Breakthrough Pain: Assessment and Management in Clinical Practice

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BREAKTHROUGH PAIN: ASSESSMENT AND MANAGEMENT

Abstract

By Sabrina Enochs Chiu
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Breakthrough pain presents a complex clinical challenge for the primary care provider and patient. Despite increased awareness and treatment options for pain management for those with chronic non-malignant and malignant pain breakthrough pain is frequently under diagnosed and under treated.

The purpose of this paper is to analyze and synthesize current literature and research to identify distinguishing characteristics of breakthrough pain, the impact of breakthrough pain on patients, providers, and society, and provide evidence-based guidelines for assessment, and treatment in clinical practice.

The data sources for this manuscript include: the PubMed search engine (part of the National Library of Medicine), Medscape, and the Cumulative Index to Nursing and Allied Health Literature databases were used to analyze peer-reviewed journal articles and literature on the assessment and management of breakthrough pain. From these data sources pertinent research articles from 1999 to 2007 were reviewed.

The conclusion is that breakthrough pain can be effectively diagnosed and managed by nurse practitioners using pertinent assessment skills, pharmacotherapy, and complementary non-pharmacological treatment.
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BREAKTHROUGH PAIN: ASSESSMENT AND MANAGEMENT

By

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Introduction

Pain represents the single most frequent reason for people to seek medical care in the United States (Burton, 2005; Fortner, Okon, Portenoy, 2002). Pain is defined by The International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” (Herskey & Bogduk, 1994). The Joint Commission on Accreditation of Hospitals and Healthcare Organization (JCAHO) mandates an individual’s “right” to appropriate pain management and focuses on pain management as an indicator of appropriate health care and a quality-of-life issue that must be addressed by health primary care providers and institutions (Brennan, Passik, Kirsh, 2003). The under treatment of pain is a major health issue and is a national quality-of-care issue for the National Agency for Healthcare Research and Quality (AHRQ) (Bennett, Burton, Fishman, Fortner, McCarberg, Miaskowski, et al., 2005a).

Pain is estimated to affect over 76 million people in the United States (National Center for Health Statistics [NCHS], 2006; American Pain Foundation [APF], 2007). Chronic pain is estimated to affect 10-45% of individuals in the industrial world (APF, 2007; Portenoy & Cruciani, 2007). Of those who are being treated for non-malignant chronic pain an estimated 19-95% experience breakthrough pain (BTP) depending on how breakthrough pain is defined and the population surveyed (Portenoy & Hagen 1990; Bennett, et al. 2005; National Cancer Institute [NCI], 2007). Over 70% of patients with cancer have pain with the prevalence of breakthrough pain (BTP) in cancer at 50-90%, and over half of those patients are under-treated for pain (APF, 2007; Portenoy, Bennett, Rauck, Simon, Taylor, Brennan, et al., 2006a; Lesage & Portenoy, 1999). Svendsen, Andersen, Arnason, et al. (2005) reported in a study of cancer patients (N=1095) that two thirds of the patients experienced breakthrough pain. Up to 50% of
individuals in hospice with non-cancer terminal illness may experience breakthrough pain (Zeppetella, 2007; Bennett, et al. 2005a).

The purpose of this paper is to analyze and synthesize current literature and research to identify distinguishing characteristics of breakthrough pain on the patient, provider, and society, and provide evidence-based guidelines for assessment, and treatment in clinical practice.

Theoretical Framework

The Gate Control Theory of pain developed by Melzack and Wall in 1962 and 1965 furthered the understanding of pain and remains fundamental to pain knowledge. Gate Control Theory guides current pain research, theory, and treatment development (McCool, Smith, Aberg, 2004). Past theories described pain as a direct response to stimuli without cognitive input. Current theories focus on the modulation of pain perception within the central nervous system. The brain perceives and thus controls the pain. Specific pain pathways allow perception and response to painful stimuli by a gating mechanism. The gate is within the spinal cord. It closes in response to fast conducting touch fibers (normal stimuli) and opens to slow conducting pain fibers that are transmitting intense sensory signals of pain (Brennan, Passik, Kirsh, 2003; McCool, et al., 2004; Simon, 2004; Benzon, Raja, Molloy, Liu, Fishman, 2005).

