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Traditional knowledge of clinical, laboratory, and endoscopic orders regarding ulcerative colitis and Crohn's disease has begun to be implemented by the revolutionary data from genetic studies. Ever since many decades ago it has been clear that inflammatory bowel diseases are complex multifactorial disorders wherein gut-confined and/or environmental factors must synergize with genetic components to effect the full-blown disorder. The sequencing of the human genome and the generation of public resources of single nucleotide polymorphisms permitted the conduction of powerful population based genome-wide association studies. The latter have increased the number of the identified susceptibility loci to 99. In this review we touched on two pathways that make true susceptibility genes for inflammatory bowel diseases; gene loci that confer specific risk for ulcerative colitis and Crohn's disease were discussed in detail.


BACKGROUND AND GOALS: Magnetic resonance (MR) enterography provides the advantages of conventional enteroclysis and those of cross-sectional imaging. Adequate luminal distension, combined with ultrafast sequences, results in excellent delineation of mural and extramural manifestations of Crohn's disease. Recent technical advances, including ultra-high-field strength MR with its capability to provide fast multiplanar images with excellent soft tissue contrast, are only rarely included in abdominal studies. STUDY: One hundred four consecutive patients with a proved or suspected diagnosis of ileitis terminalis were prospectively selected for MR imaging studies and ileocolonoscopy. The final diagnosis was based on histopathological findings or based on a combined endpoint of clinical, laboratory, endoscopic, and imaging findings. RESULTS: According to the endoscopic examination, stenosis was present in 26 patients (25%) and could be ruled out in 78 patients (75%). Total agreement between MR and endoscopy could be reached in 74 patients (71%). Histology indicated absence of inflammation in 50 patients (48%). MR and endoscopic findings were concordant in 38 patients (76%) and 37 patients (74%), respectively. Corresponding results by ileocolonoscopy were 37 true negative, 29 true positive, 4 false positive, and 12 false negative (sensitivity, 70.7%; specificity, 74%). CONCLUSIONS: MR enterography with a 3.0-T scanner is a powerful tool in the evaluation of ileal diseases, and has therefore made MR enterography the first-line modality at our institution in patients with suspected inflammatory bowel disease.


OBJECTIVE: Endoscopically confirmed mucosal healing has become an important therapeutic goal in the treatment of Crohn's disease (CD). The role of clinical indices, such as the Crohn's disease activity index (CDAI) and the Harvey-Bradshaw index (HBI), and surrogate markers, such as C-reactive protein (CRP) and fecal calprotectin, to indicate remission determined by endoscopy needs to be clarified. We analyzed the role of surrogate markers and clinical indices, separately and in combination, by comparing them with endoscopically scored disease activity in biologically treated CD patients. MATERIAL AND METHODS: Prospectively collected data of all patients with inflammatory bowel disease treated with tumor necrosis factor alpha antibodies in a tertiary center between 2007 and 2010. Altogether 210 endoscopies in 64 CD patients were analyzed. The simple endoscopic score for Crohn's disease (SES-CD) was used for scoring disease activity and compared with available data on concurrent CDAI, HBI, CRP, and calprotectin. RESULTS: Endoscopic activity demonstrated a stronger correlation with calprotectin and CRP than with the clinical indices. Neither the clinical indices nor CRP was reliable at identifying endoscopic remission. However, calprotectin alone identified endoscopic remission with a sensitivity of 84% and specificity of 74%, but was beaten, although not statistically significantly, by a combined index, based on calprotectin and the HBI. CONCLUSIONS: Clinical scores commonly used in the assessment of disease activity are unreliable at differentiating endoscopic remission from active CD. Despite this, a score based on a combination of fecal calprotectin and the HBI is a new promising tool for identifying endoscopic remission.

BACKGROUND: Perianal fistulas are frequent complications of Crohn's disease. Intravenous infliximab can control perianal disease and promote perianal fistula closure. Perifistular infliximab injections have been proposed for patients who are intolerant or unresponsive to intravenous therapy. The aim of this study was to assess the long-term efficacy of surgical treatment combined with local infliximab therapy. METHODS: A prospective cohort study was designed. Twelve patients with Crohn's disease and high/complex transphincteric and intrasphincteric perianal fistulas refractory to other treatment were submitted to core-out fistulectomies, plus perifistular injections of infliximab (20-25[NON-BREAKING SPACE]mg in 15-20[NON-BREAKING SPACE]ml of 5% glucose) every 4-6[NON-BREAKING SPACE]weeks. The main outcome measure was the clinical closure of all perianal fistulas. A 95% confidence interval was calculated for short- and long-term fistula closure rates. RESULTS: None of the procedures were associated with local or systemic adverse effects. Four patients did not complete treatment, two because of relapse of intestinal symptoms, which required intravenous infliximab. In one case, treatment with intravenous infliximab was complicated by a hypersensitivity reaction. Eight patients continued treatment until all perianal fistulas were closed and setons were removed (median: 5 sessions). Persistent closure was observed in seven (87.5%, 95% CI: 47.4-99.6) of the eight patients 12[NON-BREAKING SPACE]months after completion of treatment and in five (62.5%; 95% CI: 24.5-91.5) of eight at the end of follow-up (range: 19-43[NON-BREAKING SPACE]months, median: 35[NON-BREAKING SPACE]months). CONCLUSIONS: The cohort we examined is small, but fistulectomy combined with repeated perifistular injections of infliximab appears to be safe and may help in fistula healing. However, in most patients, permanent closure of all fistulas is not achieved.


BACKGROUND: Matrix metalloproteinases (MMPs) and their inhibitors (TIMPs), are expressed in the gastrointestinal tract by different cellular types. Nevertheless, the imbalance between MMPs and TIMPs plays an important role in the physiopathology of diverse intestinal inflammatory processes. METHODS: An immunohistochemical study was performed using tissue arrays and specific antibodies against MMPs -1, -2, -7, -9, -11, -13, -14, and TIMPs -1, -2 and -3. Immunohistochemical staining of intestinal samples from surgical interventions from 30 patients with complicated Crohn's disease (CD) and 25 patients with diverticulitis were performed at the inflamed mucosa and in adjacent noninflamed mucosa. A reverse-transcription polymerase chain reaction (RT-PCR) analysis was performed to confirm the results obtained by immunohistochemistry. In addition, western blot experiments were carried out. RESULTS: CD inflamed mucosa showed higher global expression of MMP-2, MMP-9, and MMP-13 than diverticulitis inflamed mucosa. However, inflamed and noninflamed diverticulitis mucosal samples showed higher global expression of MMP-1, TIMP-1, and 3 than the CD samples. Epithelial cells of inflamed mucosa showed higher expression of MMP-2, 9, and 13 in CD than diverticulitis. However, the latter showed higher expression of TIMP-1. Similar differences for fibroblast-like cells and mononuclear inflammatory cells were found. CD samples presented an increased expression of MMPs and a decreased expression of TIMPs compared to diverticulitis. CONCLUSIONS: These results indicate a differential pattern of expression of MMPs and TIMPs in CD and diverticulitis and the necessity to study the potential role of MMP inhibitors as new protective agents in both diseases. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Hepatitis B (HBV) is a vaccine-preventable infection that may cause severe infections, particularly in patients who are being treated with immunosuppressive therapy [(i.e., inflammatory bowel disease (IBD)]. Limited data are available about IBD patients' response rate to HBV vaccine. AIM: To assess the efficacy of HBV vaccine in IBD patients and healthy controls. METHODS: Serological markers of HBV were assessed in IBD patients, and HBV vaccine was administered to seronegative patients. The subsequent determination of anti-HBs antibody was recorded. An adequate immune response (AIR) and an effective immune response (EIR) to HBV were defined as more than 10 and 100 mIU/ml, respectively. The single dose vaccine was administered at 0, 1 and 6 months. RESULTS: A total of 102 patients with IBD (39 Crohn's disease, 63 ulcerative colitis; 54 female, 48 male) and 52 (25 female, 27 male) healthy controls were included. Mean age for patients and controls were 38 +/- 12 and 31 +/- 8, respectively (P < 0.001). Both AIR and EIR were significantly lower in patients than in controls (P < 0.001), but they were similar between patients with CD and UC (P = 0.302). Forty-four (43%) patients were on immunosuppressive therapy before vaccination. After vaccination, 76 and 53% of the patients had AIRs and EIRs, respectively, whereas 100 and 87% of the controls had AIRs and EIRs, respectively (P < 0.001 and P < 0.001, respectively). CONCLUSIONS: The response rate of IBD patients receiving HBV vaccinations were significantly lower compared to controls. The response rate of those receiving immunosuppressive therapy and with active disease was much too low. Vaccination should be given during remission and at immunosuppression-free times.
BACKGROUND: The increasing incidence of Clostridium difficile (C. difficile) infection (CDI) among patients with inflammatory bowel disease is well recognised. However, most studies have focused on demonstrating that CDI is associated with adverse outcomes in IBD patients. Few have attempted to identify predictors of severe outcomes associated with CDI among IBD patients. AIM: To identify clinical and laboratory factors that predict severe outcomes associated with CDI in IBD patients. METHODS: From a multi-institution EMR database, we identified all hospitalised patients with at least one diagnosis code for C. difficile from among those with a diagnosis of Crohn's disease or ulcerative colitis. Our primary outcome was time to total colectomy or death with follow-up censored at 180 days after CDI. Cox proportional hazards models were used to identify predictors of the primary outcome from among demographic, disease-related, laboratory and medication variables. RESULTS: A total of 294 patients with CDI-IBD were included in our study. Of these, 58 patients (20%) met our primary outcome (45 deaths, 13 colectomy) at a median of 31 days. On multiple linear regression analysis, serum albumin <3 g/dL (HR 5.75, 95% CI 1.34-24.56), haemoglobin below 9 g/dL (HR 5.29, 95% CI 1.58-17.69) and creatinine above 1.5 mg/dL (HR 1.98, 95% CI 1.04-3.79) were independent predictors of our primary outcome. Parameters such as continuous variables or shortening our primary outcome to include events within 90 days yielded similar results. CONCLUSION: Serum albumin below 3 g/dL, haemoglobin below 9 g/dL and serum creatinine above 1.5 mg/dL were independent predictors of severe outcomes in hospitalised IBD patients with Clostridium difficile infection. Copyright 2012 Blackwell Publishing Ltd.


INTRODUCTION: A significant proportion of patients with Crohn's disease (CD) lose response to antibodies directed against tumor necrosis factor alpha (TNF). Prior TNF-antagonist failure is associated with lower rates of response to subsequent TNF-antagonist therapy. In patients failing two anti-TNF agents, a choice exists between using a third anti-TNF therapy or natalizumab (NAT), an alpha-4 integrin inhibitor. A cost-effectiveness analysis comparing these competing strategies has not been performed. METHODS: A decision analytic model was constructed to compare the performance of certolizumab pegol (CZP) versus NAT in patients with moderate to severe CD. Previously published estimates of efficacy of third-line anti-TNF therapy and NAT were used to inform the model. Costs were expressed in 2010 US dollars. A 1-year time frame was used for the analysis. RESULTS: In the base case estimate, use of NAT was only marginally more effective [0.71 vs. 0.70 quality adjusted life-years (QALYs)] than CZP but was expensive with an incremental cost-effectiveness ratio (ICER) of $381,678 per QALY gained. For CZP 2 months response rate of at least 24%, NAT had an ICER above the willingness-to-pay (WTP) threshold. The model was sensitive to the costs of both therapies; for all CZP costs below $2,300 per dose, NAT had higher ICER than the WTP threshold. Substituting adalimumab for CZP resulted in similar ICER estimates and thresholds for NAT use. CONCLUSIONS: In patients with moderate to severe CD failing two TNF-antagonists, using a third TNF-antagonist therapy appears to be a cost-effective strategy without significantly compromising treatment efficacy.


BACKGROUND: Prevalence of upper gastrointestinal (GI) tract involvement in adult Crohn's disease (CD) has been reported to be very low (0.3-5%). In routine practice, upper endoscopy is recommended only in CD patients with upper GI symptoms. Available data concerning the prevalence of asymptomatic upper GI lesions in CD patients are controversial. The aim of this study was to prospectively evaluate the prevalence of upper GI CD involvement in CD patients, irrespective of upper GI symptoms. METHODS: A series of 119 consecutive CD patients underwent clinical assessment, including occurrence and score of upper GI symptoms, and upper endoscopy with biopsy samples for histological assessment and Helicobacter pylori (Hp) infection detection. In an attempt to further recognize the upper GI tract lesions as CD or other form of inflammation, in a subgroup of CD patients, the histological and endoscopic evaluation was repeated following 12 weeks of anti-TNF-alpha or other treatments in association with proton-pump inhibitors. RESULTS: Upper CD involvement was found in 19/119 (16%) patients. Hp infection was detected in 10/119 (8.4%) CD patients. Hp-negative focally active chronic gastritis was found in 34/119 (28.6%) CD patients. At presentation, 12/19 patients (63%) showing upper CD involvement were asymptomatic and 7 (37%) symptomatic. CONCLUSION: A high prevalence of upper GI tract involvement has been observed in CD patients, irrespective of upper symptoms. This finding suggests the usefulness of routine upper endoscopy in the diagnostic work-up of CD patients in order to correctly classify the distribution and extent of the disease.
BACKGROUND: Despite medical therapy, 30% of patients with ulcerative colitis (UC) need to undergo surgery. Around 50% of patients with proctocolectomy with ileal pouch-anal anastomosis (IPAA) develop complications of the pouch. Clinical evidence for the use of infliximab (IFX) in refractory pouchitis is limited. The aim of this study was to report efficacy of IFX in these patients. METHODS: A retrospective, multicenter study was designed. Patients older than 18 years with chronic refractory pouchitis treated with IFX (5 mg/kg) were included. Short-term IFX efficacy was evaluated at week 8 and mid-term efficacy at weeks 26 and 52. Complete response was defined as cessation of diarrhea and urgency and partial response as marked clinical improvement but persisting symptoms. The modified Pouchitis Disease Activity Index (mPDAI) without endoscopy was calculated when available. RESULTS: Thirty-three consecutive UC patients with chronic refractory pouchitis were included (18 male, mean age 45 years, range 21-67). At week 8, 21% patients achieved complete response and 63% showed partial clinical response. At weeks 26 and 52, 33% and 27% achieved complete response and 33% and 18% showed partial clinical response, respectively. Thirteen patients (39%) withdrew treatment (four for lack of efficacy, four for loss of response and five for adverse events). None of the potential factors analyzed had an influence on response to IFX. CONCLUSIONS: IFX was effective in the short- and mid-term in patients with chronic refractory pouchitis. However, medication had to be discontinued in a high number of patients. Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Increased intestinal permeability (IP) has been implicated in the etiopathogenesis, disease activity and relapse of Crohn's disease (CD). Glutamine, the major fuel for the enterocytes, may improve IP. AIM: We evaluated the effect of oral glutamine on IP and intestinal morphology in patients with CD.

METHODS: In a randomized controlled trial, consecutive patients with CD in remission phase with an abnormal IP were randomized to a glutamine group (GG) or active control group (ACG) and were given oral glutamine or whey protein, respectively, as 0.5 g/kg ideal body weight/day for 2 months. IP was assessed by the lactulose mannitol excretion ratio (LMR) in urine, and morphometry was performed by computerized image analysis system.

RESULTS: Patients (age 34.5 +/- 10.5 years; 20 males) were assigned to the GG (n = 15) or ACG (n = 15). Fourteen patients in each group completed the trial. The LMR [median (range)] in GG and ACG at 2 months was 0.029 (0.006-0.090) and 0.033 (0.009-0.077), respectively, with P = 0.6133. IP normalized in 8 (57.1%) patients in each group (P = 1.000). The villous crypt ratio (VCR) [mean (SD)] in GG and ACG at 2 months was 2.68 (1.02) and 2.49 (0.67), respectively, (P = 0.347). At the end of 2 months LMR improved significantly in GG from 0.071 (0.041-0.254) to 0.029 (0.006-0.090) (P = 0.0012) and in ACG from 0.067 (0.040-0.136) to 0.033 (0.009-0.077) (P = 0.0063). VCR improved in the GG from 2.33 (0.77) to 2.68 (1.02) (P = 0.001), and in ACG from 2.26 (0.57) to 2.49 (0.67) (P = 0.009). CONCLUSIONS: Intestinal permeability and morphology improved significantly in both glutamine and ACG.


OBJECTIVES: The objective of this study was to provide updated explicit and relevant consensus statements for clinicians to refer to when managing hospitalized adult patients with acute severe ulcerative colitis (UC).

METHODS: The Canadian Association of Gastroenterology consensus group of 23 voting participants developed a series of recommendation statements that addressed pertinent clinical questions. An iterative voting and feedback process was used to do this in conjunction with systematic literature reviews. These statements were brought to a formal consensus meeting held in Toronto, Ontario (March 2010), when each statement was discussed, reformulated, voted upon, and subsequently revised until group consensus (at least 80% agreement) was obtained. The modified GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria were used to rate the strength of recommendations and the quality of evidence. RESULTS: As a result of the iterative process, consensus was reached on 21 statements addressing four themes (General considerations and nutritional issues, Steroid use and predictors of steroid failure, Cyclosporine and infliximab, and Surgical issues). CONCLUSIONS: Key recommendations for the treatment of hospitalized patients with severe UC include early escalation to second-line medical therapy with either infliximab or cyclosporine in individuals in whom parenteral steroids have failed after 72[THIN SPACE]. These agents should be used in experienced centers where appropriate support is available. Sequential therapy with cyclosporine and infliximab is not recommended. Surgery is an option when first-line steroid therapy fails, and is indicated when second-line medical therapy fails and/or when complications arise during the hospitalization.

Suspicion of inflammatory bowel disease should be raised in any patient with chronic or recurrent abdominal pain and diarrhea. However, symptoms of inflammatory bowel disease (IBD) overlap with functional gastrointestinal disorders and those patients may not need endoscopy. Currently, colonoscopy with multiple biopsies is considered the gold standard to establish the diagnosis of IBD. Unfortunately, patient selection for endoscopy based on symptoms is not reliable. The use of guidelines of appropriateness for endoscopy yields significantly more significant findings but the selection criteria suffer from low specificity. Calprotectin is a calcium binding protein of neutrophil granulocytes that correlates well with neutrophil infiltration of the intestinal mucosa when measured in faeces. In the last decade, a large body of evidence on the diagnostic value of faecal calprotectin has accumulated and measurement of calprotectin in faeces has been suggested as a surrogate marker of intestinal inflammation. Testing of faecal calprotectin has been highly useful to distinguish organic from functional intestinal disorders in patients with abdominal complaints. Additionally, faecal calprotectin has reliably identified colonic inflammation in patients with suspected IBD. The use of this inexpensive and widely available test in the evaluation and risk stratification in patients with abdominal complaints is likely to increase in the future.


BACKGROUND: The Heineke-Mikulicz and Finney techniques are conventional strictureplasties that have been used to manage short (<10 cm) and medium-length (>10 cm and <20 cm) strictures from Crohn's disease. Nonconventional strictureplasty techniques have emerged to facilitate bowel conservation for atypical strictures. These techniques include the modified Finney, combined Heineke-Mikulicz and Finney, modified Heineke-Mikulicz, Michelassi, and modifications of it and others. OBJECTIVE: The aim of this study is to compare conventional vs nonconventional strictureplasties with respect to short-term complications and long-term results. DATA SOURCES AND STUDY SELECTION: A MEDLINE search was performed using "Crohn's disease", "surgical therapy", "strictureplasty", "complications", "reoperation", and "recurrence" as medical subject headings. Studies conducted between 1975 and June 31, 2010 were found via PubMed, Ovid, Embase, and Cochrane databases and categorized into 3 groups. These groups consist of centers performing conventional strictureplasties, nonconventional strictureplasties, or both. Studies with at least 3 patients were reviewed. INTERVENTIONS: A mixed-effects meta-analysis for each outcome was performed by use of Supermix software by SSI Scientific Software International. MAIN OUTCOME MEASURES: We focused on immediate and long-term complication rates among the groups. The 6 immediate complications include small-bowel obstructions, sepsis, other infections, reoperations, early postoperative GI bleeds, and other early complications. The 5 long-term complications include recurrent strictures, small-bowel obstructions, reoperations, carcinoma, and deaths. RESULTS: We reviewed 32 studies with 1616 patients who underwent 4538 strictureplasties. One thousand one hundred fifty-seven patients underwent conventional strictureplasties with an early complication rate of 15%; 459 patients underwent nonconventional strictureplasties with an early complication rate of 8%. A late complication rate of 29% for the conventional strictureplasty group and 17% for the nonconventional strictureplasty group was noted. LIMITATIONS: We are limited by the data published with the inherent risk of finding and analyzing mostly articles with positive results. CONCLUSION: The nonconventional strictureplasty techniques were noninferior to the conventional strictureplasty procedures with respect to all prespecified outcomes.


Therapeutic drug monitoring (TDM) of major metabolites of thiopurine drugs is a widely used tool for assessing treatment efficacy and toxicity in patients with inflammatory bowel disease (IBD). We report the laboratory and clinical validation of a simple and reliable high performance liquid chromatography (HPLC) method for the measurement of 6-thioguanine nucleotides (6-TGN) and 6-methylmercaptopurine (6-MMP) on paediatric patients with IBD. The aim of this paper is to develop and validate a method for the measurement of 6-TGN and 6-MMP applicable to routine practice and to evaluate the usefulness of the TDM of thiopurine drugs in children with IBD attending our Gastroenterology Unit. The HPLC method was validated following international guidelines starting from red blood cells (RBC) and whole blood (WB). A comparison between RBC and WB was assessed. The usefulness of TDM was then evaluated using the new method from WB in 47 paediatric patients with IBD treated with thiopurine drugs. WB and RBC resulted in interchangeable matrices. The majority of patients had the metabolite levels inside the therapeutic ranges. A moderate correlation was found between 6-MMP concentration and the dose of thiopurines. A higher percentage of non responders was found among patients with lower levels of 6-TGN. Toxicity was found in eight patients and was evaluated in respect to the metabolite concentration. The

BACKGROUND: Since 1999, the Crohn-Colitis Care Unit (UACC) has been dedicated to the integral management of patients with Crohn’s disease (CD) and ulcerative colitis (UC). The working methodology of the UACC is based on personalized, continued, nonphysical presence, open access and patient-centered care. From its creation, the UACC has experienced an increase in the number of its users and outpatient services. However, the impact of the activity of the UACC upon patient hospitalization is not known. OBJECTIVES: To determine the hospital activity related to CD and UC, and correlate it to the activity of the UACC. METHODS: A retrospective evaluation was made of the physical presence and non-presence activities of the UACC from January 1999 to December 2008, and of the hospital admissions and mean durations of stay due to CD and UC during that same time period. RESULTS: The number of attended patients and of presence and non-presence activities of the UACC has gradually increased. This increase contrasts with the number of annual hospital admissions, which has remained stable during the study period, with 200-300 admissions/year. Consequently, the hospitalized patients / UACC registered patients ratio has decreased from 0.36 at the start of the study period to 0.14 at the end. The median hospital stay has also decreased, from 11 days at the start of the study period to 8 days at the end. CONCLUSIONS: The UACC allows effective management of IBD patient care, since it is able to attend the needs of more patients without increasing the number of admissions, and shortening the duration of hospital stay.


BACKGROUND: Inflammatory bowel disease (IBD) is a debilitating immune disorder that impairs function and health-related quality of life (HRQOL). A goal of IBD treatment is mucosal healing, but it is not known whether it achieves normalization of the patients' perception of health. This can be assessed by using a cut-off scoring threshold of the Inflammatory Bowel Disease Questionnaire-36 (IBDQ-36). AIMS: To determine whether patients with Crohn's disease (CD) and ulcerative colitis (UC) in clinical remission and with mucosal healing normalize their HRQOL. METHODS: This is a multicentric, prospective, observational, cross-sectional study of patients who are in stable clinical remission and having mucosal healing. Patients completed the IBDQ-36, the EuroQol-5D, and the Daily Fatigue Impact Scale fatigue questionnaires. Complete restoration of health was believed to have occurred when the global score in the IBDQ-36 was at least 209 points. RESULTS: A total of 115 patients (48 with CD, 67 with UC) were included. The median activity index (the Harvey-Bradshaw or the colitis activity index) was 1.0 and the median endoscopic index (Simple Endoscopic Score for Crohn's disease or Mayo) was 0. Eighty percent of the patients (79% in CD and 82% in UC patients, P=NS) normalized their HRQOL. Type of treatment was not related to normalization of HRQOL. The lack of restoration of health was significantly related to fatigue and anxiety/depression. CONCLUSION: Mucosal healing is associated with a normalization of the perception of health by most IBD patients independently of treatment. However, a significant group of patients do not achieve restoration of HRQOL, which reinforces the necessity of a global care addressed to all patient concerns to achieve patients' complete health restoration.


Background: It is known that patients with ulcerative colitis (UC) have an increased risk of developing colorectal cancer (CCR), but there is controversy about the magnitude of this effect. Aim: To conduct a meta-analysis of studies evaluating the incidence of CCR in patients with UC. Methods: Selection of studies: studies describing the incidence and prevalence of CCR in UC. Search strategy: a MEDLINE search using the keywords: colorectal cancer, colon cancer, dysplasia, ulcerative colitis and inflammatory bowel disease, up to November 2011 was performed. Data synthesis: Cumulative incidence and incidence rates of CCR were combined and meta-analyzed using the generic inverse variance method. Subanalyses: subanalyses were performed depending on the time of follow-up, the extension of UC, the study design, and the year of publication. Results: 67 studies, including a total of 57391 patients, met the inclusion criteria. The overall cumulative incidence of CCR in patients with UC was 18.8/1000 patients (95% CI, 15.8 22; I2 = 86%). The overall incidence rate of CCR was 1.67 per 1000 patient-years (py) (1.41 1.92; I2 = 83%). When considering those studies that only included patients with extensive colitis, the incidence rate was higher: 3.7/1000 py (2.40 5; I2 = 39%). 20 studies reported results stratified into 10 years of disease duration intervals: in the first decade, the incidence rate was 1.01/1000 py (0.71 1.31; I2 = 14%), in the second decade it was 3.75/1000 py (2.51 4.98; I2 = 83%), and it was 5.85/1000 py (3.73 8; I2 = 83%) in the third decade. When only population-based studies were considered, the incidence rate was 1.24/1000 py (0.97
1.5; I2 = 79%). When results were pooled classified by the publication year, the incidence rates were as follow: 4.29/1000 py (0.95 7.64; I2 = 59%) in the 50s, 3.70/1000 py (1.98 5.42; I2 = 73%) in the 60s, 3.86/1000 py (1.24 6.74; I2 = 90%) in the 70s, 2.67/1000 py (1.75 3.57; I2 = 87%) in the 80s, 1.16/1000 py (0.75 1.57; I2 = 70%) in the 90s, and 1.09/1000 py (0.81 1.38; I2 = 80%) from 2000 to 2011. Conclusions: The risk of developing CCR in UC patients seems to be lower than previously suggested. The incidence rate of CCR was, overall, of only 1.67 per 1000 py, and this figure was even lower in population studies. The extension and the duration of the disease increase the risk of CCR. It seems to be a decreasing trend in the incidence of CCR in UC patients in the last decades.


BACKGROUND: Ulcerative colitis (UC) and Crohn's disease (CD) are inflammatory bowel diseases (IBD) of unknown aetiology. The 'hygiene hypothesis' (HH) suggests that several hygiene-related factors may have contributed to the increased incidence of IBD. The aim of the study was to evaluate risk factors for IBD related to HH in a cohort of IBD patients from the south of Italy. METHODS: We prospectively performed a one-year, questionnaire-based, case-control, multi-centre study focusing on the principal risk factors for IBD according to HH. We investigated the main surrogate markers of HH (helminthic infections and antibiotics in childhood; breastfeeding; family size/sibship;urban upbringing; personal and domestic hygiene in childhood) in UC and CD patients, in comparison with a control group of healthy subjects. In addition, the traditional risk factors for IBD were also recorded. RESULTS: The study population included 527 cases of UC, 468 CD and 562 controls. None of the surrogate risk factors of HH was significantly associated with IBD. On the contrary, the traditional risk factors confirmed their statistical significance in this IBD population. Familial aggregation: OR 4.07 for UC; OR 4.83 for CD; smoking: OR 0.38 for UC; OR 1.40 for CD; appendectomy: OR 0.28 for UC; OR 1.61 for CD. CONCLUSION: Even though risk factors associated to the HH have been proposed as a possible explanation for the increasing calendar trend of IBD incidence, their role does not appear to be statistically significant. Familial aggregation, smoking habits and appendectomy still remain the main risk factors associated with IBD. Copyright ACopyright 2011. Published by Elsevier B.V.


BACKGROUND: Ciclosporin has proven to be effective in patients with corticosteroid-refractory ulcerative colitis (UC). When therapy with this drug fails, infliximab can be considered to avoid colectomy. The efficacy and safety of this sequential approach remain unknown. AIM: To assess the efficacy and safety profile of treatment with infliximab after failure of ciclosporin in patients with a corticosteroid-refractory flare of UC. METHODS: Retrospective review of medical records of patients with a corticosteroid-refractory flare of UC who did not respond to ciclosporin and received salvage therapy with infliximab within a month of discontinuing ciclosporin. The severity of the flare and response to the treatment were graded using the Lichtiger index. Cumulative rates of colectomy were calculated using Kaplan-Meier analysis. Cox regression analysis was performed to identify predictors of colectomy. To evaluate the safety profile of this treatment strategy, any adverse event occurring after the first infusion of infliximab was considered. RESULTS: The study population comprised 47 patients with corticosteroid-refractory UC treated with infliximab after failure of ciclosporin. The median baseline Lichtiger index was 13. The mean time from the last ciclosporin dose to the first infliximab infusion was 6 days. After the first infliximab infusion, 13% of patients achieved remission, and 74% partial response. Of the 35 patients who received the third infliximab infusion, 60% achieved remission, and 37% partial response. Fourteen patients (30%) underwent colectomy. The rate of adverse events was 23%. One death occurred in a 40-year-old man who failed ciclosporin and infliximab and underwent surgery 10 days after the first infliximab infusion; he died of nosocomial pneumonia. CONCLUSIONS: Treatment with infliximab makes it possible to avoid colectomy in two-thirds of corticosteroid-refractory UC patients in whom ciclosporin fails. However, the rates of adverse events and mortality mean that the decision to administer sequential therapy (ciclosporin-infliximab) should be taken on an individual basis. Copyright 2011 Blackwell Publishing Ltd.


