Acta Neurochir (2011) 153:181–190
DOI 10.1007/s00701-010-0785-4

CLINICAL ARTICLE

Evaluation of efficacy and safety of fentanyl transdermal patch (Durogesic®D-TRANS) in chronic pain

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Received: 12 November 2009 / Accepted: 18 August 2010 / Published online: 7 September 2010

Abstract
Purpose Opioids are used in controlling several types of pain. This study was designed to evaluate the efficacy and safety of the fentanyl transdermal patch-type system (Durogesic® D-TRANS).
Methods Patients who complained of chronic moderate to severe pain were enrolled. Administration dosages of fentanyl patch started from 12.5 μg/h and could be increased by 12.5 μg/h or 25 μg/h, if the average pain score of 4 or higher occurred within 72 h. The total administration period was 12 weeks. The type, location, characteristics, and duration of pain were evaluated. Also, on day 0, weeks of 4, 8, and 12, the physician's assessment of pain intensity, the patient's assessment of pain intensity, the assessment of impact of pain on functions, and the assessment of the impact of pain on sleep were assessed. In addition, side effects were evaluated during the study duration.
Results A total of 65 cases were enrolled, and the final evaluated cases were 41. Before treatment, the average physician's assessment of pain intensity was 6.70±1.41, and the average patient's assessment of pain intensity was 7.02±1.63. In the final visit, the average physician's assessment of pain intensity was 2.58±1.72, and the average patient's assessment of pain intensity was 2.86±1.78.
Conclusions This prospective study shows that the fentanyl patch is effective in alleviating moderate to severe chronic noncancer pain including neuropathic pain down to mild pain. Therefore, the fentanyl patch should be considered before other invasive intervention procedures in chronic moderate to severe noncancer pain.

Keywords Fentanyl patch · Chronic pain · Neuropathic pain · Nociceptive pain

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Introduction

Opioids are the standard choices in drug therapy for pain control, and morphine is considered the gold standard in terms of efficacy in the relief of cancer pain [5, 6]. However, despite their potent analgesic effects, proper treatment of pain through the administration of opioids has been limited due to regulations, prejudice, and ignorance. In the review of "Tragedy of Needless Pain" in 1990, Ronald Melzack [22], known for his gate control theory of pain, reported that medical doctors have not executed proper treatment for patients with severe chronic pain due to an obscure fear of opioid addiction.

In clinical findings, no addiction to opioid analgesics has been reported in patients without a previous history of narcotic intake [30]. Additionally, in animal testing, the compensatory mechanism of morphine is blocked in chronic pain [26, 27, 33].

Conventionally, general analgesics, anti-depressants, and anti-convulsants have been used to treat neuropathic pain. However, the significance of opioids in the treatment of neuropathic pain is still under discussion [5, 15, 31]. When

pain is categorized into neuropathic pain and nociceptive pain, opioids are known to have no efficacy in treating neuropathic pain, but are efficacious for nociceptive pain [5, 15, 31]. In addition, opioids have not been widely used because adverse events occurred before the opioid concentration required to control pain can be reached [19, 20, 29]. However, in recent studies, opioids have been reported to have similar analgesic effects for both neuropathic pain and nociceptive pain [3, 25].

Morphine, unlike other medications, is used for standard opioids. It is used mainly for chronic pain as a sustained release (SR) oral medication, but one of its side effects, severe constipation, can affect the quality of life for patients [9].

In contrast, Durogesic® D-TRANS, a percutaneous deliverer of fentanyl, is a patch transdermal system in which the opioid is systemically absorbed by sustained dissolution for 3 days (72 h). Research on Durogesic® [2, 11, 12, 14, 28] showed analgesic effects on cancer pain, with less constipation and sedative actions, and patient preference was significantly higher compared to slow release morphine medications [2, 28]. Additionally, fentanyl has been found to relieve neuropathic pain, which has no susceptibility to general opioids [10]. In recent studies, it was reported that, if used carefully, opioids can be efficacious and safe for patients who have no history of opioid analgesic administration [24].

Therefore, this study was designed to evaluate the efficacy and safety of Durogesic® D-TRANS (opioids) in patients with chronic noncancer pain and to determine the usefulness of the medication by assessing patient function based on the severity of pain.

