

Prevalence and characteristics of breakthrough pain in patients receiving opioids for chronic back pain in pain specialty clinics

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ABSTRACT

Objective: We sought to assess the prevalence and characteristics of breakthrough pain (BTP) in patients with chronic back pain.

Design: Researchers utilized a telephone survey using a pain assessment algorithm. This report represents a subset of patients from a larger survey of 228 patients with chronic pain unrelated to cancer.

Participants: This study employed 117 subjects taking opioids for a primary diagnosis of back pain and receiving care at geographically dispersed pain treatment centers. Subjects had pain lasting at least six months and had "controlled" baseline pain.

Results: Eighty-seven subjects (74 percent) experienced 93 types of BTP. The median number of BTP episodes per day was two; median time to maximum intensity was 10 minutes, and median duration was 55 minutes. Onset could not be predicted for 46 percent of pains. Eighty-three percent of subjects used shorter-acting opioids for BTP. Other medications used for pain included NSAIDs, antidepressants, anticonvulsants, skeletal muscle relaxants, intrathecal local anesthetics, and transdermal local anesthetics.

Conclusions: These patients with opioid-treated chronic back pain commonly experienced BTP, which often had a rapid onset and a relatively short duration and was difficult to predict. Opioids were the mainstay of pharmacologic therapy, but nonopioid analgesics and adjuvant analgesics were commonly used.

Key words: back pain, chronic pain, breakthrough pain, prevalence, survey methodology

INTRODUCTION

Chronic low back pain is a common clinical problem that poses a significant burden to the healthcare system in the United States. A systematic review of the literature on the

prevalence of low back pain reveals a point prevalence ranging from 12 to 33 percent, a one-year prevalence ranging from 22 to 65 percent, and a lifetime prevalence ranging from 11 to 84 percent.¹ A recent study of the general population in the United Kingdom found that 6.2 percent of women and 3.9 percent of men had chronic back pain that was intense and disabling.² Chronic pain is known to have a detrimental effect on both general and psychological health, as well as social well-being.^{3,4} A recent study in patients with persistent low back pain showed that 50 to 75 percent of patients reported problems with activities of daily living, and more than 20 percent of patients required help with such activities as a result of their pain.³ Chronic low back pain also exerts an important economic toll; the annual cost associated with lower back pain (including both direct and indirect costs) has been estimated to range between \$50 billion and \$100 billion in the United States.⁵ Unfortunately, despite the economic and social burdens associated with chronic back pain, an understanding of the clinical phenomenon of this type of pain remains limited.

Breakthrough pain (BTP) is an important clinical phenomenon that has been well studied in patients with cancer pain.^{6,7} BTP has been defined as a transient flare of severe or excruciating pain that occurs in conjunction with well-controlled baseline or persistent pain.⁶ It occurs in between 50 and 90 percent of patients with cancer-related pain.⁶⁻¹⁰ Though less well studied, BTP is also thought to occur commonly in patients with chronic pain not related to cancer. One fairly recent study reported that 63 percent of patients with various types of non-cancer pain experienced BTP.¹¹ A survey of the prevalence and characteristics of BTP in 228 patients with chronic noncancer pain was recently completed (findings from this survey have been reported elsewhere).¹² The results of the survey indicated that the prevalence (74 percent) and characteristics of BTP in patients with chronic noncancer pain are similar to those in patients with cancer-related pain. This report is a subgroup analysis of the

Table 1. Characteristics of subjects with chronic back pain according to presence or absence of breakthrough pain

	BTP present (n = 87)	BTP absent (n = 30)
Median (range) age, years	48 (28 to 74)	48 (23 to 71)
Number (percentage) females	51 (59 percent)	16 (53 percent)
Median (range) number of years since diagnosis	7 (0.5 to 30)	5 (0.5 to 40)
Number (percentage) pain pathophysiology		
Somatic nociceptive	44 (51 percent)	20 (67 percent)
Visceral nociceptive	1 (1 percent)	0 (0 percent)
Neuropathic	4 (5 percent)	2 (7 percent)
Mixed pathophysiology	38 (44 percent)	8 (27 percent)

survey and describes BTP in patients with chronic back pain. It also examines both pharmacologic and nonpharmacologic methods used by these patients to manage their back pain.