Background: Objective: In an effort to detect genetic variants underlying the individual differences in efficacy to AZA treatment, DNA samples of the EIGA and ENEIDA studies, case control studies including IBD cases of documented good and bad responders, were genotyped to target non-synonymous single nucleotide polymorphisms (SNPs) in 20,000 genes. Methods: DNA samples of IBD patients of the EIGA study (n = 167, 34 cases or bad responders and 133 controls or good responders) were genotyped using the Affymetrix human 20K cSNP panel. Selected SNPs were further replicated in ENEIDA (n = 90, 30 cases or bad responders and 60 controls or good responders) by the Sequenom iPLEX Gold assay and combined meta-analysis was used for
AIM: To evaluate the usefulness of small intestine contrast-enhanced ultrasonography (SICUS) using an oral contrast agent in routine clinical practice by assessing the level of agreement with the established techniques, small bowel follow-through (SBFT) and computed tomography (CT), and diagnostic accuracy compared with the final diagnosis in the detection of small bowel Crohn’s disease (CD) and luminal complications in a regional centre. MATERIALS AND METHODS: All symptomatic known or suspected cases of CD who underwent SICUS were retrospectively reviewed. The level of agreement between SICUS and SBFT, CT, histological findings, and C-reactive protein (CRP) level was assessed using kappa (kappa) coefficient. Sensitivity was demonstrated using the final diagnosis as the reference standard defined by the outcome of clinical assessment, follow-up, and results of investigations other than SICUS. RESULTS: One hundred and forty-three patients underwent SICUS of these 79 (55%) were female. Eighty-six (60%) were known to have CD and 57 (40%) had symptoms suggestive of intestinal disease with no previous diagnosis. Forty-six (55%) of the known CD patients had had at least one previous surgical resection. The sensitivity of SICUS in detecting active small bowel CD in known CD and undiagnosed cases was 93%. The kappa coefficient was 0.88 and 0.91 with SBFT and CT, respectively. SICUS detected nine patients who had one or more small bowel strictures and six patients with a fistula all detected by SBFT or CT. CONCLUSION: SICUS is not only comparable to SBFT and CT but avoids radiation exposure and should be more widely adopted in the UK as a primary diagnostic procedure and to monitor disease complications in patients with CD. Copyright Copyright 2011 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.


Background Diagnostic imaging plays a pivotal role in the diagnosis and management of inflammatory bowel disease (IBD); however, increasing use has led to concerns about the malignant potential of ionising radiation. Several studies have demonstrated that diagnostic imaging can result in exposure to potentially harmful levels of ionising radiation in IBD patients. Aim To determine the pooled prevalence of increased exposure and pooled odds ratio of risk factors associated with exposure to potentially harmful levels of diagnostic medical radiation. Methods We searched Medline, EMBASE, CINHAL and reference lists of identified articles, without language restrictions in October 2011. Results Six studies with 1704 participants provided data on the proportion of patients receiving potentially harmful levels of radiation defined as >=50 milli-sieverts (mSv)-equivalent to 5 CT abdomen scans. The pooled prevalence was 8.8% (95% CI 4.4-16.8) for IBD patients and 11.1% (95% CI 5.7-20.5%) and 2% (95% CI 0.8-4.9%) for Crohn's disease and ulcerative colitis patients respectively. Five studies involving 2627 participants provided data for risk factors. IBD-related surgery and corticosteroid use were significant with pooled adjusted odds ratio of 5.4 (95% CI 2.6-11.2) and 2.4 (95% CI 1.7-3.4) respectively. Conclusions About 1 in 10 patients may be exposed to potentially harmful levels of diagnostic medical radiation. Corticosteroid use and IBD related surgery increased this risk. Strategies to reduce radiation exposure while assessing disease activity need to be considered. 2012 Blackwell Publishing Ltd.


AIM: The safety and short-term outcome of laparoscopic surgery for recurrent ileocolic Crohn's disease was compared with the outcome following primary resection. METHOD: Between June 2002 and June 2010, 59 consecutive unselected patients (30 of whom had recurrent disease) underwent laparoscopic ileocolic resection. Four primary resections and one revision were performed as a single incision laparoscopic surgery (SILS) procedure. RESULTS: There was no difference between the two groups in terms of age, body mass index, American Society of Anesthesiology (ASA) grade or the presence or absence of fistulating disease. The median operating time was significantly longer for the revision group (125 min vs 85 min; P < 0.001). The rate of conversion was 8.5%, morbidity was 20% and mortality was 0% (P = not significant between groups). Risk factors for conversion included a complex fistula, fibrosis and the need to carry out multiple stricturoplasty. Patients in whom surgery was converted had a longer hospital stay and a higher morbidity (40%). The median hospital stay was 3 days, the return to theatre rate was 5% and the re-admission rate was 5% (P = not significant.
between groups). CONCLUSION: Laparoscopic surgery for recurrent ileocolic Crohn's disease is safe and can lead to significant short-term benefit, including earlier discharge. Conversion increases the length of stay in hospital and the overall morbidity. Copyright 2011 The Authors. Colorectal Disease Copyright 2011 The Association of Coloproctology of Great Britain and Ireland.


Background: Intestinal proteases are involved in host defense to counteract bacterial colonization, and affect mucosal barrier integrity. In a recent systematic review of protease (inhibitor) genes in inflammatory bowel disease (IBD), the 5 top-ranked proteases in ulcerative colitis (UC) were located on 3p21: APEH, MST1, DAG1, USP4, and USP19. MST1 has repeatedly been associated with UC. We aimed to unravel the genetic makeup of this region in relation with UC. Methods: 16 haplotype tagging SNPs (tSNPs) in these 5 genes were genotyped in 2112 UC patients and 1796 healthy controls (HC); exploration: 721 UC and 542 HC; validation: 1391 UC and 1254 HC. The USP4-MST1 gene region was imputed using the 1000 genomes dataset as a reference (BEAGLE v3.2). For 23 patients, gene expression data from colonic biopsies was available. Statistical analysis was performed using SVS v7.5.2 (crude association analysis, additive genetic model), and plink v1.0.7 (meta-analysis, imputed dataset, set-based analysis, and eQTL analysis). A corrected p < 0.05 was considered statistically significant. Results: 3 ISNPs were significantly associated with UC in the meta-analysis: rs11130213, a conserved transcription factor binding site (APEH, p = 4.93e-4, OR = 1.19); rs9822268 (APEH, p = 6.26e-4, OR = 1.19); and rs6766131 (DAG1, p = 8.23e-4, OR = 1.19). 58 out of 150 imputed markers were significantly associated with UC, 51 of which were highly correlated with rs11130213 (r>sup>2</sup> < 0.8). Set-based analysis revealed 4 independent signals (r>sup>2</sup> < 0.8), with the peak signals located around USP4 (rs34343820, rs17650792) and BSN, a gene positioned between DAG1 and APEH (rs9827708, rs12497288). eQTL analysis showed no significant impact on expression of USP4, MST1, APEH or DAG1. Among the 58 markers are multiple functional variants: 1 non-synonymous coding (rs34762726, BSN), and 5 synonymous coding SNPs of which rs1801143 is a putative eQTL for USP4 (eqtl.uchicago.edu). Two SNPs are located in the 3'-UTR and 1 in the 5'-UTR. Conclusions: Multiple functional variants at 3p21 were associated with UC. The main genes implicated in this study were USP4, a deubiquitinating enzyme that plays a role in the regulation of quality control in the ER; and BSN, a presynaptic cytomatrix protein, essential for regulating neurotransmitter release. These genes warrant further followup trough functional studies in UC. Complementing genetic studies with functional studies will be indispensable to unravel the exact role for this region in UC pathogenesis.


Background: Data from both humans and experimental animals underscore the critical role of intestinal bacteria in the establishment and maintenance of inflammatory bowel disease (IBD). Host defense to counteract bacterial colonization and maintaining mucosal integrity involves intestinal proteases and protease inhibitors. Methods: We performed a genetic association study of all top-ranked protease (and inhibitor) genes in a previously published systematic review [1]. 185 haplotype tagging SNPs in 23 genes were genotyped in an exploratory dataset of 650 Crohn's disease (CD) patients, and 542 healthy controls (HC). Validation was performed in 1670 CD and 1254 HC. Statistical analysis was done using SVS v7.5.2 (crude association analysis, additive genetic model), and plink v1.0.7 (meta-analysis of exploration and validation datasets, interaction analysis). A corrected p < 0.05 was considered statistically significant. The T84 epithelial cell line was used for functional assessment of CYLD. Results: 10 markers were found to be significantly associated with CD in the meta-analysis: 4 in USP40, 1 in APEH, 1 in USP3, and 4 in CYLD. The top signals were in CYLD, a cytoplasmic deubiquitinating enzyme located next to NOD2, on 16q12: rs12324931 (p = 1.64e18), rs17314544 (p = 1.06e9), rs7205423 (p = 1.89e8), and rs1861762 (p = 1.98e8). A significant interaction between ‘NOD2 overall’ and rs12324931 was found. In patients without any NOD2 risk alleles, a significant CD-risk association with rs12324931 was present (p = 0.001, OR = 4.05 [1.68 9.73]). Upon infection of T84 cells with the adherent-invasive Escherichia coli (AIEC) strain LF82, the prototype strain of AIEC associated with ileal CD, decreased CYLD expression was observed, leading to an increased ability of LF82 AIEC to replicate within T84 cells (through CYLD siRNA transfection). Together with the AIEC LF82-induced CYLD decrease, we observed proteasome-dependent degradation of the NFB inhibitor, IB-alpha, in AIEC LF82 infected T84 cells, and an increased translocation of the NFB p65 subunit into the nucleus. Conclusions: Our data provide strong genetic and functional evidence for a role for CYLD in CD pathogenesis. We show that AIEC bacteria are able to take advantage of decreased CYLD to replicate within host epithelial cells, and that CYLD acts as a negative, NFB-mediated regulator for E. coli colonization.
Surgical-site infections (SSIs) remain a major source of morbidity after colectomy for fulminant ulcerative colitis (UC). Identifying UC patients at elevated risk of developing SSIs might improve postoperative outcomes. Our goal was to identify preoperative factors, which could predict SSI development in the postoperative UC population. The records of 59 patients treated by colectomy for fulminant UC from 2004 to 2009 were retrospectively reviewed and statistically analyzed. Few differences were observed between patients who developed postoperative complications and those who did not. Twenty patients sustained a total of 27 complications, with superficial SSIs being the single most common event. Multivariate analysis identified diabetes, white blood cell count > 15 cells/mm³, intraoperative blood loss > 200 cc, and intraoperative blood transfusion to all be independent predictors for the development of postoperative SSIs. These four factors were all able to independently predict SSIs. Postoperative UC patients with these risk factors might benefit from heightened wound surveillance or closer follow-up.


**BACKGROUND AND OBJECTIVE:** Because capsule endoscopy (CE) avoids ionizing radiation, deep sedation, and general anesthesia, CE may be valuable in pediatrics. We report a single pediatric center's experience with the use and safety of CE. **METHODS:** In a retrospective review of consecutive CE studies, 284 CE studies were performed in 277 patients with a mean age of 15 (+/-3.7) years during a 5-year period. The youngest to swallow the capsule was 4.6 years old. Twenty capsules were placed. Overall, 245 (86%) patients underwent CE for suspected (184, 65%) or confirmed (61, 21%) Crohn disease (CD); 27 (9.5%) anemia or gastrointestinal bleeding; 6 (2%) polyposis; and 4 (1.4%) celiac disease. **RESULTS:** Positive findings were observed in 205 (72%) of the studies, with 152 (54%) having small bowel findings. Of these, 72 (47%) were diagnostic. Gastric (95, 33%) and colonic (31, 11%) abnormalities were also identified. Five CE studies (1.8%) resulted in retention of the capsule in nonsurgical patients. A patency capsule before CE in 23 patients allowed 19 CE to proceed with only 1 retained capsule. In 65 (21%) patients, the video capsule did not enter the colon before the video's end. Of these, 36 (65%) had significant findings, including 27 (49%) documenting small bowel (SB) CD. **CONCLUSIONS:** CE is useful to diagnose SB disease in children. Even in a study population with a high prevalence of confirmed and suspected CD, the risk of retention remains small. The patency capsule may lessen that risk. CE may identify gastric or colonic disease even when SB lesions are not present.


**BACKGROUND:** For ulcerative colitis (UC) patients undergoing ileal pouch-anal anastomosis (IPAA), postoperative complications include chronic pouchitis and development of Crohn's disease (CD) of the pouch. **AIMS:** The aim of this study was to determine if serologic markers obtained postoperatively are associated with the development of complications in UC patients after IPAA. **METHODS:** A retrospective chart review was conducted of UC patients with IPAA were tested for expression of serologic markers. Complications abstracted from medical records included postoperative fistula, CD of the pouch, chronic pouchitis, and diversion or excision of the pouch. **RESULTS:** 142 patients were enrolled, 44 of whom developed complications. Positive serologic profiles for ASCA IgG and anti-CBir1 markers were found to be associated with the development of any complication, (P = 0.017 and P = 0.002, respectively). A positive anti-CBir1 test was also found to be associated with CD of the pouch and/or fistula formation (P < 0.001). Similarly, both ASCA IgG and anti-CBir1 titers were significantly associated with postoperative IPAA complications (P = 0.034 and P = 0.001, respectively), and anti-CBir1 titers were associated with CD of the pouch and/or fistula formation (P < 0.001). Complications developed after a median follow-up of 216 months (range 1-264). **CONCLUSIONS:** ASCA IgG and anti-CBir1 markers were associated with the development of complications after IPAA, specifically fistulie and/or CD of the pouch. The ability to identify patients at high risk for adverse outcomes may allow for early aggressive therapy, which may decrease the rate of pouch failure. A prospective study of patients with preoperative serology is ongoing.


**OBJECTIVES:** Unintended variation in the care of patients with Crohn disease (CD) and ulcerative colitis (UC) may prevent achievement of optimal outcomes. We sought to improve chronic care delivery and outcomes for children with inflammatory bowel disease by using network-based quality improvement methods. **METHODS:** By using a modified Breakthrough Series collaborative structure, 6 ImproveCareNow Network care centers tested changes in chronic illness care and collected data monthly. We used an interrupted time series design to evaluate the impact of these changes. **RESULTS:** Data were available for 843 children with CD and 345 with UC.
Changes in care delivery were associated with an increase in the proportion of visits with complete disease classification, measurement of thiopurine methyltransferase (TPMT) before initiation of thiopurines, and patients receiving an initial thiopurine dose appropriate to their TPMT status. These were significant in both populations for all process variables (P < .01) except for measurement of TPMT in CD patients (P = .12). There were significant increases in the proportion of CD (55%-68%) and UC (61%-72%) patients with inactive disease. There was also a significant increase in the proportion of CD patients not taking prednisone (86%-90%). Participating centers varied in the success of achieving these changes. CONCLUSIONS: Improvements in the outcomes of patients with CD and UC were associated with improvements in the process of chronic illness care. Variation in the success of implementing changes suggests the importance of overcoming organizational factors related to quality improvement success.


Exclusive enteral nutrition is an effective yet often underused therapy for the induction of remission in pediatric Crohn disease. The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition formed the Enteral Nutrition Working Group to review the use of enteral nutrition therapy in pediatric Crohn disease. The group was composed of 5 pediatric gastroenterologists and 1 pediatric nutritionist, all with an interest and/or expertise in exclusive enteral nutrition. Specific attention was placed upon review of the evidence for efficacy of therapy, assessment of the variations in care, identification of barriers to its widespread use, and compilation of the necessary components for a successful program. The present guideline is intended to aid physicians in developing an enteral nutrition therapy program and potentially promote its use.


We intended to see the pattern of TJ protein expression along with ultrastructural changes in colonic biopsies from patients with Crohn's disease (CD), ulcerative colitis (UC), and tuberculosis (cTB). Colonic biopsies from 11 patients with active CD and ten patients each with active UC and untreated cTB were taken along with biopsies from six patients with irritable bowel syndrome as controls. These were evaluated for expression pattern of key TJ proteins which included claudin-2 as TJ pore-forming protein, claudin-4 as pore-sealing protein, ZO-1 as scaffold protein, and occludin as TJ protein related to cell migration and polarity. Claudin-2 expression was upregulated along the whole length of intercellular junction (ICJ) in biopsies from patients with active CD and UC in comparison to the biopsies from cTB patients and controls, where its expression was limited to the uppermost part of ICJ. There was reduced expression of ZO-1 in UC, CD, and cTB. On transmission electron microscopic examination, the pentalaminar structure of TJs was destroyed in patients with CD and UC but no significant change was seen in those with cTB and in controls. The expression of claudin-2 was distinctly different in active CD and UC in comparison to its expression pattern in patients with cTB and in controls. The redistribution of claudin-2 expression was in accordance with the TJ ultrastructural changes in patients with UC, CD, and cTB. Altered claudin-2 expression, along with destroyed TJs, may result in loss of selective permeability in patients with UC and CD.


BACKGROUND AND AIM: Medical treatment of steroid-refractory ulcerative colitis (UC) is limited to either cyclosporine or infliximab. Studies comparing cyclosporine with either placebo or intravenous methylprednisone showed promise for cyclosporine, but associated it with significant toxicity. There is conflicting, but increasingly positive evidence for using infliximab. There are no studies directly comparing these two treatments. Our aim was to compare the outcomes of patients with steroid-refractory UC treated with either intravenous cyclosporine or infliximab. METHODS: We carried out a retrospective review of inpatients with steroid-refractory UC, treated with either intravenous cyclosporine or infliximab, at Waitemata District Health Board, between January 2001 and February 2010. The primary end-points were time to colectomy, and colectomy rates at 3 and 12 months. Secondary end-points were time to discharge from initiation of treatment, steroid dependence at 12 months, and reported adverse events. RESULTS: The total study population was 38, with 19 in the infliximab group. Follow up to 12 months was complete in all patients. At 3 months, the colectomy rate was 63% for cyclosporine, compared to 21% (P = 0.0094). By 12 months the rate was 68% and 37% for cyclosporine and infliximab, respectively (P = 0.06). Patients in the cyclosporine group required an additional 5 days in hospital (P = 0.0086). Steroid dependence at 12 months was 50% for cyclosporine versus 25% for infliximab (P = 0.36). Cyclosporine caused more adverse events (P = 0.17). CONCLUSIONS: Infliximab improved clinical outcomes compared to the previous use of intravenous cyclosporine in patients admitted with steroid-refractory acute severe UC. Copyright 2011 Journal of Gastroenterology and Hepatology Foundation and Blackwell Publishing Asia Pty Ltd.
BACKGROUND: Oral pathology is a commonly reported extraintestinal manifestation of Crohn's disease (CD). The host-microbe interaction has been implicated in the pathogenesis of inflammatory bowel disease (IBD) in genetically susceptible hosts, yet limited information exists about oral microbes in IBD. We hypothesize that the microbiology of the oral cavity may differ in patients with IBD. Our laboratory has developed a 16S rRNA-based technique known as the Human Oral Microbe Identification Microarray (HOMIM) to study the oral microbiome of children and young adults with IBD. METHODS: Tongue and buccal mucosal brushings from healthy controls, CD, and ulcerative colitis (UC) patients were analyzed using HOMIM. Shannon Diversity Index (SDI) and Principal Component Analysis (PCA) were employed to compare population and phylum-level changes among our study groups. RESULTS: In all, 114 unique subjects from the Children's Hospital Boston were enrolled. Tongue samples from patients with CD showed a significant decrease in overall microbial diversity as compared with the same location in healthy controls (P = 0.015) with significant changes seen in Fusobacteria (P < 0.0002) and Firmicutes (P = 0.022). Tongue samples from patients with UC did not show a significant change in overall microbial diversity as compared with healthy controls (P = 0.418). CONCLUSIONS: As detected by HOMIM, we found a significant decrease in overall diversity in the oral microbiome of pediatric CD. Considering the proposed microbe-host interaction in IBD, the ease of visualization and direct oral mucosal sampling of the oral cavity, further study of the oral microbiome in IBD is of potential diagnostic and prognostic value. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Thiopurines are considered immunosuppressive agents and may be associated with an increased risk for infections. However, few inflammatory bowel disease (IBD) patients are appropriately vaccinated, and data on their ability to mount an immune response are vague. We evaluated the effects of the thiopurines, azathioprine (AZA) and 6-mercaptopurine (6-MP), on cellular and humoral immune responses in IBD patients. METHODS: A prospective clinical investigation was conducted on IBD patients referred for thiopurine treatment. Immune competence was evaluated by assessing lymphocyte counts and phenotype, response to mitogen and antigen stimulation, immunoglobulin levels, and response to pneumococcal and tetanus vaccines (before treatment, week 0), and to Haemophilus influenza type b vaccine (at week 24). RESULTS: Thirty-one Crohn's disease and 12 ulcerative colitis patients who completed at least 24 weeks of therapy were included. The posttherapy average 6-MP dose was 1.05 +/- 0.30 mg/kg, and white blood cell counts had decreased significantly from baseline values (P < 0.002). The posttreatment response to mitogens and antigens and the immunoglobulin levels were unchanged. Responses to vaccines were normal both in thiopurine-naive and thiopurine-treated patients, suggesting that these patients were immunologically intact while on thiopurine therapy and capable of generating normal immune responses in vivo. CONCLUSIONS: There is no evidence for any intrinsic systemic immunodeficiency in IBD patients. Thiopurines at the doses used for treating IBD showed no significant suppressive effect on the systemic cellular and humoral immune responses evaluated. Thiopurine-treated IBD patients can be safely and efficiently vaccinated. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


OBJECTIVES: There are concerns that biologic treatments or immunomodulation may negatively influence anastomotic healing. This study investigates the relationship between these treatments and anastomotic complications after surgery for Crohn's disease. PATIENTS AND METHODS: Retrospective study on 417 operations for Crohn's disease performed at four Danish hospitals in 2000-2007. Thirty-two patients were preoperatively treated with biologics and 166 were on immunomodulation. In total, 154 were treated with corticosteroids of which 66 had prednisolone 20 mg or more. RESULTS: Anastomotic complications occurred at 13% of the operations. There were no difference in patients on biologic treatment (9% vs. 12% (p = 0.581)) or in patients on immunomodulation (10% vs. 14% (p = 0.263)). Patients on 20 mg prednisolone or more had more anastomotic complications (20% vs. 11% (p = 0.04)). Anastomotic complications were more frequent after a colo-colic anastomosis than after an entero-enteric or entero-colic (33% vs. 12% (p = 0.013)). Patients with anastomotic complications were older (40 years vs. 35 years (p = 0.014)), had longer disease duration (7.5 years vs. 4 years (p = 0.04)), longer operation time (155 min vs. 115 min (p = 0.018)) and more operative bleeding (200
ml vs. 130 ml (p = 0.029)). Multivariate analysis revealed preoperative treatment with prednisolone 20 mg or more, operation time and a colo-colic anastomosis as negative predictors of anastomatic complications. CONCLUSIONS: Preoperative biologic treatment or immunomodulation had no influence on anastomatic complications. The study confirms previous findings of corticosteroids and a colo-colic anastomosis as negative predictors and also that surgical complexity, as expressed by bleeding and operation time, may contribute to anastomatic complications.


Psoriasis (PS) and Crohn disease (CD) have been shown to be epidemiologically, pathologically, and therapeutically connected, but little is known about their shared genetic causes. We performed meta-analyses of five published genome-wide association studies on PS (2,529 cases and 4,955 controls) and CD (2,142 cases and 5,505 controls), followed up 20 loci that showed strongest evidence for shared disease association and, furthermore, tested cross-disease associations for previously reported PS and CD risk alleles in additional [NON-BREAKING SPACE]6,115 PS cases, 4,073 CD cases, and 10,100 controls. We identified seven susceptibility loci outside the human leukocyte antigen region (9p24 near JAK2, 10q22 at ZMIZ1, 11q13 near PRDX5, 16p13 near SOCS1, 17q21 at STAT3, 19p13 near FUT2, and 22q11 at YDJC) shared between PS and CD with genome-wide significance (p < 5 x 10(-8)) and confirmed four already established PS and CD risk loci (IL23R, IL12B, REL, and TYK2). Three of the shared loci are also genome-wide significantly associated with PS alone (10q22 at ZMIZ1, p(rs1250544) = 3.53 x 10(-9), 11q13 near PRDX5, p(rs694739) = 3.71 x 10(-9), 22q11 at YDJC, p(rs181359) = 8.02 x 10(-13)). In addition, we identified one susceptibility locus for CD (16p13 near SOCS1, p(rs4780355) = 4.99 x 10(-8)). Refinement of association signals identified shared genome-wide significant associations for exonic SNPs at 10q22 (ZMIZ1) and in [NON-BREAKING SPACE]x [NON-BREAKING SPACE]silico expression quantitative trait locus analyses revealed that the associations at ZMIZ1 and near SOCS1 have a potential functional effect on gene expression. Our results show the usefulness of joint analyses of clinically distinct immune-mediated diseases and enlarge the map of shared genetic risk loci. Copyright Copyright 2012 The American Society of Human Genetics. Published by Elsevier Inc. All rights reserved.


OBJECTIVE: The aim of the study was to evaluate thalidomide as rescue therapy for pediatric patients with severe refractory Crohn disease (CD) who failed to respond to antitumor necrosis factor (TNF) biologic agents.

PATIENTS AND METHODS: A computerized database was used to identify children with CD who had failed conventional immunosuppression therapy and received thalidomide rescue therapy. Twelve patients, mean age at diagnosis 10 years, were identified. Eight children had disease localized to the ileum and colon and 4 to the gastroduodenal area and colon. Five cases were complicated by strictures and 7 by fistulae. Previous drug therapy included azathioprine/6-mercaptopurine (11/12), methotrexate (7/12), and anti-TNF biologics (12/12). Outcome measures were Harvey-Bradshaw Index, change in prednisone dose, hospitalizations, bowel resections, and incision and drainage procedures. Laboratory evaluations were calculated before and after 1 to 6 months of thalidomide.

RESULTS: Mean Harvey-Bradshaw Index score improved from 11.8 to 3.9 (P[HAIR SPACE]=[HAIR SPACE]0.004), mean prednisone dose decreased from 13.9 to 2.3 [HAIR SPACE] mg/day (P[HAIR SPACE]=[HAIR SPACE]0.001), mean number of hospitalizations decreased from 6.3 to 1.3 (P[HAIR SPACE]=[HAIR SPACE]0.002), and erythrocyte sedimentation rate decreased from 35 to 14 [HAIR SPACE] mm/h (P[HAIR SPACE]=[HAIR SPACE]0.02). The surgery rate pre-thalidomide was 0.31 and on thalidomide was 0.004. Of the 7 patients with fistulae, 5 had complete fistula closure, 1 had partial closure, and 1 showed no improvement. Adverse reactions that resulted in discontinuation of thalidomide are as follows: 42% peripheral neuropathy, 17% worsening of the CD, 8% dizziness, and 8% allergic reaction. All 5 patients who developed peripheral neuropathy had clinical resolution of the neurologic symptoms within 2 to 3 months after stopping thalidomide. CONCLUSIONS: Thalidomide is a potentially effective rescue therapy for severe refractory CD in children who fail to respond to anti-TNF medications.


BACKGROUND: A three-stage restorative proctocolectomy with ileal pouch-anal anastomosis is the treatment of choice for the particularly debilitated patient with medically refractory ulcerative colitis (UC). Laparoscopic...
surgery has been shown to offer several advantages over the open approach in this setting. Single-incision laparoscopic surgery is an emerging minimally invasive strategy representing a truly scarless procedure for the first surgical step, namely, the total abdominal colectomy (TAC). METHODS: Nine consecutive patients with medically refractory UC underwent a single-incision laparoscopic TAC between May and October 2010. All patients were on aggressive medical therapy with corticosteroids or immunosuppressors and were selected for this approach on the basis of their body habitus and the absence of relevant comorbidities. The whole operation was performed through a single access to the abdominal cavity, placed at the ostomy site marked preoperatively.

RESULTS: Mean operating time was 142 +/- 23 min, with an estimate blood loss of 108 +/- 125 ml. No intraoperative complications or conversions to conventional laparoscopy or open surgery occurred. In all cases the postoperative course was uneventful. The return of bowel function was observed on postoperative day 1.7 +/- 0.7, and patients could tolerate a solid diet on postoperative day 3 +/- 0.5. The mean postoperative length of stay was 5.2 +/- 1.3 days. CONCLUSIONS: In our experience, a single-incision laparoscopic approach to total abdominal colectomy for refractory ulcerative colitis has been shown to be safe and feasible. Initial results suggest that this technique can lead to improvements in short-term outcomes in selected patients.


OBJECTIVES: Efficacy of 5-aminosalicylic acids (5-ASAs) in ulcerative colitis (UC) has been studied previously in meta-analyses. However, no recent meta-analysis has studied the relative efficacies of differing routes of administration. METHODS: MEDLINE, EMBASE, and the Cochrane central register of controlled trials were searched (through May 2011). Eligible trials recruited adults with mildly to moderately active UC, or quiescent UC, and compared oral 5-ASAs with either topical 5-ASAs or a combination of oral and topical 5-ASAs. Dichotomous data were pooled to obtain relative risk (RR) of failure to achieve remission in active UC, and RR of relapse of disease activity in quiescent UC, with a 95% confidence interval (CI). The number needed to treat (NNT) was calculated from the reciprocal of the risk difference. RESULTS: The search identified 3,061 citations, and 12 randomized controlled trials (RCTs) were eligible. Four compared topical with oral 5-ASAs in active UC remission, with an RR of no remission with topical 5-ASAs of 0.82 (95% CI=0.52-1.28). Four trials compared combined with oral 5-ASAs in active UC (RR of no remission=0.65; 95% CI=0.47-0.91; NNT=5). Three RCTs compared intermittent topical with oral 5-ASAs in preventing relapse of quiescent UC (RR=0.64; 95% CI=0.43-0.95; NNT=4), and two compared combined with oral 5-ASAs (RR of relapse=0.48; 95% CI=0.17-1.38). CONCLUSIONS: Combined 5-ASA therapy appeared superior to oral 5-ASAs for induction of remission of mildly to moderately active UC. Intermittent topical 5-ASAs appeared superior to oral 5-ASAs for preventing relapse of quiescent UC.


BACKGROUND & AIMS: Topical 5-aminosalicylates (5-ASAs) such as mesalamine are effective in inducing remission in patients with mild to moderately active ulcerative colitis (UC). However, there has been no meta-analysis of their efficacy in preventing relapse of quiescent UC. METHODS: We searched MEDLINE, EMBASE, and the Cochrane central register of controlled trials through July 2011 for randomized controlled trials comparing the effects of topical 5-ASAs with placebo in adults with quiescent UC. Dichotomous data were pooled to obtain relative risk (RR) of relapse of disease activity. The number needed to treat (NNT) was calculated from the reciprocal of the risk difference. Adverse events data were summarized. RESULTS: The search identified 3061 citations; we analyzed data from seven (555 patients). All trials used mesalamine, but only one included patients with extensive disease. The duration of therapy ranged from 6-24 months. The RR of relapse of disease activity in patients with quiescent UC who were given topical mesalamine, compared with placebo, was 0.60 (95% confidence interval, 0.49-0.73; NNT = 3); there was no significant heterogeneity between studies (I(2) = 21%, P = .27). No significant differences in rates of adverse events rates were detected (RR = 1.01; 95% confidence interval, 0.59-1.72). CONCLUSIONS: On the basis of a meta-analysis of 7 randomized controlled trials, topical mesalamine is effective in preventing relapse of quiescent UC, with no greater number of adverse events than placebo. However, because most studies included only patients with left-sided disease or proctitis, the efficacy of topical mesalamine in preventing relapse in patients with more extensive quiescent UC is not known. Copyright Copyright 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.


