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Original Article

Efficacy and Practicality of Opioid Therapy in Japanese Chronic Noncancer Pain Patients

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ABSTRACT

Background: Many Japanese adults suffer from chronic pain. However, 50% of these individuals discontinue treatment despite the persistence of pain. Both clinicians and patients in Japan tend to be concerned about the safety and efficacy of opioid therapy, and the use of opioids in chronic non-cancer pain remains less common in Japan than elsewhere.
Aims: This study examined the effects of opioid therapy on the daily lives of patients with chronic noncancer pain in Japan, where use of opioids for this type of pain remains uncommon.
Design: Prospective cross-sectional questionnaire study.
Setting: Data were collected over two periods, between March and April 2014 at one hospital, and between February and April 2015 at the other hospital. Subjects were recruited at the respective clinics by the study interviewer between March 1, 2014 and April 15, 2014 and between February 1, 2015 and April 15, 2015.
Participants/Subjects: This study included 34 outpatients with chronic non-cancer pain who were being treated with opioid analgesics at pain clinics in two hospitals in Sapporo.
Methods: Thirty-four Japanese patients receiving opioid medications for chronic noncancer pain in outpatient pain clinics were enrolled. Participants underwent interviews and completed the Japanese versions of the Short Form 36 (SF-36v2) and the Coping Strategies Questionnaire (CSQ).
Results: Sleep disruption, claiming compensation for work-related accidents, and current pain level were negatively correlated with opioid effectiveness ($p < .05$). Additionally, opioid effectiveness was negatively correlated with the catastrophizing subscale of the CSQ ($r = -0.50$, $p < .01$). The effects of opioid therapy had a low positive correlation with the emotional functioning role subscale of the SF-36v2 ($r = 0.38$, $p < .05$). Daily equivalent morphine dose was positively correlated with opioid therapy duration, interference with appetite, and current pain intensity. Morphine dose was also positively correlated with scores for the catastrophizing subscale of the CSQ ($r = 0.36$, $p < .05$) and negatively correlated with scores in all subdomains of the SF-36v2.
Conclusions: It is important to focus on adaptive, cognitive, and emotional factors, such as emotional role functioning, to determine the efficacy of opioid treatment for chronic noncancer pain. Moreover, patients with catastrophizing significantly increased their morphine doses, resulting in an increased risk of overdose.
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Approximately 45.2% of Japanese adults suffer from chronic pain. However, 50% of these individuals discontinue treatment despite the persistence of pain because of decreased satisfaction with treatment (Nakamura, Nishiwaki, Ushida, & Toyama, 2014). Many Japanese adults with chronic musculoskeletal pain lose or change their occupation, leave college, or are absent from work (Nakamura, Nishiwaki, Ushida, & Toyama, 2011). Chronic pain can cause physical disability, depression, and a lower quality of life, as well as financial and employment difficulties (Achterberg et al., 2010; Gillespie & Friedman, 2007; Johannes, Le, Zhou, Johnston, & Dworkin, 2010; O'Brien et al., 2017).

In the United States, 2001-2010 was defined as "The Decade of Pain Control and Research" (National Center for Health Statistics, 2006), during which pain was identified as "the fifth vital sign" for monitoring a patient's condition, in addition to body

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Key Practice Points

- Opioids are not used as widely in Japan as elsewhere, especially for chronic non-cancer pain. We used a self-reported questionnaire to assess the perceived costs and benefits of opioid treatment in a group of such patients. Most of the patients evaluated their treatment as an overall benefit, but high doses carry risks that it is important for medical professionals, including nurses, to understand.

temperature, pulse, respiration, and blood pressure. Subsequently, pain assessment became a priority for national policies concerning the treatment of pain. Some of the direct costs of treating pain include increased medical practitioner and hospital visits for diagnosis, treatment, drugs, therapy, additional medical costs, loss of work time, loss of productivity, and concentration at work or while conducting other activities (McCool, Smith, & Aberg, 2004). In 1998 total health care expenditures incurred by individuals with back pain in the United States reached $90.7 billion (Luo, Pietrobon, Sun, Liu, & Hey, 2004).

Inspired by international concern about pain treatment, the Japanese Ministry of Health, Labour and Welfare inaugurated the "Meeting on Chronic Pain" in 2009. Subsequently the ministry published a proposal in 2010 from a Study Panel on Chronic Pain that laid out a future approach for the medical treatment of pain (Labour and Welfare, 2010). The findings of this meeting were used to develop measures for improving the quality of life of patients with chronic pain. A chronic pain prevention project was started in 2011, and a survey was conducted at 19 universities across the country. A comprehensive program incorporating many social aspects, including the evaluation of activities of daily living (ADL), quality of life (QOL), and education of chronic pain patients was organized and deployed (Nakamura et al., 2011, 2014; Wakaizumi et al., 2017). In addition, Ushida (2015) preached the necessity of a multidisciplinary pain center to encourage chronic pain diagnosis and treatment. Treatment in these centers is provided by a team of specialists in anesthesiology, psychiatry, and orthopedics, as well as the relevant paramedical professionals. Consequently, they have funded a pain center for comprehensive chronic pain care in Japan (Ushida et al., 2016). However, there have been fewer Japanese nursing studies focusing on chronic noncancer pain than on chronic cancer-related pain. At least one study found that Japanese nurses often handle chronic pain incorrectly (Takai & Uchida, 2009).