METHODS

Details of the methodology of the survey have been described elsewhere.^{12,13} All subjects provided written informed consent prior to participation in the study, and an institutional review board approved the study prior to its commencement. In summary, eligible subjects participated in a telephone interview approximately one week after demographic information was collected in one of nine pain treatment centers in the United States. Surveys were conducted from February through April of 2004.

Subject selection

Subjects included in this subgroup analysis were between 18 and 75 years of age, had experienced pain for at least six months, were on daily opioid therapy, had a primary pain diagnosis of back pain, and had “controlled” baseline pain (moderate intensity or less). Subjects were excluded from participating in the survey if they had cancer-related pain, had been hospitalized within the previous month for uncontrolled pain, or had a clinically important neurological or psychiatric disorder that could compromise data collection.

Telephone survey

The survey instrument was adapted from a pain

assessment algorithm that had been used previously to assess BTP in patients with cancer pain.^{6,9} Controlled baseline pain was characterized by assessing its location, the time in weeks since its onset, and the nature of the pain (e.g., sharp; aching; cramping; radiating/shooting; pressing, squeezing, or tight; burning; throbbing; stabbing). Temporary (duration ≤ 12 hours) flares of severe or excruciating BTP were characterized by their duration, frequency (episodes per day), time from onset to maximal intensity, identifiable precipitating factors (if any), and any actions that successfully reduced the pain. Patients could describe up to three different types of BTP. The survey concluded with a series of sociodemographic questions.

RESULTS

Data from 117 subjects with chronic back pain were included in this subgroup analysis. Of the 117 subjects, 87 (74 percent) reported flares of BTP. A total of 93 distinct types of BTP were reported by these 87 subjects, indicating that individuals may experience more than one type of BTP.

Demographic data for each of the groups with or without BTP are shown in Table 1. The median age of subjects with chronic back pain was 48 years and ranged from 23 to 74 years. Fifty-seven percent of the subjects were female. Subjects had experienced back pain for a median of six years (range of 0.5 to 40 years), and the underlying pain pathophysiology could be broken down as follows: nociceptive in 56 percent of subjects, neuropathic in 5 percent, and mixed in 39 percent. There were no apparent differences in characteristics between

Table 2. Characteristics of types of breakthrough pain in subjects with chronic back pain (n = 93 pains)

	Median (range)
Frequency of breakthrough pain episodes	2/d (1/wk to 12/d)
Time in minutes to maximal pain intensity	10 (1 to 120)
Duration in minutes of episodes	55 (1 to 480)

subjects who reported having episodes of BTP and those who did not.

Characteristics of subjects' BTP are summarized in Table 2. The median number of episodes per day was two (range of less than one to 12). The median time to maximum intensity was 10 minutes (range of one to 120 minutes). Of note, 47 percent of the pains reached a maximum intensity within five minutes, and 59 percent reached maximum intensity within 15 minutes. Figure 1 illustrates the distribution of times to maximum intensity. The median duration of pain was 55 minutes (one to 480 minutes), with 67 percent of pains having a duration of 60 minutes or less (Figure 2). Subjects could identify a precipitant for 76 percent of the pains, and most of the precipitants (96 percent) were activity related. Non-volitional precipitants in subjects without activity-related pain included anxiety or stress (n = 1), change in weather (n = 1), and severe arthritis (n = 1). A precipitant could not be identified for 24 percent of the pains. Onset was unpredictable for 46 percent of BTPs, could sometimes be predicted for 35 percent of the pains, could often be predicted for 7 percent of the pains, and could almost always or always be predicted for 13 percent of the pains. Seventeen pains (18 percent) occurred at the end of the dosing interval of an analgesic medication.

Subjects could identify specific actions that could help reduce the intensity of the pain for 91 of the 93 BTPs (98 percent). Actions that reduced pain included medication (77 percent of pains); rest, lying down, or sitting (56 percent); heat (25 percent); moving, stretching, or physical

therapy (14 percent); cold (9 percent); transcutaneous electrical nerve stimulation (5 percent); relaxation (5 percent); distraction (3 percent); massage (2 percent); and spinal cord stimulation (1 percent). Subjects reported that these interventions worked successfully each time they were tried for only 27 percent of the pains.

