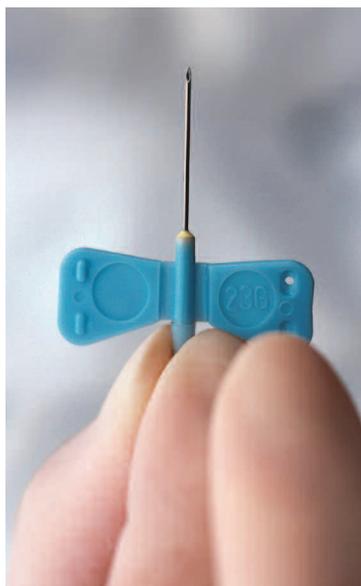


Continuous Subcutaneous Infusion: An Efficacious, Cost-Effective Analgesia Alternative at the End of Life

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Pain is an unpleasant, subjective, multidimensional sensory and emotional experience affecting the majority of children and adults with cancer and other diseases at the end of life (Hewitt, Goldman, Collins, Childs, & Hain, 2008; Middleton, Lyle, & Berger, 1996). The majority (75%) of those in the terminal phase of disease have unrelieved pain, with some requiring palliative sedation to control pain symptoms (Ferrell & Coyle, 2006). The negative consequences of uncontrolled pain include physical, psychological, social, and spiritual distress, which have a negative impact on quality of life (American Cancer Society, 2004; Easley & Elliot, 2001; Hewitt et al., 2008).

Given the high incidence of pain and the barriers precluding appropriate treatment or response, several organizations have identified standards, guidelines, and pain control priorities. In 2004, the National Consensus Project for Quality Palliative Care published Clinical Practice Guidelines for Palliative Care mandating that pain, symptoms, and treatment side effects be managed using best practices. Spiritual, religious, and existential aspects of care also are addressed (National Consensus Project,



2004). In 2007, the National Quality Forum published a set of evidence-based practices for palliative care (National Quality Forum, 2007).

The American Nurses Association (1991) reports that patients often do not fear death as much as the process of dying secondary to uncontrolled pain:

Nurses should not hesitate to use full and effective doses of pain medication for the proper management of pain in the dying patient. The increasing titration of medication to achieve adequate symptom control, even at the expense of life, thus

hastening death secondarily, is ethically justified.

The unintended outcome (i.e., death) after a good intention (i.e., administering an opioid to relieve pain) is known as the “double effect.” Laws protect medical professionals who follow this principle and do not intentionally plan to hasten death.

Best practice mandates the use of the least invasive route for analgesia delivery to achieve optimal pain control. Changes at the end of life often preclude oral administration of analgesia. Subcutaneous (SQ) analgesia infusions were first introduced in England in 1979 and in the United States during the 1980s (Anderson & Shreve, 2004; Storey, Hill, St. Louis, & Tarver, 1990). Continuous SQ infusion (CSI) is shown to be just as effective as intravenous (IV) therapy, more cost effective, and safe as an option for home care delivery (Bruera et al., 1988; Ferris et al., 1991).

Pain Assessment

A thorough assessment must be performed to identify the type of pain and to rule out non-physical distress, which can cause or contribute to pain. Inaccurate assessment can result in a subtherapeutic response from analgesics or adjuvant

medications. The nurse should assess a patient's psychological, social, and spiritual concerns in addition to a detailed pain history so a comprehensive and holistic plan of care can be implemented (Mehta & Chan, 2008).

Providing medications to relieve nonphysical distress can result in paradoxical effects that can exacerbate the individual's distress. Part of the pain assessment includes recognizing, acknowledging, and addressing common barriers to adequate pain management and myths about such management. Pathophysiologic changes occur as pain moves from an acute to a chronic phase. During this time, behaviors and emotions may not be as pronounced as they were during the acute phase, leading the clinician to question the validity of the patient's pain report. Best practice requires that the nurse accept the patient's report of pain, further explore disparities between pain rating and behaviors, and treat the patient holistically as opposed to relying only on a number scale report.

Barriers to Effective Pain Management

Many barriers exist among patients, among healthcare providers, or at a systems level that impede successful pain management (Box 1). The nurse should be aware of these barriers and acknowledge them so patient and caregiver education can be provided to reduce the fears that impede optimal analgesia therapy. The nurse also must respect personal autonomy and cultural or religious beliefs that prevent optimal pain management.