BACKGROUND: Leukocytapheresis (LCAP) is used as an adjunct therapy for patients with active ulcerative colitis (UC). Although, LCAP is routinely performed at 3,000 mL per session, we were interested to see that if this can be replaced with bodyweight (BW) adjusted volume. METHODS: In an open label prospective trial, the
Clinical response to BW adjusted LCAP (BWA-LCAP) was evaluated in 14 patients with active UC. Fourteen demography matched UC patients who had been treated with the routine 3,000 mL LCAP were randomly sampled from our database as a control group. All patients were given 10 weekly LCAP sessions. In the BWA-LCAP group, the processed blood volume (PBV) was set at 30 mL/kg x BW/session. Baseline demographic measures were not significantly different between the two groups. RESULTS: The average PBV in the BWA-LCAP group was 1971.0 +/- 330.0 mL, range 1,020-2,460. In both groups, the average UC clinical disease activity index, the endoscopic index, and the concomitant prednisolone dosage were significantly and equally reduced during the course of 10 LCAP. Accordingly, at the end of the trial, no significant difference was seen in any outcome measure between the two groups. However, a significantly higher incidence of adverse event (AE) was observed in the routine 3,000 mL LCAP group as compared with the BWA-LCAP group (P < 0.01). CONCLUSIONS: The outcomes of this investigation showed that the therapeutic efficacy of LCAP based on 30 mL/kg x BW is similar to the routine 3,000 mL per session LCAP. However, BWA-LCAP should be favored if one is to see the full potential of LCAP without AE. Copyright 2011 Wiley Periodicals, Inc.


Previously, we reported on the presence of antibodies to linear epitopes of human and mycobacterial 60 kD heat shock proteins (HSP) in the sera of healthy blood donors. Since many recent findings indicate that the levels of these antibodies may be altered in coronary heart disease (CHD) and also inflammatory bowel diseases (IBD), it seemed worthwhile to compare the epitope specificity of the anti-HSP60 and anti-HSP65 antibodies in the sera of patients with these diseases to those in healthy subjects. The multipin enzyme-linked immunosorbent assay method was applied with a large overlapping set of synthetic 10-mer peptides covering selected regions of human HSP60 and Mycobacterium bovis HSP65. Sera of 12 healthy persons (HP), 14 CHD, and 14 IBD patients with the same concentration of total anti-HSP60 and HSP65 IgG antibodies were tested. We have identified CHD-specific epitopes in the equatorial domain of the HSP60 protein but in neither region of the HSP65 molecule, indicating that the formation of anti-HSP60 antibodies is not or only partially due to the cross-reaction between human HSP60 and bacterial HSP65. IBD-specific epitopes were found in many regions of the HSP60 and in even more regions of the HSP65 molecule including an IBD-specific T cell epitope in region X as well. These findings indicate that the epitope specificity of the anti-human and anti-mycobacterial HSP60 antibodies associated with various diseases is different.


OBJECTIVES: The purpose of this study was to evaluate the accuracy of color-coded duplex sonography for the diagnosis of Crohn disease relapse and complications compared to multidetector computed tomography (CT).

METHODS: The Institutional Ethics Committee approved the protocol research, and written consent forms were obtained. Patients with a diagnosis of Crohn disease presenting with symptoms of relapse or complications (54 patients; 27 female; ages 9-80 years; mean, 34.6 years) were enrolled. Patients underwent color-coded duplex sonography and multidetector CT examinations within 2 weeks of each other. Multidetector CT was the reference standard. The location and extent of diseased bowel, wall thickness, stenosis, hyperemia, mesenteric fat thickening, lymphadenopathy, abscesses, fistulas, peritoneal fluid, and signs of hepatobiliary disease were searched for. RESULTS: About of 80% of the patients had terminal ileal involvement, and 55% had disease confined to the ileum. A significant correlation between the two modalities was found regarding wall thickness, abscesses, and fistulas (P < .05). Color-coded duplex sonography had sensitivity and specificity of 88% and 53%, respectively, for diagnosis of luminal stenosis. Hyperemia was more commonly diagnosed on color-coded duplex sonography. Color-coded duplex sonography had sensitivity and specificity of 84% and 83% for diagnosis of mesenteric fat thickening and lymphadenopathy and 66% and 86% for peritoneal fluid. Fatty liver was found in 18% and gallstone disease in 6%. CONCLUSIONS: Color-coded duplex sonography was accurate in diagnosing the disease location, wall thickness, and extraintestinal inflammatory findings associated with Crohn disease, potentially placing it as the first-line imaging modality for the diagnosis of Crohn disease relapse and complications.


BACKGROUND: There is controversy as to whether the clinicopathological features of colorectal cancer in the setting of IBD are distinct from sporadic colorectal cancer. OBJECTIVE: The aim of this study was to compare the characteristics and outcomes between IBD-associated and sporadic colorectal cancer. DESIGN: This retrospective population-based cohort study used the Surveillance, Epidemiology, and End Results Medicare-
Objective: The present UK criterion standard for assessing children with suspected inflammatory bowel disease (IBD) is upper endoscopy, ileocolonoscopy, and barium follow-through (BaFT). Significant doses of radiation, unpalatable contrast, and volume intolerance are involved with BaFT. Practice in investigating Crohn disease (CD) is changing with the increasing use of magnetic resonance imaging (MRI). The aim of the present study was to compare BaFT and a new abdominal MRI protocol in a paediatric IBD population. METHODS: All consecutive patients with a new diagnosis of IBD or requiring reassessment from September 2008 to December 2010 were investigated with both abdominal MRI and BaFT in accordance with a specific local paediatric IBD protocol. The studies were reported by nonblinded radiologists with an interest in gastrointestinal imaging. The reports were compared in conjunction with case note review. RESULTS: Eighty-seven patients underwent both BaFT and MRI abdomen. Thirty-one percent of patients had additional pathology on MRI, not seen on the BaFT. Sixty-seven percent of patients (n=59) had an MRI finding equivalent to BaFT. Using histology as a criterion standard for detecting terminal ileal disease, BaFT had a sensitivity and specificity of 76% and 67%, and MRI had a sensitivity and specificity of 83% and 95%, respectively. CONCLUSIONS: This is the largest series of small bowel MRI in a paediatric population. MRI reports were at least equivalent to BaFT. MRI had higher sensitivity and, particularly, specificity in detecting terminal ileal pathology. These findings suggest that MRI should become the criterion standard investigation in children with IBD in centres with appropriate expertise, with zero radiation exposure being highly advantageous.


Purpose: In ulcerative colitis (UC), endoscopic methods are preferred for assessment of extent and activity of disease. Due to the invasive nature of endoscopical examinations, replacement by other, reliable imaging procedures would be helpful. Contrast-enhanced ultrasound (CEUS) in combination with perfusion assessment using a specific quantification software might be such a new diagnostic tool. Thus, we compared the findings of CEUS with the results of endoscopically taken specimens applying a histopathological scoring system. METHODS: We prospectively evaluated 15 patients with proven UC undergoing endoscopy. CEUS was performed and the quantification software Qontrast [REGISTERED] applied to obtain contrast-enhanced sonographic perfusion maps. Moreover, in each patient C-reactive protein (CRP) was measured and taken biopsies were assessed using an advanced scoring system. Four patients had to be excluded from final analysis. RESULTS: There was a trend to higher Peak (%) values with increasing histological inflammation. Furthermore, a strong negative correlation between the ratio TTP (s)/Peak (%) (Spearman's correlation r[THIN SPACE]=−0.761, p[THIN SPACE]<0.01) was found. There was no significant relationship between CRP and histopathological scoring or CEUS parameters, respectively. CONCLUSION: Quantitative evaluation with CEUS, particularly the calculation of the ratio TTP (s)/Peak (%), provides a simple method for assessment of inflammatory activity in UC.

UNLABELLED: The numbers of patients with diagnosed Crohn's disease in Poland continue to be on the rise. It may be assumed that it is associated not with an increased incidence but with significant advancements in diagnostic techniques which in an increasingly better manner solve problems of abdominal pain. One of such methods is magnetic resonance enterography, which gives high hope in the diagnostics of Crohn's disease. The aim of the study was the evaluation of the results of magnetic resonance enterography (MREG) and their comparison with the results of histopathological examination of perioperative specimens. MATERIAL AND METHODS: The clinical material comprised 48 patients with suspected Crohn's disease. Colonoscopy was performed in all the patients, followed by magnetic resonance enterography, which evaluated the lesion localisation, large intestine wall thickening, small intestine stenosis, mesenteric vessel proliferation, infiltration of surrounding adipose tissue, lymph node enlargement, presence of enterointeranal, enterovesical and enterocutaneous fistulas. Next, a surgical procedure was performed, with collection of specimen for histopathology. The examination results were compared with those of magnetic resonance enterography. RESULTS: MREG was performed in 48 individuals. Suspected Crohn's disease based on the above examination was diagnosed in 35 cases, isolated small intestine inflammation—in 5, and fibrosis in the remaining 5 patients. No significant differences were found between the lesion localisation done by MREG and perioperatively. Crohn's disease was confirmed by histopathology in 36 cases. The sensitivity of MREG with histopathology was 91.6%, and the specificity—77.8%. CONCLUSIONS: Magnetic resonance enterography is a highly effective and sensitive method in the diagnostics of Crohn's disease, free of adverse effects and possible to be performed even in pregnant female patients.


BACKGROUND: The number of patients with ulcerative colitis (UC) in China has increased in the past 10 years. Thus, it is anticipated that the incidence of UC-associated colorectal cancer (UC-CRC) will also increase. However, the risk of CRC in UC patients is still unknown in Chinese. The aim of this study was to identify the risk and risk factors of UC-CRC in Chinese. METHODS: A total of 3,922 patients with UC were retrospectively collected from five central teaching hospitals in China, in which high-quality endoscopic and histological diagnoses were available from 1998 to 2009. The database of the UC and UC-associated CRC patients was evaluated. RESULTS: CRC was diagnosed 34 in patients, and the overall prevalence of CRC in patients with UC was 0.87%. The cumulative risk of developing CRC after a disease duration of 10 years was 1.15% (95% confidence interval [CI] 0.71-1.84%); 20 years, 3.56% (95% CI 2.14-5.89%); and 30 years, 14.36% (95% CI 7.57-26.3%). Longer disease duration, extensive colitis, and dysplasia found in the biopsy specimen were identified as risk factors for developing CRC. 5-ASA use was identified as a protective factor of UC-CRC. CONCLUSIONS: The period prevalence of CRC was lower than that reported from the West. However, the cumulative risk was found to be comparable to that of Western countries, which suggests that the period prevalence of UC-CRC in China may be growing in the future.


BACKGROUND AND AIMS: To evaluate the efficacy of MR enterography (MRE) in patients with known or suspected Crohn's disease without the use of anti-peristaltic pharmacologic agents compared to colonoscopy and histology. METHODS: A retrospective review of 850 consecutive patients who underwent routine MRE to evaluate known or suspected Crohn's disease was performed. Of these, 310 patients also underwent colonoscopy with biopsy(s) within 90 days. The results of the MRE were compared to the colonoscopy and pathology reports to determine the presence or absence of disease in evaluable bowel segments. Individual imaging parameters (including wall thickening, enhancement, T2 signal, mesenteric vascular prominence and adenopathy) were also separately analyzed to determine their independent predictive value. RESULTS: In 310 patients, the overall sensitivity and specificity of MRE (using endoscopy as a gold standard) were 85% and 80% respectively (kappa=0.65). The sensitivity of MRE for detection of pathologically severe disease was 87% in the terminal ileum (TI) and 88% in the colon. In the subset of 162 patients who underwent colonoscopy within 30 days of MRE, the overall sensitivity remained 85% but the specificity increased to 85% (kappa=0.69). Wall thickening and abnormal enhancement were sensitive indicators of Crohn's disease (75% and 78%), while abnormal T2 signal, mesenteric vascular prominence and adenopathy were specific (86%, 91% and 93%). CONCLUSION: MRE compares favorably to colonoscopy for evaluation of known or suspected Crohn's disease noninvasively and without the exposure to ionizing radiation associated with CT enterography (CTE). Copyright Copyright 2012. Published by Elsevier Ireland Ltd.

Background: This study compared the efficacy of an elemental formula (EF) to a polymeric formula (PF) in inducing remission for pediatric Crohn's disease (CD). Methods: Newly diagnosed CD children were randomized to EF or PF for 6 weeks. Change in the Pediatric Crohn's Disease Activity Index (PCDAI), fecal calprotectin, and plasma fatty acids were measured at 0 and 6 weeks. Patients were followed up for 2 years. Time and treatment choice for first relapse were documented. Results: Thirty-four children completed the study; EF: 15 (7 M, 8 F), PF: 19 (13 M, 6 F). The mean age was (years) EF: 12.6, PF: 11.7. Ninety-three percent of children (14/15) achieved remission in the EF group and 79% (15/19) in the PF group. One-third of patients maintained remission for 2 years. Mean time to relapse (days): EF: 183 (63-286), PF: 162 (53-301). Most children who relapsed used a treatment for that relapse (EF: 9/10 and PF: 8/13). With PF, an increase of eicosapentaenoic acid (EPA) and alpha linolenic acid was found with a reciprocal decrease in arachidonic acid (AA). With EF, AA and EPA levels were reduced with a significant decrease in docosahexaenoic acid. Fecal calprotectin measurements decreased significantly but did not normalize at the end of week 6. Conclusions: There was no significant difference between EF and PF in inducing remission. One-third of children maintained remission. Changes in plasma polyunsaturated fatty acid status were subtle and may be relevant; however, further evaluation is recommended. Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: The psychosocial functioning of caregivers of adolescents managing inflammatory bowel disease (IBD) has been understudied; yet, poor caregiver functioning can place youth at risk for compromised disease management. The current study addressed this limitation by examining a sample of caregivers of adolescents with IBD. Study aims included (1) documenting rates of paediatric parenting stress; (2) identifying associated sociodemographic predictors of parenting stress; and (3) comparing previously published rates of parenting stress to those within other paediatric chronic conditions, including cancer, type 1 diabetes, obesity, sickle cell disease, bladder exstrophy. METHODS: Caregivers of adolescents with an IBD diagnosis (M(age) = 15.4 +/- 1.4, 44.4% female, 88.7% Caucasian) and receiving tertiary care within a gastroenterology clinic (n = 62) completed the Pediatric Inventory for Parents (PIP) as a measure of paediatric parenting stress with frequency and difficulty as PIP subscales. Paediatric gastroenterologists provided disease severity assessments. RESULTS: Adolescents with IBD were experiencing relatively mild disease activity. Bivariate correlations revealed that PIP-difficulty was positively associated with Crohn's disease severity (r = 0.38, P < 0.01). Caregiver age was negatively associated with the frequency of parenting stress total (r = -0.25, P = 0.05) and communication scores (r = -0.25, P < 0.05). The frequency and difficulty of parenting stressors within the IBD sample were similar to rates within type 1 diabetes, but were significantly lower than rates identified in other paediatric chronic conditions. CONCLUSIONS: Caregivers of adolescents with IBD seem to experience low rates of parenting stress when their adolescents are receiving outpatient care and during phases of IBD relative inactivity. The sociodemographic characteristics of IBD families (i.e. primarily Caucasian, well-educated and higher socioeconomic status) likely encourage greater access to financial and psychosocial resources, which may aid in promoting more optimal stress management. Copyright 2011 Blackwell Publishing Ltd.


AIMS: To survey the practice among gastroenterologists in Australia relating to screening for latent infections and vaccination of patients with inflammatory bowel disease prior to treatment with tumour necrosis factor alpha (TNF-alpha) inhibitors. METHODS: A structured 15 question electronic survey was advertised to gastroenterologists in Australia through an email mailing list and through a hardcopy newsletter. RESULTS: Forty-four clinicians responded to the survey. Screening practice relating to latent tuberculosis infection and hepatitis B virus (HBV) was performed variably, with significant differences in screening methodology. Vaccination for HBV, influenza and pneumococcus was performed infrequently, and the timing of when vaccination should be offered varied considerably. CONCLUSIONS: Despite published guidelines advocating screening for latent infections and vaccination of patients treated with TNF-alpha inhibitors, compliance with recommendations was poor. Recommendations for screening and vaccination of these patients are provided based on these findings. Copyright 2011 The Authors. Internal Medicine Journal Copyright 2011 Royal Australasian College of Physicians.


UNLABELLED: The aim of this study was to compare the dose to organs at risk (OARs) from different craniospinal radiotherapy treatment approaches available at the Northern Centre for Cancer Care (NCCC), with a particular emphasis on sparing the bowel. METHOD: Treatment plans were produced for a pediatric...
medulloblastoma patient with inflammatory bowel disease using 3D conformal 6-MV photons (3DCP), combined 3D 6-MV photons and 18-MeV electrons (3DPE), and helical photon TomoTherapy (HT). The 3DPE plan was a modification of the standard 3DCP technique, using electrons to treat the spine inferior to the level of the diaphragm. The plans were compared in terms of the dose-volume data to OARs and the nontumor integral dose.

RESULTS: The 3DPE plan was found to give the lowest dose to the bowel and the lowest nontumor integral dose of the 3 techniques. However, the coverage of the spine planning target volume (PTV) was least homogeneous using this technique, with only 74.6% of the PTV covered by 95% of the prescribed dose. HT was able to achieve the best coverage of the PTVs (99.0% of the whole-brain PTV and 93.1% of the spine PTV received 95% of the prescribed dose), but delivered a significantly higher integral dose. HT was able to spare the heart, thyroid, and eyes better than the linac-based techniques, but other OARs received a higher dose. CONCLUSIONS: Use of electrons was the best method for reducing the dose to the bowel and the integral dose, at the expense of compromised spine PTV coverage. For some patients, HT may be a viable method of improving dose homogeneity and reducing selected OAR doses. Copyright Copyright 2012 American Association of Medical Dosimetrists. Published by Elsevier Inc. All rights reserved.


BACKGROUND: Inflammatory bowel disease (IBD) patients have a high incidence of wound and overall postoperative complications. A totally laparoscopic approach could potentially reduce these risks. We adopted totally laparoscopic total proctocolectomy (TL-TPC) using the perineal wound for extraction as the procedure of choice in IBD patients who are not candidates for a restorative procedure. This study looks at the TL-TPC results and compares them with our open cohort. METHODS: Prospectively collected data from 52 consecutive patients undergoing TL-TPC from 2002 to 2010 were compared to 31 contemporary patients undergoing open TPC.

RESULTS: Demographics and patient characteristics including body mass index were similar. Mean operative times were 340 +/- 7 minutes for TL-TPC and 337 +/- 9 minutes for open TPC (P = 0.91). Intraoperative blood loss was 228 +/- 2 mL for TL-TPC and 484 +/- 3 mL for open TPC (P < 0.001). Return of bowel function measured as an ileostomy output >100 mL per 8 hours occurred at 2.7 +/- 2.8 days for TL-TPC versus 3.3 +/- 1.8 days for open TPC (P = 0.025). The length of stay was 8.4 +/- 5.0 days for TL-TPC versus 9.2 +/- 3.2 days for open TPC (P = 0.05). The overall complication rate was 43% for TL-TPC versus 65% for open TPC (P = 0.07). Postoperative abdominal wound infections and parastomal hernias occurred in 23% and 10% of open TPC patients, respectively, versus zero (P = 0.001) and 6% (P = 0.67) for TL-TPC. CONCLUSIONS: TL-TPC is therefore considered a safe alternative to open surgery for selected IBD patients not candidates for a restorative procedure. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


AIMS: To describe the change in incidence of paediatric inflammatory bowel disease (IBD) observed at the National Centre for Paediatric Gastroenterology, Hepatology and Nutrition, and to determine whether the presenting disease phenotype and disease outcomes have changed during the past decade. METHODS: The annual incidence of IBD in Irish children aged <16 years was calculated for the years 2000-2010. Two subsets of patients, group A (diagnosed between 1 January 2000 and 31 December 2001), and group B (diagnosed between 1 January and 31 December 2008) were phenotyped according to the Paris Classification. Phenotype at diagnosis and 2-year follow-up were then compared. RESULTS: 406 new cases of IBD were identified. The incidence was 2.5/100 000/year in 2001, 7.3 in 2008 and 5.6 in 2010, representing a significant increase in the number of new cases of Crohn's disease (CD) and ulcerative colitis (UC). There were 238 cases of CD; 129 of UC; and 39 of IBD unclassified. Comparing groups A and B, no differences were found in disease location at diagnosis or, for CD, in its behaviour. CONCLUSIONS: There has been a substantial and sustained increase in the incidence of childhood UC and CD in Ireland over a relatively short period of time. However, disease phenotype at diagnosis has not changed. At 2 years follow-up, CD appears to progress less frequently than in some neighbouring countries. These variations remain unexplained. Prospective longitudinal studies will help to elucidate further the epidemiology of childhood IBD.


The purpose of this study is to review our experience with laparoscopic management of Crohn's disease including patients with prior Crohn's-related abdominal surgery. All cases of Crohn's patients who underwent laparoscopic attempt for management of disease from April 2005 to October 2010 (n = 130) at a single institution were retrospectively reviewed. Evaluated datapoints include: prior abdominal surgery for Crohn's disease, operative
time, rate of conversion, and complication rate. Of the 130 patients, 82 (63.1%) patients had no prior abdominal surgery and 48 (36.9%) patients had previous bowel surgery with mean age of 35.3 (3.5-79) and 41.3 (15-66) years, respectively. Operative time with no prior surgery was 106 (23-245) minutes, and with prior surgery was 100 (26-229) minutes. Estimated blood loss with no prior surgery was 116 (5-800) mL, and with prior surgery was 123 (5-800) mL. Conversion from laparoscopic to open surgery in those with no prior surgery was 17.1 per cent and in those with prior surgery, 20.8 per cent (P = 0.64). Postoperative complications were found in 13 patients (15.9%) without prior abdominal surgery and 13 patients (27.1%) with prior surgery (P = 0.17). The most common postoperative complication in both groups was infection/abscess (8.5%). The laparoscopic management of recurrent Crohn's disease is a safe and technically feasible option, even in those patients with prior history of Crohn's-related abdominal surgery, with a low complication rate and low conversion rate. The utility of the laparoscopic approach in Crohn's patients faced with repeat abdominal procedures may be beneficial in the long-term and should be considered as a method to limit morbidity.


BACKGROUND & AIMS: We evaluated the efficacy and safety of infliximab for inducing and maintaining benefit in children with moderately to severely active ulcerative colitis (UC). METHODS: Patients (6-17 years old) who had active UC (Mayo scores of 6-12; endoscopic subscores >= 2) and had not responded to or tolerated conventional treatment were given 5 mg/kg infliximab at weeks 0, 2, and 6. The primary end point was response at week 8 (decreases in Mayo scores >= 30% and >= 3 points and decreases in rectal bleeding subscores of >= 1 or an absolute subscore of <= 1). At week 8, only responders were randomly assigned to groups given infliximab every 8 or 12 weeks (q8w or q12w) and followed through week 54. Maintenance end points included pediatric UC activity index scores <10 points, defined as remission. RESULTS: At week 8, infliximab induced a response in 73.3% of patients (44 of 60) (95% confidence interval, 62.1%-84.5%; a positive result was defined by 95% confidence interval lower limit >40%). Among responders, twice as many were in remission at week 54 after q8w (8 of 21, 38.1%) than q12w (4 of 22, 18.2%; P = .146) therapy. Assuming the q8w remission rate for responders, the overall remission rate at week 54 would be 28.6%. Serious adverse events and infusion reactions occurred in similar proportions in the q8w and q12w groups. No deaths, malignancies, opportunistic infections, tuberculosis, or delayed hypersensitivity reactions were reported. CONCLUSIONS: Infliximab was safe and effective, inducing a response at week 8 in 73.3% of pediatric patients with moderate to severely active UC who did not respond to conventional therapy. The overall remission rate at week 54 for all enrolled patients was 28.6%, assuming the more effective q8w remission rate. Copyright © 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.


OBJECTIVES: In ulcerative colitis surveillance, chromoendoscopy improves dysplasia detection 3 - 5-fold compared with white light endoscopy (WLE). The aim of this study was to investigate whether narrow band imaging (NBI) can improve dysplasia detection compared with WLE. METHODS: This was a randomized, parallel-group trial. A total of 220 patients were needed to be recruited to detect a threefold increase in dysplasia detection. In all, 112 patients with long-standing ulcerative colitis were randomized to colonoscopic extubation with NBI (56) or WLE (56) (1:1 ratio) at two tertiary endoscopy units in the United Kingdom. Targeted biopsies of suspicious areas and quadrant random biopsies every 10 cm were taken in both groups. The primary outcome measure was the proportion of patients with at least one area of dysplasia detected. In a prespecified mid-point analysis, the criteria for trial discontinuation were met and the trial was stopped and analyzed at this point. RESULTS: There was no difference in the primary outcome between the two groups, with 5 patients having at least one dysplastic lesion in each group (odds ratio (OR) 1.00, 95% confidence interval (95% CI) 0.27 - 3.67, P = 1.00). This remained unchanged when adjusted for other variables (OR 0.69, 95% CI 0.16 - 2.96, P = 0.62). Overall, dysplasia detection was 9% in each arm. Yield of dysplasia from random nontargeted biopsies was 1 / 2,707 (0.04 % ). CONCLUSIONS: Overall, in this multicenter parallel-group trial, there was no difference in dysplasia detection when using NBI compared with high-definition WLE colonoscopy. Random background biopsies were ineffective in detecting dysplasia.


OBJECTIVE: The effect of preoperative total parenteral nutrition (TPN) on the rate of early (within 30 days) postoperative complications in patients with moderate to severe Crohn's disease (CD) was examined. MATERIAL AND METHODS: A series of 15 consecutive patients with CD (mean CD activity index score, 270) given preoperative TPN for 18-90 days (mean, 46 days) and undergoing bowel resection and primary anastomosis was compared with matching controls (105 patients) consecutively selected from all CD patients operated in
Stockholm County during a preceding 20-year period without preoperative TPN. RESULTS: During the preoperative TPN, all the patients studied displayed clinical remission of CD as reflected in improvement in their general well-being, relief of abdominal pain, and abatement of fever and diarrhea. There was no significant early postoperative complication in the TPN-treated group, whereas there were 29 patients with early postoperative complications in the control group, which means a significantly higher rate of postoperative complications when preoperative TPN was not provided. During the preoperative TPN, some crucial variables increased such as the body weight, the serum concentrations of albumin and triiodothyronine reflecting improved nutritional state, whereas the serum concentration of haptoglobin and the white cell count decreased reflecting decreased inflammatory activity. CONCLUSIONS: This study shows that preoperative TPN for at least 18 days may be recommended to be given to patients with moderate to severe CD until clinical remission is achieved in order to minimize the risk of early postoperative complications.


OBJECTIVE: In patients, with symptomatic Crohn's disease (CD), valid information about the presence or absence of small bowel disease activity and stenosis is clinically important. Such information supports decisions about medical or surgical therapy and can be obtained with MR enterography (MRE) or CT enterography (CTE).

MATERIALS AND METHODS: A total of 50 patients with symptomatic pre-existing CD and a demand for small bowel imaging to support changes in treatment strategy were included in this prospective and blinded study. MRE and CTE were performed on the same day in alternating order and subsequently compared with the gold standard: pre-defined lesions at ileoscopy (n = 30) or surgery with (n = 12) or without (n = 3) intra-operative enteroscopy. RESULTS: A total of 35 patients had active small bowel CD (jejenum 0, ileum 1, (neo)-terminal ileum 34) and 20 had small bowel stenosis. The sensitivity and specificity of MRE for detection of small bowel CD was 74% and 80% compared to 83% and 70% with CTE (p >= 0.5). MRE and CTE detected small bowel stenosis with 55% and 70% sensitivities, respectively (p = 0.3) and 92% specificities. CONCLUSIONS: MRE and CTE have comparable diagnostic accuracies for detection of small bowel CD and stenosis. In symptomatic patients with CD and high disease prevalence, positive predictive values are favorable but negative predictive values are low. Consequently, MRE and CTE can be relied upon, if a positive result is obtained whereas a negative enterography should be interpreted with caution.


BACKGROUND & AIMS: Patients with ulcerative colitis (UC) have an increased risk of developing colorectal cancer (CRC). Studies examining the magnitude of this association have yielded conflicting results. We performed a meta-analysis of population-based cohort studies to determine the risk of CRC in patients with UC.

METHODS: We used MEDLINE, EMBASE, Cochrane, and CINAHL to perform a systematic literature search. We included 8 studies in the meta-analysis on the basis of strict inclusion and exclusion criteria. We calculated pooled standardized incidence ratios (SIRs) with 95% confidence intervals (CIs) for risk of CRC in patients with UC and performed meta-regression analyses of the effect of cohort size, calendar period, observation time, percentage with proctitis, and rates of colectomy on the risk of CRC. RESULTS: An average of 1.6% of patients with UC was diagnosed with CRC during 14 years of follow-up. SIRs ranged from 1.05 to 3.1, with a pooled SIR of 2.4 (95% CI, 2.1-2.7). Men with UC had a greater risk of CRC (SIR, 2.6; 95% CI, 2.2-3.0) than women (SIR, 1.9; 95% CI, 1.5-2.3). Young age was a risk factor for CRC (SIR, 8.6; 95% CI, 3.8-19.5; although this might have resulted from small numbers), as was extensive colitis (SIR, 4.8; 95% CI, 3.9-5.9). In meta-regression analyses, only cohort size was associated with risk of CRC. CONCLUSIONS: In population-based cohorts, UC increases the risk of CRC 2.4-fold. Male sex, young age at diagnosis with UC, and extensive colitis increase the risk.

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OBJECTIVES: We hypothesised that nonadherence to thiopurines is more common in adolescents than in adults with inflammatory bowel disease. METHODS: We sought factors associated with thiopurine nonadherence defined by thiopurine metabolite levels. RESULTS: Multivariate logistic regression confirmed that adolescents (odds ratio [OR] 4.6 [95% confidence interval [CI] 1.9-11.5]; P < 0.01) compared with adults, patients with Crohn disease (OR 3.3 [CI 1.1-10.5] P = 0.04) compared with ulcerative colitis, and patients living in more socially deprived areas (OR 1.03 [CI 1.0-1.1] P = 0.02) were more likely to be nonadherent to thiopurines. CONCLUSIONS: Adolescents are more frequently nonadherent than adults: prospective studies are required to determine the reasons for nonadherence in adolescents.