Medications used by subjects are shown in Table 3. In accordance with the protocol, all subjects were receiving at least one opioid analgesic to manage their back pain, and several were using multiple analgesics. The most commonly used around-the-clock opioids were oral modified-release opioids (39 percent of subjects), methadone (20 percent), and transdermal fentanyl (15 percent). Intrathecal opioids were used by 8 percent of subjects with BTP. Shorter-acting opioids were used by 83 percent of subjects with BTP and included normal-release opioids combined with acetaminophen or a non-steroidal anti-inflammatory agent (NSAID) in 41 percent of subjects, a normal-release opioid that was not combined in 24 percent of subjects, and oral transmucosal fentanyl citrate in 28 percent of subjects.

DISCUSSION

To the best of our knowledge, this is the first study to provide a detailed description of the prevalence and characteristics of BTP in patients with chronic back pain. Understanding the phenomenon of BTP in patients with specific types of chronic pain is important not only in recognizing and diagnosing BTP but also in developing optimal

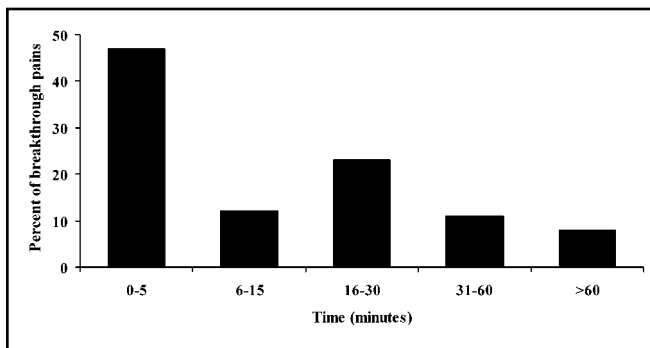


Figure 1. Distribution of times from first perception to peak intensity of breakthrough pain.

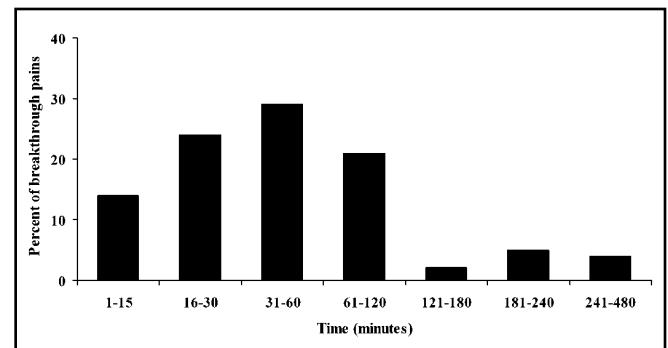


Figure 2. Distribution of durations of breakthrough pain episodes.

Table 3. Analgesics and adjuvant medications of subjects with and without breakthrough pain

Medication	BTP present (n = 87)	BTP absent (n = 30)
Opioid analgesics	87 (100 percent)	30 (100 percent)
Oral modified-release opioids	34 (39 percent)	12 (40 percent)
Transdermal opioids	13 (15 percent)	2 (7 percent)
Methadone	17 (20 percent)	5 (17 percent)
Intrathecal opioids	7 (8 percent)	0 (0 percent)
Short-acting opioids (total)	72 (83 percent)	22 (73 percent)
Combined with acetaminophen or NSAID	36 (41 percent)	11 (37 percent)
Not combined	21 (24 percent)	8 (27 percent)
Oral transmucosal fentanyl citrate	24 (28 percent)	3 (10 percent)
NSAIDs	24 (28 percent)	9 (30 percent)
Antidepressants	44 (51 percent)	13 (43 percent)
Anticonvulsants	30 (34 percent)	8 (27 percent)

treatment strategies to manage patients' pain. For example, flares of BTP that reach maximal intensity within minutes, are frequently unpredictable, and are often of relatively short duration may be alleviated by medications that are dosed as needed, have a rapid onset of analgesic effect, and have a relatively short duration. Pain that is relatively constant throughout the day is often better managed with medications that are dosed on a regular schedule around the clock, with the goal of preventing as much pain as possible. Matching the pharmacodynamic profile of medications, such as onset and duration of analgesic effect, with the individual characteristics of pain experienced by the patient offers clinicians a treatment option that may achieve better analgesia with less total medication.