The pathogenesis of chronic pain is complex, because pain can arise from a wide variety of underlying causes. Low back pain is the most common chronic pain condition (Chou et al. 2007; Iizuka et al., 2017; Yoshimura et al., 2014) and is reportedly associated with decreased activities of daily living and quality of life (Hirano et al., 2014; Nakamura et al., 2011). In addition, chronic pain can be divided into two categories: nociceptive pain (associated with damage to body tissues) and neuropathic pain (Otis, 2007). Neuropathic pain is defined as "pain caused by a lesion or disease of the somatosensory nervous system" (International Association for the Study of Pain, 2012). The severity of neuropathic pain tends to be particularly high, and its duration is often long. Neuropathic pain also substantially reduces quality of life (Bouhassira, Lantéri-Minet, Attal, Laurent, & Touboul, 2008). The prevalence of neuropathic pain in developed countries is estimated at 5%-10% of the general population (Bouhassira et al., 2008; Van Hecke, Austin, Khan, Smith, & Torrance, 2014). Postherpetic neuralgia and fibromyalgia are also chronic pain conditions. Fibromyalgia is characterized by widespread muscle pain, multiple tender points, and fatigue (Wolfe et al. 1990, 2010), often with multiple symptoms occurring together.

Chronic pain treatment includes both noninvasive treatments, such as medication, physical therapy, and psychotherapy, and invasive treatments, such as nerve blocks and spinal cord stimulation (Dosenovic et al., 2017; Xing, Zhou, Zhang, & Yan, 2017). Previous studies have reported that opioid therapy is useful for alleviating chronic pain symptoms, improving QOL, and reducing the cost of treatment (Ballantyne & Mao, 2003; Portenoy, 2000). Consequently, prescriptions of opioid medications for chronic pain have increased dramatically (Boudreau et al., 2009; Sullivan et al., 2008a, b). In older adults with chronic pain and no significant comorbidity, short-term use of opioids is associated with reduction in pain intensity and better physical functioning (Chaparro et al., 2014; Papaleontiou et al., 2010). However, this trend has been accompanied by greatly increased levels of prescription opioid overdose, abuse, addiction, and diversion (Deyo et al., 2013; Noble et al., 2010; Rolita, Spegman, Tang, & Cronstein, 2013). In a recently reported study, the evidence was found to be insufficient to validate the effectiveness of long-term opioid therapy for improvement of chronic pain (Chou et al., 2015).

The Japanese guidelines (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012) state that "opioid therapy is used for almost all diseases that produce chronic noncancer pain that patients complain about, with the exception of psychogenic pain." However, the most important statement in the guidelines is that opioid analgesics are not the first-line therapy for relieving pain in all cases of chronic noncancer pain. In Japan, opioid therapies are mostly restricted to cancer patients, and in the Japanese guidelines, the opioid drugs available to patients with chronic noncancer pain are limited to codeine phosphate, morphine hydrochloride, fentanyl, buprenorphine, pentazocine, and tramadol (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012). Moreover, clinicians, nurses, pharmacists, and patients in Japan tend to be concerned about the safety and efficacy of opioid therapy even for cancer pain (Okamoto, 2011). Japan was the first Asian nation to enact legislation and to control opioid use within its boundaries when the Japanese government severely restricted the use of opioids (Greberman & Wada, 1994). Two regulations (the Narcotics Control Law and health care insurance system) have limited the use of opioid therapy over the years in Japan. Consequently, the use of opioids in chronic noncancer pain is much less common in Japan than in the United States or Germany (Cheung et al., 2014; Duthey & Scholten, 2014). In 2010 the indications for the use of fentanyl patches in the Pharmaceutical Affairs Act were revised and a new item was added: "Pain relief with non-opioid analgesia or weak opioids for moderate to severe intractable chronic pain." As a result of this revision, fentanyl, as a strong opioid, can now be prescribed for chronic noncancer pain using health insurance. In 2011, transdermal buprenorphine patches and tramadol/acetaminophen combination tablets, which are classified as psychotropic in Japan and as strong opioids in some other countries, were released for use in chronic noncancer pain treatment. This addition constitutes official approval of opioid therapy for chronic noncancer pain in Japan. With new treatment options for patients suffering from chronic noncancer pain, Japanese society's expectations for the benefits of opioid analgesics are large and have led to increasing opioid use in Japan (Berterame et al., 2016). Further Japanese guidelines on the appropriate diagnosis of chronic noncancer pain and proper use of opioid analgesics were published in 2012 (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012). Thus the limited number of opioid analgesics available to Japanese patients with chronic noncancer pain and the established national guidelines

are expected to prevent more widespread use of opioid therapy in the future. It is expected that prescriptions by physicians who are not versed in and have little experience with opioid therapy for chronic noncancer pain will increase in the future; therefore, the Japanese guidelines emphasize protecting patients from adverse drug reactions to opioids, especially the harmful effects of high-dose or long-term prescriptions. In Europe and the United States, guidelines for the use of opioid therapy for chronic pain have been published (Chou et al., 2009), and the risks and efficacy of opioids have been evaluated (Deshpande, Furlan, Mailis-Gagnon, Atlas, & Turk, 2007; O'Brien et al., 2017). These guidelines encourage a risk-benefit assessment before the use of opioids, and patients who are treated with opioids must be carefully observed because opioids may adversely affect a patient's quality of life. The Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (Chou et al., 2009) state that the risk of abuse and dependence is greater than the benefit of treatment in cases in which 200 mg or more morphine milligram equivalent (MME) per day is administered, in which case opioid treatment should be reconsidered. In contrast, the Japanese guidelines published by Japan Society of Pain Clinicians (JSPC) established the maximum daily dose as 120 mg MME (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012). In addition, this guideline stipulated that the use of an injectable agent is not permitted under any circumstances. However, the recent standard published by the U.S. Centers for Disease Control and Prevention is stricter, at a maximum daily dose of 90 mg MME (Dowell, Haegerich, & Chou, 2016).