Four physiologic steps control nociception and response to pain: transduction, transmission, perception, and modulation. Transduction occurs when a stimulus activates peripheral nociceptive neurons creating an action potential along the afferent axons (nonmyelinated C fibers and myelinated A delta fibers) to the dorsal horn cells of the spinal cord. The signal is transmitted from the dorsal horn to the synaptic cleft where neurotransmitters are released from the afferent fibers (Brennan, et al., 2003; McCool, et al., 2004; Simon, 2004; Benzon, et al., 2005). The nociceptive afferent fibers terminate in different layers (lamina) of the
dorsal horn. The pain signal is processed for transmission, modulation, or termination. The pain impulses are controlled by a gating mechanism that opens to allow nerve impulses to reach the brain or closes to decrease or prevent pain impulse transmission to the brain. The neurotransmitters stimulate the post-synaptic fibers for further transmission of the pain signal by thalamic nuclei (via the spinothalamic tract to the thalamus) to the cerebral cortex. At the cerebral cortex there is perception of the pain signal, but it is not localized. The cerebral cortex perception of the pain signal is influenced by several factors, including autonomic responses, somatosensory localization and characterization, and limbic system factors (emotion/behavioral response). Modulation occurs with the inhibition or facilitation of the pain signal (via a gate) from the brain to the descending pathways (McCool, et al., 2004; Simon, 2004; Benzon, et al., 2005).

Chronic pain develops when the continuous or repeated transmission of a pain signal remodels the pain pathway. The pain pathway undergoes neural changes (neural plasticity). This results in resistance to antinociceptive modulation and hypersensitivity to the pain input signal. The neural changes create the perception of pain after healing has occurred and may extend to other areas of the body not involved in the initial pain event (Brennan, et al., 2003; Benzon, et al., 2005).

Barriers to Effective Pain Management

Dahl and Portenoy (2004) contend that there are several common myths that influence the treatment and management of pain (Table 1). All of these myths contribute to inadequate pain control and barriers to effective pain management. Barriers to pain management focus on three problem areas: health care professionals, patients, and health care systems (Beanett, et al.
federal) create another layer of expense for the institution and/or provider and may restrict the use of opioids (NCI, 2007; Payne, 2007). Access to adequate treatment facilities and drug availability is another barrier (Payne, 2007).

**Sociocultural Factors**

Significant racial, ethnic and gender disparities exist in health care and impact pain treatment (Green, Anderson, Baker, Campbell, Decker, Fillingim, et al., 2003; Nguyen, Ugrate, Fuller, et al., 2005, Portenoy, Ugate, Fuller, and Haas, 2004). The prevalence of chronic pain in racial and ethnic minorities has not been adequately researched. Based on available data, prevalence rates vary by population studied and research methodology (Green, et al., 2003; Portenoy, et al., 2004). A 2004 study conducted by Portenoy, Ugate, Fuller, and Haas used a cross-sectional nationwide telephone survey (N=1335) to target three populations: Hispanic, non-Hispanic white, and African-Americans. The goal of the study was to evaluate the relationship between race or ethnicity and chronic pain prevalence. Chronic pain was not associated with ethnicity or race. However, evidence indicated that racial and ethnic groups were under-treated for pain compared to non-Hispanic whites and that race and ethnicity impact the presentation of the pain experience and the treatment of chronic pain (Portenoy, et al., 2004).

Minority access to care is significantly impacted by socioeconomic factors (Green, et al., 2003; Cook & DeGood, 2006; Nguyen, et al., 2005). In addition, evidence suggests that primary care providers treat minorities and women less aggressively and treatment choices are influenced by the type of pain the patient is experiencing and the behavior or characteristics of the patient (Green et al., 2003; APF, 2007).

The elderly frequently experience pain due to aging and receive less treatment for pain (Green, et al., 2003; APF, 2007). Green, et al. (2003) note that 35-80% of nursing home patients
experience pain that goes untreated. Women seek treatment for pain more often than men and receive less treatment than men (APF, 2007). Numerous factors create these gender disparities. Women are labeled histrionic, emotional, attention seeking, and thought to be able to handle more pain than men (APF, 2007). Unfortunately, there is a dearth of research about breakthrough pain across racial and ethnic groups (APF, 2007; Green, et al., 2003).

**Economics of Breakthrough Pain Management**

The economic burden of breakthrough pain is significant due to greater use of emergency room care, hospitalizations, and physician office visits (Portenoy & Cruciani, 2007; Fortner, 2002; Green, et al. 2003). The annual monetary cost for US businesses is estimated to be 100 billion dollars due to lost productivity, health care costs and sick time (Portenoy & Cruciani, 2007; Glickman-Simon, 2006, NIH, 1998). A survey study of cancer patients with and without breakthrough pain conducted by Fortner, et al. (2002) found that the annual cost difference in health care dollars was $12,000 for those with breakthrough pain versus $2,400 for patients without breakthrough pain. Table 2 provides an overview of the effect of pain on the patient, family, and society.

**Definition of Breakthrough Pain**

There is no universally accepted definition of breakthrough pain in the literature (Portenoy & Cruciani, 2007; Bennett, et al., 2005a; Gruener, 2004; Burton, 2004; Svendsen, et al., 2004; Fishman & Moyer, 2006; Zeppetella, 2007). Breakthrough pain is interchangeably referred to as “episodic,” “incidental,” “flare,” “provoked,” or “transient” which further complicates a universal definition (Burton, 2005; Bennett, et al. 2005a; Svendsen, et al., 2004). In 1990, Portenoy and Hagen proposed that transient pain episodes in individuals with stable, controlled cancer pain be termed “breakthrough pain” (p. 274). Portenoy and Hagen (1990) further refined
the definition of breakthrough pain as “a transient increase in pain to greater than moderate intensity, occurring on a baseline pain of moderate intensity or less” (p. 274).