AIM OF THE STUDY: To determine the occurrence of intestinal and extraintestinal cancers in the 1993-2009 prospective European Collaborative Inflammatory Bowel Disease (EC-IBD) Study Group cohort. PATIENTS-METHODS: A physician per patient form was completed for 681 inflammatory bowel disease patients (445UC/236CD) from 9 centers (7 countries) derived from the original EC-IBD cohort. For the 15-year follow up period, rates of detection of intestinal and extraintestinal cancers were computed. RESULTS: Patient follow-up time was fifteen years. In total 62/681 patients (9.1%) [41 with ulcerative colitis/21 with Crohn's disease, 36 males/26 females] were diagnosed with sixty-six cancers (four patients with double cancers). Colorectal cancer was diagnosed in 9/681 patients [1.3%] (1 Crohn's disease and 8 ulcerative colitis). The remaining 53 cancers were extraintestinal. There was a higher prevalence of intestinal cancer in the Northern centers compared to Southern centers [p=NS]. Southern centers had more cases of extraintestinal cancer compared to Northern centers [p=NS]. The frequency of all observed types of cancers in Northern and in Southern centers did not differ compared to the expected one in the background population. CONCLUSIONS: In the fifteen-year follow up of the EC-IBD Study Group cohort the prevalence of cancer was 9.1% with most patients having a single neoplasm and an extraintestinal neoplasm. In Northern centers there were more intestinal cancers while in Southern centers there were more extraintestinal cancers compared to Northern centers. In this IBD cohort the frequency of observed cancers was not different from that expected in the background population. Copyright Copyright 2011 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.


OBJECTIVE: The objective of our study was to evaluate the image quality and diagnostic adequacy of the following two CT enterography protocols in patients weighing less than 160 lb (72 kg): 80-kVp imaging with the adaptive statistical iterative reconstruction (ASIR) in comparison with 120-kVp imaging with the filtered back projection reconstruction. MATERIALS AND METHODS: We retrospectively reviewed 133 CT enterography examinations of 127 patients weighing less than 160 lb, 64 80-kVp examinations, and 69 120-kVp examinations. Image quality for evaluation of the bowel wall, mesenteric vessels, and hepatic parenchyma and the overall image quality were graded on a scale of 1-5 (1 = poor, 2 = acceptable, 3 = good, 4 = very good, 5 = excellent). Diagnostic accuracy for the detection of inflammatory bowel disease was evaluated. The volume CT dose index (CTDI(vol)) was recorded and effective dose was calculated from scanner-generated dose-length product. RESULTS: There was a statistically significant decrease in the mean image quality scores for 80-kVp examinations compared with 120-kVp examinations for evaluation of the bowel wall (3.19 vs 3.70, respectively) and liver (3.12 vs 3.81) and for overall image quality (3.23 vs 3.68), but there was no significant decrease in score for evaluation of the mesenteric vessels (3.63 vs 3.67). None of the 80-kVp examinations was graded as poor, and all were considered to be of acceptable quality. Both techniques had comparable diagnostic accuracy for the detection of inflammatory bowel disease. Interobserver agreement was fair to moderate for qualitative image grading and was substantial for the detection of features of inflammatory bowel disease. The mean CTDI(vol) and effective dose for the 80-kVp examinations were 6.15 mGy and 4.60 mSv, respectively, and for the 120-kVp examinations, 20.79 mGy and 15.81 mSv. CONCLUSION: In patients weighing less than 160 lb, CT enterography examinations at 80 kVp with 30% ASIR produce diagnostically acceptable image quality with an average CTDI(vol) of 6.15 mGy and an average effective dose of 4.60 mSv.


BACKGROUND: Psychotherapy for Crohn's disease (CD) has focused on patients with psychological distress. Another approach to optimize management of CD is to target patients who do not exhibit psychological distress but engage in behaviors that undermine treatment efficacy / increase risk for flare. We sought to determine the feasibility/acceptability and estimate the effects of a program framed around Project Management (PM) principles on CD outcomes. METHODS: Twenty-eight adults with quiescent CD without a history of psychiatric disorder were randomized to PM (n = 16) or treatment as usual (TAU; n = 12). Baseline and follow-up measures were Inflammatory Bowel Disease Questionnaire (IBDQ), Medication Adherence Scale (MAS), Perceived Stress Questionnaire (PSQ), and IBD Self-Efficacy Scale (IBD-SES). RESULTS: There were significant group x time effects favoring PM on IBDQ-Total Score (F(1) = 15.2, P = 0.001), IBDQ-Bowel (F(1) = 6.5, P = 0.02), and IBDQ-Systemic (F(1) = 9.3, P = 0.007) but not IBDQ-Emotional (F(1) = 1.9, P = ns) or IBDQ-Social (F(1) = 2.4, P = ns). There was a significant interaction effect favoring PM with respect to PSQ (F(1) = 8.4, P = 0.01) and IBD-SES (F(1) = 12.2, P = 0.003). There was no immediate change in MAS (F(1) = 4.3, P = ns). Moderate effect sizes (d > 0.30) were observed for IBDQ total score (d = 0.45), IBDQ bowel health (d = 0.45), and systemic...
health (d = 0.37). Effect sizes for PSQ (d = 0.13) and IBDSES (d = 0.17) were smaller. CONCLUSIONS: Behavioral programs that appeal to patients who may not seek psychotherapy for negative health behaviors may improve quality of life and potentially disease course and outcomes. Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


Inflammatory bowel diseases (IBD) are chronic inflammatory illnesses marked by unpredictable disease flares, which occur spontaneously and/or in response to external triggers, especially personal health behaviors. Behavioral triggers of flare may be responsive to disease self-management programs. We report on interim findings of a randomized controlled trial of gut-directed hypnotherapy (HYP, n = 19) versus active attention control (CON, n = 17) for quiescent ulcerative colitis (UC). To date, 43 participants have enrolled; after 5 discontinuations (1 in HYP) and 2 exclusions due to excessive missing data, 36 were included in this preliminary analysis. Aim 1 was to determine the feasibility and acceptability of HYP in UC. This was achieved, demonstrated by a reasonable recruitment rate at our outpatient tertiary care clinic (20%), high retention rate (88% total), and our representative IBD sample, which is reflected by an equal distribution of gender, an age range between 21 and 69, recruitment of ethnic minorities ([REVERSED TILDE]20%), and disease duration ranging from 1.5 to 35 years. Aim 2 was to estimate effect sizes on key clinical outcomes for use in future trials. Effect sizes (group x time at 20 weeks) were small to medium for IBD self-efficacy (.34). Inflammatory Bowel Disease Questionnaire (IBDQ) total score (.41), IBDQ bowel (.50), and systemic health (.48). Between-group effects were observed for the IBDQ bowel health subscale (HYP > CON; p = .05) at 20 weeks and the Short Form 12 Health Survey Version 2 (SF-12v2) physical component (HYP > CON; p < .05) at posttreatment and 20 weeks. This study supports future clinical trials testing gut-directed HYP as a relapse prevention tool for IBD.


Background: Crohn's disease and ulcerative colitis are chronic debilitating diseases for which there are multiple treatment options. There are limited data on methotrexate's efficacy and safety profile. Our aim was to estimate the hepatotoxicity associated with its use in inflammatory bowel diseases (IBDs). Methods: We systematically searched the Medline, Cochrane Library, Web of Science, and EMBASE databases and manually examined references in selected articles for trials that used methotrexate as a treatment for IBDs. Thirteen trials that fulfilled the inclusion and exclusion criteria were included in the meta-analysis. Information on trial and patient characteristics, use of methotrexate as well as other treatments or placebo, and levels of hepatic aminotransferase enzymes were abstracted by two independent investigators using a standardized form. A random effects model was used to pool the incidence rates of reported abnormalities in hepatic aminotransferases. Results: The pooled incidence rate of abnormal hepatic aminotransferase levels (defined as up to a 2-fold increase over the upper limit of the normal range) in patients treated with methotrexate for IBD was 1.4 per 100 person-months, while the rate of hepatotoxicity (defined as greater than a 2-fold over the upper limit of the normal range) was 0.9 per 100 person-months. The rate of withdrawal from treatment due to these abnormalities was 0.8 per 100 person-months. Conclusions: The incidence of methotrexate-related hepatotoxicity as measured by elevation in transaminases and drug withdrawal secondary to elevated transaminases is relatively low. Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: It remains controversial whether or not cytomegalovirus infection in patients with active ulcerative colitis reflects a nonpathogenic colonization or a pathogenic disease warranting antiviral therapy. GOALS: The aim of this study was to determine the prevalence of cytomegalovirus infection in patients with active ulcerative colitis and the therapeutic efficacy of ganciclovir against cytomegalovirus infection in patients with steroid-refractory ulcerative colitis. STUDY: A prospective, multicenter study was conducted in 72 patients with moderate-to-severe ulcerative colitis who were treated with intravenous steroids. The presence of cytomegalovirus was evaluated serologically and histopathologic examination, including immunohistochemical staining. In patients with steroid-refractory ulcerative colitis, cytomegalovirus infections were treated with intravenous ganciclovir. In patients with steroid-responsive ulcerative colitis, steroid therapy was continued irrespective of cytomegalovirus infection. RESULTS: The evidence of cytomegalovirus infection was found in 31 patients (43%) with moderate-to-severe active ulcerative colitis. In patients with steroid-refractory ulcerative colitis, the cytomegalovirus infection rate increased to 67% (14 of 21). No significant clinical and endoscopic differences existed between patients with and without a cytomegalovirus infection; however, the amount of steroids used during the flare-up period was significantly higher in patients with a cytomegalovirus infection (P = 0.013). Eleven of 14 patients (79%) with steroid-refractory ulcerative colitis and a cytomegalovirus infection
improved with ganciclovir treatment. Cytomegalovirus infections in the steroid-responsive group (17 of 31) did not require ganciclovir therapy. CONCLUSIONS: Cytomegalovirus infections are frequently observed in patients with moderate-to-severe ulcerative colitis, especially steroid-refractory ulcerative colitis. Ganciclovir was effective in patients with steroid-refractory ulcerative colitis who had a cytomegalovirus infection.


BACKGROUND/AIMS: Immunosuppressive therapy in ulcerative colitis (UC) may induce cytomegalovirus (CMV) infection or reactivation in the colonic mucosa and in turn exacerbate UC. However, it is unclear whether colonic inflammation itself affects CMV infection in UC. This prospective study evaluated the prevalence and clinical outcome of CMV infection in patients with new onset UC who have not been exposed to UC medication.

METHODOLOGY: A prospective, multi-center study was conducted in 65 patients with new onset UC. The presence of CMV was evaluated by a serology test and a histopathological examination including immunohistochemical staining. The assessment of clinical outcome was performed based on CMV positivity.

RESULTS: Evidence of CMV infection was found in three (4.5%) patients with UC. Two patients with moderate disease activity improved with 5-aminosalicylate or steroid treatment. One patient with severe active colitis, however, required antiviral therapy. CONCLUSIONS: CMV infection is rare in new onset UC, which suggests that use of immunosuppressive medications is an important risk factor for CMV infection in UC. However, CMV evaluation is necessary for severe active UC, even with new onset of the disease.


In Japan, the recommended dosage regimens of infliximab (IFX) for treatment of rheumatoid arthritis (RA) and Crohn's disease (CD) are different. However, the differences have not been analyzed theoretically. In a previous study, we constructed a pharmacokinetic-pharmacodynamic model to investigate the effects of IFX for CD and found it useful to establish a rational dosage regimen of IFX for individual patients with CD. In the present study, we investigated whether the theory-based model could be used for cases of RA and also used it to evaluate the validity of the dosage regimen. The results obtained with our model were in good agreement with observed tender joint count (TJC) ratio data, which was considered to show the validity of our analysis. Thus, we concluded that the model could be used for patients with RA. Furthermore, a second administration of IFX given 2 weeks after the first infusion was important to achieve remission in the early stage of RA. We also compared the estimated pharmacodynamic parameters of RA with those of CD. The elimination rate constant of inflammation in RA was greater than that in CD, suggesting that the recovery from inflammation in RA is faster than that in CD, and indicating a reason for the difference in dosage between RA and CD. In conclusion, use of our model in light of the individual quantitative factor of tumor necrosis factor (TNF)-alpha allows establishment of IFX dosage regimens for individual patients.


BACKGROUND: Crohn's disease (CD) exhibits significant clinical heterogeneity. Classification systems attempt to describe this; however, their utility and reliability depends on inter-observer agreement (IOA). We therefore sought to evaluate IOA using the Montreal Classification (MC). METHODS: De-identified clinical records of 35 CD patients from 6 Australian IBD centres were presented to 13 expert practitioners from 8 Australia and New Zealand Inflammatory Bowel Disease Consortium (ANZIBDC) centres. Practitioners classified the cases using MC and forwarded data for central blinded analysis. IOA on smoking and medications was also tested. Kappa statistics, with pre-specified outcomes of kappa>0.8 excellent; 0.61-0.8 good; 0.41-0.6 moderate and <=0.4 poor, were used. RESULTS: 97% of study cases had colonoscopy reports, however, only 31% had undergone a complete set of diagnostic investigations (colonoscopy, histology, SB imaging). At diagnosis, IOA was excellent for age, kappa=0.84; good for disease location, kappa=0.73; only moderate for upper GI disease (kappa=0.57) and disease behaviour, kappa=0.54; and good for the presence of perianal disease, kappa=0.6. At last follow-up, IOA was good for location, kappa=0.68; only moderate for upper GI disease (kappa=0.43) and disease behaviour, kappa=0.46; but excellent for the presence/absence of perianal disease, kappa=0.88. IOA for immunosuppressant use ever and presence of stricture were both good (kappa=0.79 and 0.64 respectively). CONCLUSION: IOA using MC is generally good; however some areas are less consistent than others. Omissions and inaccuracies reduce the value of clinical data when comparing cohorts across different centres, and may impair the ability to translate genetic discoveries into clinical practice. Crown Copyright ACopyright 2011. Published by Elsevier B.V. All rights reserved.
BACKGROUND: Corticosteroids therapy, classically the first-line treatment for ulcerative colitis (UC), often causes serious side-effects. Theoretically, pulse steroid therapy where high doses are given for a shorter period may have maximal beneficial effects and minimal side-effects as induction therapy for UC. We have therefore retrospectively compared induction therapy using pulse steroids with conventional steroid treatment for children and adolescents with moderate-to-severe UC. METHODS: We utilized conventional steroid treatment (prednisolone 1-1.5 mg/kg/day) as an induction treatment in 17 UC patients between 1985 and 2006. Alternatively we used a 3-day megadose pulse steroid therapy (methylprednisolone intravenously 20-30 mg/kg/day, max. 1000 mg/day) in 20 UC patients from 1993 to 2006. RESULTS: Pulse steroid therapy successfully induced rapid remission in UC patients with moderate-to-severe disease compared with conventional treatment (13.2 days vs 25.1 days; P < 0.05). The amelioration of Pediatric Ulcerative Colitis Activity Index score between before and 1 week after pulse steroid therapy was significantly more than that of conventional treatment (P < 0.01). No serious adverse effects were observed in the patients treated with pulse steroid therapy. However, the rate of the relapse episodes during the next 12 months after pulse steroid therapy was not significantly different from that after conventional treatment. CONCLUSION: These findings suggest that pulse steroid therapy is an option to be considered in children with moderate-to-severe UC. Copyright 2011 The Authors. Pediatrics International Copyright 2011 Japan Pediatric Society.


Background: Infliximab is a chimeric monoclonal antibody directed against tumour necrosis factor alpha. When used in inflammatory bowel disease (IBD), primary non-response is seen in at least 10% of patients with secondary loss of response occurring in a further 10-15% per year. It has been suggested that this may in part be a result of the development of anti-infliximab antibodies (ATIs). The prevalence of ATIs varies according to the frequency of administration of infliximab and the use of immunosuppressants. ATIs have also been linked with infusion and hypersensitivity reactions. We aimed to perform a meta-analysis of the prevalence of ATIs in people with IBD receiving infliximab, the effect of immunosuppressive drugs on prevalence of ATIs and the effects of ATIs on infusion reactions and remission rates. Methods: MEDLINE and EMBASE databases were systematically searched from 1948 and 1980 respectively to October 2011. Inclusion criteria included randomized controlled trials, cohort studies or case series reporting on anti-infliximab antibodies in adult or juvenile IBD. Data from eligible studies were extracted into a standardized form and a meta-analysis performed. Results: Eighteen studies involving 3326 patients were included. The prevalence of ATIs was 45.8% when episodic infusions of infliximab were given and 12.4% when maintenance infliximab was given. Rates of infusion reactions were significantly higher in patients with ATIs (RR: 2.07, 95% CI 1.61-2.67). Immunosuppressants resulted in a 50% risk reduction in prevalence of ATIs. The prevalence of ATIs was 17.5% in patients using immunosuppressants and 37.7% in those who were not (RR: 0.50, 95% CI 0.42-0.59). (Figure Presented) However, the presence or absence of ATIs did not significantly affect rates of clinical remission, which was 46.5% in patients with ATIs and 60.2% in those without (p = 0.10). Conclusions: The prevalence of ATIs depends on the regimen of infliximab administration and the use of immunosuppressants. Patients who develop ATIs are at increased risk of infusion reactions, but the presence of ATIs does not, by itself, have an effect on rates of clinical remission.


BACKGROUND AND AIDS: Iron deficiency anemia (IDA) is a common problem in patients with Inflammatory Bowel Disease (IBD) and has a significant negative impact on quality of life. The aim was to compare the clinical efficacy of intravenous (IV) versus oral (PO) iron replacement in adult IBD with iron deficiency anemia (IDA). METHODS: A systematic search for randomized controlled trials comparing the efficacy of IV versus PO iron therapy in the treatment of IDA in adult IBD patients. The primary outcome was the mean change in the hemoglobin at the end of study and secondary outcomes include mean change in ferritin, clinical disease activity index, quality of life score and the adverse reaction rate. RESULTS: The search strategy identified 757 articles while only three industry-funded articles met the inclusion criteria for systematic review and meta-analysis. The total sample size was 333 patients with 203 patients receiving IV therapy. IV route was associated with a 6.8 g/L higher mean hemoglobin increment and 110 mug/L higher mean ferritin increment. The IBD activity index and Quality of Life scores were comparable between the two treatment groups. More adverse events were reported in the oral treatment group with the odds for discontinuation being 6.2 (CI 2.2, 17.1). CONCLUSIONS: Intravenous iron treatment is better tolerated and more effective than oral iron treatment in improving ferritin. The higher hemoglobin gain with the IV route was small and of uncertain clinical significance.

Background: In ulcerative colitis (UC), surgery is often recommended for patients who are not responding to conventional medical therapy [1]. We estimated the prevalence of complications of colectomy in patients with UC, using metaanalysis of published studies. Methods: A systematic literature search in PubMed (through August 2011) was conducted for "ulcerative colitis" and the following: ileum, ileal, pouch-anal anastomosis, and complications. Studies with primary data collected from reports of complication rates associated with colectomy were analysed. For complications with the highest prevalence, pooled averages across studies were estimated. The heterogeneity among studies was examined using the Cochran's Q-test to decide which model should be used (DerSimonian and Laird random-effects model with random effects applied on the logit scale if heterogeneity existed or fixed-effects model if no heterogeneity). Results: Pouchitis, chronic pouchitis, small bowel obstruction, small bowel obstruction requiring reoperation, and infertility in patients undergoing colectomy were analysed using metaanalysis; the random-effects model was used for all estimates due to heterogeneity among studies. From 16 studies, the estimated prevalence of nonchronic pouchitis (>=3 episodes per year) was 28.4% (95% CI: 21.7 36.2%) (table). From 7 studies, the estimated prevalence of chronic pouchitis (>=4 episodes per year) was 10.9% (95% CI: 6.6 17.4%). From 2 studies that included infertility data, the prevalence of infertility after surgery was about 6 times the presurgery rate. From 15 studies, the estimated prevalence of small bowel obstruction was 17.8% (95% CI: 13.5 23.2%). From 7 studies, the estimated prevalence of small bowel obstruction requiring reoperation was 24.5% (95% CI: 14.9 37.5%). (Table presented) Conclusions: Patients with moderate to severe UC experienced substantial complications associated with colectomy. This suggested that alternative therapies might need to be considered before undergoing surgical intervention if conventional medical therapies failed [1].


BACKGROUND: Patients with Crohn's disease (CD) who smoke have a more complicated disease course. AIMS: Our primary objective was to assess smoking related variables that were associated with smoking cessation versus continued smoking in patients with CD. METHODS: A multi-center study identified CD patients who were seen at the University of Chicago and University of Calgary IBD clinics. Patients were categorized into three subgroups: lifetime non-smokers, current smokers, or ex-smokers. Participants completed questionnaires assessing their cigarette smoking behavior. Current smokers were prospectively followed for 6 months to assess smoking status and attempts to quit. Logistic regression analysis was performed to identify factors associated with smoking cessation. RESULTS: Three hundred patients were enrolled with 148 identifying themselves as lifetime non-smokers, 70 as current smokers, and 82 as ex-smokers. Patients who reported their first cigarette within 5 min of waking were more likely to be current smokers (OR = 21; 95% CI 3.94-107.3) as compared to patients who waited greater than 60 min. Current smokers were more likely to have one or more household members who smoked compared to ex-smokers (P < 0.05). Nearly half (49%) of the current smokers were in the precontemplation stage of change (i.e. no intention to quit smoking). At the 6-month follow-up, only 11% reported they quit smoking. CONCLUSIONS: Patients who report a short time to first cigarette in the morning may have more difficulty in smoking cessation. Current smokers were more likely to have another smoker in the household compared to ex-smokers. Current smokers had low levels of motivation to quit smoking and consequently with no intervention, very few quit 6 months after the baseline assessment.


In the present study, we investigated the differentially expressed proteins associated with ulcerative colitis (UC) using proteomic methods. Two-dimensional electrophoresis (2-DE) technology was performed to separate the total proteins of ulcerative tissues from those of the normal tissues of UC patients. PDQuest software was applied to analyze the obtained 2-DE images. Candidate protein spots between the two groups were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and bioinformatics analysis. The well resolution and reproducible 2-DE patterns of UC and normal tissues were established. Of the 12 differentially expressed proteins, 9 were successfully identified, of which 6 proteins were up-regulated including apolipoprotein C-III, haptoglobin, receptor tyrosine kinase, aldehyde reductase, pericentriolar material 1, and heat shock factor protein 2, and 3 were down-regulated including keratin, filamin A-interacting protein 1, and tropomyosin 3. These identified proteins were related to hormonal modulation, immune response, oxidative stress, and signal conduction. The 2-DE protein expression profile of the UC tissues displays an obvious difference from that of the normal controls. Various proteins may be involved in the occurrence of UC.

**BACKGROUND:** Crohn's disease (CD), an inflammatory disease of the bowel, affects millions of people around the world. Evidence suggests that disease onset and pathogenesis differ between males and females. Yet no comprehensive efforts exist to assess the sex-specific genetic architecture of CD. **METHODS:** We used genotyping data from a cohort of 1748 CD cases and 2938 controls to investigate 71 meta-analysis-confirmed CD risk loci for sex differences in disease risk. We further validated the significant results in separate cohorts of 968 CD cases and 2809 controls, and performed a meta-analysis across datasets. **RESULTS:** The single nucleotide polymorphism (SNP) rs3792106 (C/T) in ATG16L1 showed a significant sex effect with P-value 6.9 x 10(-13) and allelic odds ratio 1.48 in females, and P-value 0.013 and odds ratio 1.22 in males (odds ratio heterogeneity P-value 0.037). Surprisingly, the difference was found to arise from a discrepancy in allele frequencies between male and female controls (P-value 0.0045) rather than cases. We found similar results for this SNP in the separate validation datasets. Using 155 HapMap 3 trios, we detected significant maternal overtransmission of the T allele at rs3792106 (P-value 0.027). **CONCLUSIONS:** Our results indicate that different transmission patterns between sexes may sustain the disparate allele frequencies at rs3792106 in healthy populations, and furthermore that a virus-risk variant mechanism implicated in CD alters the distribution in diseased patients. To our knowledge, this is the first report of sex-specific CD association in ATG16L1. The possible implications in CD and basic human biology present interesting areas for future investigation. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


Long-standing inflammatory bowel disease (IBD), either ulcerative colitis or Crohn disease, is associated with a high risk of developing colorectal adenocarcinoma (CAC). However, histomorphology of IBD-associated CAC has not been thoroughly examined, and it is unclear whether and how these patients should be screened for Lynch syndrome (LS). We evaluated the demographic and morphologic features of 108 IBD-associated CACs, including ulcerative colitis-associated (n = 95) and Crohn disease-associated CACs (n = 13), against 93 control cases of sporadic microsatellite-stable (MSS) CAC, 20 cases of sporadic microsatellite instability high (MSI-H) CAC, and 23 CAC cases of LS. The mean age of patients with IBD-associated CAC was 50 years, which was lower compared with the mean age of 63.7 years of the sporadic MSS controls and 76.5 years of the sporadic MSI-H group but not statistically different from that of the LS patients. Synchronous CACs were noted in 20.4% of the IBD patients and 13% of LS patients but in only 2.1% of the sporadic MSS controls and in none of the MSI-H patients. Right-sided CACs were significantly less frequent in the IBD group than in sporadic MSS controls, MSI-H group, and LS patients (P < 0.05 for all). In contrast to sporadic MSS CAC, IBD-associated CACs are characterized by lack of tumor necrosis, Crohn-like reaction, tumor histologic heterogeneity, the presence of mucin, and signet ring cell differentiation and tumor well differentiation. The histomorphologic similarity among IBD-associated and MSI-H tumors, either sporadic MSI-H or LS-related, is independent of MSI status. The young age of patients with IBD-associated CAC and the morphological similarities among IBD-associated, sporadic MSI-H, and LS-related CAC suggest that an age-based and morphology-based strategy before the screening test for LS may be less effective in IBD patients than in the non-IBD population.


**BACKGROUND:** "Indefinite for dysplasia" (IND) on pouch mucosal biopsy is occasionally reported during routine histopathological evaluation. The natural history and implication of this histologic entity in ileal pouch-anal anastomosis (IPAA) has not been studied. **AIM:** The aim of this study is to characterize cumulative probability, natural history, and clinical outcome of pouch IND in a cohort of patients with inflammatory bowel disease (IBD). **METHODS:** All 932 patients with restorative proctocolectomy and IPAA for IBD were included. Patients with or without IND were classified into the study and control groups. Demographic, clinical, endoscopic, and histologic variables were analyzed. **RESULTS:** The mean duration from IBD diagnosis to colectomy and from pouch construction to data entry was 8.4 +/- 8.5 and 9.7 +/- 6.2 years, respectively. A total of 2,250 surveillance or diagnostic pouchoscopies with biopsies were performed for the cohort. Twenty-one patients (2.3%) were diagnosed with anal transitional zone and/or pouch IND, for whom subsequent pouchoscopies were performed with the mean procedure number being 3.4 +/- 2.2 per patient during a mean of follow-up of 19.3 +/- 16.1 months. One patient with IND developed low-grade dysplasia and one had high-grade dysplasia in a separate endoscopy. Cox model showed the presence of primary sclerosing cholangitis was an independent risk factor for pouch IND [hazard ratio = 6.76 (95% CI 2.56-17.88)]. Interobserver agreement (kappa score) for diagnosing
Background: Data regarding the effectiveness of anti-tumor necrosis factor (TNF) agents for resolution of extraintestinal manifestations (EIMs) are scarce. The CARE study evaluated clinical effectiveness, EIM resolution, and safety of adalimumab in a large pan-European cohort of patients with moderate to severe Crohn's disease (CD).

Methods: In all, 945 patients with a Harvey-Bradshaw Index (HBI) \( \geq 7 \) enrolled in this multicenter, open-label phase IIIb trial. Patients received subcutaneous adalimumab, 160/80 mg at weeks 0/2, then 40 mg every other week. Dose adjustments were allowed for CD-related concomitant medications (from week 8) and adalimumab (from week 12). Clinical endpoints were analyzed through week 20 for all patients, and after stratification by prior infliximab exposure and by reason for discontinuing infliximab (primary nonresponse [PNR] or other). Results: The remission rate (HBI <5) at week 20 was 52% (95% confidence interval, 49%-55%) overall, and was higher for infliximab-naive versus infliximab-exposed patients (62% versus 42%, \( P < 0.001 \)). Remission rates were similar for PNR (37%) and other reasons (43%; \( P = 0.278 \)). Of 497 patients with baseline EIMs, 51% were free of EIM signs and symptoms at week 20. Serious infectious adverse events were reported in 5% of patients. Opportunistic infections and malignancies were rare (<=1%). There was one case of demyelinating disease, but no occurrences of lupus, tuberculosis, or death. Conclusions: In this large cohort of patients, adalimumab treatment resulted in rates of clinical remission and EIM resolution exceeding 50%, and substantial rates of effectiveness in patients who had PNR to infliximab. Adalimumab was well tolerated, with safety consistent with prior reports. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.
treatment by simple clinical and biological parameters. A decision-tree model for early introduction of rescue therapies is provided. Copyright Copyright 2010 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Few data are available on the efficacy of methotrexate (MTX) in ulcerative colitis (UC). AIM: To evaluate the efficacy and safety of MTX in UC patients. PATIENTS AND METHODS: UC patients who had been treated with MTX were identified from the databases of 8 Spanish IBD referral hospitals. Patients were included in the study if they received MTX for steroid dependency or steroid refractoriness. Therapeutic success was defined as the absence of UC-related symptoms, complete steroid withdrawal and no requirement of rescue therapies within the first 6 months after starting MTX. RESULTS: Forty patients were included, 70% treated for steroid dependency and 27% for steroid refractoriness. Thiopurines had been previously attempted in 87.5% of patients. The median dose of MTX used for induction was 25mg (IQR 17.5-25) weekly given parenterally in 82.5% of cases. Eighty-five percent of patients were on steroids when MTX was started. Forty-five percent of patients met criteria for therapeutic success. Initial treatment failures were mainly due to inefficacy (50%) or intolerance (36%). After a median follow-up of 28 months (IQR 22-47), 38% of patients with initial therapeutic success required new steroid courses, 22% started biological therapy, and only 1 patient required colectomy. The cumulative probability of maintaining steroid-free clinical remission was 60%, 48%, and 35% at 6, 12, and 24 months after starting MTX, respectively. Eleven patients (27.5%) experienced adverse events, leading to MTX discontinuation in only 8 of them. CONCLUSIONS: MTX appears to be effective to maintain clinical remission in UC, at least in the short-term, with an acceptable safety profile. Copyright Copyright 2011 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.


BACKGROUND: Ileal pouch-anal anastomosis (IPAA) following proctocolectomy is the preferred option for patients with medically refractory ulcerative colitis, indeterminate colitis, and familial adenomatous polyposis. However, it remains a procedure associated with morbidity and mortality. Pelvic sepsis, pouch fistulae, and anastomotic dehiscence predispose to pouch failure. We report our experience with an adaptation for the formation of the stapled ileal J pouch using the GIATM 100 stapling device (Covidien, Mansfield, Massachusetts, USA). When creating the J pouch, we remove the bevelled plastic protector from the thin fork of the stapling device, allowing the staple line to be completed to the tip of the stapled efferent limb of the pouch, thereby minimizing potential blind ending in the efferent limb and injury to the transverse staple line. METHODS: Patients undergoing elective IPAA at our institution over a 5-year period using this adapted stapling technique for creation of the ileal J pouch were reviewed. Data were collected from a prospectively maintained inflammatory bowel disease database, theater records, and patient chart review. RESULTS: Forty-one patients underwent IPAA using this technique at our institution during the study period. Postoperative morbidity was encountered in 11 of 41 patients including pelvic sepsis, pouch fistulae, anastomotic stricture, or leak. There was no morbidity observed related to a blind efferent limb or transverse staple line disruption. No mortality was observed in this series. CONCLUSION: Maximizing the length of the efferent fork of the GIA stapling device can reduce the length of redundant efferent J limb of the ileal J pouch. This may reduce the incidence of torsion, volvulus, distension, fistulae/sinuses, and pelvic sepsis/anastomotic leak following IPAA.