Moreover, the objectives of opioid therapy for chronic noncancer pain have aspects that differ from those of therapy for postoperative pain or cancer pain (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012). It is likely that many problems will appear as opioid therapy is continued. In particular, the harmful effects of opioid therapy often show up in the form of abuse or dependence when opioid analgesics are used at high dosages in overly aggressive pursuit of pain relief (Chou et al., 2015). Therefore it is necessary to be familiar with the negative aspects of opioid analgesics in opioid therapy for chronic noncancer pain. The effective goal of opioid therapy for chronic noncancer pain is to return to the kind of daily life that was lost because of chronic pain and to improve ADLs, QOL, and mental health. However, there have been limited Japanese nursing studies focusing on chronic noncancer pain, and there have been almost no studies on Japanese patients with chronic noncancer pain receiving opioid therapy.

The present study aimed to elucidate the relationships among pain level, pain self-management measures, the self-evaluated efficacy of treatment, and everyday physical, mental, and social health in Japanese patients receiving opioid therapy for chronic noncancer pain.

Material and Methods

This study was conducted with the approval of the ethics committees of our university and the participating hospitals. All patients provided written informed consent before participating in this study, and all work was carried out in accordance with the Declaration of Helsinki.

Participants

The study cohort consisted of individuals who used opioid analgesic prescriptions for noncancer pain problems. The specific inclusion criteria were adults aged 20 years and older who received opioid therapy in a pain clinic and had chronic pain that continued for 6 months or more. Individuals with a diagnosis of dementia were excluded.

This study included 34 outpatients with chronic noncancer pain who were being treated with opioid analgesics at pain clinics in two hospitals in Sapporo. Data were collected over two periods, between March and April 2014 at one hospital and between February and April 2015 at the other hospital. Participants were recruited at the respective clinics by the study interviewer between March 1, 2014, and April 15, 2014, and between February 1, 2015, and April 15, 2015. The participants completed questionnaires while waiting for treatment in the outpatient ward, either without assistance or with verbal help from the interviewer.

Medical History and Opioid Dose

Information on patient medical history was collected using a structured interview format. The following variables were recorded: age, sex, occupation, income level, health insurance, pain location, duration of continuous pain, and duration and type of opioid therapy. Opioid doses were converted to oral morphine equivalent doses to allow comparison between different opioid medications. The formula for tramadol used for calculating the morphine equivalent was taken from a previous study (Schug & Gandham, 2006). The formula for codeine used the Japanese guideline (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012), which estimated a ratio of 1:6 for oral morphine to codeine. The formula used for transdermal fentanyl was taken from Caraceni et al. (2012), who estimated a ratio of 100:1 for oral morphine to transdermal fentanyl.

Buprenorphine was not included in the source guidelines. Therefore the formula used for it was taken from Caraceni et al. (2012), who estimated a ratio of 75:1 for oral morphine to transdermal buprenorphine. Tramadol hydrochloride/acetaminophen combination tablets also were not included in the source guidelines. Therefore the formula used for them was taken from Perrot, Krause, Crozes, and Naïm (2006), who estimated that tramadol hydrochloride/acetaminophen combination tablets (37.5 mg tramadol/325 mg acetaminophen) were equivalent to 50 mg tramadol capsules.

Self-Evaluated Effectiveness of Opioid Treatments

Before further assessments, each participant rated the effectiveness of his or her previous nonopioid treatment and current opioid treatment as the percentage of pain relief (0 = no relief, 100 = complete relief). This scale used a part of the Japanese Brief Pain Inventory, which has proven validity and reliability (Uki, Mendoza, Cleeland, Nakamura, & Takeda, 1998).

The adverse effects of opioid therapy in the past month were evaluated on a 4-point categorical scale (none, mild, moderate, severe). In accordance with a previous study, the adverse effects considered were nausea, vomiting, dizziness, drowsiness, constipation, and diarrhea. These effects were examined to determine if they may have been caused by opioid therapy (Schug & Gandham, 2006).

Pain Severity Assessment Using a Visual Analog Scale

Pain severity was assessed using a visual analog scale (VAS). The VAS consisted of a 10-cm horizontal line, with start and end points labeled “no pain” and “worst possible pain,” respectively (Joyce, Zutshi, Hrubes, & Mason, 1975). Each patient was asked to mark the points corresponding to his or her worst, least, and current pain

intensity for the last month, as well as to his or her "comfort goal" pain score (Pasero & McCaffery, 2007). "Comfort goal" was defined as the pain level that would enable the patient to participate in recovery activities or normal daily life. These are commonly used as chronic pain measures, with considerable evidence supporting their reliability and validity (Jensen, Turner, Romano, & Fisher, 1999).

Measuring QOL Impairment Using the Short Form 36 Questionnaire

The Japanese version of the Short Form 36 (SF-36v2) questionnaire was used to assess QOL impairment (Fukuhara, Ware, Kosinski, Wada, & Gandek, 1998). The SF-36v2 is a commonly used measure with considerable evidence supporting its reliability and validity across samples and languages (Fukuhara et al., 1998). This questionnaire consists of eight scaled scores for assessing QOL and is useful for various diseases and for healthy individuals. The eight scales that make up this QOL assessment are physical functioning, physical role functioning, emotional role functioning (RE), social role functioning (SF), mental health (MH), body pain (BP), vitality (VT), and general health. Raw scores were converted to a 100-point scale. The responses to the 36 questions were collated, providing an overall score from 0 (worst possible health) to 100 (best possible health). Each of the eight subscales was scored on a 0-100 basis, with a higher score indicating better health-related quality of life.

