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INTERMITTENT CANCER PAIN: CLINICAL IMPORTANCE AND AN UPDATED CANCER PAIN CLASSIFICATION

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Abstract

Aim—We report the characteristics of intermittent cancer pain. And propose a new clinically based classification.

Methods—Consecutive cancer patients referred to our palliative medicine service were consented, and underwent a comprehensive pain evaluation including available laboratory and radiological studies, at the time of initial contact.

Results and Discussion—100 consecutive patients reported 158 different pain sites. Pain temporal pattern observed: 60% of patients had continuous (CP) plus intermittent (IP) pain; 29% IP alone; and 11% CP alone. The etiology of IP was somatic (58%), visceral (24%), neuropathic (7%), and mixed (11%). Median duration of IP was four months with a median daily frequency of four episodes.

Consequently we propose that IP be classified into: IP alone or non-breakthrough pain (NBP; since there is no underlying CP or around the clock opioids used), and breakthrough pain (BP; since there is underlying CP or / and around the clock opioids used). We propose that both BP and NBP be each sub-classified into 3 categories :(1) incident (2) non incident (3)mixed. And a fourth category exclusive to BP: end of dose failure. Incident pains made up (N=42, 47%) nearly half of all IP. According to our classification incident pain was part of BP in 41% (N=25) or NBP in 58% (N=17). Incident NBP received less treatment than incident BP, and it was less controlled.

CONCLUSION—1) IP is a major problem in cancer patients 2) NBP is a common but under-recognized form of cancer pain 3) NBP is a less defined and controlled than BP 4) Incident NBP

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accounts for 40% of all incident cancer pain 5) Variable IP definitions and classifications makes comparisons between studies difficult

INTRODUCTION

Pain occurs in 60–80% of those with advanced cancer.[1] Painstaking efforts have been invested with success to better understand and develop treatment guidelines however gaps remain. “Transient pain” remains a frequent and troublesome problem.[2] Breakthrough pain (BP), incident pain, intermittent pain (IP), transient pain, and episodic pain are widely but variably used terms for these events.[2–15] Although multiple terminologies are not an uncommon occurrence in medicine, for BP there seems to be confusion as to the term’s connotation. In an international survey of BP characteristics the prevalence significantly changed when reported by physicians of different countries.[16] “BP” has been defined differently by different authors (Table 1).[7–12] Further more incident pain has been defined as involuntary and/or voluntary pain brought about by movement, standing, coughing, bowel movement, or other precipitating factors.[7,17] No consensuses on definitions exist, so planning the most appropriate treatment using specific assessments for precise pain characterization is not possible.

“Transient Pain” is often a poorly managed temporal pain pattern which adversely influences both prognosis and quality of life.[17] In our experience, the opioid dose necessary for analgesia at rest may be insufficient for intermittent pain. A significant increase in the around the clock dose (ATC) may cause unacceptable toxicity without preventing intermittent pain.[4,18,19] Physicians should use two major pain treatment strategies: a continuous pain strategy (ATC dosing) and an intermittent pain strategy (rescue dosing). If continuous pain is then controlled but not the intermittent BP, the frequency or doses of the rescue medication should be altered independently of the ATC dose even if BP is mild but bothersome to the patient.

In this study we report the characteristics of intermittent pain in cancer patients at initial presentation to a palliative medicine program and also propose a new clinically based classification for intermittent cancer pain.

PATIENTS AND METHODS

During a period of about three months, consecutive patients referred to the Palliative Medicine Program of the Cleveland Clinic Foundation were screened for inclusion in this study. Patient were eligibility if they had a cancer diagnosis and had pain within the past month. They were ineligible if they were pain free, unable to provide a reliable history, language barrier, or if they declined verbal consent. At the time of consultation, a comprehensive pain evaluation was recorded including available laboratory and radiological studies. As part of the pain history, the attending physician completed a standard pain assessment form designed for routine clinical use.[20] Any pain was recorded irrespective of intensity. Medications, dosages, and response to pain medications were determined by patient history. The evaluating physicians determined anatomical location and

pathophysiological mechanisms for the pain(s) after review of clinical and radiological data. Details of the methodology are available elsewhere.[20]

The relation between the rescue morphine dose and the duration and percentage of IP relief was analyzed. All percentages were rounded off to the nearest whole number. Results are reported as numbers patients. The Chi-square goodness-of-fit test was used to test for differences between pain patterns.

