TWO BASIC PRINCIPLES of providing effective pain management are preventing pain and maintaining a pain rating that allows the patient to accomplish functional or quality-of-life goals with relative ease. These may require that the mainstay analgesic be administered on a scheduled around-the-clock (ATC) basis, rather than “as needed” (PRN) to maintain stable analgesic blood levels. ATC dosing regimens are designed to control baseline pain, defined as the pain the patient reports as being the average pain intensity experienced for 12 hours or more during a 24-hour period. In other words, ATC dosing should be used when pain itself is ATC (continuous) or present for 12 or more hours each day. Many types of persistent (chronic) cancer and noncancer pain are continuous, and most postoperative pain is continuous for at least the first 24 hours after surgery.

The use of continuous analgesia prevents the undertreatment of pain in patients who are hesitant to request pain medication and eliminates delays that patients encounter waiting for caregivers to prepare and administer pain medication. Another benefit is that patients have been shown to be more adherent to their analgesic regimen when analgesics are prescribed ATC. A five-week study of outpatient oncology patients with pain who kept a daily diary to record level of pain and analgesic intake showed that overall adherence rates for those who took their analgesics ATC ranged from 84.5% to 90.8% compared with 22.2% to 26.6% in those who took them PRN. The researchers pointed out that one might speculate that the reason for lower adherence rates for the PRN regimen was because those patients were experiencing less pain and therefore needed fewer analgesics; however, there were no significant differences in the percentage of patients who reported severe pain (numerical pain rating ≥7) in the ATC compared with the PRN group.

ATC dosing for continuous pain may be accompanied by provision of additional analgesic doses (called breakthrough doses, supplemental doses, or rescue doses) as needed to relieve pain that exceeds, or breaks through, the ongoing pain. For example, when analgesia for persistent cancer pain is provided orally, ATC dosing often is accomplished with a combination of modified-release opioid given at scheduled times, with breakthrough doses of short-acting opioid given if pain breaks through. When invasive routes are used to manage pain, such as refractory cancer pain or after surgery, a continuous infusion with PCA boluses or clinician-administered supplemental doses accomplishes the same objectives as this oral approach. Caution is recommended when using continuous infusions (basal rates) with PCA in opioid-naïve individuals; rather than routinely initiating therapy, basal rates are often added postoperatively if the patient is unable to sleep or rest adequately because of pain.

Research on ATC Dosing

There is surprisingly little research on the use of ATC analgesic dosing. An early crossover study showed that scheduled ATC dosing of analgesics improved pain relief and mood level compared with on-demand PRN dosing in patients with persistent noncancer pain. A more recent study of medical inpatients with pain from a variety of origins compared ATC scheduled opioid doses with PRN opioid doses and found that those who received ATC doses had lower pain intensity ratings. As might be expected, a significantly greater percentage of the prescribed opioid was administered when it was given ATC (70.8%) compared with PRN (38%); however, there were no differences in adverse effects between the two groups. An observational, prospective study administered ATC oral short-acting morphine to patients after orthopedic surgery, and reported average pain scores were 2.4 at rest and 4.0 during movement in bed. Nausea and vomiting, the most common adverse effects, were reported by 22%, and no one required naloxone.

Other research has shown conflicting results. A study of outpatients with pain from bone metastases found no significant differences in average, least, or worst-pain intensity in patients taking ATC or PRN opioids, but...
significantly higher opioid prescriptions and intake (12.4 times more) were reported in patients who took ATC opioids. The researchers noted that their findings challenge the accepted principle of treating continuous pain with ATC analgesics but offered a number of possible explanations. These included that the opioid analgesic regimens may not have been effective for the type of pain the patients had (bone pain), analgesic doses were not titrated to optimal effect, and the possibility that comparisons were difficult because the two groups were not receiving the same analgesics (PRN received short-acting opioids and ATC received long-acting opioids). Another study randomized children to receive ATC or PRN acetaminophen plus codeine after tonsillectomy and found no differences in pain intensity ratings or pain relief scores. Both groups experienced moderate to severe pain, and similar to the previous study, more analgesic (two times more) was consumed by those in the ATC group. There were no differences in adverse effects, such as nausea and vomiting, sedation, and dizziness, which were described as moderate to severe.