Medication Routes

Best practice recommends using the least invasive route possible to achieve optimal pain control (Anderson & Shreve, 2004). Some patients, however, are unable to swallow or may have gastrointestinal motility issues affecting absorption. The second route of choice, the rectum, often is viewed negatively by caregivers and patients.

The CSI route is a safe option that is just as effective as IV delivery and less costly. It has a lower incidence of infection than IV delivery (Anderson & Shreve, 2004). United States hospice organizations report that 73% to 75% of organizations use CSI for their patients, with morphine sulfate being the first choice for cancer pain and the most commonly prescribed medication (97%) (Anderson & Shreve, 2004; Hernon, 2001; Hunt, Fazekas, Thorne, & Brooksbank, 1999; Paix et al., 1995).

Morphine correctly titrated provides symptom relief from pain and dyspnea without causing respiratory depression (Weinstein, Arnold, & Weissman, 2006). Blood levels for CSI infusions are comparable with those for IV infusions, even for patients who are cachectic, febrile, or hypotensive. Serum levels of morphine were found to be equivalent for the IV and CSI routes (Coyle, Cherny, & Portenoy, 1994; Waldman, Eason, Rambohul, & Hanson, 1984, Weissman, 2005). Continuous infusions often are preferred over intermittent injections because they maintain steady drug levels and prevent a bolus effect, which causes nausea, sedation, and increased breakthrough pain med-

ication requirements (Watanabe, Pereira, Tarumi, Hanson, & Bruera, 2008).

Anatomy of Subcutaneous Tissue

The subcutaneous tissue is located below the dermis. It consists of large blood vessels, nerves, and fat-filled cells called adipose cells (McCance & Huether, 2006). The adipose cells are attached loosely to muscles, bones, and connective tissue to facilitate movement of the skin.

The amount of subcutaneous tissue varies from person to person and often diminishes with disease progression. No significant barriers to absorption exist. Medications delivered subcutaneously easily enter the bloodstream by passing through the spaces between cells of the capillary wall. In contrast, oral medications must first be metabolized by the liver (the primary organ of drug metabolism) before they reach the systemic circulation. Blood flow and drug solubility are the major determinants of how fast absorption takes place (Lehne, 2007).

Research on the Use and Efficacy of CSI Infusions

Limited studies have investigated the efficacy and use of CSI opioid infusions at the end of life (Anderson & Shreve, 2004). Many studies have very limited sample sizes, preventing generalization of findings to larger populations. Existing studies, however, do show that CSIs have the same analgesic affect as IVs and that they prevent the peaks and troughs associated with doses adminis-

Box 1. Barriers to Effective Pain Management

- Fear of addiction
- Concern about side effects (i.e., fatigue, constipation)
- Fear of becoming tolerant to analgesics with lessening effects at end of life
- Fear that pain is a sign of disease progression
- Reluctance to report pain (perception that reporting pain makes you a “bad” patient or distracts physician from focusing on curing illness)
- Perception that IV route is more effective than oral or SQ route
- Lack of knowledge about pain management (assessment and medications)
- Perception that infants, children, and the elderly have a decreased pain response
- Perception that behaviors, not patient report, is the best indicator of pain
- Perception that respiratory depression is a common side effect of opioids and warrants decreased dosing
- Poor access to or availability of pain specialists
- Inadequate insurance reimbursement
- Fear of incarceration due to controlled substances regulations
- Fear of litigation due to untoward outcomes

(American Cancer Society, 2004; Easley & Elliot, 2001; McCaffery & Pasero, 1999)

tered as needed (PRN) (Anderson & Shreve, 2004; Koshy, Kuriakose, Sebastian, & Koshy, 2005; Urquhart, Klapp, & White, 1988; Walsh, Perin, & McIver, 2006).

In the study of Bruera et al. (1998), 94% of the patients preferred CSI to their previous analgesia therapy, no serious toxicities were identified, and

no differences were found between morphine and hydromorphone in terms of pain control or side effects. Doyle, Morton, and McNicol's (1994) study of children receiving SQ or IV analgesia after appendectomy demonstrated that the children receiving the SQ analgesia required less morphine and had a significantly

greater percentage of valid bolus demands than those receiving IV morphine. The study of Drexel et al. (1989) showed no respiratory depression or sedation with the use of CSI. The study of Kalso, Heiskanen, Rantio, Rosenberg, and Vainio (1996) identified significantly fewer nightmares with SQ administration than with oral administration of morphine.