Measuring the Effect of Pain on Sleeping and Eating Patterns

The extent of the interference that each participant's pain had in sleeping and eating patterns for the month before enrolling in the study was evaluated using an 11-point numeric rating scale that ranged from 0 (does not interfere) to 10 (very strongly interferes).

Investigating Pain Self-Management Using the Coping Strategy Questionnaire

The Coping Strategies Questionnaire (CSQ) was used to assess the participants' behavioral strategies for managing pain. This method has proven validity and reliability for studying coping strategies in patients suffering from chronic pain (Otake & Shimai, 2002; Rosenstiel & Keefe, 1983). The CSQ (Japanese short version [CSQ-J]) classifies coping strategies as cognitive or behavioral. It assesses the use of six cognitive coping strategies (diverting attention, reinterpreting pain sensations, coping self-statements, ignoring pain sensations, praying or hoping, and catastrophizing) and two behavioral coping strategies (increasing activity level and increasing pain behavior). Using a 6-point scale, participants indicated how often they use each strategy when experiencing pain, where 0 = never, 3 = sometimes, and 6 = always. The CSQ-J contains two questions for each cognitive and behavioral strategy; therefore the scores for each coping strategy range from 0 to 12 points.

Data Analysis

All data analyses were conducted using the software IBM SPSS Version 22 (SPSS Japan, Tokyo, Japan). Several values were missing because one patient did not answer the question about side effects. Correlations among age, pain duration, opioid therapy duration, self-evaluated effectiveness of opioid treatments, daily morphine dose (low: ≤40 mg; high: >40 mg), pain severity (VAS), health insurance, SF-36v2 scores, and CSQ scores were analyzed using Spearman rank order correlations. Some of the variables were not normally distributed; therefore the data were analyzed using rank order statistics. Values of $r < 0.1$, $0.1 \geq r < 0.3$, $0.3 \geq r < 0.5$, and $r \geq 0.5$ were considered insubstantial, small, moderate, and large correlations, respectively, based on Cohen's criteria (Cohen, 1988).

Daily morphine dose was used to split the data into two groups (low: ≤40 mg, high: >40 mg) at the median rate (40 mg), in accordance with a previous study (Dunn et al., 2010). The relationship between self-evaluated effectiveness of opioid treatments and effectiveness of previous nonopioid treatment was analyzed using the Wilcoxon signed-rank test. A p value of <.05 was considered statistically significant.

Table 1
Characteristics and Analgesic History of Patients (N = 34)

	Total Mean ± SD	Median
Age, years	60.8 ± 15.8	65.0
Pain duration, years	11.3 ± 9.6	9.1
Opioid therapy, years	3.5 ± 2.8	2.5
Daily morphine equivalent dose, mg	69.1 ± 92.3	40
Sleep disruption (0 = none, 10 = worst)	3.7 ± 3.2	3
Interference with appetite (0 = none, 10 = worst)	2.7 ± 3.1	2
Visual Analog Scale (0 = no pain, 10 = pain as bad as you can imagine)		
Worst*	7.6 ± 1.9	7.6
Current pain	4.0 ± 2.6	4.4
Least	2.1 ± 1.8	1.9
Comfort goal	2.2 ± 1.7	2
	N	**%**
Sex		
Male	17	50.0
Female	17	50.0
Working		
Yes	6	17.6
No	28	82.4
Economic satisfaction*		
Yes	17	51.5
No	16	48.5
Health insurance		
Medical insurance	29	85.3
Industrial accident compensation insurance	5	14.7
Pain location		
Head	5	14.7
Chest	6	17.6
Lower back	8	23.5
Pudenda	5	14.7
Extremity	10	29.4
Daily morphine equivalent dose		
High dose (>40 mg)	14	41.2
Low dose (≤40 mg)	20	58.8
Opioid therapy (multiple other)		
Morphine, oral	12	35.3
Fentanyl, transdermal	5	14.7
Buprenorphine, transdermal	2	5.9
Tramadol hydrochloride, oral	4	11.8
Tramadol hydrochloride/acetaminophen, oral	14	41.2
Codeine, oral	2	5.9

SD = standard deviation.
* n = 33.

Results

Participant Characteristics and Analgesic Usage History

A total of 34 outpatients (17 male, 17 female) were included in the final analysis. Fifteen patients chose not to participate in this study. The participants' characteristics and history of analgesic use are presented in Table 1. The average age was 60.8 ± 15.8 years (range 22-86, median 65). The mean duration of chronic pain was 11.3 ± 9.6 years (range 0.25-33, median 9), and the mean duration of opioid administration was 3.5 ± 2.8 years (range 0.04-8.83, median 2.5).

Table 2
Adverse Effects of Opioid Therapy in Patients With Chronic Noncancer Pain (N = 34)

Adverse Effects	No. of Patients (%)	Male/Female	Morphine	Fentanyl*	Buprenorphine, Transdermal	Tramadol	Tramadol/Acetaminophen*	Codeine*
Nausea	11 (32.4)	7/4	5	2	1	1	4	0
Vomiting	4 (11.8)	2/2	3	1	0	0	1	0
Dizziness	15 (44.1)	8/7	8	3	1	1	5	0
Drowsiness	20 (58.8)	10/10	6	2	2	3	7	1
Constipation†	21 (63.6)	10/11	7	5	1	2	9	2
Diarrhea†	13 (39.4)	7/6	3	2	1	1	7	1

* Combined prescription: morphine + fentanyl, n = 3; fentanyl + tramadol/acetaminophen, n = 1; codeine + tramadol/acetaminophen, n = 1.
† n = 33.