BACKGROUND: The purpose of this study was to compare medication use and complication rates between Crohn's disease (CD) and non-CD patients undergoing ileocolic resections and right hemicolecotomies. METHODS: A review of patients who underwent ileocolic resections and right hemicolecotomies from January 1, 2003, through December 31, 2010, was performed. Data collected included demographics and clinical information, biologics use (eg, infliximab, adalimumab), other medication use (eg, steroids), complications, and mortality. RESULTS: There were 791 records reviewed, with 93 CD patients. There was no significant difference in major or minor complications, anastomotic leaks, operating room time, or postoperative ileus occurrence between the CD and non-CD groups (P > .05). Use of biologics and steroids were significantly higher among the CD patients. Mortality, age, and American Society of Anesthesiologists score were significantly higher in the non-CD group. CONCLUSIONS: Ileocolic resections and right hemicolecotomies in CD patients are not associated with an increase in complication rates even when the patients use steroids and biologics in the preoperative period. Copyright Copyright 2012 Elsevier Inc. All rights reserved.

Background & aims: Probiotics have been suggested to prevent severe necrotizing enterocolitis (NEC) and decrease mortality in preterm infants. The aim of this paper was to systematically analyze the level of evidence (LoE) of published controlled randomized trials (RCTs) on probiotics in preterm infants. Methods: Literature searches were made up to November 2010. LoE of recommendations based on single trials or meta-analyses were scored following the Oxford Center for Evidence based Medicine approach (1a - meta-analyses of 1b LoE studies; 1b - well designed RCT; 2a - meta-analyses which include 2b LoE studies; 2b - lesser quality RCT). Results: Fifteen trials were included (Two 1b LoE trials and thirteen 2b LoE trials). Methodological assessment revealed considerable heterogeneity. Some probiotics may be beneficial in relation to reduction of severe NEC (2b LoE) and reduction of mortality (2b LoE). Probiotics do not accelerate feeding advancement (1b and 2b LoE). There was no convincing benefit with regard to prevention of sepsis (1b and 2b LoE). Conclusion: There is insufficient evidence to recommend routine probiotics. However, there is encouraging data (2b LoE) which
The highest mean value of \[ e \{IQR\} = 4.0, 14.0 \) of UC than Caucasians (10.0, IQR = 6.0, 18.0) (\( P = 0.006 \)).

AIM OF THE STUDY: The aim of the study was to compare short-term outcomes of robotic and laparoscopic proctectomy in patients with inflammatory bowel disease (IBD). METHODS: This is an IRB-approved case-matched review. Seventeen robotic proctectomies (RP), 10 with ileal pouch anal anastomosis (IPAA) and 7 completion (CP), were matched to laparoscopic proctectomies (LP). Short-term and functional outcomes were compared between LP and RP. RESULTS: In CP cohort, operative times were longer in the RP group (351 RP vs 238 LP min, \( p = 0.03 \)), mean robotic time 90 min. Estimated blood loss (EBL) was similar between RP-CP and LP-CP groups (\( p = 0.18 \)). Return of bowel function (RBF) was slower in RP-CP group (3.0 vs 17 days, \( p = 0.04 \)), and length of stay (LOS) was longer (6.4 vs 4.1 days, \( p = 0.02 \)). In the IPAA group, there were no differences between operative times (\( p = 0.14 \)), robotic time 86 min; EBL (\( p = 0.15 \)), and postoperative complications. Return of bowel function (3.6 vs 2.6 days, \( p = 0.3 \)) and LOS (8.5 vs 6.1 days, \( p = 0.17 \)) were similar between RP and LP. Bowel and sexual function were equivalent between LP and RP-IPAA groups. CONCLUSIONS: Robotic proctectomy is a safe and effective technique for patients with IBD. It is comparable to LP with regard to perioperative outcomes, complications, and short-term functional results.


BACKGROUND: There has been an increase in the number of studies on the interaction of African American race and the natural history of inflammatory bowel disease (IBD). However, the results from these studies have been conflicting. We aimed to characterize the natural history of ulcerative colitis (UC) in a cohort of African American patients compared with Caucasian controls. METHODS: We performed a retrospective chart review of patients with UC who were seen in our IBD Center from 2000 to 2010. In all, 102 African American patients and 209 Caucasian patients were included. We assessed clinical variables related to the natural history of UC as well as outcome variables that reflected disease severity. RESULTS: African American patients had a shorter median duration (8.0, interquartile range [IQR] = 4.0, 14.0) of UC than Caucasians (10.0, IQR = 6.0, 18.0) (\( P = 0.006 \)). African American disease patients had more distal disease than controls. African Americans were significantly less likely to use corticosteroids (74.2% vs. 88.8%, \( P = 0.002 \)), or use immunomodulators (25.8% vs. 69.7%, \( P < 0.001 \)) than Caucasians. Adjusted multivariate analysis showed that ethnicity was not a risk factor for colectomy (hazard ratio [HR] = 1.6; 95% confidence interval [CI]: 0.78, 3.3). CONCLUSIONS: There appear to be differences in the natural history of UC in our African American patients when compared with Caucasian controls, while ethnicity was not shown to be a risk factor for colectomy. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


INTRODUCTION: Xenin is a newly discovered peptide in humans. The concentration of xenin in human plasma increases after meals and therefore this peptide is considered as a marker of satiety. The mechanism of xenin action in humans has not been thoroughly examined. MEDLINE database contains only few reports about the role of xenin in adults and none of them were performed in children. AIM OF THE STUDY: The aim of the study was to evaluate the concentration of xenin in children with energy balance disorders. MATERIAL AND METHODS: Plasma xenin concentration was measured in children with inflammatory bowel syndrome (IBD) (n=53; age 14+/−3 years) before, during and after treatment, obese children (n=26; age 14+/−2.8 years) during the OGGT test and in healthy children (n=10; age 15.7+/−2.2 years). Xenin was determined in the plasma using the radioimmunological method. RESULTS: The mean plasma xenin concentration in the healthy children was 371+/−36 pg/ml. In the children with an acute phase of IBD the mean concentration of xenin was 367+/−96 pg/ml and an increase during the treatment to the mean value 399+/−55 pg/ml was noted. The highest mean value of xenin concentration (412+/−55 pg/ml) was found during early remission. In obese children, the mean concentration of xenin (198+/−69 pg/ml) was significantly lower as compared to children with IBD and to control (p<0.001 in both cases). The glucose load did not have any effect on xenin concentration in obese children. CONCLUSIONS: Xenin takes part in the regulation of energy balance in children.


BACKGROUND: Crohn's disease (CD) and ulcerative colitis (UC), known as inflammatory bowel diseases (IBD), are characterized by an abnormal immunological response to commensal bacteria colonizing intestinal lumen and mucosa. Among the latter, strains of adherent-invasive Escherichia coli (AIEC), capable of adhering to...
and invading epithelium, and to replicate in macrophages, have been described in CD adults. We aimed at identifying and characterizing AIEC strains in pediatric IBD. METHODS: In all, 24 CD children, 10 UC, and 23 controls were investigated. Mucosal biopsies, taken during colonoscopy, were analyzed for the presence of AIEC strains by an adhesive-invasive test. Protein expression of the specific AIEC receptor, the carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6), was evaluated by western blot and immunohistochemistry, while tumor necrosis factor alpha (TNF-alpha) and interleukin (IL)-8 mRNA expression was detected by real-time polymerase chain reaction (PCR), after bacterial infection. Transmission electron microscopy and trans-epithelial electric resistance assays were performed on biopsies to assess bacteria-induced morphological and functional epithelial alterations. RESULTS: Two bacterial strains, EC15 and EC10, were found to adhere and invade the Caco2 cell line, similar to the well-known AIEC strain LF82 (positive control): they upregulated CEACAM6, TNF-alpha, and IL-8 gene/protein expression, in vitro and in cultured intestinal mucosa; they could also survive inside macrophages and damage the epithelial barrier integrity. Lesions in the inflamed tissues were associated with bacterial infection. CONCLUSIONS: This is the first study showing the presence of adhesive-invasive bacteria strains in the inflamed tissues of children with IBD. Collective features of these strains indicate that they belong to the AIEC spectrum, suggesting their possible role in disease pathogenesis. Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND & AIMS: It is not clear whether medical therapy, surgery, or both is the best approach for patients with Crohn's disease who develop an intra-abdominal abscess. METHODS: We evaluated data from patients with Crohn's disease who were diagnosed with a radiologically confirmed abdominal abscess (enhancing fluid collection, >= 1 cm) from 1999 to 2006 (n = 95; median age, 42.0 y; 50.5% female). Medical/non-surgical methods (percutaneous aspiration +/- drain placement) were used for 55 patients (mean abscess size, 6.9 +/- 3.2 cm), and 40 patients underwent surgical interventions (laparotomy +/- bowel resection; mean abscess size, 7.5 +/- 3.7 cm). We investigated risk factors for abscess recurrence. RESULTS: The median length of hospitalization was 15.5 days for patients who underwent surgery and 5.0 days for patients who did not (P < .001). The 5-year cumulative probability of abscess recurrence was 31.2% among patients who did not undergo surgery and 20.3% among those who did (P = .25). Histories of perianal or active ileal disease predicted abscess recurrence. Initiation of pharmacologic therapy after drainage reduced the risk for abscess recurrence (P < .001). Anti-tumor necrosis factor therapy, compared with no therapy, reduced the risk of abscess recurrence (P = .001) in all patients, whereas immunosuppressive monotherapy, compared with no therapy, had a trend toward significant risk reduction (P = .06). CONCLUSIONS: Among patients with Crohn's disease who have intra-abdominal abscesses, nonsurgical and primary surgical management strategies result in similar rates of abscess recurrence and complications. Initiation of anti-tumor necrosis factor and/or immunosuppressive therapy when abscesses resolve might protect against intra-abdominal penetrating disease. Copyright 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.


BACKGROUND: Germline variation in the 71 Crohn's disease (CD) loci implicated by genome-wide association studies (GWAS) only accounts for approximately 25% of estimated heritability. The contribution of epigenetic alterations to disease pathogenesis is emerging as a research priority. MATERIALS AND METHODS: The methylation status of 27,578 CpG sites across the genome was analyzed using the Illumina Human Methylation27 assay in DNA extracted from whole blood samples from 40 adult females (21 ileal CD, 19 healthy controls) and 16 girls with childhood-onset CD, all nonsmokers. Our primary analysis compared methylation profiles in adult cases and controls. RESULTS: Our data define a global methylation profile characteristic of ileal CD. In all, 1117 sites were differentially methylated (corrected P < 0.01); 50 showed significantly altered methylation in cases compared with controls (uncorrected P < 10(-6), corrected P < 0.0006), including genes altering immune activation: MAPK13, FASLG, PRF1, S100A13, RIPK3, and IL-21R. Gene ontology analyses implicated immunity-related pathways as targets of epigenetic modification (immune system processes [P = 1.3 x 10(-22)], immune response [P = 8.1 x 10(-16)], defense responses to bacteria [P = 1.8 x 10(-15)]). Ingenuity canonical pathway analyses implicated dendritic cell activity (P = 2.4 x 10(-8)) and differential regulation of cytokines by interleukin (IL)-17A and IL-17F (P = 5.8 x 10(-7)). We identified a significant enrichment of methylation changes within 50 kb of CD GWAS loci (8.6-fold [P = 0.021] in adults; 2.4-fold [P = 0.009] in adults and children combined), including IL-27, IL-19, TNF, MST1, and NOD2. Methylation status was predictive of disease status (sensitivity 0.71, specificity 0.83). Disease activity, drug therapy, NOD2 and DNMT3A genotypes were not associated with methylation changes. CONCLUSIONS: These data provide an important insight into the

BACKGROUND AND STUDY AIMS: The Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv score) was devised to measure mucosal disease activity using video capsule endoscopy (VCE). The aim of the current study was to prospectively validate the use of the scoring system in daily practice. METHODS: This was a multicenter, double-blind, prospective, controlled study of VCE videos from 62 consecutive patients with isolated small-bowel Crohn's disease. The CECDAI was designed to evaluate three main parameters of Crohn's disease: inflammation (A), extent of disease (B), and stricture (C), in both the proximal and distal segments of the small bowel. The final score was calculated by adding the two segmental scores: CECDAI = [HAIR SPACE][[A1][HAIR SPACE][B1] + [HAIR SPACE]C1] + [HAIR SPACE][[A2][HAIR SPACE][B2] + [HAIR SPACE]C2]. Each examiner in every site interpreted 6[HAIR SPACE]-[HAIR SPACE]10 videos and calculated the CECDAI. The de-identified CD-ROMs were then coded and sent to the principal investigator for CECDAI calculation. RESULTS: The cecum was reached in 72[HAIR SPACE]% and 86[HAIR SPACE]% of examinations, and proximal small-bowel involvement was found in 56[HAIR SPACE]% and 62[HAIR SPACE]% of the patients, according to the site investigators and principal investigator, respectively. Significant correlation was demonstrated between the calculation of the CECDAI by the individual site investigators and that performed by the principal investigator. Overall correlation between endoscopists from the different study centers was good, with r[HAIR SPACE] = [HAIR SPACE]0.767 (range 0.717[HAIR SPACE]-[HAIR SPACE]0.985; Kappa 0.66; P[HAIR SPACE] < [HAIR SPACE]0.001). There was no correlation between the CECDAI and the Crohn's Disease Activity Index or the Inflammatory Bowel Disease Quality of Life Questionnaire or any of their components. CONCLUSION: A new scoring system of mucosal injury in Crohn's disease of the small intestine, the CECDAI, was validated. Its use in controlled trials and/or regular follow-up of these patients is advocated. Copyright Georg Thieme Verlag KG Stuttgart . New York.


BACKGROUND: Iron isomaltoside 1000 is a novel injectable iron compound which offers potential advantages in the treatment of subjects with iron-deficiency anemia. We studied the pharmacokinetics (PK) of this novel compound in subjects with mild-to-moderate inflammatory bowel disease (IBD). METHODS: This open-label, crossover, single-center trial was conducted in 12 subjects with IBD who were allocated to one of the two single intravenous (IV) bolus sequences of iron isomaltoside 1000: 100 mg followed by 200 mg, or vice-versa. PK variables were analyzed according to a single-compartment model. RESULTS: The concentration-versus-time relationship for isomallopedia-bound iron (IBI) and total iron (TI) showed first-order kinetics with small deviations from dose-linearity. The area under the concentration-time curve (AUC) values in h * mug/mL for IBI following 100 mg and 200 mg doses were 888 and 2141 respectively, and for TI following 100 mg and 200 mg doses, the AUC values were 1010 and 2319 respectively. The corresponding maximum serum concentration (C(max)) values in mug/mL were 35.6 and 68.6 for IBI, and 37.3 and 71.1 for TI. The half-life (T(2-Jan)) values for IBI and TI were between 20.8-23.5 hours. The apparent volume of distribution (V(D)) ranged from 3.0-3.5 L. Only approximately 1% of the doses administered were excreted in the urine. No serious adverse event (SAE) was reported. One subject was withdrawn after the 100 mg dose due to abdominal pain and flushing. CONCLUSION: At the administered doses, iron isomaltoside 1000 showed first-order PK, and did not raise safety concerns in patients with IBD. The PK parameters for IBI were close to those of TI.


BACKGROUND: We report a multicenter study of oral tacrolimus (FK506) therapy in steroid-refractory ulcerative colitis (UC). METHODS: In a placebo-controlled, double-blind study, 62 patients with steroid-refractory, moderate-to-severe UC were randomized into either a tacrolimus group or a placebo for 2 weeks. Patients were evaluated using the Disease Activity Index (DAI). As an entry criterion, patients had to have a total DAI score of 6 or more as well as a mucosal appearance subscore of 2 or 3. Clinical response was defined as improvement in all DAI subscores. Mucosal healing was defined as mucosal appearance subscore of 0 or 1. Clinical remission was defined as a total DAI score <= 2 with an individual subscore of 0 or 1. RESULTS: The mean total DAI score at study entry was 9.8 +/- 1.61 in the tacrolimus group and 9.1 +/- 1.05 in the placebo group. At week 2 the clinical response rate was 50.0% (16/32) in the tacrolimus group and 13.3% (4/30) in the placebo group (P = 0.003). The rate of mucosal healing observed was 43.8% (14/32) in the tacrolimus group and 13.3% (4/30) in the placebo group (P = 0.012) and the rate of clinical remission observed was 9.4% (3/32) in the tacrolimus group and 0.0% (0/30) in the placebo group (P = 0.238). The therapies in this study were well
tolerated, with only minor side effects. CONCLUSIONS: Oral tacrolimus therapy in patients with steroid-refractory UC shortened the acute phase and induced rapid mucosal healing. These results suggest that tacrolimus therapy is useful as an alternative therapy for steroid-refractory UC. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Intestinal microbiota manipulation, one of the pathogenetic components of inflammatory bowel disease (IBD), has become an attractive therapy for ulcerative colitis (UC). AIM: To assess in children with active distal UC the effectiveness of Lactobacillus (L) reuteri ATCC 55730 enema on inflammation and cytokine expression of rectal mucosa. METHODS: A total of 40 patients (median age: 7.2 years range 6-18) with mild to moderate UC were enrolled in a prospective, randomised, placebo-controlled study. They received an enema solution containing 10(10) CFU of L. reuteri ATCC 55730 or placebo for 8 weeks, in addition to oral mesalazine. Clinical endoscopic and histological scores as well asrectal mucosal expression levels of IL-10, IL-1beta, TNFalpha and IL-8 were evaluated at the beginning and at the end of the trial. RESULTS: Thirty-one patients accomplished the trial (17 males, median age 13 year, range 7-18). Mayo score (including clinical and endoscopic features) decreased significantly in the L. reuteri group (3.2 +/- 1.3 vs. 8.6 +/- 0.8, P < 0.01) compared with placebo (7.1 +/- 1.1 vs. 8.7 +/- 0.7, NS); furthermore, histological score significantly decreased only in the L. reuteri group (0.6 +/- 0.5 vs. 4.5 +/- 0.6, P < 0.01) (placebo: 2.9 +/- 0.8 vs. 4.6 +/- 0.6, NS). At the post-trial evaluation of cytokine mucosal expression levels, IL-10 significantly increased (P < 0.01) whereas IL-1beta, TNFalpha and IL-8 significantly decreased (P < 0.01) only in the L. reuteri group. CONCLUSIONS: In children with active distal ulcerative colitis, rectal infusion of L. reuteri is effective in improving mucosal inflammation and changing mucosal expression levels of some cytokines involved in the mechanisms of inflammatory bowel disease. Copyright 2011 Blackwell Publishing Ltd.


BACKGROUND: Corticosteroids are effective in the treatment of Crohn's disease but some patients relapse during tapering or after discontinuation. We report data on efficacy and prognostic factors of response of adalimumab in steroid-dependent patients. METHODS: In all, 110 steroid-dependent patients were treated with adalimumab (80/40 or 160/80 mg every other week followed by 40 mg every other week). Clinical remission was defined as steroid discontinuation without symptomatic recurrence and clinical response as the reduction or maintenance of the initial Crohn's Disease Activity Index (CDAI) value reducing steroid dosage but without its discontinuation at week 6 and at the end of follow-up. RESULTS: At week 6, 91% of patients had a clinical benefit (remission: 45.5%, response: 45.5%). At the end of the follow-up (mean 14.6 months), 80.9% of responders maintained the clinical benefit (remission: 64.5%, response: 16.4%). At univariate analysis four variables were associated with remission at week 6: age of patients <40 years at baseline, no previous history of surgery, inflammatory pattern, and higher induction regimen. At multivariate analysis only higher induction regimen was related to remission at week 6. At the end of the follow-up, none of the variables were associated with remission. None of the variables were related to response at 6 weeks and at the end of follow-up. Adalimumab was well tolerated. CONCLUSIONS: This study shows that adalimumab is a powerful and safe weapon for steroid discontinuation in patients with steroid-dependent Crohn's disease. Higher induction regimen dosage is the better therapeutic choice for achieving clinical remission with low risk of clinical relapse. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.

Oustamanolakis, P. and I. E. Koutroubakis (2011). "Soluble transferrin receptor-ferritin index is the most efficient marker for the diagnosis of iron deficiency anemia in patients with IBD." Inflammatory Bowel Diseases 17(12): E158-159.


PURPOSES: The aim of this study was to evaluate the benefit of straight laparoscopic restorative proctocolectomy (sLRP) with ileal pouch anal anastomosis for ulcerative colitis (UC). METHODS: Twenty patients underwent sLRP or open restorative proctocolectomy. The 2 groups were retrospectively well matched with respect to sex, body mass index, and American Society of Anesthesiologists' score. RESULTS: The median operative time was longer in the sLRP group (P=0.0003). The median operative blood loss was significantly less in the sLRP group (P=0.0054). The median analgesic drug usage during the first 7 days after surgery was lower in the sLRP group (P=0.038). There were no differences in morbidity rates and long-term functional outcome measures between the groups. CONCLUSIONS: An sLRP for UC has the advantage over an open restorative
proctocolectomy of better short-term outcomes, and both groups have similar long-term outcomes. This procedure is acceptable for minimally invasive surgery in patients with UC.


Statement of Purpose, Innovation or Hypothesis: Disease metrics and biomarkers are used to define disease characteristics and evaluate therapeutic improvements. In Crohn's disease (CD), useful assessments in determining clinical manifestations of disease and treatment include Crohn's Disease Activity Index (CDAI), Clinical Response 100 (CR100), C-reactive protein concentrations (CRP) and immunogenicity to treatment. The purpose of this work was to develop kinetics of drug action (K-PD) models using meta analyses of published literature on CD and its therapies to describe the time courses of the assessments CDAI, CR100, CRP and immunogenicity. Description of Methods and Materials: Thirty-one studies of placebo and several different therapeutic agents were used to develop the meta models, using NONMEM Version 7 Level 1 with the Laplacian estimation method. Between study and between arm variability were accounted for in these models. Model evaluation was primarily graphical in nature via standard goodness of fit plots. Visual predictive checks were also conducted and demonstrated good predictive ability of the models. To understand dose response for these agents, the ranges of estimated responses for each treatment at representative doses were simulated. Box and whisker plots were generated for both induction and maintenance. Data and Results: Simulations showed good predictive ability compared to results found in the literature and validated each model for use with other treatments. Simulated CDAI responses for infliximab and adalimumab demonstrated a dose-dependent decrease, while a dose-dependent increase was seen in CR100 for both treatments. Infliximab- and adalimumab-induced dosedependent decreases were observed in simulated CRP responses. The simulated percent of subjects with human antihuman antibodies decreased with increasing dose of MLN0002 and certolizumab, as is seen in a number of biologic treatments at higher doses. Interpretation, Conclusion or Significance: The simulation results indicate that these models can be used to explore the results of other treatments and also provide an estimated range of responses that can be used as a comparator for other therapeutic agents in development for CD. Meta based models can be valuable for development of future treatments of CD and for exploration of combination treatments.


CONTEXT: Vitamin D insufficiency [serum 25-hydroxyvitamin D (25OHD) concentration less than 20 ng/ml] is prevalent among children with inflammatory bowel disease (IBD), and its treatment has not been studied. OBJECTIVE: The aim of this study was to compare the efficacy and safety of three vitamin D repletion regimens. DESIGN AND SETTING: We conducted a randomized, controlled clinical trial from November 2007 to June 2010 at the Clinical and Translational Study Unit of Children's Hospital Boston. The study was not blinded to participants and investigators. PATIENTS: Eligibility criteria included diagnosis of IBD, age 5-21, and serum 25OHD concentration below 20 ng/ml. Seventy-one patients enrolled, 61 completed the trial, and two withdrew due to adverse events. INTERVENTION: Patients received orally for 6 wk: vitamin D(2), 2,000 IU daily (arm A, control); vitamin D(3), 2,000 IU daily (arm B); vitamin D(2), 50,000 IU weekly (arm C); and an age-appropriate calcium supplement. MAIN OUTCOME MEASURE: We measured the change in serum 25OHD concentration ([Greek capital Delta]25OHD) (ng/ml). Secondary outcomes included change in serum intact PTH concentration ([Greek capital Delta]PTH) (pg/ml) and the adverse event occurrence rate. RESULTS: After 6 wk, [Greek capital Delta]25OHD +/- se was: 9.3 +/- 1.8 (arm A); 16.4 +/- 2.0 (arm B); 25.4 +/- 2.5 (arm C); P (A vs. C) = 0.0004; P (A vs. B) = 0.03. [Greek capital Delta]PTH +/- SE was -5.6 +/- 5.5 (arm A); -0.1 +/- 4.2 (arm B); -4.4 +/- 3.9 (arm C); P = 0.57. No participant experienced hypercalcemia or hyperphosphatemia, and the prevalence of hypercalciuria did not differ among arms at follow-up. CONCLUSIONS: Oral doses of 2,000 IU vitamin D(3) daily and 50,000 IU vitamin D(2) weekly for 6 wk are superior to 2,000 IU vitamin D(2) daily for 6 wk in raising serum 25OHD concentration and are well-tolerated among children and adolescents with IBD. The change in serum PTH concentration did not differ among arms.


Leukocytes are thought to play an important role in the pathogenesis of inflammatory bowel diseases; granulocyte-monocyte adsorptive (GMA) apheresis, an extracorporeal technique aimed at removing activated circulating leukocytes from the blood, may represent a safe and effective therapeutic tool in these patients. The Italian Registry of Therapeutic Apheresis performed an observational, multicentric study involving 24 Gastroenterology Units. In this study, laboratory data and clinical outcomes of 230 patients (148 males, mean age
43.5 years) affected with ulcerative colitis (UC, n = 194) or Crohn's disease (CD, n = 36) who underwent one or more cycles of GMA were analyzed. Each cycle consisted of five GMA treatments. The patients were followed up for a mean of 8.7 (min. 3 to max. 12) months. At 3 months, positive outcome was achieved in 77.7% of UC patients (72.0% remission, 5.7% clinical response) and 61.3% of CD patients (54.8% remission, 6.5% clinical response). The cumulative proportion of positive outcome at 12 months was 87.1% for UC patients (83.7% remission, 3.4% clinical response) and 77.4% for CD patients (74.2% remission, 3.2% clinical response). No single clinical or laboratory parameter among those analyzed (age, sex, disease characteristics, history of smoking, medication history, baseline values of clinical activity index (CAI)/Crohn's disease activity index (CDAI), hemoglobin, white blood cells count, and erythrocyte sedimentation rate) was independently associated with clinical outcome. The procedure was well tolerated with no significant adverse effects registered. Copyright © 2011 Wiley Periodicals, Inc.


**PURPOSE:** Evaluate the utility of multidetector-row computed tomography (MDCT) in assessing the severity of ulcerative colitis (UC) in comparison with clinical assessment, colonoscopy, and histopathology. MATERIALS AND METHODS: Patients with UC evaluated with at least one abdominal contrast-enhanced CT study (CECT) within 7 days of colonoscopy with biopsy were included. CECT of 23 patients (12 male; mean age 40 years; age range, 20-72 years) were retrospectively evaluated in consensus by two radiologists. A total of 138 lower GI tract segments were evaluated by CECT and graded for the presence of bowel wall thickening, mucosal hyperenhancement, mural stratification, mesenteric hyperemia, pericolonic stranding, and lymph nodes. A cumulative CT severity score was calculated and correlated with clinical, colonoscopic, and histopathologic severity grades. RESULTS: The cumulative CT score and individual CECT scores for bowel wall thickening, mucosal hyperenhancement, and mural stratification showed positive correlation with clinical severity (P < 0.05). All individual CECT features as well as the cumulative CT score demonstrated statistically significant correlation with colonoscopic severity (P < 0.0001). Only wall thickening on CECT demonstrated significant correlation with histopathologic severity (P = 0.01). CONCLUSION: Disease severity assessment by MDCT demonstrates positive correlation with severity established by clinical assessment and colonoscopy. Only increasing wall thickness, as graded on MDCT, correlates with histopathologic disease severity.


**BACKGROUND:** miR-143 and miR-145 are believed to function as colon cancer tumor suppressors, as they inhibit colon cancer cell growth and are downregulated in sporadic colonic tumors. We speculated that miR-143 and miR-145 might also be downregulated and contribute to malignant transformation of colonic epithelium in longstanding ulcerative colitis (UC). METHODS: Biopsies were obtained 20 cm proximal to the anus from individuals with quiescent UC and from normal controls. RNA and proteins were extracted and measured. miR-143 and miR-145 were quantified by real-time polymerase chain reaction (PCR) and miR-145 was also assessed by in situ hybridization. Putative targets of these miRNAs, K-RAS, API5, MEK-2 (miR-143), and IRS-1 (miR-145) were determined by western blotting. To assess the effects of miR-143 and miR-145 on these predicted targets, HCT116 and HCA-7 colorectal cancer cells were transfected with miR-143 and miR-145 and expression levels of these proteins were measured. RESULTS: In UC, miR-143 and miR-145 were significantly downregulated 8.3-fold (3.4-20.1) (P < 0.0001) and 4.3-fold (2.3-7.8) (P < 0.0001), respectively, compared to normal colon. In contrast, IRS-1, K-RAS, API5, and MEK-2 were upregulated in UC, consistent with their assignments as targets of these miRNAs. Furthermore, transfected miR-143 and miR-145 significantly downregulated these proteins in HCT116 or HCA-7 cells. CONCLUSIONS: Compared to normal colonic mucosa, in chronic UC miR-143 and miR-145 were significantly downregulated and their predicted targets, IRS-1, K-RAS, API5, and MEK-2 were upregulated. We postulate that loss of these tumor suppressor miRNAs predispose to chronic inflammation and neoplastic progression in IBD. Copyright © 2011 Crohn's & Colitis Foundation of America, Inc.