Morphine is considered the gold standard for CSI infusions. Hydromorphone is the opioid of choice when higher doses are required because it is more concentrated and allows for lower infusion rates required by SCI (Bruera, MacEachern, Macmillan, Miller, & Hanson, 1993; Miller, McCarthy, O'Boyle, & Kearney, 1999; Moulin, Kreeft, Murray-Parsons, & Bouquillon, 1991). Methadone, fentanyl, and ketorolac also are used (Hughes, Wilcock, & Corcoran, 1997). Methadone is shown to result in a higher incidence of skin irritation (Centeno & Vara, 2005; Mathew & Storey, 1999). Enhancement of CSI therapy can be achieved by using portable pumps that are easily programmed and have alarms, staff and caregiver education, ongoing pain assessment, and collaboration with the interdisciplinary team (Anderson & Shreve, 2004).

Site Selection and Preparation

Subcutaneous sites are selected based on the presence of adequate adipose tissue. Preference is given to sites that will interfere the least with the patient's mobility and are not easily accessible by patients who may tug at the catheter

causing accidental de-access (Anderson & Shreve, 2004; Infusion Nurses Society, 2006; McCaffery & Pasero, 1999; Weissman, 2005). Appropriate SQ sites include the abdomen, thigh, buttocks, and subclavicular areas.

Site preparation includes cleansing of the skin with an approved disinfectant—typically povidone-iodine or 2% chlorhexidine—for 30 seconds. After the site has fully dried, a 25- or 27-gauge subcutaneous needle or angiocatheter is inserted into the SQ tissue at a 45° to 60° angle (Anderson & Shreve, 2004). The needle of some needle sets is attached to the butterfly at a right angle, which results in a 90° angle insertion. An aspiration attempt should be completed to confirm that no blood return exists. If there is a blood return, the needle or catheter should be withdrawn slightly and rechecked for blood aspirate. The needle or catheter then is secured with an occlusive dressing.

Sites typically are rotated every 3 to 5 days. Some studies have reported success using a 7-day site rotation. Infusion rates of 3 to 5 mL/hour generally are well tolerated (Coyle et al., 1994; Infusion Nurses Society, 2006; Weissman, 2005). One study reported success with 5 to 7 mL/hour (Nelson, Glare, Walsh, & Groh, 1997).

Common side effects include injection-site irritation, which can be treated successfully with site rotation. Patients and caregivers should be taught to assess the SQ site twice daily and report leakage, pain, erythema, ecchymosis, burning, or swelling to the home care agency.

Case Study

Mary Jane is a 27-year-old married woman who received a diagnosis of metastatic pancreatic cancer 2 months ago and recently enrolled in a local hospice program. She has 3 small children (2, 5, and 7 years of age). Intermittent intractable vomiting prevents her from taking oral medications. She has no drug allergies or other diseases.

Mary Jane realizes that her prognosis is poor and her life span short. She wants to have her pain controlled so she has minimal fatigue and can play with her children. She rates her abdominal pain at 7 or 8 out of 10 with activity and 5 out of 10 at rest. She is getting intermittent relief from oral MS Contin 300 mg every 12 hours. She refuses to take breakthrough medications secondary to fatigue, constipation, and occasional emesis. She is having a semi-hard bowel movement every 5 to 7 days.

Mary Jane currently takes 2 Senna S twice daily. She refuses to take rectal suppositories or enemas and does not allow a rectal exam. She has no IV access and is dehydrated.

During your assessment, you identify Mary Jane's concern that her children will not remember her as they grow up. She also reveals that she was raised as a Catholic but has not practiced her faith for the past 5 years. She fears what will happen after her death and questions if she has made a difference in the world.

You help her to identify special memory gifts that she can prepare for her children (e.g., videos, letters, pictures) so they will remember her after

she has died. You identify that she is no longer affiliated with a specific Catholic church and offer visits from the hospice chaplain to discuss her spiritual concerns. You discuss the options of antiemetics, alteration of her current bowel regimen, and the use SQ analgesia instead of oral medications.

You teach Mary Jane and her husband that pain can be exacerbated if bowel function is not maintained, if oral medications are not absorbed given recurrent emesis, or if non-physical forms of distress are not addressed. You also educate them on the CSI route of analgesia administration and the use of stimulants if fatigue continues to be an issue. You listen to Mary Jane's fears that the pain medication will not be as effective as she nears death and that she will be a burden to her husband as the pain and other side effects become unmanageable.

