INTRODUCTION

The management of breakthrough pain (BTP) should be handled as a separate and distinct aspect of each patient’s pain syndrome. This approach allows the clinician to consider BTP as a therapy challenge separate from the patient’s baseline persistent pain. The treatment of BTP must be based on the individual patient factors uncovered during the pain assessment.

An analogy would be the monitoring of blood glucose in patients with diabetes. Blood glucose monitoring is used to adjust therapy on the basis of the patient’s diet, exercise, and response to pharmacological therapy in the same way that ongoing pain assessments, including the use of a pain diary, are used to tailor the management of BTP. Whereas the short-term, day-to-day objective for diabetic patients is to control blood glucose, the longer-term goal is to slow disease progression with its complications and resultant patient morbidity. Applying the chronic disease-management model to the control of both baseline persistent pain and BTP decreases both the overall morbidity associated with chronic pain and the effect of poorly controlled pain on other medical conditions as well.

In Part 1 of this series (see P&T, May 2005), BTP was defined as a transient exacerbation of pain occurring in a patient with otherwise stable, baseline persistent pain. Several subtypes of BTP can produce a spectrum of symptoms. Despite the lack of a validated tool, the assessment of BTP was highlighted in Part 1, with emphasis placed on the role of a pain diary. Part 2 in this issue describes the nonpharmacological and pharmacological management of BTP, with an emphasis on the selection and use of opioids, including a discussion of their efficacy, safety, and cost considerations.

Readily reversible causes of BTP, when present, must be treated. Examples include vertebroplasty or kyphoplasty for a vertebral compression fracture, surgical debulking of a solid tumor, or radiation therapy for bone metastases. This topic is beyond the scope of this paper and is covered elsewhere.

NONPHARMACOLOGICAL TREATMENTS

In addition to ensuring that primary treatments for the underlying cause of the pain are used to the extent that they are appropriate, clinicians should consider the utility of nonpharmacological treatments for the management of BTP. These therapies cover a wide variety of techniques, many of which are time-honored but have not been subject to specific randomized trials. In fact, patients often use many of these treatments (e.g., limitation of activities, ice, heat, corsets, counter-irritant creams, or bandage wraps) before consulting a clinician. In addition, physical medicine techniques, such as correcting poor posture or harmful lifting techniques; de-conditioning; massage therapy; transcutaneous electrical nerve stimulation (TENS); and nerve blocks, should be integrated with the pharmacological treatments as indicated.

This article was based on two teleconferences and a live Consensus Panel meeting held on December 4, 2004, in Orlando, Florida, and was supported by an educational grant from Cephalon, Inc.
Patient education is a well-accepted strategy for alleviating acute and chronic pain. Acute flares of pain can originate from many sources—for instance, medications that lose their effectiveness at the end of their half-life, diseases that are associated with periodic pain flares, and disease progression. Patients may worsen their pain by engaging in activities for an inappropriate length of time. A gardener who can tolerate only 30 minutes in the yard may find himself planting for three hours when the spring flowers arrive. People who have difficulty getting out of a chair because of pain may spend all day at the mall shopping for a granddaughter’s homecoming dress. A patient who cannot tolerate an untidy house may spend a whole day cleaning.

Even though an increase in the dose of pain medication might be considered as an option to allow the patient to engage in an inappropriate level of activity, a better intervention would be to educate patients about the need to pace their activities and to pay attention to fatigue and physical limitations. This pacing of activities is really the art of pain medicine, which consists of encouraging patients to increase their overall level of activity without performing any one activity to the point of overexertion.

Pacing allows patients to return to activities in a sensible manner, which is preferable to engaging in the “all-or-nothing” behavior exhibited by some patients with chronic pain. Pacing breaks down a desirable activity into small, manageable segments. Patients can undertake a segment at a time, with rest stops and periods of relaxation in between. Instead of planting all of the spring flowers during one three-hour period, the gardener could choose to perform the task over several days. Using a timer as a reminder of when to stop can be helpful because the enjoyment derived from this activity can mask the actual amount of time spent in the garden. For the patient who enjoys shopping at the mall, pacing might mean spending two hours there instead of eight hours; instead of walking, she could ask her granddaughter to push her in a wheelchair.