RESULTS

Demographics

Of 156 consecutive referrals,100 were eligible. Patients reported 158 separate pain pain sites. Eighty Four had intermittent pain (IP). Examining the temporal characteristic of IP: (1) 70% had intermittent plus continuous pain, and 30% intermittent pain alone (Figure 1). IN those with IP plus continuous pain, IP etiology resembled the accompanying continuous pain in most. All patients had cancer diagnosis, with a median age of 62 years (range 20–90). Most were Caucasian (81%) and had a median ECOG performance score of 3 (range: 1–4). Sixty percent were men. The most common diagnosis was lung cancer (11%), then cancers of unknown primary (8%), breast (8%), and bladder (5%). IP in general was more common in men (P=0.02) but pain severity did not correlate with gender.

Intermittent Pain

The etiologies of the IP were somatic (58%), visceral (24%), neuropathic (7%), and mixed (11%). Overall, the intensity of the intermittent pain was severe in 16%, moderate in 44%, and mild in 40%. The median duration of intermittent pain was four months with a median daily frequency of four episodes.

Analgesic Prescribing

50% of those with IP plus continuous pain were receiving either as needed analgesics or regularly scheduled opioids without any scheduled (ATC) or rescue dose (PRN) analgesics respectively. The rest were prescribed either ATC and PRN medication (45%) or no analgesics at all (5%). Twenty-five per cent of those with IP alone had not been prescribed any opioid. The most common PRN medications was oral oxycodone/acetaminophen, followed by parenteral morphine and immediate release oral morphine. IP frequency, duration and response to rescue medication are in Table 2. IP responded to rescue medications for three hours or more in only 30% of patients. The opioid responsiveness of IP was similar regardless of etiology or character; there was no relationship between morphine rescue dose and either duration or percentage of IP relief. Incident Pain made up 40% of all IP. Incident pain was present in conjunction with continuous pain or alone (Figure 1); the identified etiology was similar in either case. Incident pain with continuous pain was more likely to be treated than incident without continuous pain.

DISCUSSION

This is the first report to specifically describe the temporal types of intermittent cancer pain without preconceived definitions. This allowed as to detect all pains present (regardless of severity), and consequently propose an unbiased IP classification.

We propose intermittent pain to be defined / categorized as follows (Figure 2):

1. **Intermittent Pain only (Non-Breakthrough Pain; NBP)**: episodic pain of any intensity without any continuous pain and in the absence of prescribed ATC analgesics. NBP would be sub-classified into incident, non-incident, and mixed pains.
2. **Continuous plus Intermittent Pain (Breakthrough Pain; BP):** episodic worsening of pain of any intensity on a background of continuous pain of any intensity, or prescribed ATC analgesic. It would be sub-classified similar to NBP (incident, non-incident, mixed), in addition to end of dose failure.

Other useful definitions

Incident Pain: is intermittent but predictable pain related to a specific precipitant, which may be voluntary (e.g. after eating) or involuntary (e.g. with cough or sneeze). Incident pain may therefore be either BP or NBP in character as it may occur with or without background continuous pain, or prescribed ATC analgesics.

Non-Incident pain: is IP with no apparent precipitating factor

End of Dose failure: is IP which consistently occur before the scheduled ATC dose. It usually indicates an inadequate ATC analgesic dose.

Previous reports have reported breakthrough and incident pain as one and the same experience; our data suggests otherwise.[13] NBP as a category has not been reported before even though we found it to be common accounting for nearly a third of all IP reported. BP in our study was common. Prevalence studies suggest that BP is common but reports vary[16] based upon the definitions used. A survey of 245 hospice patients revealed that 218 (89%) had breakthrough pain.[21]. A survey 164 cancer patients noted 51% had BP.[2] It is noteworthy that the identified etiologies in our study resembled those of patients admitted to a hospice.