Materials and methods

Study materials

This study was conducted on 65 patients (male/female) who complained of chronic noncancer pain requiring opioid analgesics. The number of patients who satisfied the hypothesis (the percentage of patients, whose percent change in pain intensity was higher than 50%, was 30%, and the attrition rate was 10%; in a previous study [10] on the efficacy of fentanyl for neuropathic pain, the percentage of patients for which change in pain intensity was higher than 50% was 58%) of this study under a significance level of 0.025 (one-tailed test) and verification of 0.90 was 41, and 52 patients were registered for the study because the expected withdrawal rate was 20%.

The inclusion criteria for patient enrollment for this study was a complaint of chronic pain (persisting for more than 3 months) of the spine and limbs that scored more than 4 points (moderate pain) on the numeric rating scale (NRS) 72 h prior to baseline data, with a minimum age of 19. Patients were required to demonstrate overall good health, within two times the normal range, in terms of disease/administration history, physical examination, blood pressure/pulse, and laboratory tests prior to the administration of the study drug, and to be capable of communicating sufficiently with clinicians regarding their pain. Females with the possibility of pregnancy during the trial were advised to take measures for contraception, and only subjects who provided their written consent were allowed to participate in this study.

Patients were excluded from this study if they were participating in other clinical trials, had a history of a hypersensitivity to opioid analgesics, had a history of narcotics abuse, or had a history of mental illness. In addition, patients with a dermatological disease preventing the administration of a dermal medication, a history of CO_2 retention, a surgery (which can influence pain) in the pain areas within 7 days prior to this study, a severe illness that could have an impact on the interpretation of the study outcomes, or who had a pain complaint that was related to an insurance case such as a car accident were excluded from participation.

Study method

This study is a prospective open trial.

After the patients had voluntarily agreed to participate in this study, physical examinations and laboratory tests were executed after checking the patients' vital signs such as blood pressure and pulse. The pain intensity was evaluated using the NRS, and only those whose average pain intensity for the last 72 h exceeded 4 points, and who had pain that persisted for more than 3 months, were allowed to participate in this study. Once the patient was deemed qualified to participate in the study, previously administered medications, types/areas, and characteristics of pain were investigated; pain intensity was also evaluated, both by clinician and patient. Next, impacts of pain on daily life, gait, food intake, mood control, and sleep were evaluated. Patients were administered with the study drug for 12 weeks, and continuation of study participation was determined after evaluating the pain intensity and the adverse events related to the study drug through a phone inquiry in the first week. In the 4th, 8th, and 12th weeks, pain intensity, satisfaction, and adverse events relating to pain treatment were investigated. Patients were considered to have completed the trial if at any time during the study their number for average pain intensity was 0 (= pain is completely dissipated) on the NRS for a duration of more than 72 h. Satisfaction with pain treatment was measured by the patient and clinician. Satisfaction from the patient was evaluated on a five-point scale of "very satisfied, satisfied, average, dissatisfied, very dissatisfied," and specific reasons for satisfaction were also described.

Satisfaction from the clinician was evaluated by considering overall satisfaction with the study drug, the patient's pain management, and adverse events. In the event that a patient was unable to control pain or endure adverse events during the trial, a direct visit to the center was possible, and patients were treated accordingly.

Patients who were not already being administered opioid analgesics were administered 12.5 μg/h of the study drug. For patients already being administered opioids, the initial dosage of administration was determined based on the equianalgesic potency conversion table. Since it takes 12–24 h from the first administration to reach the maximum blood concentration, it is recommended to administer a daily dosage of the previous analgesic (taliflumate) together with the study drug on the 1st day of administration.

Administration dosage of the fentanyl transdermal patch (Durogesic® D-TRANS) could be increased by 12.5 μg/h or 25 μg/h if the patient experienced an average pain level of 4 or higher, based on the pain intensity measured at each visit. When the average scale of pain reached 4 or higher between visits, the dosage could have been increased, if the patient visited the center. Durogesic® D-TRANS was replaced within a 3-day interval, since the patch releases fentanyl at a steady rate for 3 days.