Grateful for the therapeutic presence and education, Mary Jane agrees to the proposed interventions. You identify that she currently is using a high dose of morphine, requiring increasing amounts to achieve pain control. You know that this may limit the amount of the hourly infusion you can give via CSI. You plan to evaluate her current medication usage and determine her CSI infusion needs, which include the possibility of switching to hydromorphone in addition to adjusting her bowel regimen before calling the physician for orders.

Calculation of Dose

Morphine and hydromorphone are the 2 most commonly prescribed SQ analgesics. Morphine

Box 2. Converting From an Oral Opioid to a Different SQ Opioid

Step 1. Determine current 24-hour dose of oral opioids being used.

- Your patient currently is taking Morphine extended-release tablets 300 mg PO every 12 hours. This equals 600 mg oral morphine over 24 hours.

Step 2. Convert the 24-hour oral dose of morphine to the parenteral dose. (Note: The IV/SQ morphine dose is equivalent to 1/3 of the oral morphine dose.)

- Morphine 600 mg PO = morphine 200 mg IV/SQ over 24 hours

Step 3. Convert the 24-hour opioid dose to the new opioid dose if switching to a new opioid.

- Parenteral hydromorphone is 1/6 the parenteral morphine dose.
- Morphine 200 mg IV/SQ = hydromorphone 33 mg IV/SQ over 24 hours

Step 4. Decrease the new opioid dose by approximately 30-50% to avoid incomplete cross tolerance.

- Hydromorphone 33 mg x 30% = 10 mg. Start hydromorphone at 23 mg SQ (33 mg – 10 mg) over 24 hours.

Step 5. Divide the 24-hour opioid dose by 24 to determine hourly dose.

- Hydromorphone 23 mg divided by 24 = 1.0 mg/hour starting dose.

Step 6. Determine bolus doses for breakthrough pain. (Note: Boluses usually are 50-100% of the hourly dose and are given every 10 to 15 minutes.)

- 50% of 1.0 mg/hour equals 0.5 mg every 15 minutes.
- Hydromorphone used at end of life is usually concentrated between 5-10 mg/mL depending on dosage requirements. Based on a concentration of 10 mg/mL, her CSI basal infusion rate would be 2.3 mL/hour.

Step 7. Assess pain response to current dose. The goal is to have a pain rating of 3 or less on a 0 to 10 scale.

Step 8. Assess for untoward side effects. Adjust the basal or bolus rates as required for new-onset respiratory depression or uncontrolled nausea.

Step 9. Adjust the basal and bolus rates every 8 hours if pain or dyspnea is not controlled.

(Anderson & Shreve, 2004; Storey et al., 1990)

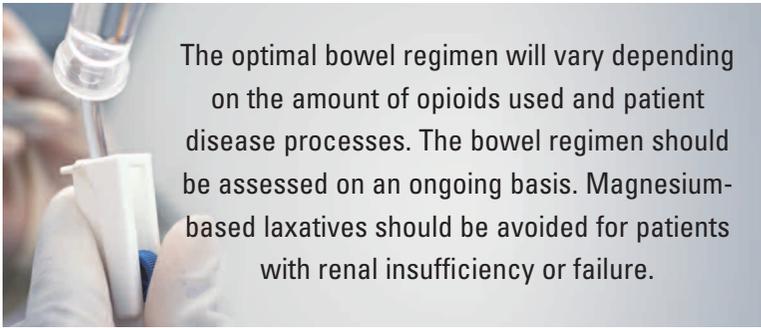
is used for low opioid requirements, whereas hydromorphone is used for higher opioid dose requirements because it is more concentrated, allowing for the lower infusion rates required for SCI. Continuous SQ infusion dosages of morphine are considered equianalgesic to IV dosages (Nelson et al., 1997).

An example of dosage calculation based on the patient in the case study is outlined in Box 2. In this case, the patient will be converted from morphine to hydromorphone. Due to the higher doses of oral morphine she currently is taking, the CSI infusion rate would exceed the recommendation of 3 to 5 mL per hour. However, in converting to a new opioid, it is recommended to reduce the new opioid dose by 30% to 50% to prevent incomplete cross tolerance such as nausea or sedation seen in opioid-naïve patients (Anderson & Shreve, 2004).

Adjunctive Bowel Regimen Therapy

Opioids cause constipation, which is a persistent side effect due to the slowing of bowel motility. The goal is for patients to have a soft bowel movement every 2 to 3 days. Scheduling a bowel stimulant plus a stool softener (i.e., docusate plus senna) often provides the best results. Starting doses should be 1 tablet twice daily, with a range up to 1 to 4 tablets twice daily.