Adverse Effects of Opioid Treatments

The major adverse effects of opioid therapy were investigated for the study cohort. Participants treated with opioids experienced the following symptoms: constipation (63.6%), drowsiness (58.8%), dizziness (44.1%), diarrhea (39.4%), and nausea (32.4%) (Table 2).

Efficacy of Current Opioid Therapy Compared with Previous Nonopioid Treatment

On average, participants rated their current opioid therapy as providing significantly better pain relief compared with previous nonopioid treatment ($p < .001$; Table 3).

SF-36v2 Scores and CSQ Scores for Opioid Treatment Responses

The SF36v2 subdomain scores and CSQ scores are listed in Table 4. All participants had QOL scores lower than the average score in Japan (Fukuhara & Suzukamo, 2011).

On the CSQ, reinterpreting pain sensations (1.85) and catastrophizing (1.97) had the lowest scores, and the highest scores were for self-assessed coping (6.03) and diverting attention (5.15).

Efficacy of Opioid Therapy, Pain, and Social Insurance

On average, participants claiming worker's accident compensation insurance rated their current opioid therapy significantly lower for pain relief compared with medical insurance patients ($p < .05$; Table 5). In addition, they rated their least pain level significantly higher than medical insurance patients. Their expectations for comfort level were lower than those of medical insurance patients. However, the difference was not significant.

Factors Influencing the Effectiveness of Opioid Therapy

Tables 6 and 7 present summaries of the Spearman rank order correlation analysis for identifying correlations among age, pain duration, opioid therapy duration, self-evaluated effectiveness of opioid treatments, daily morphine dose, pain severity (VAS), SF-36v2 scores, and CSQ scores. Sleep disruption and current pain level were negatively correlated with participants' self-evaluated effectiveness of opioid therapy. The effectiveness of opioid therapy was also negatively correlated with scores for the catastrophizing subscale of the CSQ ($r = -0.50$, $p < .01$). Opioid therapy effectiveness was positively correlated with age and had a weakly positive correlation with the RE subdomain of the SF-36v2 ($r = 0.38$, $p < .05$).

Effects of Daily Equivalent Morphine Dose

Daily equivalent morphine dose was not correlated with self-evaluated effectiveness of current opioid therapy. Daily equivalent morphine dose was positively correlated with opioid therapy duration, interference with appetite, current pain intensity, and severity of the lowest pain level experienced. Morphine dose was also positively correlated with scores for the catastrophizing subscale of the CSQ ($r = 0.36$, $p < .05$) and was negatively correlated with scores in all subdomains of the SF-36v2 and with participant age.

Effects of Current Pain Severity on Opioid Treatment Responses and QOL

Current VAS pain level was negatively correlated with the effects of opioid therapy and with scores from the BP and RE subdomains of the SF-36V2. Interference with appetite was positively correlated with current pain level. Additionally, current pain level was positively correlated with scores for the catastrophizing subscale of the CSQ ($r = 0.42$, $p < .05$).

Effects of Highest, Minimum, and Comfort-Goal Pain Severity

The presence or absence of comorbidities and appetite interference were positively correlated with VAS worst pain level. Scores for the BP, general health, VT, SF, and RE subscales of the SF-36v2 questionnaire were negatively correlated with maximum pain level. There was no correlation between highest pain level and any CSQ scores.

Sleep disruption, interference with appetite, and claiming worker's accident compensation insurance were associated with higher minimum pain levels. The score on the catastrophizing subscale of the CSQ was positively correlated with minimum pain level ($r = 0.35$, $p < .05$). Six of the eight SF-36v2 subscales, including physical functioning, BP, VT, SF, RE, and MH, were negatively correlated with minimum pain level.

Table 3
Self-Evaluated Effectiveness of Opioid Therapy in Patients With Chronic Noncancer Pain (N = 34)

Self-Evaluated Effectiveness of Therapy	Total Mean ± SD (Range)	Median (25%, 75%)	p^*
Previous nonopioid therapy (0 = no relief, 100 = complete relief)	20.6 ± 25.8 (0-100)	15 (0, 30)	<.001
Current opioid therapy (0 = no relief, 100 = complete relief)	53.6 ± 20.6 (0-80)	60 (35,70)	

SD = standard deviation.
* Wilcoxon signed rank test.

Table 4
Short Form 36 (SF-36) Scores and Coping Strategy Questionnaire (CSQ) Scores in Chronic Noncancer Pain Patients Receiving Opioid Therapy (N = 34)

Scale	Total (Mean ± SD)	Japanese Standard Score (Mean ± SD)*
SF-36 (maximum score, 100 points)		
PF; physical functioning	58.7 ± 30.2	89.1 ± 13.9
RP; physical role functioning	58.5 ± 33.2	89.2 ± 18.8
BP; body pain	36.7 ± 21.0	73.8 ± 22.4
GH; general health perception	47.2 ± 27.7	62.9 ± 18.8
VT; vitality	44.7 ± 21.8	62.8 ± 19.5
SF; social functioning	51.8 ± 37.6	86.4 ± 19.4
RE; emotional role functioning	66.9 ± 31.9	87.8 ± 20.0
MH; mental health	56.9 ± 25.9	71.6 ± 18.6
CSQ (maximum score, 12 points)		
Praying or hoping	2.97 ± 3.58	—
Catastrophizing	1.97 ± 2.55	—
Coping self-statement	6.03 ± 4.76	—
Diverting attention	5.15 ± 4.49	—
Reinterpreting pain sensations	1.85 ± 3.16	—
Ignoring pain sensations	3.88 ± 3.55	—
Increasing activity level	4.76 ± 2.58	—
Increasing pain behaviors	4.32 ± 3.80	—

SD = standard deviation.
* Suggested reference: Fukuhara & Suzukamo 2011.