If not approved by the investigator, the initiation of an administration of new medication other than analgesics, or a change in the dosage of a previously administered medication, was to be avoided. The administration of other narcotic analgesics was not permitted, but nonsteroidal anti-inflammatory drugs (NSAIDs; talniflumate) were administered if necessary. Patients steadily administered other central nervous system (CNS) depressants, such as anti-anxiety drugs, hypnotics, and tricyclic anti-depressants (TCAs), prior to participation in the study were allowed to be continuously administered the same dosage of their previous medications. When necessary, the concomitant use of anti-emetics and anti-histamines was allowed. When the administration of a systemic agent was necessary for treatment of non-pain-related symptoms, it was administered as steadily as possible during the course of this trial. However, the administration of additional medications or concomitant medications for the treatment of adverse events occurring after study participation was allowed.

Patients were considered to have completed the trial if they participated in the trial without serious violations of the clinical protocol and if, at any time during the study, the number for the average pain intensity was 0 (= pain is completely dissipated) on the NRS for the last 72 h. The clinical trial was discontinued in the following circumstances: occurrence of severe adverse events, severe drowsiness, or unresponsiveness to verbal stimuli, when deemed necessary for the safety of the patient by the investigator, when the patient did not comply with the study procedures, when the

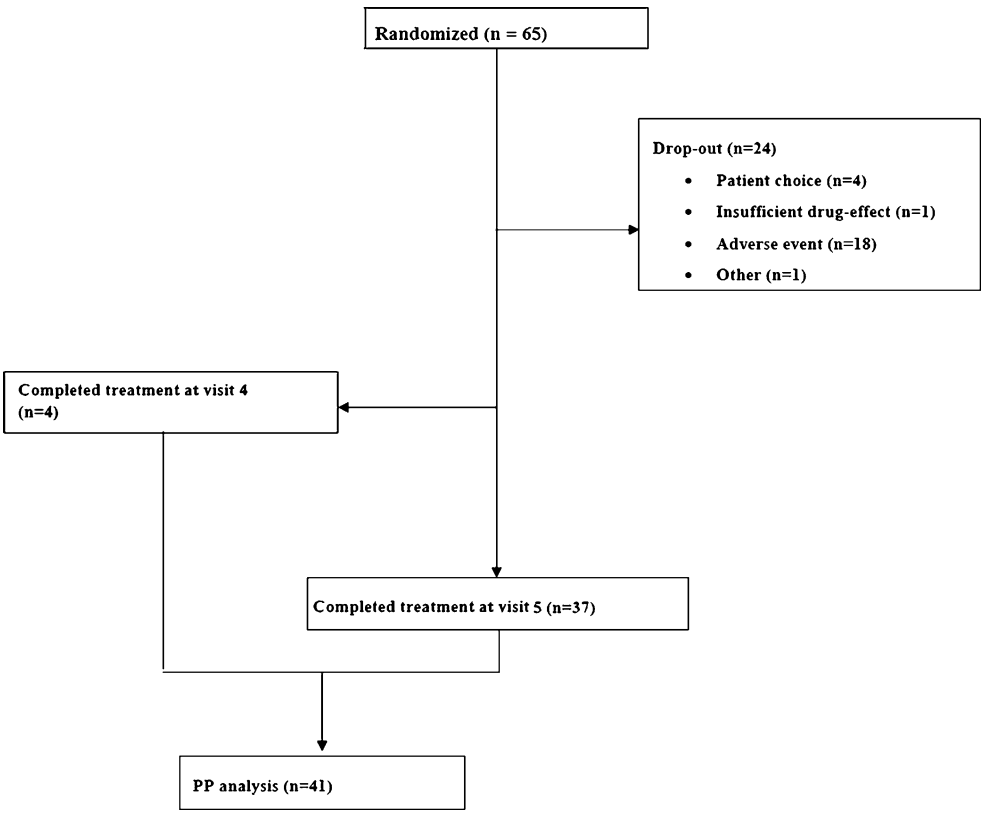

Fig. 1 Subject disposition

Table 1 Characteristics at baseline of patients

Variables	*N*=65	
Age	57.32	Range (28–80)
Weight (kg)	62.66	Range (45–82)
Height (cm)	161.21	Range (142–177)
Gender (%)		
Male	38.5	
Female	61.5	
Blood pressure (mmHg)		
Diastolic pressure	78.74	SD (7.36)
Systolic pressure	130.11	SD (13.54)
Pulse	75.09	SD (7.96)
Medical history	Yes	No
Head, eyes, ear, nose and throat	3 (4.6%)	62 (95.4%)
Cardiovascular	25 (38.5%)	40 (61.5%)
Respiratory	4 (6.2%)	61 (93.8%)
Dermatological	3 (4.6%)	62 (95.4%)
Gastrointestinal	9 (13.8%)	56 (86.2%)
Genitourinary	5 (7.7%)	60 (92.3%)
Endocrine	13 (20.0%)	52 (80.0%)
Autoimmune	1 (1.5%)	64 (98.5%)
Neurological	57 (87.7%)	8 (12.3%)