**BACKGROUND & AIMS:** Bacteria might be involved in the development and persistence of inflammation in patients with Crohn's disease (CD), and antibiotics could be used in therapy. We performed a clinical phase 2 trial to determine whether a gastroresistant formulation of rifaximin (extended intestinal release [EIR]) induced remission in patients with moderately active CD. METHODS: We performed a multicenter, randomized, double-blind trial of the efficacy and safety of 400, 800, and 1200 mg rifaximin-EIR, given twice daily to 402 patients with moderately active CD for 12 weeks. Data from patients given rifaximin-EIR were compared with those from individuals given placebo, and collected during a 12-week follow-up period. The primary end point was
At the end of the treatment period, 62% of patients who received the 800-mg dosage of rifaximin-EIR (61 of 98) were in remission, compared with 43% of patients who received placebo (43 of 101) \((P < .005)\). A difference was maintained throughout the 12-week follow-up period \((45\% \text{ [40 of 89] vs 29\% [28 of 98]; } P = .02)\). Remission was achieved by 54\% (56 of 104) and 47\% (47 of 99) of the patients given the 400-mg and 1200-mg dosages of rifaximin-EIR, respectively; these rates did not differ from those of placebo. Patients given the 400-mg and 800-mg dosages of rifaximin-EIR had low rates of withdrawal from the study because of adverse events; rates were significantly higher among patients given the 1200-mg dosage \((16\% \text{ [16 of 99]}\). CONCLUSIONS: Administration of 800 mg rifaximin-EIR twice daily for 12 weeks induced remission with few adverse events in patients with moderately active CD. Copyright © 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.


UNLABELLED: Inflammatory bowel disease (IBD) represents a heterogeneous group of chronic disorders characterized by inflammation of gastrointestinal tract, typically with a relapsing and remitting clinical course of unknown etiology. Presumably, IBD develops with response exogenous environmental factors only in persons with genetic predisposition. This predisposition was suggested to be associated with polymorphism and mutations in genes encoding proinflammatory immune system proteins. Enhanced production of macrophage migration inhibitory factor (MIF) was found in patients with inflammatory bowel disease (IBD) and mice with experimental colitis. These results suggest that MIF plays a critical role in etiology of the colitis. The aim of the study was to determine whether the MIF -173 G/C gene polymorphism is associated with the susceptibility to inflammatory bowel disease (IBD).

MATERIAL AND METHODS: A total of 99 IBD patients, including 58 patients with ulcerative colitis (UC) and 41 patients with Crohn's disease (CD) and 436 healthy controls recruited from the Polish population, were genotyped for MIF polymorphisms. Genotyping of MIF gene polymorphism was performed by a RFLP-PCR. RESULTS: We found an increased risk of UC for the C allele of the MIF-173 G/C polymorphism. The distribution of the genotypes was not significantly different in the CD group compared with the controls. CONCLUSIONS: We demonstrated that the C allele is associated with an increased risk for development of UC. This suggests that the G/C polymorphism in the MIF gene promoter may be a potential risk factor for UC in Polish population.


BACKGROUND: Patients with Crohn's disease are often investigated using MRI enteroclysis which may provide better visual quality than MRI enterography, but exposes patients to radiation. Only few data exist of the radiation dose used in fluoroscopy prior to MRI enteroclysis. SUBJECTS AND METHODS: During the 12-month study period, all 95 patients (40 men) undergoing MRI enteroclysis with nasojejunal intubation using fluoroscopy for suspicion or evaluation of Crohn's disease were included. Average age at the time of MRI was 40.1 years (range 17-79). Conversion factors from dose-area product to effective dose were determined with a Monte Carlo-based software PCXMC. The conversion factors were determined for a standard-sized adult phantom for posterior-anterior and right-posterior-oblique projections. RESULTS: The average total time of fluoroscopy was 3 min 17 s (range 0 min 7 s to 31 min). The average effective dose of ionizing radiation was 0.21 mSv (range 0.01-2.67). The average dose is equivalent to 10 PA chest x-rays. Standard deviation was 0.41 mSv. The highest effective dose of a single patient was 2.67 mSv. In comparison, a standard abdominal CT scan causes an effective dose of 12 mSv. CONCLUSIONS: The effective dose of ionizing radiation with nasojejunal intubation is relatively small in the majority of patients. When repeated imaging is necessary, it seems advisable to consider imaging techniques, which do not subject patients to ionizing radiation. Also if a previous nasojejunal intubation has been difficult, a different imaging technique is recommended.


Background: The rate of wound infection after appendectomy without antibiotic prophylaxis is 10%-30%. The role of prophylactic antibiotic therapy in nonperforated appendicitis is still controversial. Metronidazole is against anaerobic organisms and its bioavailability after oral and parenteral administration has been shown to be similar. The objective of the present study is to compare the infective complications rate after open appendectomy for nonperforated appendicitis receiving either oral or intravenous metronidazole as prophylaxis. Methods and Materials: From June 2007 to July 2009 in a randomized controlled trial, 204 patients with nonperforated appendicitis underwent an open appendectomy; 122 male and 82 female with mean age of 25 years. Among these, 102 (case group) received oral metronidazole and in 102 (control group) metronidazole was administered intravenously before surgery. The rate of wound infection and duration of the postoperative hospital stay was
studied in the two groups. Results: The rate of wound infection was not significantly different in the two groups. (6% and 4% in study and control group, respectively, P = 0.861). Also the hospital stay was equal in two groups (2.3 days and 2.7 days in study and control group, respectively, P = 0.293). Conclusion: Single dose of oral metronidazole prior to operation can provide a sufficient prophylaxis for nonperforated appendicitis; so, it can be substitute the parental route of antibiotic administration. 2011 Ravari et al, publisher and licensee Dove Medical Press Ltd.


The current study examined factors associated with adolescent and parent participation in a coping skills intervention for adolescent girls with inflammatory bowel disease (IBD) and examined factors associated with attrition related to intermittent missing data. Thirty-one adolescent girls with IBD and their parents enrolled in the intervention. Psychosocial and disease factors related to participation in the 6-week web component of the coping skills intervention were examined as were baseline group differences between those who provided post-treatment data and those who did not. Adolescents experiencing more difficulties related to their disease and psychosocial functioning participated less in the web component of the treatment intervention. Families who attrited had higher baseline levels of parental catastrophic thoughts, parenting stress, and adolescent depression. Families experiencing greater levels of psychological and disease-related difficulties may be at risk for low participation and eventual dropout from pediatric IBD psychological treatment interventions.


Background Infliximab is effective treatment for Crohn's disease and has been associated with rare, but serious infectious complications. Emerging data suggest a benefit of infliximab in preventing postoperative Crohn's disease recurrence. It is not known whether administration of infliximab shortly after resective surgery for Crohn's disease increases postoperative complications. Aims To evaluate the risk of developing postoperative complications among Crohn's disease patients receiving infliximab within 4 weeks of intestinal resection. Methods As part of a randomized placebo-controlled infliximab postoperative prevention study, adverse events were prospectively monitored. Crohn's disease patients undergoing intestinal resection were randomized to placebo or infliximab 2-4 weeks after surgery. Study infusions were administered at 0, 2, and 6 weeks then every 8 weeks for 1 year. To evaluate whether infliximab increased postoperative complications, we analyzed all adverse events for 1 year after surgery. Results Twenty-four patients were randomized to infliximab or placebo after intestinal resection for Crohn's disease. Mean time to first postoperative infusion was 20 days (range 14-25 days). Over the course of 1 year, there were 22 total adverse events, but no difference between infliximab and placebo patients (12 versus 10, respectively, P = 1.0). In the immediate postoperative period, within 8 weeks of surgery, the number of adverse events was also similar between the two groups (3 infliximab and 5 placebo patients, P = 0.68). There were no serious adverse events and no complications related to wound healing or infection. Conclusions Initiation of infliximab within 4 weeks of intestinal resection was not associated with postoperative complications. Springer Science+Business Media, LLC 2011.


BACKGROUND: The aim was to evaluate long-term efficacy, quality of life, and safety in ulcerative colitis patients who received infliximab during the ACT-1 and -2 extension studies. METHODS: Adults with moderate-to-severely active ulcerative colitis in the 54-week ACT-1 and 30-week ACT-2 studies who achieved benefit from infliximab were eligible to participate in extension studies and receive up to 3 additional years of therapy. Patients received randomized study medication until all sites were unblinded; placebo-treated patients were discontinued. Patients receiving 5 or 10 mg/kg infliximab continued to receive open-label infliximab every 8 weeks. Patients receiving infliximab 10 mg/kg could decrease to 5 mg/kg; patients receiving infliximab 5 mg/kg could increase to 10 mg/kg if response was lost. RESULTS: A total of 229 of 484 infliximab-treated patients from the ACT-1 and ACT-2 main studies entered the long-term extensions. Overall, 70 (30.6%) patients discontinued infliximab infusions for adverse events (24 [10.5%], lack of efficacy (11 [4.8%]), required a colectomy (1 [0.4%]), or for other reasons (34 [14.8%]). Proportions of patients whose Physician's Global Assessment scores were indicative of no or mild disease (score = 0 or 1) were maintained during the extension studies; 76.5% at Extension week 0 and ranged between 90.0% and 94.3% through Extension week 152. Improvement in Inflammatory Bowel Disease Questionnaire scores observed in the main studies was maintained. During the long-term extension, the infliximab safety profile was consistent with that of the main studies; no new or unexpected safety signals were observed. CONCLUSIONS: Long-term treatment with infliximab for up to 3 additional years was effective and well tolerated. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.

Background Secondary loss of response to anti-TNF-alpha therapy is observed in Crohn's disease patients. Aim Serum C-reactive protein (CRP) levels at baseline and after infliximab induction therapy at week 14 were assessed as predictors for maintained response or remission through 54 weeks of treatment in patients with Crohn's disease who responded to induction therapy. Methods ACCENT I was a multicenter, randomised, placebo-controlled study. Patients who received infliximab induction (weeks 0, 2 and 6) and maintenance (5 or 10 mg/kg every 8 weeks beginning at week 14) therapy were considered. Patients in clinical response or remission to induction therapy at week 14 (n = 212 or n = 138 respectively) were analysed. Associations between CRP levels (cut-off points 0.5-3.0 mg/dL), baseline disease variables and maintained clinical response or remission during maintenance therapy were assessed. Results A significant association was observed between baseline CRP levels and maintained remission. Forty-five percent of patients with baseline CRP >= 0.7 mg/dL vs. 22.0% with CRP < 0.7 mg/dL maintained remission (P = 0.012). CRP normalisation during infliximab treatment (decrease from 0.5 mg/dL at baseline to < 0.5 mg/dL at week 14) resulted in higher probability of maintained response (P < 0.001) or remission (P = 0.052). At week 14 low CRP levels were associated with maintained response (56.6% of patients with CRP < 0.5 mg/dL vs. 37.2% with higher CRP, P = 0.005). No optimal predictive CRP cut-off point was observed. Conclusions High baseline CRP levels increased the likelihood of maintained remission. Normalised CRP levels at week 14 increased the likelihood of maintained response or remission during 1 year of infliximab maintenance therapy (Clinical trial: NCT00207662). 2012 Blackwell Publishing Ltd.


Despite being a mainstay of inflammatory bowel disease (IBD) therapy, glucocorticoids (GCs) still carry significant risks with respect to unwanted side effects. Alternative drugs with a more favorable risk/benefit ratio than common GCs are thus highly desirable for the management of IBD. New and supposedly selective glucocorticoid receptor (GR) agonists (SEGRAs), with dissociated properties, have been described as promising candidates for circumventing therapeutic problems while still displaying full beneficial anti-inflammatory potency. Here, we report on compound A [CpdA; (2-(4-acetophenyl)-2-chloro-N-methyl)ethylammonium-chloride] and N-4-methyl-1-oxo-1H-2,3-benzoxazine-6-yl)-4-(2,3-dihydrobenzofuran-7-yl)-2-hydroxy-2- (trifluoromethyl)-4-methylpentanamide (ZK216348), two GR agonists for the treatment of experimental colitis. Their therapeutic and anti-inflammatory effects were tested in the acute trinitrobenzene sulfonic acid-mediated colitis model in mice against dexamethasone (Dex). In addition to their influence on immunological pathways, a set of possible side effects, including impact on glucose homeostasis, steroid resistance, and induction of apoptosis, was surveyed. Our results showed that, comparable with Dex, treatment with CpdA and ZK216348 reduced the severity of wasting disease, macroscopic and microscopic damage, and colonic inflammation. However, both SEGRAs exhibited no GC-associated diabetogenic effects, hypothalamic pituitary adrenal axis suppression, or development of glucocorticoid resistance. In addition, CpdA and ZK216348 showed fewer transactivating properties and successfully dampened T helper 1 immune response. Unlike ZK216348, the therapeutic benefit of CpdA was lost at higher doses because of toxic apoptotic effects. In conclusion, both SEGRAs acted as potent anti-inflammatory agents with a significantly improved profile compared with classic GCs. Although CpdA revealed a narrow therapeutic window, both GR agonists might be seen as a starting point for a future IBD treatment option.


BACKGROUND AND AIMS: Patients with Crohn's disease (CD) may need anti-inflammatory drugs for decades. Anti-TNF-alpha agents have good efficacy and adverse events similar to placebo in randomized controlled trials (RCTs), but there are still questions about long-term safety and efficacy. In this respect, reports from clinical practice may be useful. We currently report on the clinical experience with infliximab and adalimumab in a single-center cohort of patients with CD. MATERIAL AND METHODS: Patients with CD treated with infliximab or adalimumab from 2000 to 2010 were reviewed. Patient and disease characteristics at start, reason for discontinuation, and adverse events were recorded retrospectively. Corticosteroid use, the need for hospitalization, and surgeries before and during anti-TNF-alpha therapy were recorded. RESULTS: Eighty-three patients had received anti-TNF-alpha treatment against CD, median treatment duration was 11.4 months (0.2-99.5), and follow-up time 59 months (8-135). Eighteen of 43 patients using corticosteroids at treatment start discontinued corticosteroids during TNF-alpha therapy. Need for hospitalizations (6.13 vs. 3.28 days/year, p < 0.001) and surgeries (0.56 vs. 0.16 operations/year, p < 0.001) were lower during anti-TNF-alpha therapy than
before treatment. Twenty-six percent discontinued therapy due to adverse events and 26% due to lack of response. Two of four deaths observed during follow-up were believed to be related to anti-TNF-alpha treatment. CONCLUSIONS: Anti-TNF-alpha therapy was beneficial in many patients with CD, but the majority of patients discontinued treatment during follow-up. Reports from clinical experience with anti-TNF-alpha treatment may be valuable for clinicians treating patients with CD.


BACKGROUND: Crohn's disease is an inflammatory condition of the gut, thought to involve an overactive immune response to gut flora. A novel theory postulates possible immunodeficiency as a cause, and aims to use sargramostim (granulocyte macrophage colony stimulating factor, GM-CSF) to boost the immune system in an effort to test this hypothesis. OBJECTIVES: The primary objectives were to determine the efficacy and safety of sargramostim for induction of remission in patients with clinically active Crohn's disease. SEARCH METHODS: A systematic search of MEDLINE, EMBASE, and CENTRAL was conducted from inception to April 2011. Reference lists of relevant review articles were also searched. Trial registries and abstract databases including Digestive Diseases Week (1980-2010) and United European Gastroenterology Week (2005-2009) were searched to identify studies published in abstract form. SELECTION CRITERIA: Randomized controlled trials of sargramostim for the treatment of patients with active Crohn's disease were considered for inclusion. DATA COLLECTION AND ANALYSIS: Data from selected articles were extracted and the Cochrane Risk of Bias tool applied independently by two authors. The primary outcome was induction of clinical remission as defined by a Crohn's Disease Activity Index (CDAI) of < 150 at the end of treatment. Secondary outcomes included clinical responses measures on the CDAI and safety outcomes. Pooled risk ratios (RR) and 95% confidence intervals (CI) were calculated for dichotomous outcomes, in most cases using a random effects model due to high heterogeneity. MAIN RESULTS: Three studies were identified, 2 published as full papers and one in abstract form (537 patients). The risk of bias was low for the 3 included studies. There was no statistically significant difference in the proportion of patients (GM-CSF 25.3% versus placebo 17.5%) who achieved clinical remission (RR 1.67; 95% CI 0.80 to 3.50; P = 0.17; 3 studies; 537 patients). There was no statistically significant difference in the proportion of patients (GM-CSF 38.3% versus placebo 24.8%) who achieved a 100-point clinical response (RR 1.71 95% CI 0.98 to 2.97; P = 0.06; 3 studies; 537 patients). There was no statistically significant difference in the proportion of patients (GM-CSF 54.3% versus placebo 44.2%) who achieved a 70 point clinical response (RR 1.23; 95% CI 0.83 to 1.82; P = 0.30; 1 study; 124 patients). There was no statistically significant difference in the proportion of patients (GM-CSF 95.8% versus placebo 89.3%) who experienced at least one adverse event (RR 1.07; 95% CI 0.99 to 1.16; P = 0.08; 2 studies; 251 patients), or serious adverse events (GM-CSF 12.0% versus placebo 4.8%; RR 2.21; 95% CI 0.84 to 5.81; P = 0.11; 2 studies; 251 patients). The incidence of bone pain, musculoskeletal chest pain, and dyspnea were higher in patients treated with sargramostim compared to placebo. Other adverse events commonly associated with sargramostim such as pulmonary capillary leak syndrome, pulmonary edema, heart failure, fever, and neurotoxicity were not reported in these studies. AUTHORS' CONCLUSIONS: Sargramostim does not appear to be more effective than placebo for induction of clinical remission or clinical improvement in patients with active Crohn's disease. However, the GRADE analysis indicates that the overall quality of the evidence for the primary (clinical remission) and secondary outcomes (clinical response) was low indicating that further research is likely to have an impact on the effect estimates.


BACKGROUND: Nutritional deficiencies and anemia are common in Crohn's disease (CD). METHODS: We evaluated the effect of adalimumab on changes in laboratory values using data from CHARM, in which patients were randomized to adalimumab 40 mg every other week (eow), adalimumab 40 mg weekly, or placebo for 56 weeks. Mean changes in laboratory values from baseline to Weeks 26 and 56 were compared between adalimumab and placebo using analysis of covariance models. Percentages of patients with suboptimal laboratory values at Weeks 26 and 56 were compared between treatment groups using Cochran-Mantel-Haenszel (CMH) tests. Pearson correlation coefficients for associations between changes in Crohn's Disease Activity Index (CDAI) score and changes in laboratory values were estimated at Weeks 4, 26, and 56. RESULTS: The intention-to-treat analysis included 778 patients randomized to adalimumab eow (N = 260), adalimumab weekly (N = 257), or placebo (N = 251). Baseline abnormalities in laboratory values were common across treatment groups. CMH tests revealed significantly lesser rates of suboptimal laboratory values with adalimumab vs. placebo at Week 26, including hypoalbuminemia, calcium deficiency, low hemoglobin, low hematocrit, low red blood cell count, elevated platelet count, and elevated C-reactive protein concentration (all P < 0.05). These improvements persisted at Week 56. Improvements in CDAI from baseline to Weeks 4, 26, and 56 were significantly correlated with changes from baseline for albumin, hemoglobin, and C-reactive protein (all P < 0.001). CONCLUSIONS: Adalimumab therapy for moderately to severely active CD was associated with significant improvements in

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**BACKGROUND & AIMS:** We investigated the efficacy of adalimumab for inducing and maintaining mucosal healing in patients with Crohn's disease (CD). METHODS: A randomized, double-blind, placebo-controlled trial (extend the safety and efficacy of adalimumab through endoscopic healing [EXTEND]) evaluated adalimumab for induction and maintenance of mucosal healing in 135 adults with moderate to severe ileocolonic CD. The baseline degree of mucosal ulceration was documented by ileocolonoscopy. All patients received induction therapy (subcutaneous adalimumab 160/80 mg at weeks 0/2). At week 4, patients were randomly assigned to groups given 40 mg adalimumab or placebo every other week through week 52. Open-label adalimumab was given to patients with flares or no response, starting at week 8. Mucosal healing was reassessed by ileocolonoscopy at weeks 12 and 52. RESULTS: Twenty-seven percent of patients receiving adalimumab had mucosal healing at week 12 (the primary end point) versus 13% given placebo (P = .056). At week 52, rates of mucosal healing were 24% and 0, respectively (P < .001). Remission rates, based on the Crohn's Disease Endoscopic Index of Severity, were 52% for adalimumab and 28% for placebo at week 12 (P = .006) and 28% and 3%, respectively, at week 52 (P < .001). Rates of clinical remission based on the Crohn's Disease Activity Index were greater among patients given continuous adalimumab therapy versus placebo at weeks 12 (47% vs 28%; P = .021) and 52 (33% vs 9%; P = .001). Five serious (1 during induction and 4 during open-label therapy) and 3 opportunistic infections (1 in each group during double-blind therapy and 1 during open-label therapy) were reported (n = 135). CONCLUSIONS: Following induction therapy with adalimumab, patients with moderately to severely active CD who continue to receive adalimumab are more likely to achieve mucosal healing than those given placebo. Copyright Copyright 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.


**BACKGROUND AND AIMS:** Epstein-Barr virus (EBV) is present in the malignant epithelial cells of 10% of all gastric adenocarcinomas; however, localization of the virus in normal gastrointestinal mucosa is largely unexplored. In the present study, we measured EBV DNA and localized viral gene products in gastritis specimens (n = 89), normal gastric and colonic mucosa (n = 14), Crohn's disease (n = 9), and ulcerative colitis (n = 11) tissues. METHODS: A battery of sensitive and specific quantitative polymerase chain reactions targeted six disparate regions of the EBV genome: BamH1 W, EBNA1, LMP1, LMP2, BZLF1, and EBER1. EBV infection was localized by EBV-encoded RNA (EBER) in situ hybridization and by immunohistochemical stains for viral latent proteins LMP1 and LMP2 and for viral lytic proteins BMRF1 and BZLF1. B lymphocytes were identified using CD20 immunostains. RESULTS: EBV DNA was essentially undetectable in normal gastric mucosa but was present in 46% of gastritis lesions, 44% of normal colonic mucosa, 55% of Crohn's disease, and 64% of ulcerative colitis samples. Levels of EBV DNA exceeded what would be expected based on the numbers of B lymphocytes in inflamed tissues, suggesting that EBV is preferentially localized to inflammatory gastrointestinal lesions. Histochemical staining revealed EBER expression in lymphoid cells of some PCR-positive lesions. The viral lytic viral proteins, BMRF1 and BZLF1, were expressed in lymphoid cells of two ulcerative colitis tissues, both of which had relatively high viral loads by quantitative PCR. CONCLUSION: EBV-infected lymphocytes are frequently present in inflamed gastric and colonic mucosa. Active viral replication in some lesions raises the possibility of virus-related perpetuation of gastrointestinal inflammation.


**BACKGROUND:** Methotrexate is considered a treatment for Crohn's disease, whilst few data in ulcerative colitis are available. AIM: To evaluate frequency, indications, efficacy and safety of methotrexate in inflammatory bowel disease patients. METHODS: 5420 case histories were reviewed. RESULTS: Methotrexate was prescribed for induction and maintenance of mucosal healing in 135 adults with moderate to severe ileocolonic CD. The baseline degree of mucosal ulceration was documented by ileocolonoscopy. All patients received induction therapy (subcutaneous adalimumab 160/80 mg at weeks 0/2). At week 4, patients were randomly assigned to groups given 40 mg adalimumab or placebo every other week through week 52. Open-label adalimumab was given to patients with flares or no response, starting at week 8. Mucosal healing was reassessed by ileocolonoscopy at weeks 12 and 52. RESULTS: Twenty-seven percent of patients receiving adalimumab had mucosal healing at week 12 (the primary end point) versus 13% given placebo (P = .056). At week 52, rates of mucosal healing were 24% and 0, respectively (P < .001). Remission rates, based on the Crohn's Disease Endoscopic Index of Severity, were 52% for adalimumab and 28% for placebo at week 12 (P = .006) and 28% and 3%, respectively, at week 52 (P < .001). Rates of clinical remission based on the Crohn's Disease Activity Index were greater among patients given continuous adalimumab therapy versus placebo at weeks 12 (47% vs 28%; P = .021) and 52 (33% vs 9%; P = .001). Five serious (1 during induction and 4 during open-label therapy) and 3 opportunistic infections (1 in each group during double-blind therapy and 1 during open-label therapy) were reported (n = 135). CONCLUSIONS: Following induction therapy with adalimumab, patients with moderately to severely active CD who continue to receive adalimumab are more likely to achieve mucosal healing than those given placebo. Copyright Copyright 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.
methotrexate could be more widely administered to inflammatory bowel disease patients with complicated disease. Copyright Copyright 2011 Editrice Gastroenterologica Italiana S.r.l. Published by Elsevier Ltd. All rights reserved.


Inflammatory bowel disease (IBD) is fundamentally a relapsing and remitting disease appearing in forms of ulcerative colitis (UC) or Crohn's disease (CD) with a non-well-known etiology. With the hope to prevent adverse drug events and to increase the efficacy of therapies for IBD, in the recent years, other than new monoclonal antibodies such as infliximab, the novel phosphodiesterase inhibitors (PDEIs) have been introduced. Among PDE4Is, rolipram, OPC-6535, mesopram, roflumilast and tetomilast have shown beneficial effects in experimental colitis. Unfortunately until now, human studies have not been successful in showing significant superiority of PDE4Is in the treatment of IBD. Parallel with discovery of PDE4Is and their anti-inflammatory properties, inhibiting other PDE isoenzymes in immune and proinflammatory cells is on the way. PDE7Is have shown synergistic effect with PDE4Is and they may act similar to PDE3Is in experimental settings. Sildenafil as the PDE5I has shown good effects in experimental colitis by balancing oxidantantioxidant status. Although the present data about PDE superfamily and their specific roles in gastrointestinal tract is limited but inhibitors of PDE4, PDE5 and PDE7 seem good candidates as the next generation of effective drugs. The synergistic anti-inflammatory effect of PDE4Is and PDE7Is is also important. 2012 Informa UK, Ltd.


BACKGROUND: Ulcerative colitis is a chronic inflammatory disease of the colon for which current treatments are not universally effective. One additional treatment may be tofacitinib (CP-690,550), an oral inhibitor of Janus kinases 1, 2, and 3 with in vitro functional specificity for kinases 1 and 3 over kinase 2, which is expected to block signaling involving gamma chain-containing cytokines including interleukins 2, 4, 7, 9, 15, and 21. These cytokines are integral to lymphocyte activation, function, and proliferation. METHODS: In a double-blind, placebo-controlled, phase 2 trial, we evaluated the efficacy of tofacitinib in 194 adults with moderately to severely active ulcerative colitis. Patients were randomly assigned to receive tofacitinib at a dose of 0.5 mg, 3 mg, 10 mg, or 15 mg or placebo twice daily for 8 weeks. The primary outcome was a clinical response at 8 weeks, defined as an absolute decrease from baseline in the score on the Mayo scoring system for assessment of ulcerative colitis activity (possible score, 0 to 12, with higher scores indicating more severe disease) of 3 or more and a relative decrease from baseline of 30% or more with an accompanying decrease in the rectal bleeding subscore of 1 point or more or an absolute rectal bleeding subscore of 0 or 1. RESULTS: The primary outcome, clinical response at 8 weeks, occurred in 32%, 48%, 61%, and 78% of patients receiving tofacitinib at a dose of 0.5 mg (P=0.39), 3 mg (P=0.55), 10 mg (P=0.10), and 15 mg (P<0.001), respectively, as compared with 42% of patients receiving placebo. Clinical remission (defined as a Mayo score <=2, with no subscore >1) at 8 weeks occurred in 13%, 33%, 48%, and 41% of patients receiving tofacitinib at a dose of 0.5 mg (P=0.76), 3 mg (P=0.01), 10 mg (P<0.001), and 15 mg (P<0.001), respectively, as compared with 10% of patients receiving placebo. There was a dose-dependent increase in both low-density and high-density lipoprotein cholesterol. Three patients treated with tofacitinib had an absolute neutrophil count of less than 1500. CONCLUSIONS: Patients with moderately to severely active ulcerative colitis treated with tofacitinib were more likely to have clinical response and remission than those receiving placebo. (Funded by Pfizer; ClinicalTrials.gov number, NCT00787202.).


Background & Aims: Adalimumab is a fully human monoclonal antibody that binds tumor necrosis factor (TNF)-alpha. Its efficacy as maintenance therapy for patients with ulcerative colitis has not been studied in a controlled, double-blind trial. Methods: Ulcerative colitis long-term remission and maintenance with adalimumab 2 (ULTRA 2) was a randomized, double-blind, placebo-controlled trial to evaluate the efficacy of adalimumab in induction and maintenance of clinical remission in 494 patients with moderate-to-severe ulcerative colitis who received concurrent treatment with oral corticosteroids or immunosuppressants. Patients were stratified based on prior exposure to TNF-alpha antagonists (either had or had not been previously treated with antiTNF-alpha) and randomly assigned to groups given adalimumab 160 mg at week 0, 80 mg at week 2, and then 40 mg every other week or placebo. Primary end points were remission at weeks 8 and 52. Results: Overall rates of clinical remission at week 8 were 16.5% on adalimumab and 9.3% on placebo (P =.019); corresponding values for week 52 were 17.3% and 8.5% (P =.004). Among antiTNF-alpha nave patients, rates of remission at week 8 were 21.3% on adalimumab and 11% on placebo (P =.017); corresponding values for week 52 were 22% and 12.4% (P =.029). Among patients who had previously received anti-TNF agents, rates of remission at week 8 were 9.2% on
adulimumab and 6.9% on placebo (P = .559); corresponding values for week 52 were 10.2% and 3% (P = .039). Serious adverse events occurred in 12% of patients given adalimumab or placebo. Serious infections developed in 1.6% of patients given adalimumab and 1.9% given placebo. In the group given adalimumab, 1 patient developed squamous cell carcinoma and 1 developed gastric cancer. Conclusions: Adalimumab was safe and more effective than placebo in inducing and maintaining clinical remission in patients with moderate-to-severe ulcerative colitis who did not have an adequate response to conventional therapy with steroids or immunosuppressants. 2012 AGA Institute.