These strategies, which are cost-effective, simple, and devoid of side effects or drug–drug interactions, are underused. Clinicians would be well advised to actively promote these commonsense approaches, which help patients to recognize their limitations and adapt their behaviors accordingly.

**PHARMACOLOGICAL TREATMENTS**

A primary goal of pharmacological treatment of BTP is to ensure that baseline persistent pain is treated effectively with around-the-clock (ATC) doses of an analgesic. If an immediate-release (IR) opioid is being used to treat the baseline persistent pain, the dose should be slowly tapered during conversion and titration of the ATC analgesic (opioid) dose. After this conversion to an ATC opioid is complete and an effective,

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**Figure 1** General approach to the management of breakthrough pain (BTP). ATC = around the clock; PRN = as needed; R/O = rule out. (See Part 1 of this series in the May 2005 issue of P&T.)

<table>
<thead>
<tr>
<th>R/O treatable causes of pain</th>
<th><strong>Treatment of baseline persistent pain</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Use patient diary &amp; nonpharmacological options</strong></td>
<td><strong>ATC analgesia for baseline persistent pain</strong></td>
</tr>
<tr>
<td></td>
<td><strong>p.r.n. analgesic for BTP</strong></td>
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<tr>
<td><strong>Reassessment of pain and patient outcomes</strong></td>
<td><strong>Effective analgesia</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Baseline persistent pain controlled</strong></td>
</tr>
<tr>
<td><strong>Refer to pain specialist</strong></td>
<td><strong>Unsuccessful</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Successful</strong></td>
</tr>
<tr>
<td>1. Dose-limiting toxicities</td>
<td>1. Ongoing use of patient diary</td>
</tr>
<tr>
<td>2. Aberrant drug-related behavior</td>
<td>2. Assess for the 4 As*</td>
</tr>
<tr>
<td></td>
<td><strong>Effective analgesia increased patient function</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Baseline persistent pain controlled</strong></td>
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<td></td>
<td><strong>Modify treatment</strong></td>
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<td></td>
<td><strong>Refer to pain specialist</strong></td>
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<td></td>
<td><strong>Unsuccessful</strong></td>
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<tr>
<td><strong>Successful</strong></td>
<td><strong>Unsuccessful</strong></td>
</tr>
</tbody>
</table>

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*The “four As” are analgesia, activities of daily living, adverse events, and aberrant drug-related behavior.
tolerated dose of the ATC opioid is established, the use of the IR opioid should not be continued for the management of baseline persistent pain.

Baseline persistent pain should be assessed at regular intervals to ensure effective control with ATC doses of the analgesic. If end-of-dose BTP is identified, two treatment options are available:

1. increasing the total daily dose of the ATC opioid by 25% to 50% and then re-evaluating for a response. This approach may result in the development of intolerable side effects, such as drowsiness.
2. shortening the dosing interval if the patient is already taking the maximally tolerated dose

Finally, because of unpredictable variability among patients, some may require the dosing interval to be shorter than generally recommended. For example, a transdermal fentanyl patch (Duragesic®, Janssen) would be replaced every 48 hours instead of every 72 hours, or controlled-release oxycodone (e.g., OxyContin®, Purdue) might be prescribed every eight hours instead of every 12 hours.

**Case Study: T. G.**

T. G. is a 62-year-old woman with stage IV breast cancer (see Part 1 of this series in the May 2005 issue of P&T). She reports that she had been tolerating opioid therapy without any side effects except for constipation. Because of the frequent disturbance in T. G.’s sleep resulting from pain, the choice was made to increase her evening dose of sustained-release morphine and to increase her dose of her stimulant laxative, which was used to treat opioid-induced constipation.

After control of the baseline persistent pain has been achieved, the management goal is to decrease the frequency and intensity of BTP (Figure 2). This latter goal is particularly important, because it may reduce the patient’s level of discomfort or disability.

The ideal treatment of BTP would match its onset and duration and would therefore typically have a rapid onset (within minutes) and a short duration of action (approximately 30 minutes in most cases) (Figure 3). Because no currently available pharmacological agent is ideal, management should be adjusted according to the following: (1) the chemical class, (2) the route of administration, (3) the dosage, (4) the setting (inpatient or outpatient), and (5) the subtype of BTP.