Musculoskeletal	10 (15.4%)	55 (84.6%)
Allergy	0 (0.0%)	65 (100.0%)
Others	4 (6.2)	–
Physical examination	Normal	Abnormal
General appearance	65 (100%)	–
Skin	64 (98.5%)	1 (1.5%)
Head, eyes, ear, nose and throat	65 (100%)	–
Neck	65 (100%)	–
Heart	65 (100%)	–
Lung	65 (100%)	–
Abdomen	65 (100%)	–
Genitourinary	65 (100%)	–
Extremities	65 (100%)	–
Musculoskeletal	65 (100%)	–
Neurological	65 (100%)	–
Others	–	–
Result of laboratory test		
Within normal range	45 (69.2%)	
Out of normal range, but clinically not significant	20 (30.8%)	
Out of normal range, and clinically significant	0 (0.0%)	
Type of pain		
Nociceptive	1 (1.5%)	
Neuropathic	47 (72.3%)	
Combined	17 (26.3%)	
Diagnoses of underlying disease		
Nociceptive pain		
Myofacial pain	1 (1.5%)	
Neuropathic pain		
FBSS		
Cervical	1 (1.5%)	
Thoracic	1 (1.5%)	
Lumbar	23 (35.4%)	
Degenerative spondylosis		
Cervical	1 (1.5%)	
Thoracic	1 (1.5%)	
Lumbar	8 (12.3%)	
Spinal cord injury	9 (13.8%)	
Chronic pain after compression fracture	1 (1.5%)	
Peripheral neuritis	1 (1.5%)	
Perineural cysts	1 (1.5%)	
Combined pain		
Lumbar FBSS	6 (9.2%)	
Degenerative spondylosis		
Cervical	1 (1.5%)	
Lumbar	9 (13.8%)	
Chronic pain after compression fracture	1 (1.5%)	
Locations of pain[a]		
Neck	13	
Upper limb	14	
Right	1	
Left	5	
Both	8	
Back	7	
Lumbar	47	
Lower limb	47	
Right	14	
Left	9	
Both	24	
Duration of pain		
3–6 months	12 (18.5%)	
6–12 months	10 (15.4%)	
12–36 months	17 (26.1%)	
>36 months	26 (40.0%)	
Pain intensity (numeric rating scale)		
Physician's assessment	6.49	SD (1.42)
Patient's assessment		
Average pain	6.85	SD (1.52)
Pain at resting	5.12	SD (2.39)
Pain at moving	7.17	SD (1.83)
Impact of pain on subjects		
Daily life	7.22	SD (1.68)
Walking	6.60	SD (2.27)
Eating	3.46	SD (2.79)
Mood	7.17	SD (1.76)

Table 1 (continued)

Variables	*N*=65
Sleep disturbance due to pain (number of awakenings due to pain at night)	
0	23 (35.4%)
1–2	19 (29.2%)
3–4	14 (21.5%)
≥5	9 (13.9%)
Previous analgesic medication	
Acetaminophen	1
NSAIDs	15
ULTRACET	23
Tramadol	1
SR morphine	1
Gabapentin	15

[a] One or more locations from each patient were reported

study drug was detached from skin for more than 12 h, or when the patient or his or her legal guardian withdrew their consent to participate. In the event of study discontinuation or withdrawal, the date and the reason for discontinuation or withdrawal were recorded on the Case Report Form.

