Management of Breakthrough Pain Due to Cancer

Author: Simmonds MA
Source: Oncology 13(8), 1999, 1103-8

Scientific Implications

The following is an excellent review of breakthrough pain in cancer patients. Breakthrough pains have a rapid onset and severe intensity with a short duration. It is a complex, frequent, yet poorly understood cancer pain syndrome. Hence, reviews of breakthrough pain are appropriate and needed. Mechanisms, etiologies, and most importantly, treatments of breakthrough pain are reviewed. The most difficult aspects of managing breakthrough pain are discussed, most notably the balancing of adequate pain relief and toxicity of increasing opioid medications. Therefore, alternative and supplemental analgesics, such as corticosteroids, are also discussed. In addition, the management of common side effects to opioid pain medications is reviewed as is the difference between breakthrough pain and end-of-dose exacerbation of pain.

The article by Dr. Simmonds is subsequently reviewed in the same edition of *Oncology* (Bruera E, *Oncology* 13(8), 1999, 1110; Manfredi P, *Oncology* 13(8), 1999, 1113-4) who further elucidate on titrating dose, routes of administration, and the differences in the types of pain commonly encountered (bone pain vs. neuropathic pain, spontaneous vs. triggered pain).

Summary of Key Points in the Simmonds Article

- Approximately 75% of patients with advanced cancer will experience pain
- Cancer pain syndrome commonly includes "breakthrough pain", which is an addition to baseline pain the patient may experience
- Breakthrough pains characteristically include a rapid onset, severe intensity, but a brief duration
- Breakthrough pain commonly requires the use of supplemental doses of analgesics

Characteristics and Classification

- Breakthrough pain may be caused by somatic, visceral, or neuropathic etiologies
- It is usually related to the same mechanism that causes the patient's persistent pain
- The onset of pain is paroxysmal (peaking in intensity within 3 minutes) or developing gradually
- Breakthrough pain can be related to movement (termed incident pain) that may be volitional (caused by voluntary movements) or non-volitional (caused by involuntary movements, such as bowel movements)

Treatment

- Breakthrough pain is managed primarily with supplemental opioid medications
- Primary treatment measures, including antineoplastic therapy, should be considered. This commonly includes radiation therapy, or even chemotherapy to reduce tumor bulk.
- Increasing baseline dosage of medication may be considered, though it may be associated with

unacceptable side effects

Primary Therapy

- There are many instances where primary cancer therapy would substantially alleviate pain.
- Usually, this involves radiation therapy, in instances of bone metastases, tumor pressing on a nerve, painful skin metastases, etc.
- Chemotherapy has also been shown to decrease pain in instances such as pancreatic cancer, small cell lung cancer, and with hormonal manipulation in prostate cancer.
- Primary therapies may also be effective by treating underlying causes, such as antitussives to alleviate breakthrough pain due to coughing.

Supplemental Analgesics

- In the past, frequent episodes of breakthrough pain have been treated with increased dosages of regularly scheduled "baseline" analgesic medication. These medications often take a long time to provide relief and there is concern over opioid side effects.
- Shorter acting, "rescue" analgesics have therefore been used, to provide quicker relief. A general rule has been to use 5%-15% of the daily baseline medication every 1-2 hours. However, this breakthrough pain medication should be titrated to provide good relief with acceptable side effects.
- Obviously, these analgesics used to treat breakthrough pain have a time to achieve pain relief as well. However, treatment of breakthrough pain requires an effective analgesic that has a rapid onset and short duration.
- The route of administration is a key component of the breakthrough medication:
- - " **Oral route:** Oral agents are convenient for those patients who can swallow, though their onset of action is relatively slow.
  - **Rectal route:** This route provides a fairly rapid onset but is less convenient and in many instances, unacceptable for patients
  - **Sublingual route:** This route is potentially useful, as it provides a rapid onset. However, morphine and other narcotics are not absorbed well through the sublingual mucosa, so its use has been minimal.
  - **Oral transmucosal route:** This route is promising, as oral transmucosal fentanyl citrate (OFTC) has been shown to have excellent absorption through the transbuccal mucosa. Peak plasma levels are reached in 5-10 minutes, with pain relief proven to be efficacious. This method of analgesia should prove to be very efficacious in the treatment of breakthrough pain.

Treatment of End-of-Dose Exacerbations

- Some patients report exacerbations of pain that occur at the end of the dosing periods. These episodes are not considered breakthrough pain but rather inadequate treatment of the baseline pain.
- These painful episodes should be treated by increasing the dosage of scheduled analgesics
- These episodes may also suggest a need for investigation into the possibility that the patient's disease has progressed

Preventing or Managing Analgesic Side Effects

- An increase in analgesic medication is often associated with an increase in side effects

- Nausea is a common toxicity, most often treated with dopamine-blocking agents (eg, phenothiazine), other central acting agents (eg, ondansetron), or prokinetic agents (eg, metoclopramide)
- Constipation is the most common side effect, which must be managed with an aggressive bowel regimen and prophylactic prescription of stool softeners and/or laxatives
- If side effects cannot be managed effectively, adjuvant analgesics, such as corticosteroids, NSAIDs, etc, should be used

Overall, the management of breakthrough pain is a clinical challenge, due to its prevalence, severity and rapid onset. The supplemental analgesic agent that is selected should be fast acting, effective, and proportional to the amount of analgesic given for persistent pain. Toxicities of analgesic use must also be considered. The management of breakthrough pain must be individualized to maximize efficacy and safety.