Definitions—Prior definitions of cancer pain, especially, IP are an inadequate guide to patient management because all pain intensities were not included (Table 1). In addition some definitions are confusing, and hard to understand (IASP classification of chronic pain; 1986). We believe it is the temporal pattern of pain, which is of primary importance in determining analgesic scheduling. Failure to identify these temporal pain patterns, may result in inadequate analgesic prescribing. Our population was seen as palliative medicine consultations while other studies involved persons referred to a pain service.[2,8] We would have anticipated more BP (not less) in those studies. NBP, which has not been reported before, is common and accounted for just under a third of all cancer pains. Incident pain (whether BP or NBP) seems under reported in the literature as in our population it made up

almost half of all intermittent pains. The proportion of men and women with bone metastases were the same, and do not explain the greater prevalence of IP in man. This may be due to gender differences in pain thresholds or cancer primary site.

Inadequate Treatment—Intermittent pain in general (and incident pain in particular) may be more difficult to treat than continuous pain.[22–24], In our study amongst the intermittent pains, a significant minority were untreated before assessment. Incident NBP received less treatment than incident BP. This may be due to 1) the unpredictable nature of NBP and the better defined nature of BP 2) poor assessment due to inadequate knowledge of NBP and its treatment 3) physicians may ignore NBP due to the lack of continuous pain and 4) patient reluctance to report pain particularly if only intermittent. Almost half with BP were receiving both ATC and PRN medication at assessment but despite this many still complained of moderate or severe pain. The other half with BP received either PRN alone, ATC alone or no medication; unacceptable practice.

Pain Classification—Based on these observations we recommend: 1) Cancer pain be re-categorized to help routine treatment and improve clinician communication (Figure 2) 2) Breakthrough pain should be defined as a transient exacerbation of any intensity occurring in the presence of baseline pain of any intensity or while patients are receiving continuous around the clock opioid dosing 3) NBP should be defined as a transient pain of any intensity in the absence of baseline pain or scheduled opioid dosing 4) Incident pain should be specifically recorded within both the BP and NBP categories (Figure 2) 5) Incident pain (whether BP or NBP) should be treated proactively.

CONCLUSIONS

We conclude; 1) Intermittent pain is a major problem in cancer patients, 2) Intermittent NBP is common in cancer, 3) Intermittent incident NBP is common and accounts for 40% of incident cancer pain, 4) Variable definitions and classifications of intermittent pain makes comparisons between studies difficult, 5) There was no relation between rescue analgesic doses and degree or duration of intermittent pain relief, 6) The etiology of IP was somatic (58%), visceral (24%), neuropathic (7%) or mixed 16% whether BP or NBP in nature, 7) Incident pain is the most common single cause of intermittent cancer pain whether BP or NBP in character.

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REFRENCES

1. Twycross R, Fairfield S. Pain in far-advanced cancer. Pain. 1982; 14(3):303–310. [PubMed: 6218464]
2. Portenoy R, Payne D, Jacobsen P. Breakthrough pain: characteristics and impact in patients with cancer pain. Pain. 1999; 81:129–134. [PubMed: 10353500]
3. Bruera E, MacMillian K, Hanson J, MacDonald RN. The Edmonton staging system for cancer pain: preliminary report. Pain. 1989; 37:203–209. [PubMed: 2748193]