Efficacy evaluation criteria and methods

The subjects for efficacy evaluation were subjects who completed the trial without a serious violation of the clinical protocol and who were administered with the study drug according to the instructions of dosage during the course of the trial with available data for efficacy evaluation. The primary endpoint was the percentage of change in pain intensity from before the administration of the study drug to 12 weeks after administration, and the secondary endpoint was the degree of satisfaction on the part of the patient and the investigator

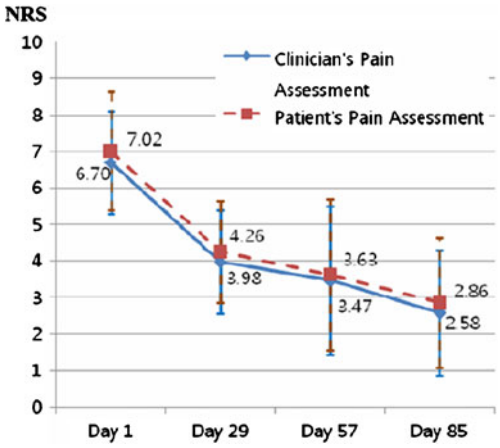

Fig. 2 Changes in pain intensity: clinician and patients's pain assessment (*NRS* numeric rating scale; $p<0.0001$, Wilcoxon signed ranksum test)

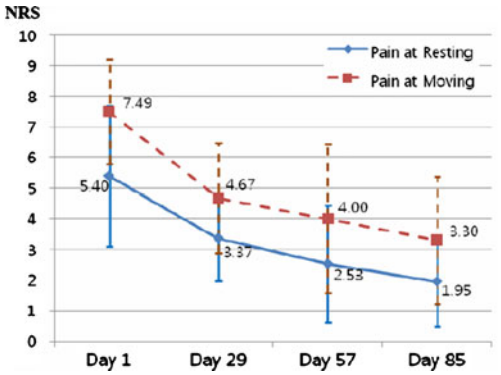

Fig. 3 Changes in pain intensity: patient's pain assessment at resting and moving ($p<0.0001$, Wilcoxon signed rank-sum test)

(clinician) with the dosage of the study drug, the patient's functions/sleep interference, and the study drug itself.

Evaluation methods for safety

Safety of the study drug was analyzed when safety data were available after the attachment of study drug, and all adverse events reported during the trial were recorded in the Case Report Form and put into a chart. Subsequently, the types and frequencies of adverse events experienced by the patient were assessed.

Statistical analyses

The analysis of outcomes was conducted using a full analysis set, which excluded cases in which patients violated the inclusion/exclusion criteria, were never administered the study drug, or could not evaluate the pain on the 2nd evaluation date. When there were missing data on major endpoints, it was processed using the Last Observational Carried Forward (LOCF) method, which substitutes the most

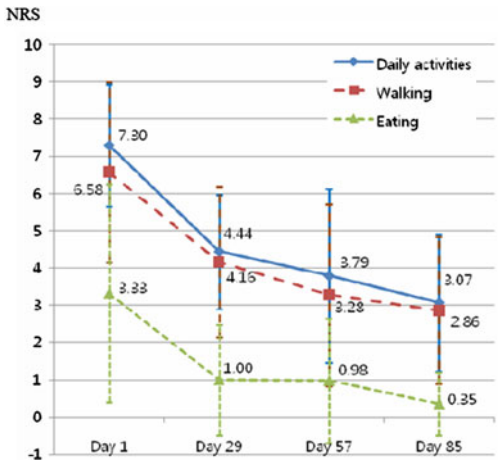

Fig. 4 Changes in interference with daily activities: interference with daily activities, walking and eating ($p<0.0001$, Wilcoxon signed rank-sum test)

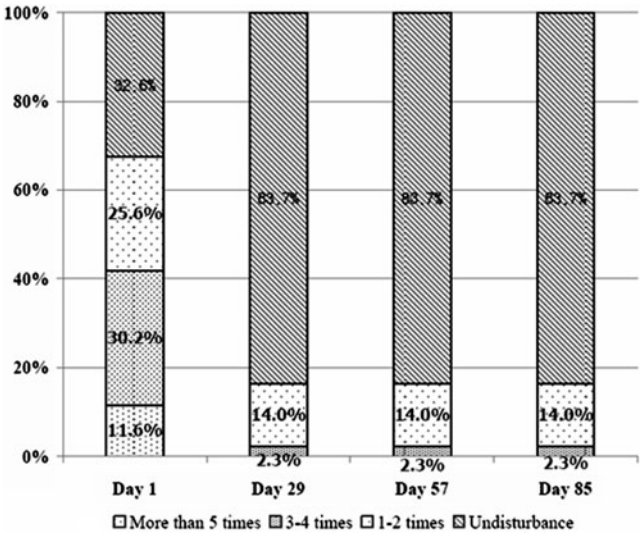

Fig. 5 Changes in the frequency of sleep disturbance due to pain at night ($p<0.001$, McNemar's test)

recently acquired data prior to the occurrence of the missing data for the missing data. For major endpoints, per protocol (PP) analysis was additionally executed for patients who completed the study without violations of the clinical protocol, and the patient selection criteria included in PP analysis was determined according to whether they violated the clinical protocol and whether the major endpoints were measured. Those included in PP analysis were patients whose Case Report Form was recorded on every evaluation date.