In 2004, a consensus panel of experts in pain management (chronic, cancer, and acute), palliative care, oncology, and anesthesiology was formed to review the literature and provide practice guidelines for the assessment and management of breakthrough pain. The review and discussion resulted in the formation of Consensus Panel Recommendations for the Assessment and Management of Breakthrough Pain: Part 1 Assessment and Part 2 Management. Bennett, et al. (2005a) contend that breakthrough pain be defined as “a transient exacerbation of pain that occurs in patients with otherwise stable, baseline persistent pain” (p. 297). This definition proposes that the baseline persistent pain, regardless of cause, is stable and controlled with around-the-clock analgesics and that the pain generally shares the same etiologic cause (Bennett, et al., 2005a). The definition clarifies that persistent chronic baseline pain (malignant or non-malignant in nature) is distinct from breakthrough pain and that breakthrough pain should be treated as a separate entity (Bennett, et al., 2005a; Payne, 2007). Breakthrough pain can be characterized as abrupt, intense pain that occurs quickly in a predictable or unpredictable manner that has a short duration one to four times a day (McCaffrey & Pasero, 2003; Bennett, et al., 2005).

The cause of breakthrough pain generally arises from the etiology of the baseline pain condition and includes somatic, visceral, and neuropathic origins (Svendsen, et al., 2004; Payne, 2007). Visceral pain is described as a sharp, aching, twisting, throbbing pain that is difficult to isolate because it arises from internal organs and linings of body cavities (Payne, 2007). Examples of visceral pain include renal colic, irritable bowel pain, liver metastases, and angina. Somatic pain is described as sharp, throbbing, aching, and constant (Payne, 2006). The pain is
generally well localized and usually musculoskeletal in origin. Frequent causes of somatic pain include bone metastases, low back spasms, and osteoarthritic pain (Payne, 2007). Neuropathic pain is described as shooting, burning, tingling, or electrical-like intense pain and is related to central nervous and peripheral nervous system structural changes (Payne, 2007). Examples of types of neuropathic pain are chronic regional pain syndrome, diabetic neuropathy, polyneuropathy, and central pain syndromes.

Three subtypes of breakthrough pain have been identified and defined by the Agency for Healthcare Research and Quality (AHRQ): incident pain, (predictable and unpredictable), idiopathic and end-of-dose related pain (Fishman & Moyer, 2006; Bennett, et al., 2005a).

Incident pain is characterized as predictable or unpredictable. Predictable pain is related to volitional movement activities such as standing, sitting, walking, bending, touch (Bennett, et al., 2005a; Fishman & Moyer, 2006; Zeppetella, 2007; Svendsen, et al., 2004). Predictable incidental pain accounts for approximately 50% of breakthrough pain and it is more amenable to preemptive treatment with immediate release analgesics (Bennett, et al., 2005a; Payne, 2007). Unpredictable incident pain is inconsistent pain related to activity (Bennett, et al., 2005a). Examples include pain from visceral organs such as bladder spasm, renal colic, irritable bowel pain (Payne, 2007). Unpredictable incident pain is more difficult to treat due to its spontaneous occurrence (no pretreatment with analgesics) and the rapid escalation of pain (Bennett, et al., 2005a).

Idiopathic pain is pain associated with an unknown cause and is spontaneous. Idiopathic pain has a rapid onset and intensification (referred to as crescendo pain) and it lasts longer (>30 minutes) than incident pain and should be treated with immediate-release analgesics (Bennett, et
Idiopathic pain in patients with cancer is frequently related to disease progression (Bennett, et al., 2005a).

End-of-dose pain occurs when the scheduled dose of prescribed analgesic does not control pain before the next prescribed dose of analgesic (Bennett, et al., 2005a). The baseline analgesic is inadequate to control the pain. Some experts contend that this type of pain is not actually breakthrough pain, because the baseline analgesic needs to be adjusted to control the pain throughout the prescribed dose range (Bennett, et al., 2005a). The onset of end-of-dose breakthrough pain is generally more gradual and lasts longer than incident pain (Bennett, et al., 2005a; Payne, 2006). Table 3 is an overview of the types, etiology, and treatment of breakthrough pain.

Assessment and Diagnosis of Breakthrough Pain

Diagnosis and assessment of breakthrough pain is dependent on the etiology of the pain, the patient’s understanding of breakthrough pain, and the provider/patient relationship. Patient (if able) or family self-report is essential for accurate assessment and evaluation (Bennett, et al., 2005a; Payne, 2007). A comprehensive, detailed history is the key to assessment and diagnosis of breakthrough pain. The physical examination will provide clues to the pathophysiology of the pain, trigger the implementation of further diagnostic evaluation if indicated, and help guide therapeutic intervention (NCI, 2007; Payne, 2007, Burton, et al., 2005).