**Chemical Class**

Although a variety of drugs are used to treat chronic baseline persistent pain, most published and clinical experiences with BTP, regardless of etiology, involve opioids. Oral transmucosal fentanyl citrate (Actiq®, Cephalon) is the only opioid approved by the Food and Drug Administration (FDA) that is specifically indicated for cancer-related BTP, but the use of many other opioids, although they are “off-label,” is supported by extensive research. The wide experience with opioids is a consequence, in part, of the lack of a “ceiling effect” (similar to insulin in the treatment of hyperglycemia); that is, analgesia is related to the dose with no upper limit, even though the dose may be limited by side effects.

Using the same opioid for the treatment of baseline persistent pain and BTP is not unusual, but it is not clear whether this affords any benefit in terms of efficacy, compared with using a different opioid. However, using the same opioid does have some advantages, such as easier titration of the ATC opioid, as well as management of opioid-related side effects. On the other hand, any IR opioid can be used with longer-acting agents, such as methadone and levorphanol (e.g., Dolophine® or Levo-Dromoran®, Roxane) to avoid possible accumulation with repetitive doses of these agents. Similarly, a different IR opioid might be used for BTP in patients who have been treated with transdermal fentanyl.

Non-opioid analgesics, such as acetaminophen (e.g., Tylenol®, Ortho-McNeil) and cyclooxygenase type 2 (COX-2)
selective and nonselective nonsteroidal anti-inflammatory drugs (NSAIDs), should be efficacious in treating BTP because of their nociceptive mechanisms. However, the use of these agents is complicated by dose-limiting toxicities, an onset of a half-hour or more, a duration of action of several hours, and recent concerns about cardiovascular morbidity. In addition, no published evidence exists to support their use in BTP.

A similar situation exists with bisphosphonates for bone pain and with antidepressants, anticonvulsants, and other adjuvant analgesics for neuropathic BTP. Some evidence exists that subcutaneous midazolam (Versed®, Roche) and intranasal ketamine are efficacious in BTP, but the results are preliminary. Consequently, the Consensus Panel’s treatment recommendations focus on the use of opioids.

An approach for selecting an IR opioid to treat BTP should be based on the sustained-release or ATC opioid that is used for baseline persistent pain. In addition, a careful review of the patient diary by the clinician can suggest when to administer the IR opioid. Finally, cost differences exist among opioids—a fact that clinicians need to consider when choosing an opioid for BTP.

### Routes of Administration

Because the time from onset to peak pain intensity of BTP is generally only a few minutes and the average duration is one-half hour, the opioid that is used to manage most cases of BTP should have a rapid onset of effective analgesia and a duration of action appropriate for the characteristics of the BTP.

#### Oral and Oral Transmucosal Routes

Morphine, hydromorphone, and oxycodone are the oral opioids most often used to treat BTP when they are administered in their IR formulations of tablets, capsules, or liquid concentrates (Table 1). However, these agents typically have an extensive first-pass effect and are hydrophilic in nature, which slows the onset of analgesia to approximately 30 minutes or more. In the opinion of the Consensus Panel, this makes these three opioids less well suited for severe idiopathic or unpredictable incident BTP. Oral IR opioids, however, may be appropriate in patients with predictable incident pain when they are given 30 to 45 minutes before the precipitating event (such as movement).

Although methadone is commonly used in other settings because of its longer duration of action, recent evidence suggests that it may have a role in the management of BTP as a result of its relatively rapid onset of action. Caution is essential with frequent dosing of methadone because of its long elimination half-life and the potential for accumulation, resulting in toxicity.

Fentanyl, by contrast, is well suited for absorption through the oral mucosa with minimal local irritation. These attributes led to the development of and the FDA’s subsequent approval of oral transmucosal fentanyl for BTP. The oral transmucosal delivery system incorporates fentanyl citrate within a matrix of sucrose fitted onto a plastic handle for dissolution within the oral cavity.

For all opioids, ongoing reassessment and titration are critical for successful pain relief and for minimizing the risk of clinically significant adverse events. Only clinicians with experience in the use of opioids should prescribe them.