4. Cleary J. Pharmacokinetic and pharmacodynamic issues in the treatment of break-through pain. Seminars in Oncology. 1997; 24 Suppl 16(5):S16. [PubMed: 9381223]
5. Petzke K, Radbruch L, Zech D, Loick G, Grond S. Temporal presentation of chronic cancer pain: transitory pains on admission to a multidisciplinary pain clinic. J Pain Symptom Manage. 1999; 17:391–401. [PubMed: 10388244]
6. Portenoy R, Hagen N. Breakthrough pain: definition and management. Impact in patients with cancer pain. Pain. 1989; 81:129–134. [PubMed: 10353500]
7. Portenoy R, Hagen N. Breakthrough pain: definition, prevalence and characteristics. Pain. 1990; 41(3):273–281. [PubMed: 1697056]
8. Hanks, G.; Portenoy, RK.; MacDonald, N.; Forbes, K. Difficult pain problems. In: Doyle, D.; Hanks, GWC.; MacDonald, N., editors. Oxford Textbook of Palliative Medicine. 2nd edition. New York: Oxford University Press; 1998. p. 454-477.
9. Coluzzi PH. Cancer pain management: Newer perspectives on opioids and episodic pain. Am J Hosp Palliat Care. 1998; 15:13–22. [PubMed: 9468974]
10. Bennett D, Burton A, Fishman S, et al. Consensus panel recommendations for the assessment and management of breakthrough pain. Part 1 Assessment. Pharmacy & Therapeutics. 2005; 30:296–301.
11. Abrahm, JL. Assessing the patient in pain. In: Abrahm, JL., editor. A Physician's Guide to Pain and Symptom Management in Cancer Patients. 2nd edition. Baltimore, MD: Johns Hopkins University Press; 2005. p. 107-147.
12. National Cancer Institute. [accessed December 12, 2005] Pain (PDQ® health professional version. 2005. Available at: http://www.nci.nih.gov/cancertopics/pdq/supportivecare/pain/HealthProfessional
13. Payne R. Recognition and diagnosis of breakthrough pain. Pain Med. 2007 Jan-Feb;8(Suppl 1):S3–S7. [PubMed: 17280600]
14. Swanwick M, Haworth M, Lennard R. The prevalence of episodic pain in cancer: a survey of hospice patients on admission. Palliat Med. 2001; 15(1):9–18. [PubMed: 11212475]
15. Fine P, Busch M. Characterization of breakthrough pain by hospice patients and their caregivers. J Pain Symptom Manage. 1998; 16:179–183. [PubMed: 9769620]
16. Caraceni A, Martini C, Zecca E, Portenoy RK, et al. Working Group of an IASP Task Force on Cancer Pain. Breakthrough pain characteristics and syndromes in patients with cancer pain. An international survey. Palliative Medicine. 2004; 18(3):177–183. [PubMed: 15198130]
17. Mercadante S, Radbruch L, Caraceni A, Cherny N, Kaasa S, Nauck F, Ripamonti C. De Conno F Steering Committee of the European Association for Palliative Care (EAPC) Research Network. Episodic (breakthrough) pain: consensus conference of an expert working group of the European Association for Palliative Care. Cancer. 2002; 94(3):832–839. [PubMed: 11857319]
18. Walsh D. Pharmacological management of cancer pain. Semin Oncol. 2000; 27(1):45–63. [PubMed: 10697021]
19. Twycross, R. Pain relief. In: Twycross, R., editor. Symptom management in advanced cancer. Abingdon Oxon: Radcliffe Medical Press; 1997. p. 13-59.
20. Gutgsell T, Walsh D, Zhukovsky DS, Gonzales F, Lagman R. A prospective study of the pathophysiology and clinical characteristics of pain in a palliative medicine population. American Journal of Hospice & Palliative Care. 2003; 20(2):140–148. [Journal Article]. [PubMed: 12693647]
21. Zepetella G, O'Doherty C, Collins S. Prevalence and characteristics of breakthrough pain in cancer patients admitted to a hospice. J Pain Symptom Manage. 2000; 20:87–92. [PubMed: 10989246]
21. Caraceni A, Portenoy RK. An international survey of cancer pain characteristics and syndromes. IASP Task Force on Cancer Pain. International Association for the Study of Pain, Pain. 1999; 82(3):263–274.
22. Paice, J. Pain. In: Groenwald, SL.; Frogge, MH.; Goodman, M.; Yarbro, CH., editors. Cancer symptom management. Subury, Massachusetts: Jones and Bartlett publishers; 1996. p. 100-136.
23. Walsh D. Oral morphine in chronic cancer pain. Pain. 1984; 18:1–11. [PubMed: 6200818]
24. Walsh D. Symptom control in patients with advanced cancer. Am J Hosp Palliat Care. 1990 Nov-Dec;7(6):20–29. [PubMed: 14686467]