The consensus panel notes that often patients are asked about their pain, but not specifically about breakthrough pain (Bennett, et al., 2005a). Furthermore, patients frequently do not have an accurate definition of breakthrough pain (Bennett, et al., 2005). Key questions to be queried should focus on the frequency and onset of additional pain episodes (pain flare-ups) above the baseline pain, severity, character, location, source, duration, intensity, contributing
Numerous unidimensional evaluation tools are available that assess pain (Numerical Rating Scale, Visual Analog Scale, Wong-Baker Faces Pain Rating Scale), but none have been researched and validated for breakthrough pain (Bennett, et al., 2005). These scales quantitatively measure pain intensity (severity), so have a limited use in assessing all of the factors involved in breakthrough pain (Bennett, et al., 2005a, Payne, 2007). The benefits of unidimensional scales are that they are easy to administer, can be done quickly, and do not require provider assistance. The Wong-Baker Faces scale can be used in children, in those with cognitive impairment and across cultures (Payne, 2007).

Multidimensional scales such as the Brief Pain Inventory and patient pain diary provide quantitative and qualitative analysis of breakthrough pain, but are time consuming and require provider assistance (Brief Pain Inventory) and evaluation (Pain Diary) (McMillan, 2001; Bennett, et al., 2005a; Payne, 2007). The advantage of these tools is the primary care provider and patient can review and analyze the pain problem comprehensively (Bennett, et al., 2005; Burton, 2004). The Pain Diary is the most telling of all of the tools. If used correctly, it assesses the type of pain, duration of pain, severity and predictability of pain over time (Payne, 2007; Bennett, et al., 2005a; McMillan, 2001). Limitations of the pain diary are: patient input (is the patient documenting and is the patient capable of documenting), provider input (is the provider reading the diary?), interpretation (is there congruence between the patient and provider, is the “diary” the whole picture?). The American Pain Foundation provides a pain diary that is easy to use and available at their website (Figure 1).
Reassessment is crucial to determine therapeutic outcomes. Bennett, et al. (2005a) advocate for using the “four A’s” in the ongoing assessment and subsequent management of breakthrough pain. The four A’s are: “(1) analgesia, (2) activities of daily living (3) adverse events, and (4) aberrant behavior” (Bennett, et al., 2005a, p. 300). Reevaluation of the cause and treatment of breakthrough pain is indicated for those who have more than four episodes a day (Bennett, et al., 2005a; Payne, 2007). Table 4 provides guidelines for assessment and diagnosis.

**Management of Breakthrough Pain**

The management of breakthrough pain in those with chronic malignant and nonmalignant pain presents challenges for primary care providers and patients (Barrie, 2005, Bennett, et al., 2005b). Management focuses on: assessment and determination of underlying source of the pain, patient variables, pharmacologic treatment, and non-pharmacologic treatment (Zeppetella, 2007; Barrie, 2005; Burton, 2005). Optimizing baseline pain medication and therapy is of paramount importance prior to breakthrough pain treatment (Bennett, et al., 2005b). The goal is to determine cause, and decrease breakthrough pain frequency and intensity with rescue medications and non-pharmacologic treatment modalities (Burton, 2005). Reassessment of around-the-clock (ATC) analgesics is needed if the patient is having more than four episodes of breakthrough pain a day. Breakthrough pain should be treated as a separate entity from the baseline pain (Bennett, et al., 2005). Therapeutic options include non-pharmacologic treatment and pharmacologic treatment options with immediate-release opioids, nonopioid analgesics, and adjuvant agents (Driver, 2007). Patient education is a key component of the treatment strategy and has been shown to reduce pain severity and symptoms, decrease stress and depression, decrease fear, and help patients and their family cope with pain (Burton, 2005).
A multidisciplinary approach is frequently used to manage chronic pain conditions. The use of specialists in physical medicine, psychiatry, psychology, occupational medicine, nutrition, pain medicine, and social services provides additional support for the patient and helps guide the care provided by the primary care provider. Referral to a pain specialist is indicated, when the patient is not responding to therapy (dose-limiting toxicity of opioid or poorly controlled pain), the primary care provider has concerns about diversion or aberrant drug behavior, the primary care provider is unsure of a treatment strategy, and/or additional assessment is indicated for interventional pain management (Bennett, et al., 2005b). Consultation with a pain specialist can provide a treatment plan for the primary care provider to follow, plus act as an additional resource for ongoing pain management concerns.

Concerns regarding medical-legal ramifications in prescribing narcotic analgesics can be addressed by using safe-practice standards for assessment and management, following local, state, and federal regulations for prescribing narcotics, and thorough medical record documentation (Bennett, et al., 2005b).

