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STERILITY, STABILITY AND POTENCY OF MEDICATIONS ADMINISTERED BY CARERS IN HOME-BASED PALLIATIVE CARE

The Practice

Nurses providing palliative care to people at end-of-life in the community sometimes prepare and leave single doses of medications in a client's refrigerator. The client's carer, who is usually a relative, will administer the injectable medications subcutaneously (SC), as prescribed, in order to alleviate the palliative care client's symptoms. The medications administered in this way can include Morphine, Hydromorphone, Fentanyl, Midazolam, Clonazepam, Haloperidol and Metoclopramide. When less than 0.5 ml of the medication is prescribed, nurses will add 0.5 ml normal saline, as 0.3 ml is retained in the subcutaneous device. The access is called an Intima (subcutaneous butterfly). The syringes are labelled and carers are well informed and prepared to carry out the administration.

What was the problem with this practice?

Although this practice has evolved to be regularly and successfully utilised in the community setting for a number of years, the safety, quality and risks associated with this practice had not been scientifically demonstrated.

What did we do?

During 2006/2007 we undertook research which included:

- Finding out whether other researchers in Australia or overseas had investigated this practice in palliative care;
- Defining sterility, stability and potency of the injectable medications;
- Providing a risk assessment for this practice;
- Making recommendations for community Palliative Care practice and policies.

How did we do it?

We carried out a literature review, investigated the sterility, stability and potency of specified palliative care medications and commissioned a risk assessment of this practice.

Ethical considerations

Ethical approval to conduct interviews with nurses and carers was obtained from the RDNS Ethics Committee. All interviewees were provided with an information sheet about the research and a consent form which indicated, *inter al.*, that the interview would be audio-taped and that they were free to withdraw from the study at any time. All interviewees signed a consent form.

What did we find?

Data Set One: Literature Review

The aim was to review the literature relating to:

- Place of death and issues associated with symptom control and out-of-hours medication management in the home
- Current best practice of injectable medication management used for palliation in the home
- Medications used in palliative care
- Pharmaceutical sterility, potency and stability testing.

During the course of the project, further literature was accessed in relation to sterility and, more broadly, infection control.

For details of the electronic databases used to carry out this search, please refer to the project report.

What did the literature tell us?

All people experiencing life-limiting illness will be faced with decisions about their preferred place of death. Most people prefer to die at home in familiar surroundings (National Council for Palliative Care, 2006; Canadian Hospice Palliative Care Association (CHPCA), 2006; Thomas, 2001; Hughes *et al.*, 2006; Watson *et al.*, 2005); however, there are a range of factors which may work against this actually happening. Statistics indicate that even though most people prefer to die at home, only one quarter actually do (Thomas, 2001; National Hospice and Palliative Care Organization (NHPCO), 2006; Canadian Hospice Palliative Care Association (CHPCA), 2006; Costello, 2001; Watson *et al.*, 2005). One reason for admission to hospital in the last weeks of life is for better pain or symptom management (Watson *et al.*, 2005; Amass, 2006).

The symptoms that commonly occur at end of life may include pain, nausea, fatigue, anorexia, anxiety, gastrointestinal obstruction and weakness (Fielding *et al.*, 2000; West Midlands Palliative Care Physicians, 2003; Watson *et al.*, 2005); Amass *et al.*, 2005). A major challenge in palliative home care is the effective control of symptoms and maintaining the person in a comfortable state. Frequently, the condition of the dying person changes rapidly and this often happens during the night or at the weekends, which can cause distress to the person and their carer, especially when access to health services is limited. Therefore, it can be important that carers have the ability to quickly access and administer medications in the home to provide relief and comfort (Amass *et al.*, 2005; National Advisory Committee on Palliative Care (NACPC), 2001; Australian Government Department of Health and Ageing, 2004; Thomas, 2001; Canadian Hospice Palliative Care Association (CHPCA), 2006; Jones, 2003; Ellershaw *et al.*, 2003; National Institute for Clinical Excellence (NICE), 2004).

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Lee and Headland (2003) have found that there were few references in the literature to carers administering "as required" (prn) medication. They suggest that the idea of lay carer administering medication is a new development in the UK and acknowledge the need for education and support. In Australia, medications for subcutaneous administration are left drawn up by health professionals for lay carers to use as required (Watson *et al.*, 2005). However, in common with other countries, such as the UK, there is little discussion of the feasibility of this practice. At the time of carrying out the review, no protocols or guidelines regarding the practice of storing prefilled syringes of prn medication in the home could be found.

Which Medications are used in Palliative Care?