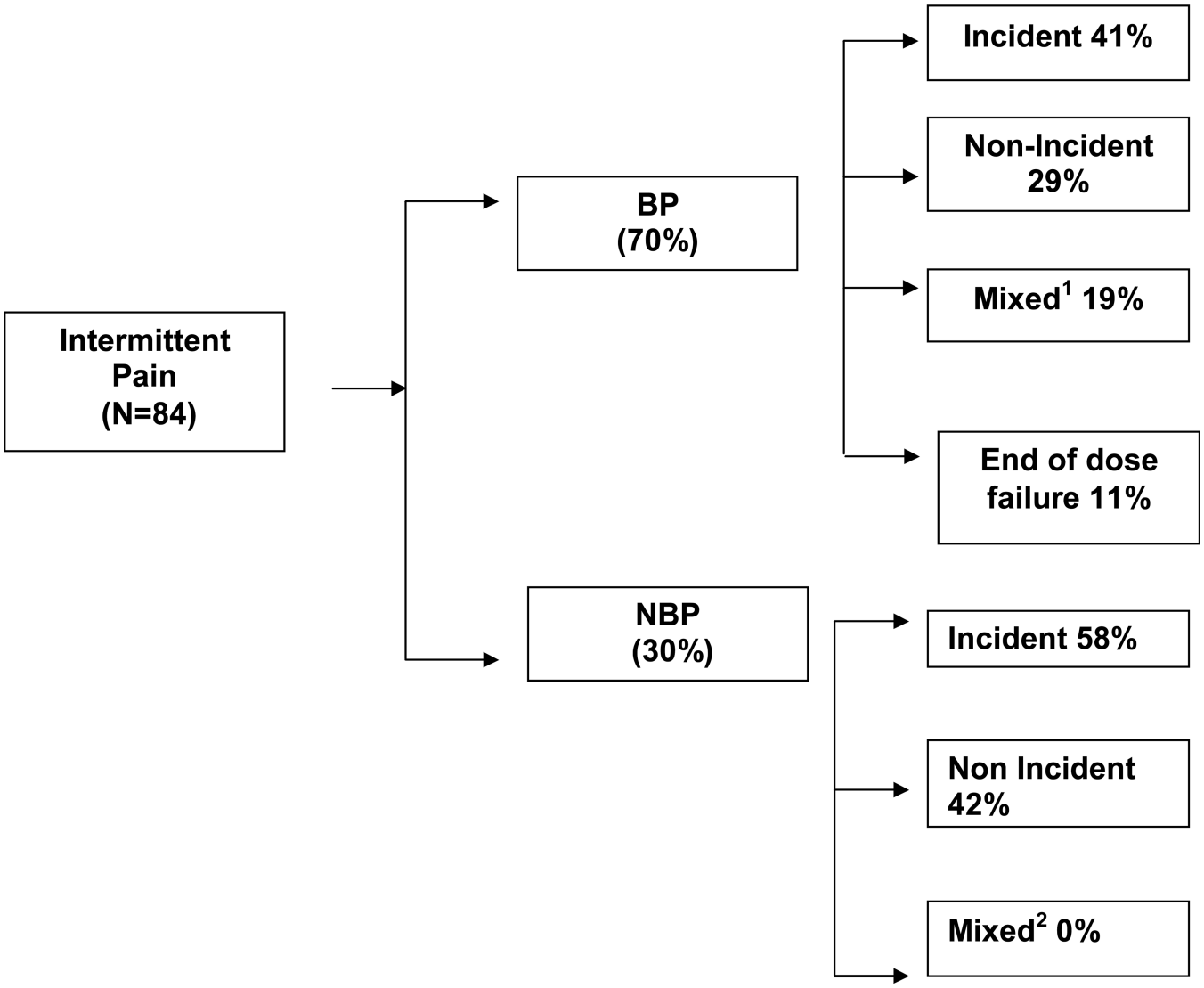

FIGURE 1.
INTERMITTENT PAIN
EODF=End of dose failure, [1]Mixed=incident, non-incident, [2]Mixed=incident, nonincident, and EODF, BP=Breakthrough or intermittent plus continuous pain, NBP=Non-Breakthrough or intermittent pain only