Non-pharmacologic Treatment

Non-pharmacologic treatment should be incorporated before or along with pharmacologic intervention. The aim of physical and cognitive-behavioral interventions is to empower patients to control their breakthrough pain episodes. The key to successful use of non-pharmacological treatment is patient education (McCarberg, 2007; Bennett, et al., 2005b). Many physical interventions are common sense and are frequently used by patients before they seek medical care (Burton, 2005). Examples include: limiting or pacing activity, hot/cold applications, massage, over-the-counter (OTC) remedies, analgesic creams, and binders/ace wraps (NCI, 2007; Burton, 2005; Bennett, et al., 2005b; Pray & Pray, 2003). Optimizing the
patient’s physical condition with exercise, physical therapy, and/or water therapy may help decrease the frequency of incident breakthrough pain episodes (McCarberg, 2007). Treatment with transcutaneous electrical nerve stimulation (TENS) may be of benefit in predictable, incident pain (Fishman & Moyer, 2006; Brosseau, 2006). Acupuncture and naturopathy are alternative therapies used and anecdotally of benefit to some patients with breakthrough pain (NCI, 2007; Payne, 2007). The efficacy of these therapies for breakthrough pain has not been validated in scientific studies (NCI, 2007; Payne, 2007).

Cognitive-behavioral therapy, relaxation techniques, hypnosis, and distraction techniques may be of benefit, but have not been validated as effective treatments for breakthrough pain in scientifically controlled studies (Gruener, 2004). Counseling and education promote patient understanding and the relationship between the provider and the patient. The National Cancer Institute provides a comprehensive analysis of nonpharmacologic treatment options at their website (see references).

**Pharmacologic Treatment**

Opioid analgesics are the foundation treatment for breakthrough pain. Ideally, breakthrough pain medication (rescue medication) should be efficacious, have a rapid onset of action (within minutes), have a short duration of effect (ideally less than 30 minutes), have minimal side effects, be non-invasive and easy to use, plus be cost effective (Burton, 2005, Bennett, et al., 2005; Fishman & Moyer, 2006). There is no optimal opioid analgesic medication available that meets all of these criteria. Thus, providers and patients must consider a multitude of factors to determine the most appropriate treatment. See table 5 for an overview of narcotic analgesics.
The use of the same opioid analgesic for baseline pain management and breakthrough pain management is common practice, but the efficacy of this practice has not been demonstrated (Bennett, et al., 2005b; Burton, 2005). Sustained release (for baseline persistent pain) and immediate release (rescue) formulations of the same opioid offers the advantages of easier opioid titration and management of side effects (Bennett, et al., 2005b). Disadvantages include problems of overmedication and untoward side effects occurring when the clinician increases the around the clock (ATC) or slow release (SR) analgesic to cover breakthrough pain episodes (Burton, 2005). While using the same opioid analgesic is common any immediate release opioid analgesic can be used with any long-acting opioid or transdermal opioid analgesic (Burton, 2005; Bennett, et al., 2005b; McCarberg, 2007; Davis, Walsh, Lagman, et al., 2005).

Predictable incident pain should be treated with a preemptive short-acting opioid given approximately 30 minutes before activity. Unpredictable and idiopathic breakthrough pain cannot be preemptively treated and optimal treatment would use a rapid onset lipophilic agent or an immediate release agent (McCarberg, 2007; Bennett, et al., 2005b; Davis, et al., 2005). Using one of the following two options can treat end-of-dose breakthrough pain: increase the daily dose of the ATC analgesic (this may be limited by side-effects) or decreasing the dosing interval (Bennett, et al., 2005b).

No randomized controlled studies to establish the optimal dose for rescue pain medications for breakthrough pain have been conducted (Davis, Walsh, Lagman, et al., 2005). Dosage guidelines, based on expert opinion, promote using a fixed proportion (5-17%) of the daily dose of medication and adjusting as needed to provide breakthrough pain relief (Bennett, et al., 2005b; Davis, Walsh, Lagman, et al., 2005). Titration rescue strategies promote doubling the
rescue dose, if the patient has less than 50% relief and increasing the rescue dose by 50%, if the patient has 50-100% relief (Davis, et al., 2005).

There is no correlation between the daily opioid dose and medication needed to treat the breakthrough pain episode because breakthrough pain varies in cause, onset, duration, and severity (Bennett, et al., 2005b). Further considerations when prescribing rescue medication include assessment of onset, cause, severity and duration of the breakthrough pain, current baseline medication, patient tolerance to the opioid, potential side effects and drug toxicity, plus the pharmacokinetics and pharmacodynamics of the drug (McCarberg, 2007; Bennett, et al., 2005b; Davis, Walsh, Lagman, 2005).

