Morphine, Diamorphine and Oxycodone Combinations in Palliative Care: A Compatibility Study

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Background

The issue of Patient Safety Alert 20: Promoting safer use of injectable medicines by the National Patient Safety Agency in March 2007 includes the recommendation that healthcare staff need to have full technical information about stability in solution and compatibility information for commonly used mixtures in specialist areas only. This covers the mixing of injectable medicines in the same syringe [1].

In end of life care, injectable medicines are sometimes combined in order to treat a single symptom, or because multiple symptoms need to be treated simultaneously. It is often found that the oral route of administration is no longer available and an alternative route is required. Continuous subcutaneous infusion (CSCI) is the preferred alternative [2].

CSCI’s are delivered using a syringe driver or pump. There are a number of different syringe drivers or pumps available but this research concentrates on the use of a McKinley T34 Syringe Pump, as presently it is the most popular syringe pump being adopted nationwide.

It is widely known that combining drugs for CSCI could potentially result in interactions between and amongst the different drugs. There is limited, if any, compatibility data available about them. Sources concentrate on physical compatibility data but this cannot rule out chemical incompatibilities within the syringe, which could be contributing to decreased drug concentrations.

Aim

The aim of this study was to obtain chemical compatibility information on the most commonly encountered supportive drugs in end of life care. A database search has identified these as being:

- Cycliczine and haloperidol
- Cycliczine and midazolam
- Levomepromazine and metoclopramide
- Haloperidol and midazolam
- Hyoscine butylbromide and levomepromazine
- Levomepromazine and midazolam
- Metoclopramide and midazolam
- Cycliczine, haloperidol and midazolam

The combinations are administered with an opioid via CSCI and this study concentrates on the opioids morphine hydrochloride and oxycodone hydrochloride.

Methodology

To achieve the aim of the study:

- Analytical methods were developed to separate the individual drug solutions in each combination using High Performance Liquid Chromatography-Diode Array Detection (HPLC-DAD).
- Individual drug solutions were heated at high temperature prior to being analysed by HPLC-DAD to identify possible degradants.
- Syringes were prepared containing the drug combination as close to clinical practice as practically possible.
- A McKinley T34 Syringe Pump was used to simulate infusion of the syringe preparation over a 24hr period.
- Samples were taken at set time points from the administration line and analysed by HPLC-DAD to obtain individual drug concentrations.
- Results assessed to determine whether drug combinations are compatible and stable.

Results

<table>
<thead>
<tr>
<th>Morphine 100mg</th>
<th>Diamorphine 100mg</th>
<th>Oxycodone 50mg</th>
<th>+ Supportive Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ (24h)</td>
<td>✓ (24h)</td>
<td>✓ (24h)</td>
<td>Cycliczine and Haloperidol</td>
</tr>
<tr>
<td>✓ (24h)</td>
<td>✓ (24h)</td>
<td>✓ (24h)</td>
<td>Cycliczine and Midazolam</td>
</tr>
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<td>✓ (24h)</td>
<td>✓ (24h)</td>
<td>✓ (24h)</td>
<td>Levomepromazine and Metoclopramide</td>
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<tr>
<td>✓ (24h)</td>
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<td>Haloperidol and Midazolam</td>
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<tr>
<td>✓ (24h)</td>
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<td>Hyoscine butylbromide and Levomepromazine</td>
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<td>✓ (24h)</td>
<td>✓ (24h)</td>
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<td>Metoclopramide and Midazolam</td>
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<td>✓ (24h)</td>
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<td>✓ (24h)</td>
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</tr>
</tbody>
</table>

* (24h) chemically compatible over 24hrs

Combinations remained clear and free from visible particulate matter and pH remained constant over the 24 hour infusion.

Conclusion

The following have been identified as physically and chemically compatible and stable over 24hrs infusion:

- All eight morphine sulphate supportive drug combinations
- Five diamorphine hydrochloride and six oxycodone hydrochloride supportive drug combinations

This is the first step towards providing technical information required by healthcare staff for the mixing of injectable medicines in the same syringe, a recommendation in Patient Safety Alert 20.

Future Work

To assess the remaining supportive drug combinations with diamorphine hydrochloride and oxycodone hydrochloride for chemical compatibility.

The potential exists to extend the study to include other opioids that are often used in end of life care.

References