These studies suggest the need for more research evaluating the best method for analgesic dose administration in a variety of populations and for a variety of types of pain. It is important that future research includes the effect of dosing regimens on functional outcomes as well as pain relief. Until research proves otherwise, prevention of the recurrence of pain with scheduled ATC dosing is recommended for continuous types of pain.

Awakening Patients for Analgesic Administration

Nurses often wonder whether patients taking ATC short-acting opioids should be awakened and given pain medication and whether they should teach patients in the home setting to wake themselves during their normal sleep time to take their pain medications to keep pain under control. There is very little research guiding this practice, and none could be found in opioid-naïve patients with acute pain. The consensus expert opinion of the European Association for Palliative Care (EAPC) regarding palliative care patients with moderate to severe pain who are taking short-acting (not modified-release) opioids is to give a double dose of the short-acting opioid at bedtime, rather than a single dose, and awaken the patient for a second dose four hours later. This is based on the assumption that doubling the dose will prolong the duration of analgesia long enough to prevent awakening with pain.

Some research on the efficacy of double dosing versus usual dosing has been done in patients with cancer pain. A double-blind, randomized, crossover study that compared the two methods found that average pain, strongest night pain, and sleep quality were slightly better in patients who took a double dose compared with those who took a single dose, but the difference was not clinically significant. The researchers suggested that the slight difference may have been because of initial higher exposure to morphine’s metabolite M6G, which is a potent analgesic. An earlier prospective study of palliative care patients found all of the pain scores were worse in patients who took a double dose of opioid compared with those who took a single dose at bedtime followed by another dose four hours later. Further, those in the double-dose group required more breakthrough analgesia and experienced more adverse effects.

Double doses of opioids should not be given to opioid-naïve patients, but outpatients who are opioid-tolerant and have persistent pain can be told to try double dosing and usual dosing, as described before, to see which works best to keep their pain under control. Alternatively, patients taking short-acting opioids can be switched to a modified-release formulation in an effort to improve sleep at night.

Both opioid-naïve and opioid-tolerant patients with continuous pain in the hospital setting after surgery should be awakened to take their pain medication. Awakening postoperative patients with moderate-to-severe pain to take their pain medication is especially important during the first 24 to 48 hours of therapy to keep pain under control. Patients should be told that this helps to avoid waking with severe pain and that if their pain is well controlled, they are more likely to go back to sleep quickly. A sedation and respiratory status assessment should be conducted before administration. The patient can transition gradually to PRN dosing and sleeping during the night as pain resolves.

Breakthrough Pain

Breakthrough pain (sometimes called “pain flare,” “episodic pain,” or “transient pain”) is defined as a transitory exacerbation of pain in a patient who has relatively stable and adequately controlled baseline pain. The intensity of pain is sometimes included in the definition of breakthrough pain, ie, a transient increase in pain to greater than moderate intensity occurring on a baseline pain of moderate intensity or less.

Like its definition, there is variation in the description of breakthrough pain. Some describe it as occurring spontaneously (not related to activity), rapidly increasing to a high intensity level, and having a short duration (30-45 minutes). Others describe subtypes of breakthrough pain, noting that it can have a sudden or gradual onset and can be brief or prolonged; some episodes are spontaneous and others are associated with an identifiable precipitant. When breakthrough pain is brief and precipitated by a voluntary action, such as movement, it is referred to as incident pain. Another subtype, idiopathic pain, is
not associated with a known cause and often has a longer duration than incident pain. **End-of-dose failure**, the last of the subtypes, is characterized by a return of pain before the next analgesic dose is due. The occurrence of increased pain at the end of the scheduled dosing period suggests a need to maintain a higher plasma drug concentration throughout the dosing interval. In these cases, the dose of the scheduled analgesic should be increased, or in some patients the interval between doses should be shortened, which ultimately results in an increased dose. End-of-dose failure is seen in some patients receiving intravenous PCA postoperatively who make multiple unsuccessful attempts to obtain a PCA dose. Often, their pain can be improved dramatically by shortening the lockout (delay interval), eg, from 10 minutes to 6 to 8 minutes.

