Managing Cancer-Related Breakthrough Pain With FENTORA

Introduction

Breakthrough pain (BTP) in patients with cancer is a common, distressing and costly problem. It interferes with functional capacities and virtually all quality-of-life measures, and adds appreciably to physical and psychological morbidity.

Epidemiology, Characteristics and Impact of BTP

BTP is a transitory exacerbation, or flare, of moderate to severe pain that occurs in patients with otherwise stable, persistent pain. The prevalence of BTP in patients with persistent cancer-related pain syndromes varies widely, from 51% to 89%.\(^4\) BTP appears to become more prevalent with advancing disease. In one survey, up to 86% of hospice patients capable of responding experienced BTP.\(^2\)

BTP has been categorized by pathophysiology (neuropathic, nociceptive and mixed) and subtype (incident, spontaneous and end-of-dose failure)\(^2\) (Table). Patients with cancer-related BTP appear to have more intense pain, more substantial functional impairment and greater psychological distress than patients with cancer pain but without BTP.\(^4\) Similarly, in one study, cancer patients with BTP had fivefold higher costs for pain-related hospitalizations, emergency room visits and physician office visits than did those without BTP.\(^9\)

Appropriate pain assessment considers pathophysiology, source, intensity, location, radiating/referred pain patterns, severity and temporal patterns. Successful treatment is important because BTP can have an impact on the patient’s quality of life and the costs of healthcare. Effective management of BTP requires a clear understanding of each patient’s pain in terms of its cause(s), predictability, duration, relationship to the dosing of routinely scheduled analgesic medications, and, most importantly, its onset of action.

Treatment of BTP: Match Drug Delivery With Pain Characteristics

The goal of BTP treatment is to manage an episode effectively with nonpharmacologic and pharmacologic means. The most commonly used nonparenteral treatment strategy for patients with cancer-related BTP has been oral short-acting opioids (often referred to as “immediate release”).\(^10\) These have been prescribed as supplemental medication and are taken on an as-needed basis, along with an around-the-clock opioid regimen to control baseline pain.\(^10\) However, traditional short-acting, immediate-release oral agents often fail to provide adequate pain relief because of a mismatch between the temporal characteristics of a typical BTP episode and the onset of analgesia of orally administered supplemental opioids.\(^11,12\)

Optimally, the pharmacokinetic and resultant pharmacodynamic qualities of an analgesic agent should match the

| Case 1 |

Recognition and Treatment of Breakthrough Pain

A 55-year-old woman was recently diagnosed with metastatic lung cancer, after several months of intractable cough and more recent onset of persistent, severe pain in her chest and upper extremities. Motivated by a desire to “get as much time as I can,” she took disability leave from her full-time job to pursue aggressive chemotherapy. Her pain has been both nociceptive and neuropathic, determined to be caused by bone metastases, pleuritic infiltrations of tumor and brachial plexopathy from tumor encroachment. Baseline pain was well controlled after a course of dexamethasone and daily use of nonsteroidal anti-inflammatory drugs (NSAIDs). Celecoxib (Celebrex, Pfizer) twice daily was chosen for its “platelet-sparing” properties—especially important while undergoing chemotherapy—along with maximum titration of gabapentin (Neurontin, Pfizer) to tolerability (800 mg three times per day) and controlled-release oxycodone (OxyContin, Purdue Pharma 40 mg three times daily, as twice-daily dosing resulted in end-of-dose failure and higher twice-daily doses caused excessive sedation). Prior use of morphine was discontinued because it made her feel “spaced out.” On this analgesic regimen, the patient continued to have a few episodes of spontaneous and incident pain each day. Spontaneous pain was predominantly neuropathic, affecting her right upper extremity, occurring rapidly and becoming “excruciating” within minutes. Incident pain in her chest wall region was highly predictable, occurring after standing and walking for more than a few minutes. The pain interfered greatly with her quality of life. She had been taking supplemental doses of hydrocodone/APAP and oxycodone, but these took too long to relieve her pain—especially when spontaneous—and lasted too long, causing her to be drowsy much of the day if she took more than a single dose.

Considering the etiology and temporal patterns of this patient’s cancer-related pain, it was determined that FENTORA would provide the flexibility required to meet her needs. Her physician discussed its use, benefits and risks, and initiated therapy with the lowest dose, 100 mcg. The patient then met with the supportive care nurse to review proper use of FENTORA, including an instruction sheet that had been prepared (Figure). They spoke briefly by phone each day to determine the optimum dose and timing of the BTP medication.