BACKGROUND: The single nucleotide polymorphism (SNP) rs2542151 within the gene locus encoding protein tyrosine phosphatase non-receptor type 2 (PTPN2) has been associated with Crohn's disease (CD), ulcerative colitis (UC), type-1 diabetes, and rheumatoid arthritis. We have previously shown that PTPN2 regulates mitogen-activated protein kinase (MAPK) signaling and cytokine secretion in human THP-1 monocytes and intestinal epithelial cells (IEC). Here, we studied whether intronic PTPN2 SNP rs1893217 regulates immune responses to the nucleotide-oligomerization domain 2 (NOD2) ligand, muramyl-dipeptide (MDP). MATERIALS AND METHODS: Genomic DNA samples from 343 CD and 663 non-IBD control patients (male and female) from a combined German, Swiss, and Polish cohort were genotyped for the presence of the PTPN2 SNPs, rs2542151, and rs1893217. PTPN2-variant rs1893217 was introduced into T(84) IEC or THP-1 cells using a lentiviral vector. RESULTS: We identified a novel association between the genetic variant, rs1893217, located in intron 7 of the PTPN2 gene and CD. Human THP-1 monocytes carrying this variant revealed increased MAPK activation as well as elevated mRNA expression of T-bet transcription factor and secretion of interferon-gamma in response to the bacterial wall component, MDP. In contrast, secretion of interleukin-8 and tumor necrosis factor were reduced. In both, T(84) IEC and THP-1 monocytes, autophagosome formation was impaired. CONCLUSIONS: We identified a novel CD-associated PTPN2 variant that modulates innate immune responses to bacterial antigens. These findings not only provide key insights into the effects of a functional mutation on a clinically relevant gene, but also reveal how such a mutation could contribute to the onset of disease. Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


Background: The aetiology of Necrotising enterocolitis (NEC) is unknown and the pathogenesis of NEC appears to be multifactorial. Various different antibiotic regimens have been widely used in the treatment of NEC. This review was undertaken to clarify this issue. Objectives: To compare the efficacy of different antibiotic regimens on mortality and the need for surgery in the empirical treatment of neonates with NEC. Selection criteria: All randomised and quasi randomised controlled trials where antibiotic regimen were used for treatment of NEC. Data collection and analysis: Eligibility of studies for inclusion was assessed independently by each review author. The criteria and standard methods of the Cochrane Neonatal Review Group was used to assess the methodological quality of included trials. Results: Two eligible trial were included. Faix et al randomised 42 premature infants (mean gestation 29 weeks) with NEC to receive parenteral ampicillin, gentamicin +/- clindamycin. Hansen et al. randomised 20 infants (gestation range 28-40 weeks) with NEC to receive parenteral ampicillin, gentamicin +/- enteral gentamicin. There was no statistically significant difference in bowel perforation, death or development of strictures. One of the studies reported a significant increase in risk of stricture in infants randomised to receive clindamycin (odds ratio 11.3, 95% CI 1.18, 109.26). Conclusions: There was insufficient evidence to recommend a particular antibiotic regimen for the treatment of NEC. There were concerns about adverse effects following the usage of clindamycin, related to the development of strictures. To address this issue a large randomised controlled trial needs to be performed.


BACKGROUND: While ulcerative colitis (UC) is a risk factor for colorectal cancer, the association of UC with survival after colorectal cancer has not been studied in an older population. AIMS: The objective of our study was to compare the survival of colorectal cancer between persons with and without UC. METHODS: All cases of colorectal cancer (CRC) in persons 67 and older residing in a SEER catchment area and enrolled in the Medicare between 1993 and 1999 were assessed. We identified diagnosis of UC using ICD-9 codes on Medicare outpatient, office, and inpatient claims in the 2 years prior to the date of diagnosis. We used Cox proportional hazards model and Kaplan-Meier curves to compare survival between individuals with UC and CRC (UC-CRC) and sporadic CRC RESULTS: We identified 47,543 cases of colorectal cancer. Cases with UC-CRC tend to be diagnosed at earlier stages compared to sporadic CRC (42 vs. 37% local (TNM stage 1 and 2) and 11 vs. 17% distant spread (TNM stage 4), respectively; P value = 0.04). Controlling for age, gender, race and stage, diagnosis of UC did not
affect the 3-year survival for CRC. CONCLUSIONS: Colorectal cancers tend to be diagnosed at earlier stages among persons with UC, but there is no difference in 3-year survival rates for colorectal cancer among individuals with and without UC.


OBJECTIVES: An association between celiac disease (CD) and peripheral neuropathy (PN) has been reported. METHODS: Patients with CD and/or inflammatory bowel disease (IBD) were recruited from the gastroenterology clinics at a medical center and local support groups. Control subjects without CD or IBD were recruited from the staff of the medical center as well as relatives and attendees at support groups. Each participant completed a survey that used two validated PN instruments to define and characterize PN. RESULTS: In the CD group, 38.9% met criteria for PN compared with 38.7% in the IBD group (P = 0.97) and 20.5% in the control group (P < 0.001). On multiple logistic regression, the odds of PN after adjusting for age, gender, diabetes, vitamin B12 deficiency, and cancer history were increased for CD (odds ratio, 2.51; 95% confidence interval, 1.82-3.47) and IBD (odds ratio, 2.78; 95% confidence interval, 1.85-4.18). CONCLUSIONS: PN is more often found in patients with CD and/or IBD than in the general population.


BACKGROUND: The incidence of ulcerative colitis (UC) varies between Western and Eastern ethnicities. A distinct genetic background may play a role in the differences. Until now, very little was known of the UC genetics in Asian populations. Here we performed a haplotype-based analysis of six known UC susceptibility loci in Han Chinese patients. METHODS: In all, 245 UC patients and 300 healthy controls of Han Chinese descent were genotyped for 27 single nucleotide polymorphisms (SNPs), which cover the major haplotypes of the chromosome regions containing IL10, IL2/IL21, MYO9B, ECM1, MST1, and IL23R in Han Chinese. RESULTS: In contrast to the tight linkage disequilibrium (LD) block of the IL2/IL21 region in Caucasians, IL2 and IL21 reside in two independent LD blocks in Han Chinese. The IL2 SNP rs2069762 (P = 7.0 x 10(-4), odds ratio [OR] = 1.54, 95% confidence interval [CI] 1.20-1.99) and the IL21 SNP rs2055979 (P = 1.2 x 10(-4), OR = 1.50, 95% CI 1.17-1.92) were independently associated with UC. We identified one risk haplotype in IL2 and another independent risk haplotype in IL21. In addition to the IL2/IL21 locus, we observed association of the TT genotype of SNP rs1545620 in MYO9B with UC (P = 0.0169; OR = 2.38, 95% CI 1.41-4.02) and association of rs17375018 in IL23R with pancolitis in Chinese UC patients (P = 0.002; OR = 2.38, 95% CI 1.41-4.02). CONCLUSIONS: Our study confirmed the association of the IL2/IL21 region with UC in Han Chinese patients, and further implied both IL2 and IL21 as genetic risk factors for UC. Han Chinese UC patients share part of their genetic susceptibility with Caucasian patients. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Cyclosporine (CsA) or infliximab (IFX) are used as rescue therapies in steroid-refractory, severe attacks of ulcerative colitis (UC). There are no data comparing the efficacy of these two alternatives. METHODS: Outcome of rescue therapy was retrospectively studied in two cohorts of patients hospitalized due to steroid-refractory moderate to severe UC: 1) a Swedish-Danish cohort (n = 49) treated with a single infusion of IFX; 2) an Austrian cohort (n = 43) treated with intravenous CsA. After successful rescue therapy, maintenance immunomodulator treatment was given to 27/33 (82%) of IFX; 2) an Austrian cohort (n = 43) treated with intravenous CsA. After successful rescue therapy, maintenance immunomodulator treatment was given to 27/33 (82%) of IFX patients and to 31/40 (78%) of CsA patients. Endpoints were colectomy-free survival at 3 and 12 months. Kaplan-Meier and Cox regression models were used to evaluate the association between treatment groups and colectomy. RESULTS: At 15 days, colectomy-free survival in the IFX cohort was 36/49 (73%) versus 41/43 (95%) in the CsA cohort (P = 0.005), at 3 months 33/49 (67%) versus 40/43 (93%) (P = 0.002), and at 12 months 28/49 (57%) versus 33/43 (77%) (P = 0.034). After adjusting for potential confounding factors, Cox regression analysis yielded adjusted hazard ratios for risk of colectomy in IFX-treated patients of 11.2 (95% confidence interval [CI] 2.4-53.1, P = 0.002) at 3 months and of 3.0 (95% CI 1.1-8.2, P = 0.030) at 12 months in comparison with CsA-treated patients. There were no opportunistic infections or mortality. CONCLUSIONS: Colectomy frequencies were significantly lower after rescue therapy with CsA than with a single infusion of IFX both at 3 and 12 months' follow-up. The superiority of CsA was seen principally during the first 15 days. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.

BACKGROUND AND AIMS: Colectomy rates for ulcerative colitis (UC) and data on postcolectomy complications in children are limited. Thus, we assessed colectomy rates, early postcolectomy complications, and clinical predictors in children with UC undergoing a colectomy. METHODS: Children (18 years old or older) with UC who underwent colectomy from 1983 to 2009 were identified (n=30). All of the medical charts were reviewed. The diagnostic accuracy of International Classification of Diseases codes for UC and colectomy were validated. The primary outcome was postoperative complications defined as Clavien-Dindo classification grade II or higher. The yearly incidence of colectomies for pediatric UC was calculated and temporal trends were evaluated. RESULTS: The sensitivity and positive predictive value of UC and colectomy International Classification of Diseases codes were 96% and 100%, respectively. The median ages at UC diagnosis and colectomy were 10.9 and 12.1 years, respectively. All of the children had pancolitis and 63% underwent emergent colectomy. Postoperatively, 33% experienced at least 1 complication. Patients with emergent colectomy were more likely to have a postoperative complication compared with patients with elective colectomy (90% vs 50%; P=0.03). For emergent colectomy, postoperative complications were associated with a disease flare of >=2 weeks before admission (60% vs 0%; P=0.03) and 2 weeks after admission to colectomy (78% vs 22%; P=0.04). The average annual rate of pediatric colectomy was 0.059/100,000 person-years and stable from 1983 to 2009 (P>0.05). CONCLUSIONS: Colectomy UC was uncommon and rates have remained stable. Postcolectomy complications were common, especially in patients undergoing emergent colectomy. Optimizing timing of colectomy may reduce postoperative complications.


BACKGROUND: Current data indicate that infliximab-given immediately after surgery—may be very effective in preventing postsurgical recurrence of Crohn's disease. However, it is unknown whether a similar benefit would result from early diagnosis and treatment, rather than prevention of endoscopic recurrence. AIMS: The primary outcome of this study was to clarify whether infliximab, given after diagnosis of postoperative endoscopic recurrence of Crohn's diseases (Rutgeerts score>=2) can induce endoscopic remission (score<2) at 54 weeks. The secondary outcomes were improvement in the endoscopic score and clinical recurrence at 54 weeks. METHODS: In this prospective open label multicenter pilot study 43 patients with ileocolonic Crohn's disease subjected to curative surgery underwent colonoscopy 6 months after surgery. Patients with endoscopic recurrence (Rutgeerts score>=2) were treated with either mesalamine 800mg tid or infliximab 5mg/kgbw on a maintenance basis. Colonoscopy was performed after 54 weeks. RESULTS: A total of 24/43 patients were diagnosed with endoscopic recurrence at 6 months. Thirteen were treated with infliximab and 11 with mesalamine. None of the 11 mesalamine-treated patients had endoscopic remission at 54 weeks. Two had clinical recurrence at 8 and 9 months. Fifty-four percent of patients treated with infliximab had endoscopic remission at 54 weeks (P=0.01) while 69% had an improvement in the endoscopic score. None had clinical recurrence. CONCLUSIONS: Treatment of postsurgical endoscopic lesions by infliximab appears superior to mesalamine. However, a sizeable proportion of patients did not fully benefit from this strategy.


OBJECTIVES: To validate the Dudley Inflammatory Bowel Disease Questionnaire (DISQ) for determining the presence and severity of bowel symptoms in axial SpA. METHODS: Seventy-seven SpA patients were assessed for disease activity using the BASDAI. All participants, including 32 healthy controls and 29 patients with Crohn's Disease (CD), completed the DISQ and an assessment of stool form and frequency. Validation of the DISQ was undertaken in accordance with OMERACT criteria. RESULTS: Validity of the DISQ for measuring bowel symptoms in SpA was confirmed (Cronbach's alpha 0.79). Mean DISQ scores (s.d.) were: controls 2.6 (2.6), SpA 8.7 (6.1) and CD 17.1 (10.2). Differences were significant between controls and SpA, and SpA and CD, and correlated with disease activity (rho 0.27, P=0.02). In SpA, DISQ scores of those taking NSAIDs (n=THIN SPACE)=THIN SPACE59) did not differ from those not taking NSAIDs (n=THIN SPACE)=THIN SPACE18) (P=0.31). Stool form and frequency differed significantly between SpA patients and healthy controls (P=0.001). Using the DISQ the prevalence of clinically relevant bowel symptoms in SpA is 31%, and 7.8% experience bowel symptoms equivalent to active CD. CONCLUSION: The DISQ is a valid measure of bowel symptoms in SpA. Bowel symptoms are prevalent in SpA and correlate with disease activity. Symptoms do not relate to treatment

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BACKGROUND: The role of single-site laparoscopy (SSL) for the treatment of ileocolic Crohn's disease complicated by an abscess, a phlegmon, or fistulizing disease has not been thoroughly assessed. METHODS: A prospectively maintained database of SSL surgeries performed between October 2010 and March 2011 was reviewed. Consecutive patients with ileocolic Crohn's disease complicated by a paracolic abscess, a phlegmon, or a fistula were included for analysis. Data recorded included demographic information, body mass index (BMI), estimated blood loss (EBL), length of surgery, rate of conversion to standard laparoscopic surgery or open surgery, length of hospital stay, and rate of complications. RESULTS: A total of six patients were identified. Complications from Crohn's disease included four (66%) patients who developed a paracolic abscess that required drainage upon admission, one (16%) patient who developed a phlegmon, and one (16%) patient who developed an enterocutaneous fistula. Mean age of the study population was 25 years, with a mean BMI of 21 and a mean ASA score of 3. Five (83%) of the patients were immunosuppressed with high-dose steroids. Mean operative time was 160 min, with a median EBL of 60 mL. One patient required the insertion of an additional trocar, whereas there were no conversions to laparotomy. Four (66%) patients required diversion with a loop ileostomy. Median time to flatus was 1 day. All patients tolerated a diet on the day of surgery, with a median length of stay of 3 days. There were no deaths and no complications related to bleeding, organ injury, surgical site infections, or anastomotic leaks. CONCLUSIONS: A single-site laparoscopic approach for complicated ileocolic Crohn's disease can be performed safely, with short lengths of hospital stay and with a low rate of complications. A multicenter study would be beneficial to validate these findings.


BACKGROUND AND AIMS: The neutrophil protein calprotectin has been investigated as a surrogate marker for intestinal inflammation. This study was designed to contrast fecal calprotectin levels in patients with inflammatory and non-inflammatory intestinal diseases and to compare the results obtained from the standard ELISA-based method with those obtained from a novel desk-top device. METHODS: Soluble proteins were extracted from stool samples of 50 participating patients, including those diagnosed with Ulcerative Colitis, Crohn's Disease or IBS, and volunteers with no known intestinal problems. Calprotectin was assessed in the extracted material using the "desk top" Buhlmann Quantum Blue Reader[REGISTERED] or by standard ELISA techniques. RESULTS: The mean concentration of calprotectin in the IBD patients group was significantly higher than the mean concentration found in IBS patients and healthy controls (p=0.01). Calprotectin concentrations in IBS patients and controls were indistinguishable. IBD patients that had undergone recent surgery displayed scores similar to controls and IBS patients. Excluding these patients yielded a specificity of 100% for results from both CD and UC patients and an accuracy rate of 1 for CD and 0.89 for UC patients in ROC analysis. Quantum Blue Reader[REGISTERED] calprotectin levels were available within 30 min and correlated well with results derived from standard ELISA assays, which took over 8h to complete. CONCLUSION: Our results confirm the effective use of fecal calprotectin levels in differentiating non-inflammatory from active inflammatory intestinal diseases. The desk top Buhlmann Quantum Blue Reader[REGISTERED] exhibits a fast, non-invasive, and reliable way of identifying an inflammatory intestinal disease. Copyright Copyright 2011 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.


BACKGROUND: Thromboembolism (TE) is a common extraintestinal complication of inflammatory bowel disease (IBD). Catheter-directed thrombolysis (CDT) is being increasingly used to treat TE but often evokes fears of hemorrhagic complications (HCs) in patients with IBD. We reviewed clinical outcomes with anticoagulation (AC) and CDT in IBD patients with TE. METHODS: Published cases of IBD patients with TE were identified by a PubMed search. Cases were divided into two groups based on treatment modality: AC alone or CDT. Pretreatment variables and treatment-related outcomes were compared between treatment groups. RESULTS: Fifty-two cases of IBD-associated TE were identified. Thirty-five cases were treated with AC alone and 17 with CDT. There were no significant differences in pretreatment variables. Patients treated with CDT tended to be more likely to achieve complete or partial symptomatic (P = 0.02) and radiologic resolution (P = 0.06). Gastrointestinal (GI) and non-GI HCs tended to occur more frequently with CDT, although these differences were not statistically significant (P = 0.44 and 0.15, respectively). CONCLUSIONS: CDT and AC both appear to be well tolerated by IBD patients with TE. CDT may be used preferentially in patients with life-threatening TE, while AC may be preferable in patients with less clinically significant TE or patients at higher risk for bleeding.
Further prospective studies are warranted to confirm these results and more definitively identify the best therapeutic approach for patients with IBD-associated TE. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


OBJECTIVE: The aim of this study was to assess whether power Doppler ultrasound (PDU) can serve as a reliable replacement for endoscopy in follow-up assessment of disease activity in children with Crohn disease. METHODS: Nineteen children (13 boys), median age 14.8 (5.4-15.8) years, with macroscopically diagnosed Crohn disease were included in the study. Clinical parameters, histological evaluation, and graded PDU assessments were undertaken in all patients at diagnosis and following their initial treatment. Discriminant analysis was used to build predictive models from the PDU data for the histological evaluation. RESULTS: The median Pediatric Crohn's Disease Activity Index (PCDAI) was 31.5 (15.5-42.0) at diagnosis. All clinical and ultrasonographic parameters and the histological evaluation showed an improvement between pre- versus posttreatment results; 1-way analysis of variance showed a significant difference because of treatment (P[HAIR SPACE]<[HAIR SPACE]0.005) for all variables apart from the superior mesenteric artery flow (SMA); paired sample t tests indicated that these differences were statistically significant (P[HAIR SPACE]<[HAIR SPACE]0.001), with the exception of SMA (P[HAIR SPACE]<[HAIR SPACE]0.178). There was a statistically significant correlation (P[HAIR SPACE]<[HAIR SPACE]0.001) between the platelet count and the bowel wall stratification (STRAT). Significant correlation was also observed between the histology findings and the mean mucosal, transmural, and segmental flow (MFL) and STRAT and between platelets and both MFL and small bowel thickening (SBT) (P[HAIR SPACE]<[HAIR SPACE]0.01 in all cases). There was a statistically significant correlation (P[HAIR SPACE]<[HAIR SPACE]0.05) between C-reactive protein and MFL and between histology and SBT, MFL, and STRAT. Discriminant analysis using discriminating factors SBT, STRAT, and MFL could assign 84.6% of cases to the correct classification of "no/mild inflammation" or "medium/severe inflammation." CONCLUSIONS: Results obtained using power Doppler ultrasonography and endoscopy showed statistically significant correlations. Power Doppler sonography, in the hands of an experienced examiner, can be used for follow-up assessment of disease activity in children with Crohn disease.


OBJECTIVE: To systematically review the efficacy and safety of once-daily (OD) mesalamine for the treatment of ulcerative colitis (UC) compared with multiple-daily (MD) mesalamine. METHODS: Electronic databases up to July 2011 were searched for related studies evaluating the efficacy of OD vs MD for treatment of UC. Only randomized controlled trials (RCTs) were considered eligible. Remission rates or relapse rates were analyzed using intention-to-treat (ITT) and per-protocol (PP) analysis. Pooled relative risk (RR) and 95% confidence interval (CI) were calculated. Publication bias was assessed with a funnel plot. RESULTS: Overall 10 RCTs including 9 full-text manuscripts and one abstract met the inclusion criteria. OD dosing of mesalamine was shown to be as effective as MD dosing for the maintenance of clinical remission in patients with quiescent UC (RR = 1.00, 95% CI 0.89-1.12) by ITT analysis. For active UC, a mild but significant benefit was achieved by OD dosing compared with MD dosing (RR = 0.80, 95% CI 0.64-0.99). Total adverse events were similar using OD and MD mesalamine in quiescent UC (RR = 1.06, 95% CI 0.93-1.20). Compliance with OD was slightly better than with MD (RR = 0.92, 95% CI 0.82-1.03). CONCLUSIONS: OD mesalamine is as effective and has a comparable safety profile as MD regimens for the maintenance treatment of UC, and is even more effective for inducing remission in active UC. Copyright 2012 The Authors. Journal of Digestive Diseases Copyright 2012 Chinese Medical Association Shanghai Branch, Chinese Society of Gastroenterology, Renji Hospital Affiliated to Shanghai Jiaotong University School of Medicine and Blackwell Publishing Asia Pty Ltd.


BACKGROUND: Variability in endoscopic assessment necessitates rigorous investigation of descriptors for scoring severity of ulcerative colitis (UC). OBJECTIVE: To evaluate variation in the overall endoscopic assessment of severity, the intra- and interindividual variation of descriptive terms and to create an Ulcerative Colitis Endoscopic Index of Severity which could be validated. DESIGN: A two-phase study used a library of 670 video sigmoidoscopies from patients with Mayo Clinic scores 0-11, supplemented by 10 videos from five people without UC and five hospitalised patients with acute severe UC. In phase 1, each of 10 investigators viewed 16/24 videos to assess agreement on the Baron score with a central reader and agreed definitions of 10 endoscopic descriptors. In phase 2, each of 30 different investigators rated 25/60 different videos for the descriptors and assessed overall severity on a 0-100 visual analogue scale. kappa Statistics tested inter- and
intraobserver variability for each descriptor. A general linear mixed regression model based on logit link and beta distribution of variance was used to predict overall endoscopic severity from descriptors. RESULTS: There was 76% agreement for 'severe', but 27% agreement for 'normal' appearances between phase I investigators and the central reader. In phase 2, weighted kappa values ranged from 0.34 to 0.65 and 0.30 to 0.45 within and between observers for the 10 descriptors. The final model incorporated vascular pattern, (normal/patchy/complete obliteration) bleeding (none/mucosal/luminal mild/luminal moderate or severe), erosions and ulcers (none/erosions/superficial/deep), each with precise definitions, which explained 90% of the variance (pR(2), Akaike Information Criterion) in the overall assessment of endoscopic severity, predictions varying from 4 to 93 on a 100-point scale (from normal to worst endoscopic severity). CONCLUSION: The Ulcerative Colitis Endoscopic Index of Severity accurately predicts overall assessment of endoscopic severity of UC. Validity and responsiveness need further testing before it can be applied as an outcome measure in clinical trials or clinical practice.


BACKGROUND: The Pediatric Crohn's Disease Activity Index (PCDAI) has become the standard outcome measure in pediatric Crohn's disease (CD) clinical research. Other versions have been proposed but without systematic evaluation. The aim was to assess validity and responsiveness of the abbreviated PCDAI (abbrPCDAI), short PCDAI (shPCDAI), and modified PCDAI (modPCDAI) as measures of disease activity and to compare these with a mathematically weighted version developed here (wPCDAI). METHODS: The raw data from four prospectively collected datasets were used, totaling 437 children with CD (including two clinical trials). Discriminant validity utilized physician global assessment of disease activity (PGA), and construct validity the correlation with PGA and laboratory results. Feasibility and face validity were ascertained by a survey of 33 experts in pediatric CD. RESULTS: The wPCDAI had better performance than the PCDAI in construct validity and responsiveness and it discriminated better between the disease activity categories (area under the receiver operator characteristic [ROC] 0.97; 95% confidence interval [CI]: 0.95-0.99). In comparison to the original PCDAI, the noninvasive versions (abbrPCDAI and shPCDAI) had lower face, construct, and discriminant validity but were judged to be significantly more feasible. The modPCDAI performed well in the construct validation but was consistently inferior in all other parameters. Cutoffs that correspond to remission, response, and gradations of disease activity were determined for each index. CONCLUSIONS: The newly weighted wPCDAI performed better than the original PCDAI and is more feasible. The noninvasive versions (shPCDAI and abbrPCDAI) are inferior to the full PCDAI, but when needed in retrospective studies either may be equally used. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: There has not been an extensive comparison of CRP and ESR in ulcerative colitis (UC), and thus, we aimed to explore their utility in UC. METHODS: Four previously enrolled cohorts of 451 children with UC were utilized, all including laboratory, clinical and endoscopic data. A longitudinal analysis was performed on prospectively collected data of 75 children. Disease activity was captured by both global assessment and pediatric UC activity index (PUCAI). RESULTS: The best thresholds to differentiate quiescent, mild, moderate and severe disease activity, were <23, 23-29, 30-37, >37 mm/h for ESR, and <2.5, 2.5-5, 5.01-9, >9 mg/L for CRP (area under the ROC curves 0.70-0.81). Correlation of endoscopic appearance with CRP and ESR were 0.55 and 0.41, respectively (P<0.001). Both CRP and ESR may be completely normal in 34% and 5-10% of those with mild and moderate-severe disease activity, respectively. Elevated CRP in the presence of normal ESR or vice versa was noted in 32%, 38%, 30% and 17% of those with quiescent, mild, moderate and severe disease activity. Over time, the utility of CRP and ESR in reflecting disease activity remained stable in 70-80% of cases. CONCLUSION: In ~2/3 of children, both CRP and ESR values reflect disease activity to a similar degree and in the remaining, either CRP or ESR may be sufficient, with slight superiority of CRP. CRP is more closely correlated with endoscopic appearance. When either CRP or ESR performs well for a given patient, this is likely to remain so over time. Therefore, it may not be justified to routinely test both ESR and CRP in monitoring disease activity. Copyright Copyright 2011 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.


BACKGROUND: Ileocecal resection is the most commonly performed operation in patients with Crohn's disease. Anastomotic-associated complications, with their associated morbidity, are the most feared risks of surgery. OBJECTIVE: This study aimed to assess the influence of a variety of putative risk factors in a homogenous group of patients undergoing first or subsequent surgery for Crohn's disease to quantify the
cumulative risk for anastomotic-associated complications. DESIGN AND PATIENTS: All patients undergoing ileocolic or ileocolic resections for Crohn's disease from 2000 to 2010 were studied with the use of a prospective database. Demographics, operative details, possible risk factors, and anastomotic-associated complications were recorded. Patients having strictureplasties, multiple resections, or subtotal colonic resections were excluded from analysis. Statistical analysis was by univariate analysis (Mann-Whitney U test) and binary logistic regression. OUTCOMEs: An anastomotic-associated complication was defined as a proven anastomotic leak, postoperative fistulation, or intra-abdominal abscess formation. RESULTS: Two hundred seven patients (109 female) with a median age of 35 years (range, 13-75 years) were identified. One hundred seventy-three underwent primary anastomosis, 94 as an emergency procedure. Fifty-three had laparoscopic (5 converted) procedures. Nineteen of 173 anastomotic complication events (11%) were recorded. Steroid usage (OR 2.67, 95% CI 1.0-7.2) and the presence of preoperative abscess formation (OR 3.4, 95% CI 1.2-9.8) were identified as independent predictors of anastomotic-associated complications. In the absence of both steroids and intra-abdominal abscess, the risk of anastomotic complications was 6%, which increased to 14% if either risk factor was present. When both risk factors were present, complication rates reached 40%. CONCLUSION: Steroid usage and preoperative abscesses were associated with higher rates of anastomotic complications following ileocolic resection for Cohn's disease. When both risk factors are present, it is best to avoid primary anastomosis.


BACKGROUND: Both ulcerative colitis (UC) and Crohn's disease (CD) have a complex etiology involving multiple genetic and environmental factors. Many genome-wide association studies (GWAS) and subsequent replication studies revealed that both diseases share some of the susceptibility loci; however, common genetic factors for both diseases are not fully elucidated. This study is aimed to identify the common genetic factors for CD and UC by a meta-analysis of published studies. METHODS: We first reviewed the 10 GWAS for CD to select candidate single nucleotide polymorphisms (SNPs). Next, we performed a PubMed literature search up to June 30, 2010 and carried out a systematic review of published studies that examined the association of CD susceptibility loci in UC patients. Meta-analysis was carried out using the inverse variance-weighted method or the DerSimonian-Laird method after estimating the heterogeneity among the studies. The data for highly linked SNPs were combined. Finally, we performed a meta-analysis of 43 published studies in 45 SNPs located at 33 loci by using a total of 4852 to 31,125 subjects. RESULTS: We confirmed the association of 17 reported common susceptibility loci. Moreover, we found associations at eight additional loci: GCKR, ATG16L1, CDKAL1, ZNF365, LRRK2-MUC19, C13orf31, PTPN2, and SBNO2. The genetic risk of each locus was modest (odds ratios ranged from 1.05-1.22) except IL23R. CONCLUSIONS: These results indicate that CD and UC share many susceptibility loci with small genetic effect. Our data provide further understanding of the common pathogenesis between CD and UC. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Inflammatory bowel diseases (IBDs) are comprised of two major disorders: Crohn's disease (CD) and ulcerative colitis (UC). No curative treatment options are available, but gene therapy may offer an alternative therapeutic approach. For this a safe and reliable vector is needed. The adeno-associated viruses (AAV) have attracted considerable interest as gene therapy vectors. However, neutralizing antibodies (nAb's) made in response to wildtype AAV have been associated with a partial to complete block of transduction in case of reexposure. Therefore, and in order to define AAV vector candidates to treat IBD patients, we characterized preexisting humoral responses to AAV in this population. METHODS: We measured circulating antibodies against AAV serotypes 1, 2, 3, 4, 5, 6, and 8 using a previously established virus neutralization assay. In all, 100 healthy donors and 200 IBD patient's serum samples (101 CD and 99 UC) were analyzed. RESULTS: A significant difference was detected in the prevalence of nAb's for AAV types 1, 5, 6, and 8 between the healthy donors and the patient population. Furthermore, various disease phenotypic characteristics correlated with the prevalence of nAb's to all the serotypes studied. CONCLUSIONS: Our study establishes a foundation for the development of an AAV-based gene therapy approach as a novel treatment for IBD. Furthermore, we show a relationship between disease phenotype in IBD patients and the humoral immune response to AAV. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


That gut and joint inflammation are linked in spondyloarthritis (SpA) has been recognized for almost three decades. Intriguingly, microscopic gut inflammation, which occurs frequently in patients with SpA, is an important risk factor for clinically overt Crohn's disease and ankylosing spondylitis. This Review describes current insights into the underlying mechanisms that lead to chronic gut inflammation in patients with SpA. We
propose that the development of chronic bowel inflammation in these individuals occurs through a transition phase, in which inflammation evolves from an acute into a chronic state. Our transition model implies that different cell types are involved at different stages during disease progression, with stromal cells having an important role in chronicity. In addition, deficient regulatory feedback mechanisms or genetically determined alterations in antigen presentation, endoplasmic reticulum stress, autophagy or cytokine signaling might also favor a transition from self-limiting acute inflammation to chronic inflammation. We anticipate that this transition phase might be an important window for therapeutic intervention.


