Degree of Pain Intolerance and Adverse Outcomes in Chronic Noncancer Pain Patients

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Introduction

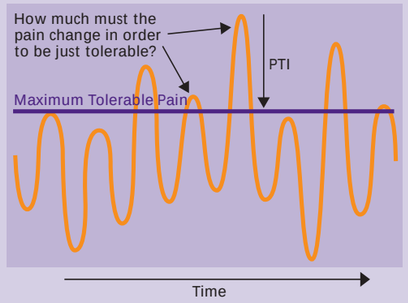
- Variations in pain intensity that occur over time in patients with chronic pain are often described in terms of breakthrough pain (BTP) and baseline or persistent pain
- Breakthrough pain (BTP) was initially defined in patients with chronic cancer pain as a transient flare in pain, increasing in intensity to severe or excruciating, occurring in conjunction with controlled baseline or persistent pain that is mostly absent due to therapy or is no more than mild or moderate intensity[1]
- Breakthrough pain in cancer patients has been shown to be a predictor of poor medical outcome.[2,3,4,5] Patients with breakthrough pain:
  - are often less satisfied with their opioid therapy
  - have decreased functioning because of their pain
  - have increased levels of anxiety and depression[6]
- Temporal variations in pain have not been well described in patients with chronic pain without cancer
- Our approach was to survey noncancer patients with chronic pain. We used a pain assessment algorithm initially developed for cancer patients[1] to determine the prevalence and characteristics of BTP. These results are reported elsewhere[7]
- We also administered three patient self-assessment surveys to assess the impact of pain on various heath related outcomes. These surveys included:
  - Brief Battery for Health Improvement 2 (BBHI 2)
  - Brief Pain Inventory (BPI) (modified short form)
  - Physical Function Scale from SF-36 (10 specific items from the SF-36)
- The BBHI 2 test is a 63 item self-report, multiple- choice instrument designed for the psychological assessment of medical patients. It has 6 scales organized into 3 domains as outlined below. An additional BBHI 2 Quality of Life scale is under development and was included in this study
  - Validity Scale
    - Defensiveness
  - Physical Symptom Scales
    - Somatic Complaints
    - Pain Complaints
    - Functional Complaints
  - Affective Scales
    - Depression
    - Anxiety
  - Psychosocial Context Scale
    - Quality of Life

Pain definitions

Breakthrough pain is defined as an affirmative response to the question: "Do you experience temporary flares of severe or excruciating pain in addition to your baseline pain?" (Note that the duration had to be 12 hours or less to qualify as "temporary")

Pain Tolerance Index is a score derived from the BBHI 2. Initially, a Peak Pain score is calculated by finding the patient's highest rated pain on the BBHI 2 (which may be either whole body pain or pain in only one bodily area). Patients are also asked to rate their Maximum Tolerable Pain score. The difference between these scores (Maximum Tolerable Pain - Peak Pain) was called the Pain Tolerance Index (PTI) (Figure 1). The PTI represents the change in Peak Pain needed to produce just tolerable levels. The more negative this number the more the patient's highest level of pain exceeds their maximum tolerated level. This peak level of pain could occur each day with temporary flares of pain (e.g. BTP) or could have occurred only once or several times per month with a duration that exceeds the 12 hour limit for defining BTP

Figure 1. Pain Tolerance Index (PTI)



Objective

- Determine the relationship of temporal variations in pain to adverse health outcomes including disability, depression, anxiety and quality of life

Methods

- Survey was conducted in nine, geographically dispersed, US pain treatment centers
- Entry criteria
  - Ages 18-75
  - Chronic noncancer pain for at least 6 months
  - Controlled baseline or persistent pain
  - Chronic opioid therapy
- Exclusion criteria
  - Cancer related pain
  - Hospitalized within previous month for surgery or uncontrolled pain
  - Neurological or psychological disorder that would, in the investigator's judgment, comprise the patient's ability to reliably respond to the questionnaire
- Three self-assessment surveys were administered after patient gave informed consent
  - BBHI 2
  - BPI modified short form
  - Physical function scale from SF36
- BTP Questionnaire
  - Administered as a telephone interview
  - First assessed characteristics of baseline pain
  - Asked if patients experience temporary flares of severe or excruciating pain in addition to their baseline pain
    - If no, patients were classified as having controlled baseline pain without BTP
    - If yes, patients were classified as having controlled baseline pain with BTP
  - For BTP patients, questionnaire
    - Allowed description of type(s) of BTP (up to 3)
    - Characterized BTP frequency, intensity and duration

Results

- 228 patients met all entry criteria

Table 1. Patient demographics

	Total (n=228)
Age, years	
Median (range)	47 (21-81)
Sex, %	
Male	41
Female	59

Table 2. Characteristics of controlled baseline pain

	Total (n=228)
Type of chronic pain, %	
Abdominal pain	5
Arthritis	
Osteoarthritis	4
Rheumatoid	1
Back pain	51
Central pain	1
Cervical neck pain	7
Complex regional pain syndrome	7
Fibromyalgia	6
Headache	
Migraine	2
Other	2
Neuropathy	
Diabetic	<1
Peripheral	2
Postherpetic neuralgia	1
Other	9
Pelvic pain	<1
Other	2
Time since diagnosis, yrs	
Median (range)	6 (0.1-55)
Pathophysiology	
Nociceptive somatic	41
Nociceptive visceral	4
Neuropathic	18
Mixed	37

BTP as a predictor of adverse outcomes

- The presence of BTP did not predict adverse outcomes in these patients as assessed by the BBHI 2 Function scale, the BPI Pain Interference scale, the SF36 Physical Function Scale, or measures of affective distress