#### Parenteral Route

The parenteral administration of opioids may serve as an important alternative to the oral route, mainly in patients experiencing multiple daily episodes of BTP that respond poorly to oral opioids. However, even though parenteral opioids are used extensively in inpatient and hospice settings, technical problems limit their use in the outpatient setting to carefully selected patients, including those with pain refractory to more standard approaches.

#### Rectal Route

Administration of medication through the rectum is an alternative route, although the onset and peak effects lag behind those necessary for managing BTP. There is also considerable variability in the medication’s absorption among patients and within the same patient. Only morphine and hydromorphone are commercially available as a rectal suppository.

### Table 1: Characteristics of Immediate-Release Opioids Useful for Breakthrough Pain (BTP)

<table>
<thead>
<tr>
<th>Immediate-Release Opioid</th>
<th>Onset of Analgesia</th>
<th>Duration of Effect</th>
<th>Advantages (A)/Disadvantages (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine (oral)</td>
<td>30–40 minutes</td>
<td>4 hours</td>
<td>A — available in multiple dosage forms, liquid concentrate D — slow onset of analgesia for idiopathic BTP</td>
</tr>
<tr>
<td>Oxycodone (oral)</td>
<td>30 minutes</td>
<td>4 hours</td>
<td>Same as morphine</td>
</tr>
<tr>
<td>Hydromorphone (oral)</td>
<td>30 minutes</td>
<td>4 hours</td>
<td>D — no liquid concentrate, slow onset of analgesia for idiopathic BTP</td>
</tr>
<tr>
<td>Methadone (oral)</td>
<td>~10–15 minutes</td>
<td>4–6 hours</td>
<td>A — faster onset of analgesia in one small study D — complex pharmacology, pharmacokinetics</td>
</tr>
<tr>
<td>Fentanyl (transmucosal)</td>
<td>~5–10 minutes</td>
<td>1–2 hours</td>
<td>A — fastest onset of analgesia D — requires ongoing patient cooperation in use</td>
</tr>
</tbody>
</table>
Breakthrough Pain: Management

Sublingual and Intranasal Routes
Because of its highly vascular nature, the oral cavity is also used as a site for local rapid absorption of opioids. Sublingual morphine has been used for many years in patients with terminal cancer, but this route of administration is less than ideal as a result of its bitter taste and its delayed onset of action, caused by poor absorption.8–10 Preliminary evidence suggests that sublingual sufentanil solution,11,12 sublingual buprenorphine (Subutex®, Reckitt Benckiser),13 and fentanyl and alfentanil sprays14 provide rapid, effective pain relief. Various opioids have also been administered via the intranasal route, including morphine,15,16 sufentanil,17 and fentanyl.18,19 These unique delivery systems await further investigation for use in daily clinical practice.

Dosage
The best method of determining the most effective dose of an opioid for BTP remains unclear. Guidelines have advocated a fixed proportion of the daily maintenance dose, typically in the range of 5% to 17% of the total daily dose.20–23 However, BTP may vary in cause, severity, and duration, and the dose of medication for BTP may need to be titrated in much the same way as the dose of opioid is titrated for baseline persistent pain.

Little correlation exists between the daily opioid dose and the dose needed for BTP.5,24,25 Given this disparity, the dose of an IR opioid should be tailored to the individual according to:

- the onset of the BTP episode.
- the duration of BTP.
- the patient’s tolerance to the IR opioid used.

Patients who are already taking opioid therapy may require a higher initial opioid dose than opioid-naïve patients.

Case Study
A reassessment and review of T. G.’s pain diary reveals several predictable episodes of BTP. Most episodes of BTP are linked to activity, especially when she stands or walks. The characteristic of the BTP is similar to her baseline persistent pain.

T. G. wishes to restore her ability to work around her home as much as possible until the pain-relieving effects of the radiation therapy occur. A trial of immediate-release (IR) morphine 30 mg orally 30 minutes prior to any of these predictable episodes of BTP is initiated with the understanding that this dosage will be re-evaluated in one week.

T. G. is reminded to document her episodes of BTP, including her response to her pre-emptive dose of morphine. She is also reassured that if this dose proves ineffective in reducing the overall severity of BTP; it will be titrated to effect, just as her sustained-release morphine was adjusted for her baseline persistent pain.