Background: Loss of response to infliximab (IFX) is seen in up to 50% of IBD patients. This is often a result of antibody formation and subsequent low infliximab concentrations (trough levels). Loss of response is managed clinically by decreasing the interval between infusions or increasing the dose. We hypothesised that sustained good anti-TNF trough levels are associated with a better long term outcome. Aim: To investigate the value of individualised treatment with IFX based on therapeutic drug monitoring in a randomised controlled trial. Methods: 270 consecutive IBD patients on IFX maintenance therapy were randomised to dosing based on IFX trough levels (TLI) (group1: TLI kept in a window between 3 and 7 mg/ml) or dosing and optimisation based on clinical symptoms (group 2). Before randomisation, trough levels were first optimised to have a baseline TLI between 3 and 7 mg/ml. The primary endpoint is defined as clinical and biological (CRP <5 mg/l) remission rates at one year after randomisation. TLI (expressed in mg/ml) and antibodies to infliximab (ATI; expressed in mg/ml equivalents) were measured with an in-house developed ELISA. We here report on the results of the optimisation phase. Results: In the total cohort of patients (n = 270) in clinical remission, 117 patients (43%) had a TLI between 3 and 7 mg/ml and needed no dose adjustment, 71 patients (26%) had a TLI higher than 7 mg/ml and in these patients the dose of IFX was reduced. 59 patients (22%) had a detectable TLI lower than 3 mg/ml and 23 patients (9%) even had undetectable TLI of which 17 patients (77%) were ATI positive: (median; IQR) (5.92; 2.76 7.68 mg/ml eq.). In these patients the dose of IFX was increased to reach the target level. In 6 patients IFX therapy was discontinued due to absent TLI and ATI >8 mg/ml eq. and they were excluded from the randomised study. Patients with TLI <3 mg/ml had a significantly higher CRP (2.75; 1.03 7.53 mg/l) compared to patients with a TLI between 3 and 7 mg/ml (1.45; 0.60 3.28 mg/l) (P-value = 0.001) and patients with a TLI >7 mg/ml (1.20; 0.60 4.80 mg/l) (P-value = 0.01). Conclusions: The results of this optimisation phase of the TAXIT trial show that in this large cohort of patients in remission under treatment with maintenance infliximab only 43% have optimal TLI. In the others dose adjustment was carried out. 9% of the patients have undetectable TLI despite staying in remission. The current controlled study will show whether long term adjustment of treatment based on IFX levels is a superior strategy.


BACKGROUND: Neutropenic patients are at risk of abdominal complications and yet the incidence and impact of these complications on patients' morbidity and mortality have not been sufficiently evaluated. We aimed to assess a clinical rule for early detection of abdominal complications leading to death or transfer to intensive care in patients with chemotherapy-associated neutropenia. DESIGN AND METHODS: This observational multicenter study was carried out in seven German hematology-oncology departments. For inclusion, neutropenia of at least 5 consecutive days was required. Risk factors for "transfer to intensive care" and "death" were assessed by backward-stepwise binary logistic regression analyses. Chemotherapy-associated bowel syndrome was defined as a combination of fever (T >37.8 degreesC) and abdominal pain and/or lack of bowel movement for 72 hours or more. Five hundred and twenty-one neutropenic episodes were documented in 359 patients. RESULTS: The incidence of chemotherapy-associated bowel syndrome was 126/359 (35%) in first episodes of neutropenia. Transfer to intensive care occurred in 41/359 (11%) and death occurred in 17/359 (5%) first episodes. Chemotherapy-associated bowel syndrome and duration of neutropenia were identified as risk factors for transfer to intensive care (P<0.001; OR 4.753; 95% CI 2.297-9.833, and P=0.003; OR 1.061/d; 95% CI 1.021-1.103). Chemotherapy-associated bowel syndrome and mitoxantrone administration were identified as risk factors for death (P=0.005; OR 4.611; 95% CI 1.573-13.515 and P=0.026; OR 3.628; 95% CI 1.169-11.256). CONCLUSIONS: The occurrence of chemotherapy-associated bowel syndrome has a significant impact on patients' outcome. In future interventional clinical trials, this definition might be used as a selection criterion for early treatment of patients at risk of severe complications.


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BACKGROUND: Crohn's disease patients have a decreased Quality of Life (QoL) which is in part due to extreme fatigue. In a pilot study we prospectively assessed the feasibility and effect of psychological interventions in the management of fatigue. METHODS: Patients with quiescent Crohn's disease and a high fatigue score according to the Checklist Individual Strength were randomized to Problem Solving Therapy (PST), Solution Focused Therapy (SFT) or to a control group (treatment as usual, TAU). Patients completed the Inflammatory Bowel Disease Questionnaire, the EuroQol-5D, and the Trimbos questionnaire for Costs. RESULTS: Twenty-nine patients were included (12 TAU, 9 PST, 8 SFT), of these 72% were female, mean age was 31 years (range 20-50). The SFT group improved on the fatigue scale in 85.7% of the patients, in the PST group 60% showed improved fatigue scores and in the TAU group 45.5%. Although not significant, in both intervention groups the QoL increased. Medical costs lowered in 57.1% of the patients in the SFT group, in the TAU 45.5% and the in PST group 20%. The drop out rate was highest in the PST group (44%; SFT 12.5%; TAU 8.3%). CONCLUSIONS: PST and SFT both positively affect the fatigue and QoL scores in patients with Crohn's disease. SFT seems most feasible with fewer dropouts and is therefore a promising new tool in the management of fatigue in Crohn's disease patients. Copyright Copyright 2011 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.


Purpose: Necrotizing enterocolitis (NEC) is the most common acquired disease of the gastrointestinal tract in preterm infants, whereas probiotic supplementation might reduce NEC risk and potentially provide benefits to preterm infants. We performed an updated meta-analysis of all relevant randomized, controlled trials to assess the benefits of probiotic supplementation for preterm very low-birth-weight (VLBW) infants. Methods: We searched in PubMed, Embase, and Chinese BioMedical Literature Database (CBM) databases, and 20 randomized, controlled trials (a total of 3816 preterm VLBW infants) were finally included into this meta-analysis. Incidence and relative risk (RR) were calculated using a random-effects or fixed-effects model depending on the heterogeneity of the included studies. Results: Probiotic supplement was associated with a significantly decreased risk of NEC in preterm VLBW infants (RR = 0.33; 95% confidence interval [CI], 0.24-0.46; P <.00001). Risk of death was also significantly reduced in the probiotic group (RR = 0.56; 95% CI, 0.43-0.73; P <.0001). There was no difference in the risk of sepsis between the probiotic group and placebo group (RR = 0.90; 95% CI, 0.71-1.15; P =.40). Conclusions: Probiotic supplement can reduce risk of NEC and mortality in preterm VLBW infants. However, the optimum type of probiotic supplement and the long-term effects need further study. 2012 Elsevier Inc. All rights reserved.


BACKGROUND: Inflammatory complications of ileal pouch-anal anastomosis (IPAA), including pouchitis and Crohn's disease (CD) of the pouch, are common in patients with restorative proctocolectomy for ulcerative colitis. It is not clear whether these inflammatory conditions can affect upper GI tract. The aim of the study was to evaluate correlation between duodenal and pouch histology in patients with healthy and diseased pouches. METHODS: All IPAA patients who had esophagogastroduodenoscopy with biopsy after colectomy (N = 96) were included. H&E slides of gastric, duodenal, neo-terminal ileum, and pouch body biopsies were blindly re-reviewed by an expert GI pathologist for acute and chronic inflammation. Demographic and clinical variables and pouch outcome were analyzed. RESULTS: There was a significant correlation between acute inflammation in the duodenum as measured by neutrophil infiltration score and the presence of chronic pouchitis (kappa coefficient = 0.21, P <.05). Intraepithelial lymphocytosis of the duodenum, though uncommon, only occurred in patients with irritable pouch syndrome, chronic pouchitis, or CD of the pouch. Crypt distortion of duodenal epithelium was only seen in patients with inflammatory or structural diseases of the pouch, including acute (18.2%) and chronic (5%) pouchitis, CD of the pouch (14.3%), and surgical complications of the pouch (14.4%). CONCLUSION: Histologic evaluation of duodenal biopsy may provide additional information in patients with ileal pouches, as patients with normal histology of the pouch may have an abnormal duodenal histology.


BACKGROUND: Current therapy for inflammatory bowel disease (IBD) patients often involves agents that suppress the immune system, placing patients at an increased risk for developing infections, of which several are potentially vaccine preventable. Many IBD patients are not being vaccinated appropriately. The aims of this study were to assess gastroenterologist's knowledge regarding vaccinating the IBD patient, eliciting the barriers that prevent vaccinations, and defining the gastroenterologist's role in vaccinations. METHODS: One thousand gastroenterologists, randomly selected from the membership of the American College of Gastroenterology, were
asked to complete a 19 question electronic survey regarding the suitable vaccines for the immunocompetent and immunosuppressed IBD patient and the barriers to recommending the vaccines. The perceived role of the gastroenterologist versus the primary care physician (PCP) was also assessed. RESULTS: In all, 108 responses were analyzed; 68 (62%) gastroenterologists managed 40+ IBD patients, with 65 (52%) asking their patients about immunization history most or all of the time. The majority believed that the PCP should determine which vaccinations to give (64%) and to administer the vaccines (83%). Overall, 66%-88% of gastroenterologists correctly recommended the inactivated vaccines for their IBD patients not on immunosuppressive therapies while 20%-30% incorrectly recommended administering the live vaccines to their immunosuppressed patients. CONCLUSIONS: Gastroenterologist knowledge of the appropriate immunizations to recommend to the IBD patient is poor and may be the primary reason why the majority of gastroenterologists believe that the PCP should be responsible for vaccinations. Educational programs on vaccinations directed to gastroenterologists who prescribe immunosuppressive agents are needed. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.


BACKGROUND: Calprotectin is an acute-phase protein used extensively in the assessment of gastrointestinal inflammation. It can readily be measured by enzyme-linked immunosorbent assay (ELISA) and recently by point-of-care testing (POCT). We evaluated the Quantum Blue[REGISTERED] POCT in this study and compared it with our existing ELISA method. METHODS: The method comparison study used faecal samples (n = 47) sent to the laboratory for routine calprotectin analysis. Linearity was assessed by serial dilution of extracted faeces (n = 4). Extraction efficiency was determined by repeat extraction of three different stools. The variation in results as a consequence of reading the POCT cartridges either side of the recommended 12 min was also assessed. RESULTS: The assay was linear across the range stated by the manufacturer. When multiple samples were taken from the same stool, results varied from -31.3% to +31.5%. For the clinical arm of our study, strictly applying the 50 mug/g cut-off recommended for both assays as positive for gastrointestinal inflammation, there were four patients where results fell a different side of the clinical cut-off; two patients had results higher by Quantum Blue[REGISTERED] and two higher by ELISA. CONCLUSIONS: In our hands, the Quantum Blue[REGISTERED] method was a suitable screening test for excluding inflammatory bowel disease. It may be of value to laboratories wishing to offer calprotectin but who do not have sufficient numbers to warrant ELISA methodology or in 'one stop' gastrointestinal clinics where an immediate result is required.


Background and aims: Adalimumab has been shown to be efficacious and well-tolerated in Western patients with Crohn's disease. These 2 randomized, double-blind clinical trials evaluated adalimumab efficacy and safety in Japanese patients with moderate to severe Crohn's disease. Methods: 90 patients enrolled in the induction trial and were randomized to receive adalimumab 160/80. mg, adalimumab 80/40. mg or placebo at Weeks 0/2. At Week 4, patients who achieved a decrease in CDAI >= 70 points versus Baseline entered the maintenance trial and were randomized to adalimumab 40. mg every other week or placebo for 52. weeks. All other patients received 4 more weeks of blinded adalimumab before entering the open-label portion of the maintenance trial. At/after Week 4 of the maintenance trial, blinded patients who flared/failed to respond entered the open-label portion. Open-label maintenance patients received adalimumab 40. mg every other week with the option of 80. mg every other week for flare/non-response. Results: Clinical remission rates at Week 4 in the induction trial were 33.3%, 17.6% and 13.0% in the adalimumab 160/80. mg, adalimumab 80/40. mg and placebo groups, respectively. Maintenance remission rates were 38.1% for adalimumab and 9.1% for placebo at Week 52. Anti-TNF naive patients achieved greater efficacy than anti-TNF exposed patients. Patients randomized to adalimumab achieved greater quality of life improvement versus placebo. There were no clinically relevant differences in safety between adalimumab and placebo. Conclusions: Adalimumab is effective and well-tolerated for inducing and maintaining clinical remission in Japanese patients with moderate to severe Crohn's disease. NCT00445939; NCT00445432. 2011 European Crohn's and Colitis Organisation.


BACKGROUND: Steroids, immunomodulators, and biologics, often in combination with one another, are frequently used in the treatment of Crohn's disease. Retrospective studies have yielded conflicting results regarding the influence of preoperative immunosuppressive therapy on postoperative complications after surgery in Crohn's disease. Unplanned hospital readmission is considered to be an index of quality surgical care. OBJECTIVE: The aim of this study was to examine the association, if any, between the number of preoperative immunosuppressive therapies and unplanned hospital readmission after surgery in patients with Crohn's disease.
DESIGN: Consecutive patients with Crohn's disease requiring abdominal surgery were identified from a prospectively maintained database. Preoperative immunosuppressive therapy within 3 months before surgery was categorized into 3 classes: steroids, immunomodulators, and biologics. MAIN OUTCOME MEASURES: Unplanned readmission occurring within 30 days of hospital discharge was assessed. Trend analysis was performed with the use of the Cochrane-Armitage test. RESULTS: The study group included 338 patients. Preoperative medical therapy included steroids (n = 199; 59%), immunomodulators (n = 162; 48%), and biologics (n = 59; 18%). Sixty-three patients (19%) were not treated with any immunosuppressive medications preoperatively, whereas 148 patients (44%), 108 patients (32%), and 19 patients (6%) were treated with 1, 2, or 3 classes of immunosuppressive medications. Twenty-eight patients (8.3%) had an unplanned readmission. The incidence of unplanned readmission was similar among patients treated with steroids (11%), immunomodulators (9%), and biologics (12%). The incidence of unplanned readmission was 3%, 7%, 11%, and 16% in patients treated with 0, 1, 2, or 3 preoperative medication classes (trend analysis p = 0.02). No significant differences were observed between patient groups treated with 0, 1, 2, or 3 preoperative immunosuppressive therapies with respect to patient, disease, or surgical factors. CONCLUSIONS: Unplanned hospital readmission occurs frequently (8.3%) after surgery for Crohn's disease. Combination immunosuppressive therapy before surgery in patients with Crohn's disease appears to be associated with an increased incidence of postoperative unplanned hospital readmission.


Background. Acute onset vomiting and diarrhoea is one of the most common illnesses of infancy, and is second only to respiratory illnesses as a cause of childhood deaths worldwide. Existing guidelines for management of diarrhoea are often ignored in public and private practice, possibly because of a perception that the guidelines are too simple, or because of expectations of the need to give 'real' drug therapy to stop diarrhoea. Objectives. This guideline provides a problem-based approach to the basics of present-day management of acute gastroenteritis, and discusses the evidence for the recommendations. Recommendations. Each episode of diarrhoea must be seen as an opportunity for caregiver education in the prevention of the illness, in the 'what' and 'how' of oral rehydration and re-feeding, and in the recognition of when to seek help. The vast majority of patients recover rapidly, but serious complications do occur and must be recognised and managed correctly. Validation. The guidelines are endorsed by the Paediatric Management Group (PMG) in South Africa. Conclusion. The aim of management is to help the child to maintain or regain hydration, and to recover from diarrhoea, with careful attention to adequate oral rehydration and judicious re-feeding.


AIM: The diagnostic accuracy of chromoendoscopy for dysplasia in ulcerative colitis (UC) was systematically evaluated. METHOD: [en space] Original studies in any language were searched from PubMed and Embase. Meta-analysis of prospective studies that compared chromoendoscopy with histological diagnosis was carried out. Sensitivity, specificity, and diagnostic odds ratio (DOR) were calculated for each study and pooled together; summary receiver operating characteristic (ROC) and subgroup analyses were performed, while the quality of the study and heterogeneity were assessed. RESULTS: Six randomized controlled trials were included, which used methylene blue or indigo carmine dye spray. The meta-analysis demonstrated a pooled sensitivity of 83.3% (95% confidence interval (CI), 35.9-99.6%), specificity of 91.3% (95% CI, 43.8-100%), and DOR of 17.544 (95% CI, 1.245-247.14). Subgroup analyses revealed that both the methylene blue dye spray subgroup and the unspecified endoscopist subgroup include the same studies, and their pooled sensitivity and specificity were 0.737 and 0.917, respectively. The other subgroup, which used indigo carmine dye spray, had overall higher sensitivity (0.930) and lower specificity (0.910). CONCLUSION: Chromoendoscopy has medium to high sensitivity and a high diagnostic accuracy for dysplastic lesions in UC. Copyright 2010 The Authors. Colorectal Disease Copyright 2010 The Association of Coloproctology of Great Britain and Ireland.


Tumor necrosis factor-alpha (TNF-alpha) has been regarded as a candidate gene for Crohn's disease (CD) based on its inflammatory function in immune reaction and the clinical effectiveness of anti-TNF-alpha therapy. However, studies to date have reported inconsistent findings for the association between TNF-alpha and CD. The PubMed, EMBASE, and Medline databases were systematically reviewed from all English language publications up to April, 2011. A total of twenty-nine studies concerning the association between CD and the TNF-alpha promoter polymorphisms of -308G/A, -857C/T and -238G/A were identified, among of them only twenty-three studies match the inclusion criteria (including 3,843 cases and 6,260 controls) and were selected for the statistical test. We found that neither the G allele of -308G/A (OR 1.02, 95% CI 0.87-1.19, P = 0.84), C allele of -857C/T

PURPOSE: Percutaneous drainage (PD) of Crohn's related abscesses is becoming popular with the development of techniques. We retrospectively analyzed the outcome of initial PD versus initial surgical drainage for intra-abdominal abscesses in Crohn's disease. METHODS: Twenty-three patients of Crohn's disease complicated with intra-abdominal or pelvic abscesses treated in our institution between July 2001 and April 2010 were retrospectively identified from 188 patients with proven Crohn's disease. Outcome measures included abscess recurrence after different treatments, post-drainage complications, ultimate stoma creation, and subsequent surgery for Crohn's disease. RESULTS: Patients were divided into initial PD group (n=10) and initial surgery group (n=13): post-drainage complications were more common in initial surgery group (2/10 vs 9/13, P=0.036), abscess recurred in three patients (2/10 vs 1/13, NS), and subsequent surgery was needed in 10 patients (6/10 vs 4/13, NS). Ultimate stoma creation were significantly more in initial surgery group (1/10 vs 9/13, P=0.01). CONCLUSIONS: Initial PD group had lower rate of post-drainage complications and ultimate stoma creation compared to the initial surgery group. Although subsequent surgery may not be avoided after PD, it can provide safe anastomosis for resections. Long-term follow-up should be done to assess the outcome of PD.


PURPOSE: Although a number of genetic studies have attempted to link organic cation transporter 1/2 (OCTN1/2) polymorphisms to susceptibility of Crohn's disease (CD), the results were often inconsistent. The present study aimed at investigating the associations. METHODS: The PubMed, EBSCO, and BIOSIS databases were searched to identify eligible studies which were published in English before April 2011. The association was assessed by odds ratio (OR) with 95% confidence intervals (CI). RESULTS: A total of 15 case-control studies, containing 4,489 cases/5,351 controls for OCTN1 and 4,474 cases/5,377 controls for OCTN2 were included. Overall, significant associations were found between OCTN1/2 polymorphisms and susceptibility of Crohn's disease for all genetic models. In the subgroup analyses, significant associations were found in the Caucasian population for OCTN1 (TT vs. CC: OR=1.425, 95% CI 1.247-1.628; TT vs. CT: OR=1.299, 95% CI 1.149-1.468; dominant model: OR=1.344, 95% CI 1.197-1.508; and recessive model: OR=1.179, 95% CI 1.066-1.305) and for OCTN2 (CC vs. GG: OR=1.309, 95% CI 1.078-1.588; CC vs. GG: OR=1.200, 95% CI 1.002-1.438; dominant model OR=1.231, 95% CI 1.036-1.462; recessive model: OR=1.148, 95% CI 1.031-1.279). Significant associations were not found in the East Asian population. CONCLUSIONS: This meta-analysis suggests that OCTN1/2 polymorphisms were associated with susceptibility of CD in the Caucasian population but not in the East Asian population.


BACKGROUND/AIM: Metabolic syndrome (MetS) is a clinical condition characterized by central obesity, elevated triglycerides, low-density lipoproteins, impaired fasting glucose, and hypertension. There is insufficient data on the prevalence of MetS in patients with inflammatory bowel disease (IBD). This study sought to determine the prevalence of MetS in a Turkish cohort of patients with IBD and the association between insulin resistance (IR) and the MetS parameters, in this population. PATIENTS AND METHODS: A total of 177 patients over 18 years of age (62 with Crohn's disease (CD) and 115 with ulcerative colitis (UC)) were enrolled in the study. The presence of at least three criteria of the International Diabetes Federation (IDF) was accepted for the diagnosis of MetS. The Homeostasis Model Assessment (HOMA) was used to determine IR. HOMA values < 1 were considered normal and values > 2.5 indicated a high probability of IR. RESULTS: MetS frequency was higher in patients n=34 (29.5%) with UC than in patients n=11 (17.7%) with CD (P<0.01). MetS was detected in 12 of the 117 patients (10.3%) with IBD, under 45 years of age, and in 33 of 60 patients (55%) over 45 years of age. HOMA value in n=31 patients (27%) with UC was > 2.5. Body mass index, insulin (P<0.001), waist circumference, fasting plasma glucose, leucocyte count (P<0.01), triglycerides, C-reactive protein, and uric acid values (P<0.05) were significantly higher in UC patients with IR than those without IR. CONCLUSION: Frequent occurrence of MS with increasing age in IBD, particularly in UC, showed the importance of early diagnosis and treatment of cardiovascular disease risk factors in the long-term follow-up of these diseases.

BACKGROUND: Hitherto, therapeutic depletion of granulocytes and monocytes by adsorption (GMA) has been associated with significant and insigificant efficacy in patients with ulcerative colitis (UC). Further, the processed blood volume in one GMA session has been fixed at 30,[NON-BREAKING SPACE]mL/min,[NON-BREAKING SPACE]60,[NON-BREAKING SPACE]min, regardless of patients' body weight (BW). We were interested to see the efficacy and safety of GMA when administered in relation to patients' BW. METHODS: Sixty patients were randomly assigned to the routine GMA ([n][NON-BREAKING SPACE]=30) and to GMA adjusted to patients' BW, 60,[NON-BREAKING SPACE]mL/kg ([n][NON-BREAKING SPACE]=30). GMA was done with the Adacolumn, up to 10 sessions over 10,[NON-BREAKING SPACE]weeks. At entry and 1,[NON-BREAKING SPACE]week post last GMA, patients were clinically and endoscopically evaluated. Remission was defined as clinical activity index (CAI) <=4, whereas mucosal remission was defined as endoscopic index (EI) <=3.

RESULTS: In the BW group, the processed volume/session was 3,260,[NON-BREAKING SPACE]!=/[NON-BREAKING SPACE]581 versus 1,800,[NON-BREAKING SPACE]mL in the routine group ([P][NON-BREAKING SPACE]<[NON-BREAKING SPACE]0.001). In the BW group, 25 of 30 patients (83.3%) achieved remission versus 19 of 30 patients (63.3%) in the routine group. The average CAI in the BW group fell from 9.6,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]2.6 to 2.3,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]2.1 versus from 9.1,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]2.4 to 4.0,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]2.1 ( [P][NON-BREAKING SPACE]<[NON-BREAKING SPACE]0.05) in the routine group. Similarly, the EI in the BW group fell from 9.4,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]1.3 to 2.1,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]1.8 to 4.5,[NON-BREAKING SPACE]+/[NON-BREAKING SPACE]2.3 ([P][NON-BREAKING SPACE]<[NON-BREAKING SPACE]0.01). CONCLUSIONS: GMA adjusted to patients' BW and at a vastly greater processed volume produces significantly higher efficacy as compared with the routine GMA protocol. Further, in this study, up to twofold higher processed volume caused no safety concern.


BACKGROUND: Embryonic ectoderm development (EED) protein is involved in multiple cellular protein complexes. EED mediates the repression of gene activity through histone deacetylation, and it may act as a specific regulator of integrin's function. This gene was identified as a candidate gene for the susceptibility to IBD by our previous cDNA microarray analysis. AIM: The present study aimed to validate the expression level of the EED gene in patients with IBD by performing RT-PCR, and we investigated whether the polymorphisms in the EED gene are associated with the susceptibility to UC, and whether a functional EED promoter polymorphism is related to UC. METHODS: Genotype analysis of the EED SNPs was performed by single-base extension analysis. The haplotype frequencies of the EED gene for multiple loci were estimated using the expectation maximization algorithm. The promoter region of the human EED gene, including the g.-1850G>C allele, was isolated by PCR. The amplified PCR products were inserted into the pGL3-basic vector and the luciferase activity was analyzed. RESULTS: The expression level of the EED gene was significantly decreased in both the UC and CD patients and it was significantly higher in the liver and ileum than in the other tissues of the human digestive system. The genotype and allele frequencies of the g.-1850G>C polymorphism of the EED gene in the UC patients were significantly different from those of the healthy controls (p = 0.018 and 0.017, respectively). The luciferase activity assay showed that the promoter activity was decreased about twofold in the construct containing the g.-1850G allele compared to that of the construct containing the g.-1850C allele, which means that the allele G could produce less EED mRNA. CONCLUSIONS: These results suggest that the g.-1850G>C polymorphism in the EED gene might be associated with the susceptibility to UC by the change of the EED expression level.


Probiotics are used for the prevention of necrotizing enterocolitis (NEC) because of their positive effects on modulation of inflammatory response and mucosal barrier function. The aim of this study was to evaluate the role Lactobacillus paracasei in Bell's stage 2 in order to prevent the clinical progression to stage 3. A randomized, controlled clinical trial was approved and started in September 2009; patients were infants weighing from 750 to 15,009 g at birth. The intervention group received probiotic supplementation (L. paracasei) and a control group received only medical standard treatment. The primary outcome was the progression to stage 3 as defined by Bell's modified criteria. After ethical committee approval the study was conducted in three Italian centres and one
Uruguayan centre. Inclusion and exclusion criteria were created and discussed with parents before treatment at present 12 patients were treated with L. paracasei and 24 without. None of study group patients developed a stage 3 NEC; three patients of group 2 had a clinical history of Bell's stage 3 Nec (p<0.05). Oral supplementation of L. paracasei reduced the clinical progression of NEC. It was considered that an improvement in intestinal motility might have contributed to this result. This trial was registered at the Azienda Ospedaliera di Verona (Randomized Controlled Trial).


BACKGROUND: Peroxisome proliferator-activated receptor gamma (PPARgamma), a nuclear receptor, has been implicated playing a role in the development of inflammatory bowel disease (IBD). However, previous studies evaluating the association between the PPARgamma2 Pro12Ala polymorphism and IBD are inconsistent. We performed a meta-analysis to determine whether the PPARgamma2 Pro12Ala mutation was associated with the presence of IBD. METHODS AND FINDINGS: Electronic databases were searched for case-control studies evaluating the association between the Pro12Ala mutation and the presence of IBD. Effects were summarized with the methods recommended by the Cochrane Collaboration. A total of 7 studies including 1002 ulcerative colitis (UC) cases, 1090 Crohns disease (CD) cases and 1983 controls were involved in this meta-analysis. In the overall analysis, no significant association of this polymorphism with UC or CD was found. In the subgroup analyses in different populations, AlaAla genotype seemed to protect the European Caucasian population against the development of CD (Pro vs Ala: OR[HAIR SPACE]=1.135, 95%CI[HAIR SPACE]=[HAIR SPACE]1.000-1.273, P=0.027, Bon[HAIR SPACE]=1.094, 95%CI[HAIR SPACE]=[HAIR SPACE]1.000-1.228, P=0.027). There was no significant association of this polymorphism with UC or CD in the East Asian population and the Turkish population. CONCLUSION: AlaAla genotype may be a protective factor in the European Caucasian population against the development of CD in a recessive way.


OBJECTIVES: Several trials have demonstrated that oral delayed-release mesalazine might be administered once daily. We aimed to conduct a meta-analysis to investigate this. METHODS: A comprehensive and multiple-source literature search was carried out. Only randomized-controlled trials (RCTs) were investigated by comparing a once daily-dosing regime with a divided (twice or thrice daily)-dosing regime of oral delayed-release mesalazine formulations for induction or maintenance of remission in patients with mild-to-moderate ulcerative colitis. The quality of RCTs was assessed using the Jadad scores. Meta-analysis of pooled odds ratios was carried out using Review Manager 5.1. RESULTS: Nine RCTs were finally included. With regard to meta-analyses for induction trials, there were no significant differences for all comparisons between the once daily and the divided groups, including maintenance of just clinical remission (P=0.52) and just endoscopic remission (P=0.23), maintenance of combined clinical and endoscopic remission (P=0.78), and the overall incidence of adverse events (P=0.61). With regard to meta-analyses for maintenance trials, there were also no significant differences for all comparisons between once daily and divided groups, including maintenance of just clinical remission (P=0.73) and just endoscopic remission (P=0.43), maintenance of combined clinical and endoscopic remission (P=0.43), the overall incidence of adverse events (P=0.12) as well as compliance with the prescribed medication (P=0.34). CONCLUSION: The present work showed that oral delayed-release mesalazine administered as a single or a divided dose demonstrated a good safety profile, which was well tolerated and effective as either maintenance or induction treatment. High clinical and/or endoscopic remission rates can be achieved with once-daily dosing.
Zintzaras, E. (2012). "Is there evidence to claim or deny association between variants of the multidrug resistance gene (MDR1 or ABCB1) and inflammatory bowel disease?" *Inflammatory Bowel Diseases* **18**(3): 562-572.

**BACKGROUND:** Inflammatory bowel disease (IBD) is a complex disease with a genetic background. Crohn's disease (CD) and ulcerative colitis (UC) are the two main types of IBD. There is indication that variants in the MDR1 gene are associated with development of IBD. However, the 20 published genetic association studies (GAS) for the three most popular variants in the MDR1 gene (C3435T, G2677T/A, and C1236T) have produced inclusive results. **METHODS:** In order to decrease the uncertainty of pooled risk effects and to explore the trend and stability of the risk effects, a meticulous meta-analysis, including cumulative and recursive cumulative meta-analysis, of the GAS related to the MDR1 gene with susceptibility to IBD was conducted. The risk effects were estimated based on the odds ratio (OR) of the allele contrast and the generalized odds ratio (OR(G)). **RESULTS:** The analysis showed marginal significant association for the C3435T variant in UC: the risk estimate for the allele contrast was OR = 1.11 (1.00-1.22) and OR(G) = 1.12 (1.01-1.27), indicating that a subject with high mutational load has a 12% higher probability of being diseased. The respective cumulative meta-analysis indicated a downward trend of association, as evidence accumulates with the association being significant during the whole published period. The cumulative meta-analysis for the other variants showed lack of any trend of association. However, the recursive cumulative meta-analysis showed that there is no sufficient evidence for denying or claiming an association for all variants. **CONCLUSIONS:** More evidence is needed to draw safe conclusions regarding the association of MDR1 variants and development of IBD. Copyright Copyright 2011 Crohn's & Colitis Foundation of America, Inc.

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