Morphine remains the narcotic analgesic of choice or benchmark for breakthrough pain treatment, because of its multiple routes for administration, extensive clinical use, and equivalent efficacy to other analgesics (Davis, et al., 2005). Over the last ten years different narcotic analgesics with alternate formulations have come into use and randomized controlled studies have demonstrated these formulations to be equivalent to morphine (Davies, et al., 2005). Promising research is being conducted on an intranasal morphine-chitosan agent (onset appears to be comparable to IV morphine) for the relief of breakthrough pain (Brennan, Passik, Kirsh, 2003).

Fentanyl citrate has been specifically developed for breakthrough pain (Zeppetella, 2006). Two immediate acting formulations are available: oral fentanyl transmucosal lozenge (OTFC) and fentanyl buccal tablets (FBT). These agents are classified as rapid-onset opioids (ROOs) (Gudin, 2006). OTFC has been studied extensively and reported as efficacious in the treatment of breakthrough pain in cancer patients (Burton, et al., 2004; Zeppetella & Ribeiro, 2006; Rhiner, Palos, Termini, 2004). Studies in chronic pain conditions (migraine, sickle cell,
neuropathic, and nocioceptive) reported OTFC to be efficacious with greater ease of use and patient satisfaction, higher adherence rates, lower medication needs, and fewer side-effects (Simon, 2004; Tenet, Herman, Reinking, Snyder, 2002). Portenoy, Taylor, Messina, Tremmel (2006) findings from a double blind randomized, placebo-controlled study (N=77) indicating that FBT is safe, well tolerated, and efficacious for breakthrough pain in patients with cancer. Sublingual fentanyl, aerosolized liposome encapsulated fentanyl, fentanyl nasal spray, and a matrix transdermal fentanyl controlled heat-assisted drug delivery system are all novel fentanyl delivery products that are currently under research development.

**Adjuvant Medications and Interventional Devices**

It is beyond the scope of this paper to discuss adjuvant medications and interventional devices used in pain management in detail, but it is important for primary care providers to be aware of the use of these medications and advanced interventional approaches to treat pain. Types of adjuvant medications in current use for nonmalignant and malignant chronic pain include antidepressants, anticonvulsants, alpha 2 agonists, and N-methyl-D-aspartic (NMDA) receptor antagonists (Luessier, Huskey, Portenoy, 2004). These agents have some analgesic properties and enhance the analgesic effect of opioids. Table 6 is a review of some of the adjuvant medications currently in use. Interventional approaches include nerve blockade, peripheral and spinal cord stimulation, and intrathecal infusion pump systems. Newer infusion systems have a patient controlled activation bolus function for breakthrough pain. Spinal cord stimulation systems are controlled and adjusted by the patient (Bennett, 2005c).

Non-opioid analgesics (acetaminophen, non-steroidal anti-inflammatory agents) can be used, but are limited in effectiveness due to dose-related toxicities, slow onset and long duration
of action, less analgesic potency, and potential cardiovascular and gastrointestinal morbidity (Burton, 2005; Payne, 2007).

Cost Considerations

Medication cost has an important impact on the type of narcotic analgesic used in breakthrough pain. The consensus panel promotes the use of an immediate release opioid as the most cost-effective treatment for patients with slow-onset, prolonged pain and in those with predictable pain (Bennett, et al., 2005b). Fentanyl citrate agents should be used in patients with rapid-onset idiopathic and unpredictable pain and may be more cost-effective if improved quality of life and decreased emergency health care, hospitalization, and parenteral opioid costs are realized (Burton, 2005; Burton, et al., 2004).

Conclusion

A specific, working definition of breakthrough pain has been proposed and refined by Bennett, et al. (2005a) providing clinical guidance for primary care providers. Breakthrough pain is a distinct clinical entity that should be treated separately from the baseline pain condition. Treatment consists of non-pharmacologic and pharmacologic agents. Narcotic analgesics are the mainstay of pharmacologic treatment.

Areas for research in breakthrough pain assessment and management include myths regarding pain, disparities and barriers in pain management, and nurse practitioner beliefs and attitudes and how these beliefs and attitudes impact pain management. Further research is necessary in nurse practitioner prescribing patterns for narcotic analgesics, use of multidisciplinary systems to manage pain, and practice management of patients with breakthrough pain.
Primary care nurse practitioners can successfully treat patients with breakthrough pain. Continued medical education assures that primary care providers are current in their understanding of breakthrough pain and available treatment options. A multidisciplinary approach facilitates appropriate treatment options.