The patient’s response to therapy should be reassessed on a frequent basis, especially after changes in the management regimen have been made. If more than four episodes of BTP occur within a 24-hour period, an increase in the total daily dose of opioid for the baseline persistent pain should be considered.

This situation would be viewed as different from one in which a patient has predictable incident BTP and is using a scheduled dose of an IR opioid.

Inpatient and Outpatient Settings
All of the options for BTP can be used in the inpatient setting, but parenteral administration may be less applicable in the outpatient setting. Patients who might be appropriate candidates for parenteral opioid therapy in the outpatient setting include those who are highly motivated to comply with the regimen, are receiving a relatively stable dose for BTP, and are not experiencing significant adverse effects, chiefly respiratory depression or confusion. For most outpatients, however, the oral and oral transmucosal routes are generally preferred.

Subtypes of Breakthrough Pain
The subtype of BTP serves as a basis for tailoring the treatment approach (Table 2). For end-of-dose pain, the ATC dosing needs to be carefully calculated (see Part 1, Table 1, in the May 2005 issue of P&T). For predictable incident pain, such as that occurring with movement, the pre-emptive use of a hydrophilic IR opioid given 30 minutes prior to the incident is reasonable. Of course, when incident pain is predictable but occurs with little advance notice (e.g., as in coughing), oral transmucosal fentanyl citrate is a good choice because of its rapid onset of action.

A trial of an IR opioid should be initiated for unpredictable incident pain or idiopathic pain. An oral IR hydrophilic opioid (e.g., morphine or oxycodone) may be a reasonable choice if the onset of BTP is slower than the average three to five minutes or longer than the average duration of 15 to 30 minutes.

Case Study (continued)
T. G. returns in one week for a re-evaluation. A discussion with her and a review of her patient diary indicate that IR morphine is effective when it is given pre-emptively before she stands or walks for an extended time. However, the IR morphine has been ineffective on several occasions of the severe, sharp, shooting pain (9 on a scale of 1 to 10) in her right hip and leg—pain that seems to have no precipitating features when she is at rest.

Although she has taken the morphine when these episodes have occurred, it has been ineffective because of the speed and intensity of the pain. As the pain lessens, T. G. is left feeling “hung over” from the effects of the morphine—which had not been a problem with her opioid therapy until now.

A trial of oral transmucosal fentanyl is discussed. T. G. is to use oral transmucosal fentanyl citrate 200 mcg over 15 minutes for each episode of BTP for the next week. This dosage is to be re-evaluated at her follow-up visit. T. G. is then reminded to use her pain diary to record her response to therapy and to document the variability of her pain daily.

Alternatively, acetaminophen or another NSAID may be considered for episodes of BTP with a slow onset or a long duration. Conversely, oral transmucosal fentanyl citrate may
be a good choice if the BTP is unpredictable and has an onset within several minutes and a short duration.

**CLINICAL TRIALS**

**Morphine**

In a study by Mercadante et al., intravenous (IV) morphine was effective in reducing cancer-related BTP when administered as a dose equivalent to one-fifth of the oral daily morphine dose.26 Pain was reduced from a mean intensity of 7.9 on a scale of 1 to 10 to 3 out of 10 within a mean of 17.7 minutes. This is the only retrieved study that formally assessed the use of a fixed dose of an opioid as a percentage of the daily opioid dose.

**Oral Transmucosal Fentanyl Citrate**

Oral transmucosal fentanyl citrate has been investigated for the management of cancer-related and non–cancer-related BTP.24,25,27–32 Two dose-ranging studies that involved 127 patients with cancer-related BTP demonstrated significant efficacy in reducing BTP, with doses varying from 550 to 650 mcg (range, 200–6,400 mcg).24,25 In both cases, there was no correlation between the effective dose of oral transmucosal fentanyl citrate and the ATC dose of an opioid. Approximately 50% of the reduction in pain intensity from oral transmucosal fentanyl citrate occurs within 15 minutes.25

In a direct comparison with IR oral morphine, oral transmucosal fentanyl citrate was found to be more effective in reducing the intensity of cancer-related BTP.26 The use of this agent over a mean of three months showed no trend toward decreased effectiveness.29