Medications in addition to this regimen should be considered if optimal bowel function is not achieved. These can include 2 to 3 tablets of bisacodyl taken orally at bedtime, a 10-mg bisacodyl rectal suppository at bedtime, and milk of magnesia 30 mL 1 to 2 times daily. If these ad-



The optimal bowel regimen will vary depending on the amount of opioids used and patient disease processes. The bowel regimen should be assessed on an ongoing basis. Magnesium-based laxatives should be avoided for patients with renal insufficiency or failure.

ditional medications do not aid regular bowel movements, the nurse should perform a rectal check to rule out impaction and remove the stool if possible. Additional medications that should be evaluated include 30 to 60 mL of lactulose taken orally twice daily, 8 ounces of magnesium citrate taken orally, or a phosphate enema (i.e., Fleet).

Some patients, however, are unable to swallow these medications or do not achieve optimal bowel functioning with this regimen. In April 2008, the Food and Drug Administration (FDA) approved the use of methylnaltrexone bromide (Relistor) for opioid-induced constipation (FDA, 2008). It can be used alone or in conjunction with other bowel medications.

Methylnaltrexone bromide is a peripheral opioid antagonist and a derivative of naltrexone. It has a methyl group added at the nitrogen ring, which makes it water soluble rather than lipid soluble, thus diminishing its ability to cross the blood-brain barrier. This prevents the drug from reversing analgesia effects because it does not operate on the centrally located receptors. One randomized, double-blind study found that the median time to laxation (successful passage of a bowel movement) was 1.26 hours for patients receiving SQ Relistor injections of 5 mg or

more every other day (Portenoy et al., 2008). The most common side effect was mild abdominal pain. Relistor comes in a 12.5-mg vial, with retail prices averaging from \$100 to \$150.

Another peripheral opioid antagonist—pegylated, modified naloxone (PEG-naloxol)—currently is in phase 2 testing (Thomas, Cooney, & Slatkin, 2008). Additional research is needed to identify which laxatives best synergize peripheral opioid antagonists.

The optimal bowel regimen will vary depending on the amount of opioids used and patient disease processes. The bowel regimen should be assessed on an ongoing basis. Magnesium-based laxatives should be avoided for patients with renal insufficiency or failure.

Case Summary Continued

You determine that Mary Jane most likely needs a change of opioid from morphine to hydromorphone given her current morphine needs. You call the physician and discuss her spiritual and emotional distress and the proposed interventions, her current oral morphine dose, your proposed hydromorphone basal dose of 0.9 mg/hour with a 0.5-mg bolus every 15 minutes PRN for breakthrough pain, and your proposed increase of 4

Senna S twice daily given the patient refuses to use any rectal medications or other bowel medications considering that she has thrown up when taking liquid medications in the past. The physician agrees with your recommendations and faxes an order to the pharmacy to begin the CSI infusion today.

You plan a visit for later in the day to begin the CSI infusion and to educate Mary Jane and her husband on assessing the SQ site, side effects of the therapy, use of the portable pump, and changes to the bowel regimen. Mary Jane's husband states that he wants to learn how to change the SQ needle should it become dislodged given activity with the children. Mary Jane does not want to participate in the direct care of the CSI infusion but is willing to have her husband render the care. You contact the hospice chaplain, who will meet with the patient tomorrow. The care plan is updated.

Summary

Many children and adults who still have uncontrolled pain at the end of life. National and global organizations have made pain management a moral imperative (Ferrell, 2007; World Health Organization, 2008). A thorough pain assessment includes assessing and addressing physical, psychological, spiritual, or social distress. Such assessment is required to ensure adequate pain control. Nurses are legally protected by the principle of "double effect," which states that no fault can result from an untoward outcome that results from an intended good.

Studies show that CSIs are as efficacious as IVs, less ex-

pensive than IVs, well tolerated by patients, safe, and a viable option to be considered for the treatment of pain at the end of life in both the hospital and home setting (Crane, 1994; Letizia, Shenk, & Jones, 1999). Future research should explore the efficacy of other SQ medications (e.g., antiemetics, anti-anxiety medications) and their affect on sleep disturbance at the end of life (Bottomley & Hanks, 1990; Dawson, Brockbank, Carr, & Barrett, 1999). ■

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