The key to successful management of breakthrough pain is a comprehensive evaluation (patient history and assessment) of the background pain condition and breakthrough pain characteristics (Zeppetella, 2007). Individualized treatment is guided by the patient report, type of breakthrough pain and impact on quality of life. Patient education plays a critical role in assisting the patient to use proactive techniques that improve quality of life and enhance breakthrough pain management.
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Table 1

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<th>Common Pain Myths</th>
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<td>Fear of narcotics: physical dependency, tolerance, and addiction.</td>
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<td>Narcotic side effects are unavoidable.</td>
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<td>Functioning will be impaired using narcotics.</td>
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<td>Pain medication should be used when absolutely necessary when pain occurs.</td>
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<td>Pain is a part of serious illness. Fear that disease is progressing if pain occurs/increases.</td>
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<td>Pain builds character.</td>
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<td>Use of narcotics at the end of life will facilitate an earlier death.</td>
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<td>You can’t treat pain and disease—its one or the other.</td>
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Table 2

Effects of Pain

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<td><strong>Quality of Life:</strong></td>
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<td>Demoralizing for patient and family. Family-marital stress and altered relationships.</td>
</tr>
<tr>
<td><strong>Economic:</strong></td>
<td>Underemployment, unemployment, financial difficulties.</td>
</tr>
<tr>
<td><strong>Patient Morbidity:</strong></td>
<td>Decreased self-esteem, anxiety, depression, insomnia, isolation, suicidal ideation.</td>
</tr>
<tr>
<td><strong>Treatment:</strong></td>
<td>Increased use of narcotics, noncompliance with treatment.</td>
</tr>
<tr>
<td><strong>Overuse of Health Care Resources:</strong></td>
<td>Increased emergency room, clinic visits, hospital use.</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Subtype</th>
<th>Etiology</th>
<th>Onset/Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident</td>
<td>Related to movement.</td>
<td>Rapid/abrupt.</td>
</tr>
<tr>
<td>(predictable)</td>
<td>Examples: Musculoskeletal spasm, coughing, movement.</td>
<td>Lasts 5-15 min.</td>
</tr>
<tr>
<td>Incident</td>
<td>Visceral pain.</td>
<td>Rapid, escalation is common.</td>
</tr>
<tr>
<td>(unpredictable)</td>
<td>Examples: Renal colic, irritable bowel pain.</td>
<td>Duration depends on cause.</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Unknown cause.</td>
<td>Rapid, escalation (crescendo)</td>
</tr>
<tr>
<td></td>
<td>R/O disease progression</td>
<td>Lasts longer (&gt;30 min)</td>
</tr>
<tr>
<td>End-of-dose Failure</td>
<td>Baseline pain RX does not last to the next dose.</td>
<td>Gradual onset over time. Longer duration.</td>
</tr>
</tbody>
</table>


Table 4

Assessment and Diagnosis Guidelines for Breakthrough Pain (BTP)

<table>
<thead>
<tr>
<th>Patient Report</th>
<th>What is the patient’s definition of BTP?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>How does the patient report breakthrough pain?</td>
</tr>
<tr>
<td></td>
<td>Is BTP affecting ADL, quality of life (QOL)?</td>
</tr>
<tr>
<td></td>
<td>Onset, duration, and quality of BTP.</td>
</tr>
<tr>
<td></td>
<td>Aggravating and alleviating factors.</td>
</tr>
<tr>
<td></td>
<td>Are there beliefs, attitudes, and socioeconomic factors impacting the patient’s pain and pain treatment?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>What are the physical findings?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Is the diagnosis correct?</td>
</tr>
<tr>
<td></td>
<td>Has the pathology changed?</td>
</tr>
<tr>
<td></td>
<td>Are additional diagnostic tests indicated?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication</th>
<th>Is the medication adequately treating the baseline pain?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Is the patient experiencing side effects?</td>
</tr>
<tr>
<td></td>
<td>Is the patient taking the OTC analgesics as prescribed?</td>
</tr>
<tr>
<td></td>
<td>Are there concerns regarding addiction, tolerance, diversion?</td>
</tr>
<tr>
<td></td>
<td>Is the cost of the medications prohibitive?</td>
</tr>
<tr>
<td></td>
<td>What are the alternatives?</td>
</tr>
<tr>
<td></td>
<td>Is assistance available?</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Medication</th>
<th>Onset/Duration</th>
<th>Formulations</th>
<th>Oral Equianalgesic Dose</th>
<th>Pain Indications</th>
<th>Advantages/disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine (Morphine IR)</td>
<td>30-40 minutes</td>
<td>Oral, IM, IV</td>
<td>30 mg q 3-4 hours</td>
<td>Moderate/severe</td>
<td>Predictable, incident, Readily available, known side effects, lower cost.</td>
</tr>
<tr>
<td>Oxycodone (exp. Percocet)</td>
<td>30 minutes</td>
<td>Liquid, capsule, Tablet</td>
<td>20 mg q 3-4 hours</td>
<td>Moderate/severe</td>
<td>Predictable, incident, Similar to morphine. Compounded with acetaminophen/ aspirin/ibuprofen—potential toxicities. Expensive, diversion potential.</td>
</tr>
<tr>
<td>Hydromorphone (exp. Vicodin)</td>
<td>30 minutes</td>
<td>Tablet</td>
<td>30 mg q 3-4 hours</td>
<td>Moderate/severe</td>
<td>Predictable/incident, Compounded—limited use due to toxicities. Readily available, inexpensive.</td>
</tr>
<tr>
<td>Hydrocodone (Dilaudid)</td>
<td>30 minutes</td>
<td>Tablet, liquid, IV, suppository</td>
<td>7.5 mg q 3-4 hours</td>
<td>Moderate/severe</td>
<td>Predictable, incident, Less puritus and sedation.</td>
</tr>
<tr>
<td>Methadone (Methadose)</td>
<td>10-15 minutes</td>
<td>Oral, tablet</td>
<td>20 mg q 6-8 hours</td>
<td>Moderate/severe pain</td>
<td>Less dose escalation, inexpensive, can be used in renal failure. Long and unpredictable half-life (15-60) hr.</td>
</tr>
<tr>
<td>OTFC</td>
<td>5-10 min. 1-2 hours</td>
<td>Transmucosal lozenge</td>
<td>--</td>
<td>Moderate/severe pain Unpredictable, incident, Idiopathic</td>
<td>Caution in opioid naïve patients. Very expensive. Potential drug interactions</td>
</tr>
<tr>
<td>TBF</td>
<td>5-10 min.</td>
<td>Buccal</td>
<td>--</td>
<td>Moderate/severe pain</td>
<td>Smaller dose requirement than OTFC.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Adjuvant Medications for Breakthrough pain (not inclusive)</th>
</tr>
</thead>
</table>