The BP and MH SF-36v2 subscales were negatively correlated with comfort-goal pain level. The daily equivalent morphine dose and self-evaluated effectiveness of current opioid therapy were not correlated with comfort-goal pain level.

Discussion

To our knowledge, the present study is the first to use a self-reported questionnaire to investigate the effects of long-term opioid therapy in Japanese outpatients with chronic noncancer pain. Our results indicate improvements in pain relief after long-term opioid therapy. We report a negative correlation between current pain measured using the VAS and self-evaluated opioid effectiveness. Although pain is known to fluctuate throughout the day, the level of pain that causes patients to visit the hospital could have an impact on their self-assessments of treatments.

Claiming worker's accident compensation insurance was negatively correlated with the efficacy of opioid therapy. In a situation where injury has occurred as a result of someone else's error or negligence, the victim might experience a sense of injustice (Miller, 2001). It has been previously reported that this feeling is a risk factor for poor recovery outcomes, particularly if this perception pertains to physical function and return to work (Sullivan et al., 2008a, b; Sullivan, Scott, & Trost, 2012). McCracken (1998) defined the acceptance of chronic pain as "acknowledging that one has pain, giving up unproductive attempts to control pain, acting as if pain does not necessarily imply disability, and being able to commit one's efforts toward living a satisfying life despite pain" (p. 22). The relevant data support some of these components. For example, a previous study reported that current pain levels and pain acceptance are important predictors for QOL in patients with chronic pain (Mason, Mathias, & Skevington, 2008). Furthermore, if treatment of the injury is paid for using worker's compensation insurance, symptoms may consciously or unconsciously be influenced for the purposes of primary or secondary gain.

We also found that many participants experienced nausea (32.4%) and constipation (63.6%) after receiving opioid therapy. Gastrointestinal symptoms are known side effects of opioid medications (Michna et al., 2014; Kalso, Edwards, Moore, & McQuay, 2004). This finding is also supported by a Taiwanese study (Lin, Hsu, Lu, Tsai, & Ho, 2010), in which the major adverse effects of opioids were found to be constipation (48%) and nausea and vomiting (21%). Compared with previous studies, this study reports a higher incidence of nausea and constipation. Additionally, in this study interference with appetite was positively correlated with the various VAS pain levels and daily opioid dose. Thus an increase in daily opioid dose because of increased pain intensity may interfere with appetite. Furthermore, opioid-induced constipation negatively affects pain management and QOL (Bell et al., 2009; Panchal, Müller-Schwefe, & Wurzelmann, 2007), which results in increased health care utilization and costs (Fernandes et al., 2016). Better pain management with opioid treatment therefore requires further assessment of the gastrointestinal side effects of these drugs.

Self-evaluated effectiveness of opioid therapy had a significant positive correlation with age. However, daily morphine dose was negatively correlated with age, suggesting that older patients might control pain with smaller doses of opioids. It has been previously suggested that interdisciplinary pain rehabilitation incorporating opioid withdrawal can more effectively improve long-term psychological, social, and physical functioning in geriatric chronic pain patients compared with middle-aged and young patients (Darchuk, Townsend, Rome, Bruce, & Hooten, 2010). However, opioid

Table 5
Effectiveness of Opioid Therapy, Pain, and Social Insurance (N = 34)

Parameter	Medical insurance	Worker's Accident Compensation Insurance	*p*
Self-Evaluated Effectiveness of Current Opioid therapy*			**.044**†
N (Median)	28 (60)	5 (40)	
Mean ± SD (Range)	56.4 ± 20.9 (0-80)	38.0 ± 8.4 (30-50)	
Visual analog scale			
Current pain			.318
N (Median)	29 (4.0)	5 (5.0)	
Mean ± SD (range)	3.8 ± 2.7 (0-8.9)	5.1 ± 2.1 (2.0-7.3)	
Worst*			.305
N (Median)	29 (7.4)	4 (8.2)	
Mean ± SD (range)	7.5 ± 2.0 (3.3-10)	8.5 ± 1.0 (7.6-10)	
Least			**.013**†
N (Median)	29 (1.6)	5 (4.2)	
Mean ± SD (range)	1.8 ± 1.7 (0-5.0)	4.0 ± 1.2 (2.0-4.9)	
Comfort goal			.327
N (Median)	29 (2.0)	5 (0.0)	
Mean ± SD (range)	2.3 ± 1.6 (0-6.0)	1.6 ± 2.3 (0-5.0)	

SD = standard deviation.
Bold is emphasize $p < .05$ score.
* n = 33, Mann-Whitney test.
† $p < .05$.

Table 6
Correlation Between Effectiveness of Opioid Therapy and Social Variables (N = 34)

Parameter	Self-Evaluated Effectiveness of Current Opioid Therapy*	Daily Morphine Equivalent Dose (0 = Low Dose, 1 = High Dose)
Age, years	0.46†	−0.45†
Pain duration, years	0.05	0.27
Opioid therapy, years	−0.33	0.38‡
Self-evaluated effectiveness of previous nonopioid therapy*	0.074	0.15
Economic satisfaction	−0.06	0.06

* 0 = no relief, 100 = complete relief; Spearman's rank correlation coefficient.
† $p < .01$.
‡ $p < .05$.

management requires special consideration for elderly patients because age is positively associated with increased sensitivity to opioid analgesics (Kaiko, 1980; Scott & Stanski, 1987). Elderly patients undergoing opioid therapy have a greater risk of experiencing adverse drug reactions, including sedation, nausea, vomiting, constipation, urinary retention, and respiratory depression (Weiner & Hanlon, 2001). Opioid medications may also exacerbate preexisting conditions that are common in the elderly, such as dementia, impaired mobility, and urinary retention in men with benign prostatic hypertrophy (Ensrud et al., 2002; Weiner, Hanlon, & Studenski, 1998). Therefore long-term opioid treatment for elderly patients with chronic pain requires careful management.