Although much about the epidemiology of breakthrough pain remains to be elucidated, some early data strongly suggest that, if not addressed adequately, breakthrough pain can have significant negative effects on function and quality of life. One study also indicated that the presence of breakthrough pain in U.S. cancer patients increases the economic burden for patients and the health care system.

**Treatment of Breakthrough Pain**

The routine treatment of breakthrough pain is considered, in general, to be conventional practice in populations for which opioid therapy is the mainstay for the long-term management of moderate to severe pain—specifically those with active cancer or other types of advanced medical illness.

Addressing the cause of breakthrough pain can eliminate the need for analgesic therapy in some patients. For example, surgery, chemotherapy, or radiation therapy in some cancer patients may eliminate the cause. Adjusting the scheduled analgesic regimen, such as by increasing the dose, is another approach that targets cause.

A variety of analgesic interventions may be considered to treat breakthrough pain. Nonsteroidal anti-inflammatory drugs can be used, based on an analysis of the patient’s risk for adverse gastrointestinal or cardiovascular risk. More often, a short-acting mu agonist opioid is selected and provided on a PRN basis. If a patient is taking a modified-release formulation for control of baseline pain, a short-acting formulation of the same drug as the modified-release formulation is often selected. For example, short-acting oral morphine is prescribed for breakthrough pain in patients taking modified-release morphine. Similarly, a short-acting oral or oral transmucosal opioid may be prescribed when baseline pain is treated with transdermal fentanyl.

**PRN Dosing**

PRN dosing requires patients to request analgesia. Effective PRN dosing relies on the patient’s active participation. Patient teaching must include reminding patients to “stay on top of pain” and request analgesia before pain is severe and out of control. Obviously crucial to the effective use of PRN dosing is a rapid response to reports of pain and to requests for an analgesic.

In addition to its use for breakthrough pain, PRN dosing of opioid analgesics may be appropriate for other types of pain, such as intermittent pain. It is also useful when initiating opioid analgesic therapy in opioid-naive patients with moderate to severe persistent pain, especially when pain is escalating rapidly. In these cases, PRN dosing allows for a rapid response to the patient’s need for pain relief while minimizing the chance of overdose. PRN dosing is also helpful when pain is decreasing rapidly. When patients with acute pain recover and pain resolves, ATC dosing may be replaced with PRN dosing.

Although PRN dosing may be effective in these scenarios, there is abundant clinical experience suggesting the potential for negative outcomes. As mentioned before, some research has shown that overall adherence rates for those who take PRN analgesics are poor compared with those who take ATC analgesics for persistent cancer pain. When PRN dosing is used in the inpatient setting, patients may be reluctant to ask for pain medication for a variety of reasons and request it only when pain is severe and out of control despite instructions to stay on top of the pain. After the patient’s request, the nurse must check the record to ensure enough time has elapsed since the last dose the patient received; then the nurse must obtain and prepare the analgesic and, if it is an opioid, account for removal of the drug from the drug security system. These activities are time consuming and result in further loss of pain control.

Research shows that the most vulnerable of patients are at high risk for undertreatment of pain when the PRN approach is used for continuous pain. A study of older adults hospitalized for hip fracture, a condition associated with moderate-to-severe pain, found that most of the analgesics were prescribed for PRN administration and the nurses were unaware that ATC administration of PRN-prescribed analgesics would be preferable for this type of pain; only 22.3% of the patients received ATC analgesic administration of the PRN analgesics, and less than 25% of the minimum morphine equivalents of the opioids prescribed were administered. Patients with dementia received significantly less pain medication than those without dementia, and eight patients with dementia in this study received no opioid at all during the first 72 hours after admission. It is important for nurses to recognize that
PRN-prescribed analgesics may be administered ATC within the parameters of the PRN prescription and that this is the preferred dosing method for patients with continuous pain. Because there are so many disadvantages to PRN dosing, the appropriateness of its use should be evaluated carefully in all cases.

References


Calendar of Events

October 7, 2010. FLASPAN Preconference.

October 8-10, 2010. FLASPAN’s 41st Annual Conference "Humanity & Technology in Harmony...The Future of Perianesthesia Nursing.” Regal Sun Resort, Lake Buena Vista, Florida. Contact Emma Pontenila at cordeliacr@aol.com for further information.