**Antidepressants:**

- **TCA:** Amitriptyline, Nortriptyline, Desipramine
- **SSRI’s:** Paroxetine, Citalopram
- **SNRI’s:** Duloxetine, Venlafaxine

**Anticonvulsants:** Gaspentin, Pregabalin

**NMDA Receptor Antagonists:** Memantine, amantadine, ketamine, dextomethorphan.

Figure 1
Pain Diary

Name ______________________
Day ______________________
Date ______________________

1 DAILY PAIN CHART: Connect the points on your Daily Pain Chart so your medical team can see when and why your pain levels changed. Every day start a new chart.

2 DAILY PAIN LOG: Record your medication intake, pain level, and any other relevant information. Note any changes in your pain levels and how they affect your daily life.

MEDICATION: Name / Dose

#1 ________________________
#2 ________________________
#3 ________________________
#4 ________________________
#5 ________________________

NON-MEDICINE THERAPY (other than prescription medicines)

ACTIVITIES / EXERCISE

COMMENTS AND MORE INFORMATION: Make notes for and about work with your healthcare providers. Record any changes you may be experiencing and any problems you are having coping with your pain. You may also want to write notes about some of your answers on the previous page.

____________________________________________________________________
____________________________________________________________________
____________________________________________________________________
____________________________________________________________________
____________________________________________________________________
____________________________________________________________________
Name ____________________________
Day ____________________________
Date ____________________________

3

DAILY PAIN SUMMARY

Did you have pain today? ____NO ____YES

Did you avoid or limit any of your activities or cancel plans today because of pain or changes in your pain?

____NO ____YES: What activities?

Did you take all your pain medicine today according to instructions? ____NO ____YES

Even though you took your pain medicine for persistent pain on schedule, were there times during the day that you experienced unrelieved breakthrough pain? ____NO ____YES

How many times did this happen today?
1 2 3 4 5 6 7 8 9 10 more than 10

Did any specific activity start your breakthrough pain? ____NO ____YES What activities?

What was your average level of pain today?
0 1 2 3 4 5 6 7 8 9 10

Other than prescription medicine, did you do anything else today to relieve the pain?

____NO ____YES (Check any that you used.)

___ Non-prescription drugs (e.g., acetaminophen, ibuprofen)
___ Herbal remedies
___ Hot or cold packs
___ Exercise
___ Changing position (such as lying down or elevating your legs)
___ Physical therapy
___ Massage
___ Acupuncture
___ Rest
___ Psychological counseling
___ Talk to trusted friend, family, clergy
___ Prayer, meditation, guided imagery
___ Relaxation technique (hypnosis, biofeedback)
___ Creative technique (art or music, therapy)
___ Other (describe):

Check any of these common side effects that you've noticed after taking your pain medicine.

___ Drowsiness, sleepiness
___ Nausea, vomiting, upset stomach
___ Constipation
___ Lack of appetite
___ Other (describe)

Did you skip any of your scheduled pain medicines today? ____NO ____YES Why?

Did you call your doctor's office or clinic between visits because of pain? ____NO ____YES

Overall, are you satisfied with your pain management? ____YES ____NO (Explain what makes you satisfied or not satisfied. Use Log section.)

What pain level overall would you find acceptable?
0 1 2 3 4 5 6 7 8 9 10