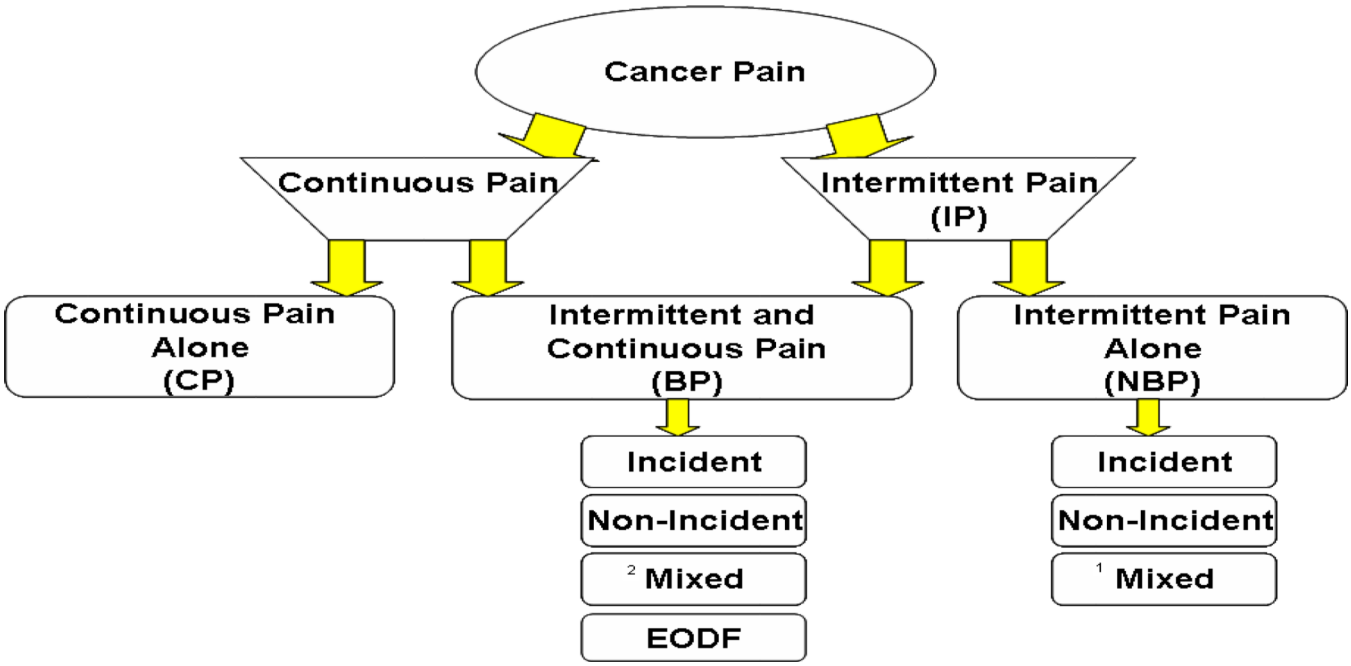

Figure 2.

PROPOSED INTERMITTENT CANCER PAIN CLASSIFICATION (CONTINUOUS PAIN IS INCLUDED JUST FOR COMPREHENSIVENESS)

EODF=End of dose failure, [1]Mixed=incident, non-incident, [2]Mixed=incident, non-incident, and EODF, BP=Breakthrough or intermittent with continuous pain, NBP=Non-Breakthrough or intermittent pain only

TABLE 1

INTERMITTENT CANCER PAIN DEFINITIONS

Transitory ↑ in Pain to > Moderate Intensity + Baseline Pain of Moderate Intensity or Less & Receiving Chronic Opioid
Transitory Exacerbation of Pain + Relatively Stable Controlled Baseline Pain
Transitory Flare of Pain + Stable Pain Pattern + Opiates
Transient Exacerbation of Pain + Stable Persistent Pain
Moderate to Excruciating Acute Pains Intermittently + Often on a Background of Well-controlled Chronic Pain
Transitory Increase in Pain That Occurs + Persistent Pain

TABLE 2

INTERMITTENT PAIN FREQUENCY, DURATION AND RESPONSE TO PRN MEDICATION AT INITIAL REFERRAL TO PALLIATIVE MEDICINE

	BREAKTHROUGH PAIN	NON-BREAKTHROUGH PAIN	INCIDENT PAIN
Frequency / 24 Hours Median (Range)	4(1–13)	3(1–24)	5(1–12)
Duration of pain before assessment; Median (Range)	4 months(1 day– 6 years)	3 months(2 days– 3 years)	4 months(1 week– 6 years)
Pain improvement > 70% Response After Rescue medication	63%	64%	50%