The drugs commonly used to control symptoms in palliative care include:

- Opioid (e.g. morphine hydrochloride, hydromorphine, fentanyl) for alleviation of pain
- Non-steroidal anti-inflammatory drugs (NSAIDs) (e.g. ibuprofen, naproxen) have anti-inflammatory, analgesic and antipyretic effects
- Corticosteroids (e.g. dexamethasone, methylprednisolone) are useful in treating pain, anorexia, vomiting
- Anti-emetics (e.g. haloperidol, metoclopramide hydrochloride) to alleviate nausea and vomiting
- Anticholinergic drugs (e.g. atropine sulphate, butylhyoscine bromide) to treat terminal bronchial secretions, colic, internal obstruction
- Muscle relaxants (e.g. midazolam) for terminal restlessness, myoclonic jerking, sedation.

(Schrijvers *et al.*, 1998; West Midlands Palliative Care Physicians, 2003; Costello, 2001).

How are medications administered in palliative care?

Most medications are administered orally; however, many people receiving palliative care find swallowing difficult as their condition deteriorates. Intramuscular injections are painful and therefore not appropriate (Jones, 2003). The main alternative to oral administration is the SC route. The advantages of this route are that it is safe, more comfortable and enables easier access. SC administration of medication is well suited to home care. There are two ways of delivering medication subcutaneously:

Bolus: intermittent injections or extra doses of prn medication, which often occurs in conjunction with the use of a syringe driver. e.g. breakthrough pain.

SC infusion: syringe driver pump which delivers a combination of medications slowly and continuously, maintaining a constant level of palliation over a fixed period of time (Kennedy *et al.*, 1999); (Hernandez, 2005).

Syringe drivers are the mainstay of medication administration for symptom control for people who cannot take medication orally; however, they are not effective for breakthrough pain (South Western Staffordshire Primary Care Trust, 2004). To this end, SC medication is prescribed 'as needed', to supplement medications administered via the syringe driver. According to a number of authors, this type of prescribing equates to good practice (Ellershaw *et al.*, 2001; National Institute for Clinical Excellence (NICE), 2004; Australian Government Department of Health and Ageing, 2004).

What about the Sterility, Potency and Stability of Palliative Care Medications drawn up and stored in the Community Setting?

Infection control guidelines deal with matters such as hand washing, personal protective equipment, waste disposal and equipment and supplies (Australian Government Department of Health and Ageing, 2004).

Unlike nurses in the hospital setting, community nurses do not have the same degree of control over their environment (Lawrence, 2005). In order to minimise the risk of infection, nurses should have a good 'aseptic technique', such that the transmission of micro-organisms to wounds or other susceptible sites is minimised or prevented. Hand hygiene is the single most effective measure to prevent healthcare associated infection (Cole, 2007). Alcohol-based hand rubs have excellent anti-microbial efficacy and are an acceptable alternative to hand washing when hands are not badly soiled. In Australia, waste disposal must be carried out in accordance with local and State/Territory regulations (Australian Government Department of Health and Ageing, 2004).

With respect to the stability and potency of drugs commonly used SC in palliative care, there are a number of guidelines and booklets developed by palliative care services, providing comprehensive, definitive information. These publications have been developed as a result of collating data from a wide range of credible sources. Most of these publications relate to drugs used in syringe drivers; however, some publications include bolus delivery (Capital Health *et al.*, 2005; Northern Health and Social Services Board (NHSSB), 2003; West Midlands Palliative Care Physicians, 2003; Back, 2001).

There are a number of publications which provide comprehensive information about a wide range of medications (not specific to palliative care), which may include stability, potency and compatibility data. These resources are intended to assist health professionals in ensuring safe and effective medication therapy. The Australian Medicines Handbook (Rossi, 2006), Australian Injectable Drugs Handbook (The Society of Hospital Pharmacists of Australia, 2005) and The Handbook of Injectable Drugs (Trissel, 2005) are examples.

What was our conclusion?

Limited research has been reported about the practice of the drawing up of syringes of medications for SC administration by carers to provide symptom relief in the community setting and the appropriateness of such a practice. There is a need to have reliable information about the sterility, stability and potency of the drugs commonly being prescribed. This information needs to be collated and presented in a usable format for health professionals. By so doing, the potential of palliative care to be provided in the community setting will be maximised, the person receiving palliative care will be safeguarded and health professionals and carers will be secure in the knowledge of the appropriateness of their care.

Data Set Two: The sterility, stability and potency of palliative care medications

The research team assembled the following list of

medications widely used in palliative care in the Adelaide metropolitan area and a rural district adjacent to Adelaide:

Narcotics • Morphine • Hydromorphone • Methadone • Fenantyl	Anti-emetics • Metoclopramide • Haloperidol
Sedatives • Levomepromazine • Clonazepam • Midazolam	Other drugs • Ranitidine • Octreotide • Hyoscine • Atropine • Dexamethasone • Ketamine

What did the sterility testing reveal?

a. Clean technique

The clean technique of nurses was tested in the following manner:

- Twenty four vials of tryptone soya broth were supplied by Ms Anna Covino, Women's and Children's Hospital (WCH), Adelaide.
- Nurses from RDNS Southern Division drew up 1ml of media out of each vial, which was then returned to the vial. Without prompting from members of the project team present, the nurses used the alcohol-based hand cleaner, Aqium, before drawing up the media.
- Vials were taken to the WCH for microbial testing.