Opioid effectiveness was negatively correlated with the catastrophizing subscale of the CSQ. This finding is supported by a previous study, which reported that the catastrophizing subscale is not only related to pain severity but also to other important pain-related behaviors (Keefe, Rumble, Scipio, Giordano, & Perri, 2004). Other studies have found that catastrophizing is significantly related to negative moods, such as anxiety (Geisser, Robinson, & Henson, 1994), and that patients who catastrophize have higher levels of disability (Martin et al., 1996; Robinson et al., 1997). Furthermore, catastrophizing behavior is consistently associated with increased depression, pain, and patient-reported physical disability (Jensen, Turner, & Romano, 2001). For example, chronic pain symptoms improve when catastrophizing behavior decreases after treatment and pain management (Burns, Kubilus, Bruehl, Harden, & Lofland, 2003; Spinhoven et al., 2004).

The present study demonstrates that the self-evaluated effectiveness of current opioid therapy is not correlated with any subscale of the CSQ other than catastrophizing. However, the self-evaluated effectiveness of current opioid therapy did have a positive correlation with the SF-36v2 RE subscale. In a recent study, participants with chronic pain tended to believe that long-term opioid therapy helped them control their pain and allowed them to participate in important activities, such as work (Robinson, Dansie, Wilson, Rapp, & Turk, 2015). Participants who were unable to work because of chronic pain reported higher levels of affective distress, catastrophizing, and functional interference compared with working participants. The mental ability required for daily work and subsequent decreases in catastrophizing behavior could be an important predictor of opioid treatment effectiveness.

Surprisingly, morphine dosage did not appear to be significantly associated with self-evaluated effectiveness of current opioid therapy. Although there were no differences in effect by opioid dosage, we did identify a positive correlation between dosage and interference with appetite, which is a hindrance to QOL as assessed by the SF-36. In addition, opioid treatment period was positively correlated with morphine daily dose. Moreover, catastrophizing scores increased significantly with increasing morphine dose. Pain catastrophizing is associated with intentional overdose or past attempted suicide (Sansone, Watts, & Wiederman, 2014). Catastrophizing thoughts have been associated with greater pain and disability and reduced treatment efficacy in most studies (Wertli et al., 2014). These variables may help to determine the

Table 7
Correlation of Effectiveness of Opioid Therapy With Visual Analog Scale, SF-36, and CSQ Scores (N = 34)

Parameter	Self-Evaluated Effectiveness of Current Opioid Therapy*	Daily Morphine Equivalent Dose	Visual Analog Scale			
			Current Pain	Worst	Least	Comfort Goal
Self-evaluated effectiveness of current opioid therapy*	10.00	−0.16	−0.45†	−0.17	−0.17	−0.33
Daily morphine equivalent dose (0 = low dose, 1 = high dose)	−0.16	10.00	0.39‡	0.21	0.38‡	0.11
Sleep disruption (0 = none, 10 = worst)	−0.42‡	0.24	0.28	0.23	0.59†	0.18
Interference with appetite (0 = none, 10 = worst)	−0.25	0.39‡	0.43‡	0.44‡	0.66†	0.15
Other diseases (0 = none, 1 = yes)	0.01	0.01	0.01	0.44‡	−0.06	0.07
SF-36 (full score 100 points)						
PF; physical function	0.01	−0.43‡	−0.15	−0.31	−0.43‡	−0.25
RP; physical role functioning	0.29	−0.63†	−0.32	−0.31	−0.34	−0.06
BP; body pain	0.15	−0.56†	−0.38‡	−0.51†	−0.56†	−0.34‡
GH; general health perception	0.23	−0.42‡	−0.31	−0.38‡	−0.24	−0.31
VT; vitality	0.13	−0.36‡	−0.32	−0.41‡	−0.57†	−0.27
SF; social functioning	0.15	−0.42‡	−0.33	−0.52†	−0.44‡	−0.29
RE; emotional role functioning	0.38‡	−0.49†	−0.41‡	−0.36‡	−0.53†	−0.10
MH; mental health	0.22	−0.48†	−0.30	−0.31	−0.47†	−0.34‡
CSQ (full score 12 points)						
Praying or hoping	−0.05	0.04	−0.12	−0.24	−0.08	0.05
Catastrophizing	−0.50†	0.36‡	0.42‡	0.30	0.35‡	0.30
Coping self−statement	0.23	−0.21	−0.18	0.11	−0.09	−0.15
Diverting attention	−0.01	0.13	0.12	0.11	0.30	0.11
Reinterpreting pain sensations	0.14	−0.03	0.07	−0.03	0.25	−0.01
Ignoring pain sensations	−0.00	−0.13	−0.11	−0.13	0.02	−0.08
Increasing activity level	−0.13	0.11	−0.06	0.14	−0.18	−0.11
Increasing pain behaviors	0.17	0.03	−0.07	−0.14	0.10	0.06

SF-36 = Short Form 36; CSQ = Coping Strategies Questionnaire.
* 0 = no relief, 100 = complete relief; Spearman's rank correlation coefficient.
† $p < .01$.
‡ $p < .05$.