Oral transmucosal fentanyl citrate is also effective in the outpatient management of sickle cell pain.32 A recent review of four previously conducted trials of this agent for the treatment of BTP in patients with cancer demonstrated similar efficacy in both nociceptive and neuropathic pain.33 Common side effects include somnolence, constipation, nausea, dizziness, and vomiting, all with an incidence of less than 15%.25,29,30

**ECONOMIC AND QUALITY-OF-LIFE CONSIDERATIONS**

BTP is a common cause of hospital admissions and accounts for 4.4% to 7.6% of readmissions.34,35,37 Patients with BTP have higher direct pain-related costs than patients without BTP ($1,080 vs. $750, respectively) and are approximately 2.5 times more likely to seek care in an emergency department than patients with chronic pain but without BTP.25

To reduce the economic and the health-related quality-of-life burden of BTP and pain in general, various strategies have been employed with mixed results. Bookbinder et al. observed improvement in pain-related knowledge and attitudes in nurses but a reduction in patient satisfaction related to pain relief following the implementation of accepted standards.38 Two other groups of investigators noted a reduction in the hospitalization rate for uncontrolled pain following staff education and other interventions,34,39 although the readmission rate for BTP actually increased in one group.34 Patient education initiatives have provided favorable results and have been associated with reductions in pain severity, anxiety, and fear of addiction and improved pain-coping skills.30–42

The selection of a management approach to BTP often includes cost as a factor. For BTP, the acquisition costs vary widely with oral IR morphine and other generic formulations that are several-fold less expensive than oral transmucosal fentanyl. Although this is an important consideration, this narrow focus on acquisition cost ignores the impact of a specific therapy on the total cost of care. The importance of total cost of care is underscored by a recent retrospective review that demonstrated that the outpatient use of oral transmucosal fentanyl citrate was associated with a reduced need for emergency-department visits, parenteral opioids, and hospitalization.31 Because the acquisition cost of a specific drug often varies widely among health care organizations and purchasing groups and there are few data describing the effect on the total cost of care for specific therapies for BTP, it is not possible to make ironclad recommendations regarding the preferred therapy for all situations involving BTP.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>General Management Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-of-dose</td>
<td>Carefully tailored around-the-clock dosing</td>
</tr>
<tr>
<td>Incident, predictable</td>
<td>Pre-emptive use of a hydrophilic immediate-release opioid, given 30 minutes prior to activity</td>
</tr>
<tr>
<td>Incident, unpredictable</td>
<td>Trial of hydrophilic immediate-release opioid; if a poor patient response, switch to a lipophilic immediate-release opioid or a parenteral opioid in carefully selected patients</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Trial of a lipophilic immediate-release opioid</td>
</tr>
</tbody>
</table>

In general, however, the Consensus Panel believes that the use of an oral IR opioid may be cost-effective in many patients, such as those with slow-onset or prolonged BTP, and may be appropriate for patients with predictable incident BTP who have sufficient warning of anticipated pain. However, oral transmucosal fentanyl citrate may be more cost-effective in patients with rapid-onset idiopathic or unpredictable incident pain, especially if the BTP causes significant impairment of activities of daily living or if it prompts the patient to seek emergency medical care.

**Referral to a Pain Specialist**

A primary care clinician can effectively manage most patients with BTP, but referral to a pain specialist might be considered under certain conditions, such as:

- dose-limiting opioid toxicity in a patient
- pain that is poorly controlled with IR opioids (oral or oral transmucosal)
- past or present aberrant drug behavior of the patient
- patients needing assessment for interventional pain techniques
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Medical–Legal Issues

Although the relief of pain and suffering is a core commitment shared by all health care professionals, legal and regulatory issues related primarily to opioids are often cited as barriers to fulfilling this commitment. Because opioids are an important management option and pain relief has become an important societal concern (a fact that has been underscored by the Federation of State Medical Boards [FSMB] in its adoption of the 2004 Model Policy), various organizations and U.S. governmental agencies have established standards and provided guidelines to assist health care professionals in treating patients with a pain syndrome. Although the FSMB makes it clear that inappropriate treatment of pain, including undertreatment, is a departure from an acceptable standard of practice, the FSMB also describes appropriate steps that clinicians can take when treating patients with a pain syndrome. These steps are similar to those recommended by the American Academy of Pain Management.