After a few days, most spontaneous pain episodes could be well controlled with a single, 100-mcg dose of FENTORA. For incident pain, the patient took a dose a few minutes before initiating activity, and she would carry a second dose in the sealed blister pack if she took a walk, went shopping, attended medical appointments, etc., for additional use if needed. The result was that her pain was sufficiently well managed.

| Table. Subtypes, Characteristics, and Impact of BTP |

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<tr>
<th>SUBTYPE OF BTP</th>
<th>CHARACTERISTICS</th>
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<td>Incident</td>
<td>Predictable: consistent temporal relationship with a precipitating factor. Although predictable, the onset and severity cannot always be foreseen. Unpredictable: inconsistent temporal relationship, but usually occurring with some type of a precipitating factor.</td>
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<td>Spontaneous (idiopathic)</td>
<td>Not induced by a readily identifiable cause; these seem to occur more commonly as a consequence of neuropathic conditions.</td>
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<td>End-of-dose failure</td>
<td>Occurs prior to a scheduled dose of an around-the-clock analgesic; most easily identified through use of pain diaries that include pain episode(s) timing, intensity, duration and time of all medication dosing.</td>
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| IMPACT OF BTP |

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<th>PATIENTS MAY HAVE:</th>
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<tr>
<td>• Be less satisfied with their opioid therapy</td>
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<tr>
<td>• Demonstrate decreased levels of function</td>
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<tr>
<td>• Have increased levels of anxiety and depression</td>
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<td>• Incur higher healthcare-related costs</td>
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FENTORA may be an appropriate treatment choice for some patients with chronic cancer pain who experience BTP. Patient-reported outcomes have been evaluated only in an open-label study with FENTORA.
**Figure. FENTORA for BTP in Cancer Patients: Patient/Caregiver Instructions.**

- Remove the tablet from the blister unit and immediately place the entire tablet in the buccal cavity above a rear molar tooth.
- The tablet dissolves in saliva, with no water needed. The tablet should not be sucked, chewed or swallowed, as this may result in lower amounts getting into the bloodstream than when taken as directed. Do not attempt to split the tablet.
- If little pieces from the tablet remain after 30 minutes, they may be swallowed with a glass of water.
- In cases where the BTP episode is not relieved within 30 minutes, patients may only take ONE additional dose of FENTORA. Patients MUST wait at least 4 hours before treating another BTP episode.
- Keep this, and all your medicines, in a safe place where no one has access to them but you and a trusted caregiver.

BTP: breakthrough pain

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**Switching Therapies**

A 64-year-old man with advanced renal cell carcinoma had widespread bone metastases, including disease in the thoracic spine, lumbar spine and pelvis. He complained of pain in his lower back and hips that were present at rest but more severe on movement. As a result of the incident pain, he was bedridden and he refused to undergo palliative radiation. Moreover, movement while in bed also resulted in significant pain.

The patient had several comorbidities that complicated his pharmacologic management.

A history of severe peptic ulcer disease precluded the use of NSAIDs. In view of his reduced creatinine clearance, morphine also was a concern, so he was started on immediate-release oxycodone tablets, with the dose gradually titrated upward in an attempt to control the pain. He was successfully switched to the fentanyl transdermal patch (Duragesic, Janssen), 100 mcg per hour, with a patch change every three days. The patch was his preference so that he would not have to think about taking pills on a fixed schedule.

The pain at rest was well controlled and he was able to sleep comfortably. However, transferring from bed to chair or during short walks continued to cause severe pain, and further upward titration of the fentanyl patch resulted in excessive sedation. For BTP, OTFC was titrated to a dose of 800 mcg, but the patient did not like having to actively rub it against his cheek. Furthermore, as he became more active and interested in having visitors, he was very self-conscious about using this form of pain control.

Based on conversion recommendations and after explanation of its correct use, 200 mcg of FENTORA was prescribed up to four times throughout the day to encourage ambulation and social interaction. This regimen provided satisfactory prevention and relief of the patient’s incident BTP. Subsequently, following a course of palliative radiotherapy to the lumbar spine, the dose of transdermal fentanyl was reduced to 50 mcg per hour, but he continued to use FENTORA up to four times a day for BTP.

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**Conclusions**

Breakthrough pain is highly prevalent among cancer patients with pain conditions from multiple etiologies, and timely treatment is important to prevent pain-related morbidity and optimize therapeutic outcomes. In appropriately selected patients, BTP can often be successfully treated through the use of FENTORA, which has an onset and duration that closely matches the majority of BTP flares. When used properly, FENTORA is safe and well tolerated in most opioid tolerant patients. As with all opioid therapies, regularly scheduled and ongoing assessment for appropriate medically indicated use is required.
References