therapeutic effects of opioids and the risk of high opioid dose, using only self-evaluations by the patient. It is now known that higher opioid dose is associated with increased risk (Gomes, Mamdani, Dhalla, Paterson, & Juurlink, 2011). High doses and prolonged use of opioid therapy have been known to cause serious problems such as intestinal dysfunction, sexual dysfunction, cognitive dysfunction, immune dysfunction, abuse dependence, analgesic tolerance, and pain sensitivity (Ballantyne & Mao, 2003; Dunn et al., 2010; Noble et al., 2010). Therefore physicians should ensure that patients take the minimum opioid dose required for effectiveness. In particular, the results of an evidence-based structured review indicate that estimates of the fraction of patients in whom long-term opioid therapy exposure leads to abuse or addiction range from less than 1% to 40% (Cheatle, 2015; Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008; Martell et al., 2007). A recent population-based study reported that addictive behaviors were identified in 22.6% of long-term opioid users with chronic pain, compared with 11.5% of nonopioid users with chronic pain and 8.9% of the individuals without chronic pain (Højsted, Ekholm, Kurita, Juel, & Sjøgren, 2013). Therefore a strong association was found between long-term opioid use and addictive behaviors. The European Federation of Chapters of the International Association for the Study of Pain recommends that opioid treatment should not be considered a lifelong treatment (Kalso, et al., 2003). Opioid treatments have to be discontinued, or the dose reduced, if the patient experiences a significant improvement in the painful condition (such as improvement of ADLs and QOL) or a poor outcome of treatment. It is important to caution the patient about opioid-caused side effects and to halt treatment not only when negative signs and deteriorating quality of life appears but also when the quality of the patient's life is improved. In addition, a recent study reported that patients treated with long-term opioid therapy for chronic noncancer pain and followed in a tertiary care pain center are at low risk for opioid misuse or abuse because of screening and monitoring of the patents with a comprehensive examination (Vargas-Schaffer & Cogan, 2017). For this reason, when opioid therapy begins to be prescribed in Japan, it will be necessary to select patients by conducting a comprehensive examination to determine whether they are suitable for an opioid prescription. Moreover, we should explain to patients beforehand all the side effects and opioid abuses risks and gain agreement that opioid therapy is not a permanent treatment method.

Limitations

It is important to acknowledge the limitations of the present study. First, as with all cross-sectional studies, we were unable to establish the direction of associations or any causal relationships. Second, this study was restricted to a small sample of patients from Hokkaido in the northernmost area of Japan. A Japanese study reported that their chronic pain was adversely influenced by bad weather and also by oncoming bad weather (Inoue et al., 2015). Therefore it may not be representative of individuals with chronic noncancer pain from other parts of Japan.

Nursing Implications

Awareness of the benefits and consequences of opioid therapy in adults with chronic noncancer pain enables clinicians to intervene appropriately and to act as advocates for patients using chronic opioid therapy. Although our results did indicate that patients with noncancer pain evaluated opioid therapy as effective, the data also identified several nursing problems in Japan. First, when physicians select opioid therapy for patients with noncancer chronic pain, it is important that nurses perform comprehensive pain assessments, evaluating mental condition and pain history. Opioid therapy may be ineffective in patients who have a history of occupational injury or catastrophizing. Nurses should assess, together with physicians, whether a patient is suitable for opioid therapy, by gathering information such as case histories, medical histories, and family histories. Nurses should perform comprehensive, continuing interviews, and consult about daily life and psychosocial factors.

Second, medical professionals should assess both mental state and daily life functions to prevent overdose. This includes administration of a VAS to assess daily tasks and roles. In particular, elderly patients undergoing opioid therapy have a greater risk of experiencing adverse drug reactions. Opioid medications may also exacerbate preexisting conditions that are common in the elderly, such as dementia and impaired mobility. Therefore long-term opioid treatment for elderly patients with chronic pain requires the same sort of careful management and monitoring that are used for clinical research patients. If patients cannot regularly consult a doctor, nurses should call them and check the reason.

Moreover, the objectives of opioid therapy for chronic noncancer pain have aspects that are entirely different from those of therapy for postoperative pain or cancer pain (Committee for the Guidelines for Prescribing Opioid Analgesics for Chronic Noncancer Pain of JSPC, 2012). In particular, the harmful effects of opioid therapy often become significant when opioid analgesics have been used at high doses in an overly aggressive pursuit of pain relief. Therefore it is necessary to be familiar with the risks of opioid analgesics in opioid therapy for chronic noncancer pain. The goal of opioid therapy for chronic noncancer pain is to return to the kind of daily life that was lost because of chronic pain and to improve performance of ADLs, QOL, and mental health. Nurses should be familiar with guidelines for opioid treatment of chronic noncancer pain as well as for cancer pain. Therefore ongoing education regarding chronic noncancer pain is crucial in the nursing field.

Conclusions

Patients with chronic noncancer pain rated opioid therapy as significantly more effective compared with previous nonopioid treatments. Patients who evaluated opioid therapy as less effective tended to demonstrate more catastrophizing coping behavior. Furthermore, patients who rated opioid therapy as highly effective had higher RE scores. These findings suggest that it is important to focus on adaptive, cognitive, and emotional factors, such as RE, to determine the effectiveness of opioid treatments for chronic noncancer pain. Additionally, more than half the participants in this study experienced constipation and/or drowsiness after receiving opioid therapy. The presence of comorbidities and appetite interference increased the severity of the worst pain levels experienced by patients. Hence these factors require further assessment to identify the most appropriate treatment options for chronic noncancer pain.

Even though we did not identify a correlation between self-evaluated effectiveness of opioid therapy and opioid dosage, we did find that appetite interference was positively correlated with dosage. In addition, opioid treatment period was positively correlated with morphine dose. Moreover, catastrophizing scores increased significantly with increasing morphine dose. These variables appear to be helpful in determining the therapeutic effects of opioids and the risk of opioid overdose using only self-evaluations.

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