Chemical Compatibility/Stability of Alfentanil with Commonly Used Supportive Drug Combinations Administered by Continuous Subcutaneous Infusions for End of Life Care

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\section*{BACKGROUND}

A continuous subcutaneous infusion (CSCI) is an effective method of drug administration that is commonly encountered in palliative medicine.\textsuperscript{11} When the oral route is no longer available, the use of a CSCI is the preferred method of drug administration to maintain symptom control.

The National Patient Safety Agency (NPSA) issued a patient safety alert promoting the safer use of injectable medicines in March 2007.\textsuperscript{12} In order to reduce medication error risks, the NPSA recommended that healthcare staff need to have full technical information about compatibility of commonly used mixtures readily available. In 2008, the Commission on Human Medicine (CHM) made several recommendations to the Medicines and Healthcare products Regulatory Authority, one of which proposed that research should be commissioned to develop authoritative national advice on mixing of medicines to encompass compatibility and stability data.\textsuperscript{13}

Exploration and analysis of common practice in national practice identified 8 drug combinations administered by CSCI comprising alfentanil that lacked compatibility data.\textsuperscript{21}

\section*{AIMS}

To determine the chemical compatibility/stability of alfentanil with other supportive drugs in 8 drug combinations, at minimum and maximum concentrations.

\section*{METHODS}

The chemical compatibility and stability of the 8 combinations (see Table 1) were studied. Drug combinations were prepared in duplicate and attached to a CME T34 syringe pump (Figure 1). Each combination was examined under normal use conditions, i.e. a CSCI was set to run over 24 hours at room temperature/light. Samples were taken from the giving set at four set time points over the 24 hour infusion period (0, 1-3 hours, 4-6 hours and 24 hours). At each time point the appearance of the contents of the syringe and giving set were monitored visually, pH was measured and individual drug concentrations were assayed by high performance liquid chromatography diode array detection (HPLC-DAD). Chromatograms (see Figure 2) were produced for each combination to aid with detection of any degradation. Statistical analysis of the data allowed uncertainty to be calculated.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{Name} & \textbf{Retention Time} & \textbf{Area} & \textbf{Resolution (DAB)} \\
\hline
Alfentanil & 8.65 & 8679025 & 0.00000 \\
Cyclizine & 10.027 & 276369595 & 15.90237 \\
Methylpridol & 20.057 & 13802564 & 15.45916 \\
Midazolam & 21.133 & 276369595 & 15.90237 \\
Methadone & 21.251 & 13802564 & 15.45916 \\
Morphine & 21.351 & 13802564 & 15.45916 \\
Ondansetron & 21.451 & 13802564 & 15.45916 \\
Oxycodon & 21.551 & 13802564 & 15.45916 \\
Vincristine & 21.651 & 13802564 & 15.45916 \\
\hline
\end{tabular}
\caption{Identified drug combinations comprising alfentanil (min/max doses in brackets)}
\end{table}

Seventeen combinations were identified as stable and compatible by HPLC-DAD. These combinations also remained clear and free from visible particulate matter and the pH remained constant over the monitored period. One combination, alfentanil 2mg and cyclizine 150mg, will require additional analysis due to the high level of uncertainty between the two syringes analysed.

\section*{CONCLUSION}

From our work it can be concluded that these 8 commonly encountered drug combinations comprising alfentanil are chemically and physically stable and compatible for infusion over 24hrs. This research contributes to the knowledge that is steadily addressing the recommendations of the NPSA and CHM by providing technical information required by healthcare staff for the mixing of injectable medicines in the same syringe. This information will help to inform local and national policy and practice.

\section*{REFERENCES}


\section*{RESULTS}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{CHE T34}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Example of a chromatogram}
\end{figure}