In general, clinicians can minimize their personal risk of legal and regulatory scrutiny by:

• using sound assessment and monitoring techniques.
• adhering to accepted principles of medication prescribing.
• thoroughly documenting the patient’s medical record.
• following the regulations of their state and the U.S. Drug Enforcement Administration (DEA).

In August 2004, the DEA issued a statement regarding the prescribing of pain medications, to answer questions frequently asked by health care professionals and law enforcement personnel. Citing misstatements, the DEA subsequently withdrew this announcement and indicated its intent to clarify appropriate principles related to the dispensing of controlled substances for the treatment of pain in a future issue of the Federal Register.

CONCLUSION

BTP is an important clinical problem commonly experienced by patients with chronic pain. Several subtypes of BTP exist, including incident, idiopathic, and end-of-dose pain. BTP is commonly characterized by severe or excruciating pain that typically peaks within minutes of its onset and remits within 15 to 30 minutes, but the spectrum of clinical presentations may vary. BTP must be assessed separately from baseline pain. A thorough history and physical examination are essential to assess BTP, and the evaluation should take into consideration the pain diary or one or more unidimensional assessment tools.

The management of BTP involves pharmacological and nonpharmacological measures, coupled with patient education. The initial management of BTP involves addressing readily correctable causes when present. Nonpharmacological measures (pacing, limiting activities, and applying physical medicine techniques) are often effective and prevent many of the complications associated with pharmacological therapy.

Opioids are the mainstay of pharmacological therapy for BTP. The opioid, dose, and route of administration must be tailored for all patients. Oral IR opioids are commonly used for BTP, as their actions are well established and they are relatively inexpensive. Their comparatively slow onset makes them less suitable for most cases of idiopathic or unpredictable incident pain.

The rapid onset of oral transmucosal fentanyl citrate makes it appropriate for most types of BTP, although its acquisition cost is greater than that for oral IR opioids. In addition to efficacy, safety, and acquisition cost, the impact on function and health-related quality of life are important considerations in selecting an opioid for BTP.

REFERENCES

Breakthrough Pain: Management


Disclosure

Dr. Bennett reports no relationships to disclose with respect to his participation in this project.

Dr. Burton reports that he receives Research Support from Elan, Celgene, and Glaxo; he is on the Speakers’ Bureau of and has been a Consultant for Medtronic, Inc., and Merck.

Dr. Fishman reports the following relationships: Consultant, Cephalon; Consultant, Speakers’ Bureau of, and Grants/Research Support from Elan, Endo, Janssen, Merck, Pfizer, Purdue Pharma, and Eli Lilly.

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Dr. McCarberg reports that he is on the Speakers’ Bureau of Endo, Janssen, Ligand, Ortho-McNeil, Pfizer, and Purdue Pharma.

Dr. Miaskowski reports the following relationships: Cephalon: Chair of Nursing Advisory Board; Endo: Speakers’ Bureau, Research Support; Janssen: Advisory Board, Research Support; Merck: Advisory Board, and Purdue Pharma: Advisory Board, Research Support.

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Dr. Payne reports the following relationships: Consultant for AstraZeneca, Eisai, Elan, Endo, Ionix, Janssen, Johnson & Johnson, Merck, Pfizer, Purdue Pharma, and Xanodyne; Speakers’ Bureau of Janssen and Purdue; and Major Shareholder of Rinat and Xanodyne.

Dr. Ray reports the following relationships: Consultant for PharmaCia/Pfizer; Speakers’ Bureau for Purdue and Janssen; and Advisory Panel for Ligand.

Dr. Viscusi reports the following relationships: Honorarium: Cephalon; Advisory Boards: Alza, Endo, Ortho-McNeil, and Skye Pharma; Grants: Adolor, Alza, Bristol-Myers Squibb, Endo, Ortho-McNeil, Progenics, and Skye Pharma; and Speakers’ Bureau: B. Braun and Pfizer.

Dr. Wong reports that he has no relationships to disclose with respect to his participation in this project.