Dexmedetomidine: admixture compatibility with palliative care drugs

INTRODUCTION

Dexmedetomidine (DXM) is an alpha-2 adrenoreceptor agonist of interest in palliative care.[1 2] It has been conventionally used in intensive care for sedation (with rousability) and refractory neuropathic pain, and ventilator weaning.[3] There is minimal literature in palliative care, with case reports for use in refractory cancer pain, and as a sedative, and retrospective chart analyses of use for sedation in terminal heart failure.[4–6]

End-of-life-care drugs in palliative medicine are often given subcutaneously, with the syringe driver the tool of choice in multiple settings.[7] A syringe driver allows multiple medications in a single syringe, if compatibility permits.[7] Although DXM is well tolerated subcutaneously with minimal side effects,[8] it is unclear whether it can be given along with other medications in a single syringe, which would expand utility. There are laboratory compatibility data in a single site with multiple agents.[9] In our centre, DXM has been used in a pilot clinical trial in a separate syringe driver, and is currently investigated as an alternative to benzodiazepines for terminal sedation. Although anecdotally compatible in admixture with opioids, complex admixtures have not been formally tested.

METHODS

Common admixtures were determined in discussion with nursing and pharmacy staff on the palliative care unit in a regional centre. The most common included an opioid, an anticholinergic, a benzodiazepine and an antiemetic. Standard care includes first-line haloperidol as an antiemetic and hyoscine butylbromide as an anticholinergic, with morphine and hydromorphone the most common opioids.

We performed admixtures of them in two, three and four drug combinations, with DXM replacing the benzodiazepine. This admixture was determined by our pharmacist, clinical nurse educator and the palliative medicine registrar, who is the chief investigator for DXM studies. Doses mixed were determined by ampoule size and our standard practice. DXM dose was determined from trial protocol in development, as 12 μg/kg, but rounded to nearest vial size for test applicability.

Admixtures were compounded by the clinical nurse educator, pharmacist and registrar. Medications were drawn up in individual 20 mL syringes, with normal saline as a diluent up to 18 mL volume; visual and pH testing was then done and repeated after 24 hours. Visual inspection was aided by external light source. After preparation, mixed syringes were securely stored in the hospital pharmacy in a locked cabinet. After repeat observations at 24 hours, all mixtures were securely discarded.

RESULTS

All solutions with DXM were both visually compatible and pH stable at time zero and 24 hours (table 1). No particles were visualised when using a light source. No precipitation was seen either at time of mixture or time of assessment.

DISCUSSION

DXM in common two, three and four drug admixtures, appeared visually and pH stable at combination time and at 24-hour assessment point. This provides some surety for combination in clinical practice, although not robust. Caution should be taken in that the admixtures were tested via visibility and pH only, without formal chemical testing, which may determine other compatibility issues. In addition, the pH test kit used was accurate to the nearest full integer, and possibly some small pH shifts were not observable.

It is common in palliative medicine practice to rely on visual compatibility alone[7] and the tests done accord with clinical practice. This lack of robust evidence is of concern, and more extensive compatibility needed, given that most combinations in palliative

Table 1 Admixtures and compatibility tests at time zero and time 24 hours

Morphine test	M + Dex	M + Dex + Hyo	M + Dex + Halo	M + Dex + Halo + Hyo
Initial visual	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction
Initial pH	5	5	5	5
24 hours visual	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction
24 hours pH	5	5	5	5
Hydromorphone test	**HM + Dex**	**HM + Dex + Hyo**	**HM + Dex + Halo**	**HM + Dex + Halo + Hyo**
Initial visual	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction
Initial pH	5	5	5	5
24 hours visual	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction	Clear, nil reaction
24 hours pH	5	5	5	5

Medications tested included morphine 30 mg (M), hydromorphone 10 mg (HM), haloperidol 2.5 mg (Halo), hysoscine butylbromide 60 mg (Hyo) and dexmedetomidine 800 microg (Dex).

medicine are based on observational rather than laboratory data.[7 10]

DXM tests with other commonly used opioids like fentanyl and methadone, or antiemetics such as metoclopramide and cyclizine, may be warranted, given the developing interest in DXM in palliative medicine.

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