The result was that no bacterial growth was found.

b. Samples of drawn up medications – "test syringes"

Using medications no longer required by carers, 2 "test syringes" of each of the following medications were drawn up and stored in an opaque container in a domestic refrigerator for 28 days:

- Haloperidol 5mg/ml
- Midazolam 5 mg/ml
- Dexamethasone Sod Phos 8mg/ml
- Buscopan 20 mg/ml
- Atropine 600 ug/ml
- Maxolon 10mg/2ml
- Clonazepam 1mg/ml
- Morphine.

The temperature of the refrigerator was monitored during this time and varied by 5°C.

The syringes and intact ampoules with the same batch numbers were then sent to Silliker Microtech, Sydney, New South Wales, for analysis of levels of microbial contaminants. Analysis of the "test" drugs indicated that no aerobic bacteria, yeast or mould were detected in any product after storage in syringes for up to 28 days. *For more details about the nature of the testing carried out, please refer to the final project report.*

What is known about the stability and potency of the identified medications?

Stability data relating to the identified medications in polypropylene syringes is summarised in Table 1. The potency of all medications was maintained beyond 7 days.

Table 1: Summary of stability and potency data of medications in polypropylene syringes (Trissel, 2005)

Drug	*Storage Temp*	*Presence of Light*
Atropine	*No data*	
Dexamethasone	Refrig/RT	*not mentioned*
Fentanyl	Refrig/RT	yes
Haloperidol	*No data*	
Hydromorphone	Refrig/RT	no
Ketamine	RT	*not mentioned*
Methadone	*No data*	
Metoclopramide	Refrig/RT	*not mentioned*
Midazolam	RT	no
Morphine Sulph	RT	no
Octreotide	Refrig	no
Rantidine	Refrig	*not mentioned*
Clonazepam	*No data*	
Hyoscine	*No data*	
Levomepromazine	*No data*	

As no data could be located relating to the stability and potency of a number of medications in polypropylene syringes, stability testing of the following medications drawn up and stored in polypropylene syringes was undertaken by Forensic Science SA: Hyoscine Butylbromide, Atropine, Levomepromazine, Haloperidol and Methadone. Syringes were stored under refrigeration (between 3-5°C) and in the absence of light. Samples were analysed using Gas Chromatography and it was concluded that there was no observable decrease in concentration of these pharmaceutical preparations. However, due to the variability in the average relative percentage concentrations for Atropine and Hyoscine, Associate Professor Robert Milne, School of Pharmacy and Medical Sciences, University of South Australia, recommended that further testing be carried out on these two medications in the future. *Please refer to the project report for more detail about the testing carried out.*

What was the outcome of the risk assessment?

A risk assessment of the process, using the RDNS Multiple Risk Assessment Tool, was carried out. The outcome of the assessment was that the training and education of carers, in conjunction with the testing of nurses' aseptic (clean) technique and the syringes stored for 28 days, has reduced the risk of this practice in the community to a low and acceptable level.

What were the limitations of this study?

The results of this study are limited by:

- Findings of the literature review are potentially limited by the search terms used and databases accessed.
- Interviews carried out with nurses and carers were in one geographical location of Australia and findings may not be replicated in other Australian states or countries.

- Sterility testing:
  - ⇒ Clean technique of nurses in one location was assessed. Findings may be different if nurses in other locations were tested.
  - ⇒ Testing was only carried out on one batch of syringes drawn up and stored in one domestic refrigerator. Test results may be different if carried out on syringes drawn up in a variety of locations at different times of the year.

What was our conclusion?

The practice of drawing up and leaving medications in syringes, for SC administration by carers to provide responsive to symptomatic relief for people in the terminal phase of their condition, has been shown to be feasible by demonstration of the sterility, stability and potency of the majority of medications.

What recommendations did we make?

On the basis of the findings of this research, the recommendations for community nursing practice included:

- *Sterility testing:*
  - ⇒ With respect to the practice within RDNS, that the findings of this research be referred to RDNS Risk Management Unit to make a decision as to the ongoing testing of medications stored in clients' refrigerators. Medications to be considered in this assessment should include those used in palliative care and other conditions, eg, insulin.
- *Stability of Atropine and Hyoscine:*
  - ⇒ Further testing of stability of atropine and hyoscine in polypropylene syringes to be carried out.
  - ⇒ Polypropylene syringes containing atropine and hyoscine should be prepared for immediate use only and not prepared and stored for later administration.
- *Medication storage:*
  - ⇒ Drawn up syringes to be stored in opaque containers in clients' refrigerators for a period of no longer than 7 days.
  - ⇒ Bulk medications to be stored securely in a cool cupboard.
- *Education/resources:*
  - ⇒ Work instruction on the drawing up of medications and storage in clients' homes to be developed.
  - ⇒ Information leaflet to be produced for nurses about storage recommendations for medications commonly used in their palliative care practice.

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