PTI as a predictor of adverse outcomes

- The distribution of PTI Scores is shown in Figure 2
- PTI Mean -4.47; Median -5.0
- Correlations between the PTI and adverse outcomes are shown in Table 3. Similar correlation assessments with Pain Right Now score from the BPI were made for comparison purposes. Many times a single pain score is all that is available
- The PTI from the BBHI 2 and Pain Right Now from the BPI both correlated strongly with the degree to which pain interferes with a variety of life activities (BPI Pain Interference), and correlated significantly with a number of other variables as well
- The PTI correlated only -0.22 with Pain Right Now. Similarly, PTI correlated -0.27 with Overall Pain Now from the BBHI 2. This suggests that PTI may be assessing a different aspect of pain related disability
- A stepwise regression was performed to further test this hypothesis (see Table 4). Using this procedure, Pain Right Now produced an R^2 of 0.29, indicating that it accounted for 29% of the variance in Pain Interference. When PTI was included in the stepwise regression, the R^2 increased to 0.41

Figure 2. Distribution of PTI Scores

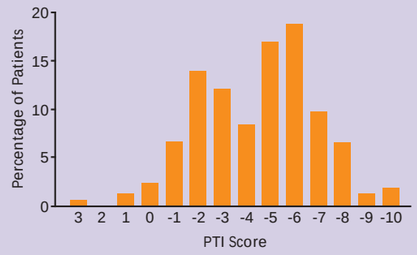


Table 3. Correlation between PTI and adverse outcomes

	PTI		Pain right now (BPI)	
	Correlation	P value	Correlation	P value
BPI Pain Interference	-0.42	<0.0001	0.52	<0.0001
SF 36 Function	0.29	<0.0001	-0.24	0.0001
BBHI 2 Function Complaints	-0.37	<0.0001	0.19	0.0071
BBHI 2 Somatic Complaints	-0.29	<0.0001	0.22	0.0011
BBHI 2 Pain Complaints	-0.34	<0.0001	0.38	<0.0001
BBHI 2 QoL	0.34	<0.0001	-0.28	<0.0001
BBHI 2 Depression	-0.23	0.0006	0.09	NS
BBHI 2 Anxiety	-0.16	NS	-0.01	NS

Table 4. Stepwise regression results

	BPI Pain Interference % variance accounted for	BBHI 2 Disability % variance accounted for
BPI Pain Right Now	29	7
PTI	21	13
BPI Pain Right Now + PTI	44	15

- The distribution of PTI scores (Figure 2) suggests a bimodal distribution. Patients were separated into an "At risk PTI group" and "Not at risk PTI group" using criteria outlined in Table 5

Table 5. Definition of At risk PTI score

Group	PTI scores	n[a]
At risk PTI	-5 or worse	106
PTI	-4 or better	93

[a]29 patients were excluded from the MANOVA due to missing data

- The At risk PTI score as a predictor of adverse outcomes was examined using a multivariate analysis of variance (MANOVA) test of between-subject effects for At risk PTI vs. Non at risk PTI. See Table 6
- Overall, the at-risk group as defined by PTI had significantly higher levels of disability on three different measures (SF 36 Function, BBHI 2 Functional Complaints and BPI Pain Interference). This group also had significantly higher levels of diffuse pain complaints, somatic preoccupation, and a significantly lower quality of life. Although PTI correlated significantly with BBHI 2 Depression, PTI was not associated with Depression or Anxiety when using MANOVA, which was a more stringent test of this relationship

Table 6. MANOVA Tests of Between-Subjects Effects for At risk PTI vs. Not at risk PTI Patients

Dependent Variable	Type III Sum of Squares	df	Mean Square	F	P value
BPI Pain Interference	5170.701	2	2585.351	15.018	<0.001
SF 36 Function Score	213.451	2	106.725	6.398	0.002
BBHI 2 Somatic Complaints	622.471	2	311.235	4.061	0.019
BBHI 2 Pain Complaints	1202.777	2	601.388	9.808	<0.001
BBHI 2 Functional Complaints	1662.549	2	831.274	7.506	0.001
BBHI 2 Depression	389.393	2	194.697	1.936	NS
BBHI 2 Anxiety	4.334	2	2.167	0.017	NS
BBHI 2 Quality of Life	322.390	2	161.195	8.356	<0.001

- It is important to note that in the clinical setting, there may be two ways to improve the PTI. One is to lower the level of Peak Pain (for example through pharmacological approaches) and the other is to increase the level of Maximum Tolerable Pain (for example through the used of behavioral approaches to increase pain tolerance). Thus, an advantage of PTI is that it is one index that can assess the combined influence of treatment in a multidisciplinary pain program

Summary

In the survey of 228 non-cancer patients with controlled baseline pain

- The presence of BTP did not predict adverse health related outcomes
- PTI, which is a measure of how much peak pain in the last month exceeds maximum tolerated pain, did predict adverse health related outcomes including:
  - Physical Function (SF 36, BBHI 2)
  - Quality of Life (BBHI 2)
  - Somatic Complaints (BBHI 2)
  - Diffuse Pain Complaints (BBHI 2)
  - Pain Interference (BPI)
  - Depression (BBHI 2)
- When PTI is assessed as a continuum, BBHI 2 Depression was significantly related. However, when the PTI was reduced to a dichotomous high/low variable, Depression was no longer significantly related
- The PTI provides different information than a single assessment of Pain Right Now and may a better assessment of multidisciplinary pain management approaches that use both pharmacologic and nonpharmacologic modalities

CONCLUSION

These findings suggest that the pain tolerance index (PTI), which is the degree to which a patient's maximal pain score over the past month exceeds the reported tolerable pain score, is an important but previously unresearched dimension of chronic pain associated with adverse outcomes. Clinically, it may be a useful index to monitor responses to multidisciplinary pain management approaches

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