The prevalence of BTP in this group of subjects—74 percent—is similar to that found in both patients with cancer-related pain and patients with noncancer pain.⁶⁻¹² Characteristics of the BTPs were also similar to those described by patients with cancer-related BTP. Specifically, they were rapid in onset (from baseline to peak intensity), had a relatively short duration, and were difficult to predict. Typically, longer-acting opioids were dosed around the clock to manage baseline pain, and shorter-acting opioids were dosed as needed to manage flares of BTP. These

subjects also required a number of nonopioid and adjuvant analgesics to manage their pain.

The chronic use of opioid analgesia for noncancer pain is controversial and is less well studied than its use for cancer pain.¹⁴⁻¹⁶ However, several studies have demonstrated the efficacy of opioids for chronic back pain, and pain specialists generally support the notion that chronic pain responds to opioid therapy in a manner similar to that of cancer-related pain.¹⁷⁻²⁰ Recent reviews have also supported the use of opioids for chronic pain not associated with cancer, including low back pain, for carefully selected patients.²¹⁻²³ However, some studies have failed to show improved back pain and function in patients using opioids relative to patients not on opioids.²⁴ Moreover, a comprehensive review of the literature on opioid therapy for chronic pain revealed that most of the literature on opioid therapy consists of reports of surveys and uncontrolled studies.²³ Evidence on long-term opioid therapy is lacking, and well-controlled studies are needed to evaluate the efficacy and safety of opioids in patients with pain not associated with cancer. There is also a need to study the potential adverse impact of BTP in patients without cancer and the role of rapid-onset, short-duration opioids in managing these adverse outcomes.

Physicians' concerns regarding the use of opioids for chronic pain are a frequent barrier to opioid management of back pain. Physicians are often reluctant to prescribe opioids for back pain, not only because of concerns about the safety and efficacy of treatments but also due to concerns about opioid abuse and its legal and regulatory ramifications.²⁵⁻²⁷ A recent survey of 230 primary care physicians showed that 35 percent would never prescribe Schedule II opioids on an around-the-clock basis for patients with chronic pain not associated with cancer, and 57 percent would never prescribe them for chronic low back pain, even after exhaustive evaluation and attempts at treatment. Concern about physical dependence was identified as one of the most important barriers to the use of opioids for chronic pain.²⁶ Another survey of physician attitudes toward opioid use for chronic pain found that 35 percent of general practitioners and 23 percent of physicians with a defined interest in palliative care would never use opioids for noncancer pain, even when the pain was described as severe.²⁷

This study has several limitations that warrant comment. First, the survey was based on subject self-report and therefore was dependent on subject recall. Second, our sample comprised subjects who were being seen at a pain clinic and who were receiving opioids for their pain. It is probable that patients who are receiving care outside a pain clinic are less likely to receive opioids for their pain and may therefore have a considerably different pain experience than subjects in our survey. As noted previously, many physicians who are not pain specialists may be reluctant to prescribe opioids, even for patients with severe pain. Indeed, a recent cross-sectional analysis of more than 25,000 patients with spine disorders showed that only 3.4 percent of patients with spine disorders at 23 specialty spine care centers across the United States were recommended, prescribed, or continued on opioid therapy.²⁸ These limitations notwithstanding, the results of this study suggest that BTP is an important clinical occurrence in patients with chronic back pain.

While pharmacologic management of cancer-related pain has improved considerably over the past 20 years, management of chronic noncancer pain remains a challenge. For noncancer pain management to achieve the same level of success as management of cancer-related pain, the clinical phenomena of specific types of pain must be understood. This article represents an important first step in understanding the prevalence and characteristics of BTP in patients with chronic back pain. Additional, well-controlled studies are needed to more fully elucidate the phenomenon of BTP in chronic pain not associated with cancer, including its impact on patients' lives and the safety and efficacy of various treatment approaches such as rapid-onset, short-duration opioids.

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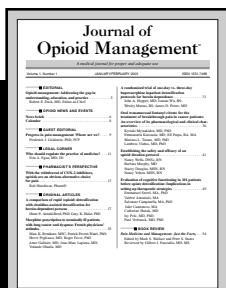
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