For demographic data, exploratory data analysis was used. For efficacy evaluation variables, the continuous variables were analyzed using the Wilcoxon signed rank sum test while the categorical variables were analyzed

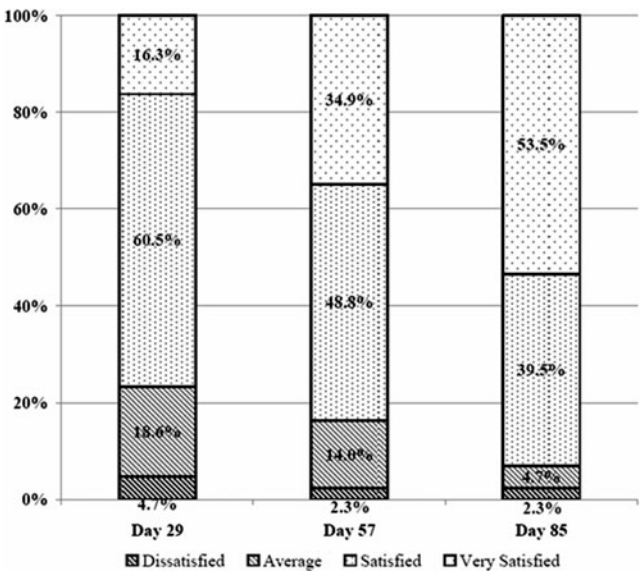

Fig. 6 Patient's satisfaction (satisfied group: sum of very satisfied group and satisfied group, $p<0.05$, McNemar's text)

using McNemar's test. All p values were two-sided, and a probability value of $p<0.05$ was considered significant.

Results

From October 24th of 2005 to August 31st of 2006, a total of 65 patients were registered, out of which 24 withdrew from the study and 41 completed the study (Fig. 1). The characteristics of the patients who participated in this study at baseline are shown in Table 1. Patients who participated in the study could be described as healthy, overall, based on history of disease/administration, physical examinations, and laboratory tests. Pain could be classified into three types: nociceptive, neuropathic, and combined, and most were patients who complained of neuropathic pain of the spine and limbs. The diagnoses of underlying diseases and the locations of pain are shown in Table 1. The neuropathic pain was diagnosed when patients without surgical lesion show characteristics of neuropathic pain such as hypesthesia, allodynia, paresthesia, and dysesthesia. In terms of the duration of pain, 66.2% of patients complained of chronic long-term pain that had persisted for longer than 1 year. The average pain intensity at baseline was relatively serious pain, close to the level "severe", and patients complained that the pain interfered with their life in terms of difficulties associated with performing daily activities, such as walking, eating, and sleeping. Analgesics administered for pain treatment were mostly non-narcotic analgesics.

Changes in pain intensity

The changes in average pain intensity experienced by the patient, as evaluated by a clinician, decreased from a level of 6.70 on the NRS prior to the administration of study drug to 2.58 (61.5%) at the end of the study period (Fig. 2). The average individual pain intensity, evaluated by the patients themselves, decreased to from 7.02 to 2.86 (59.3%; Fig. 2). This difference was statistically significant ($p<0.0001$). The pain intensities evaluated by the patient, at rest and when moving, were decreased from 5.40 to 1.95 (63.9%), and from 7.49 to 3.30 (55.9%), respectively (Fig. 3), a statistically significant decrease ($p < 0.0001$). This statistical significance was observed on all intent-to-treat (ITT), and PP analyses.

Evaluation of patients' functions and sleep

Patients' functions were evaluated using NRS in terms of interference with daily life, walking, and eating due to pain. Following administration of the study drug for the study period, each function showed a decrease as follows: from 7.30 to 3.07, from 6.58 to 2.86, and from 3.33 to 0.35, respectively (Fig. 4), which were statistically significant

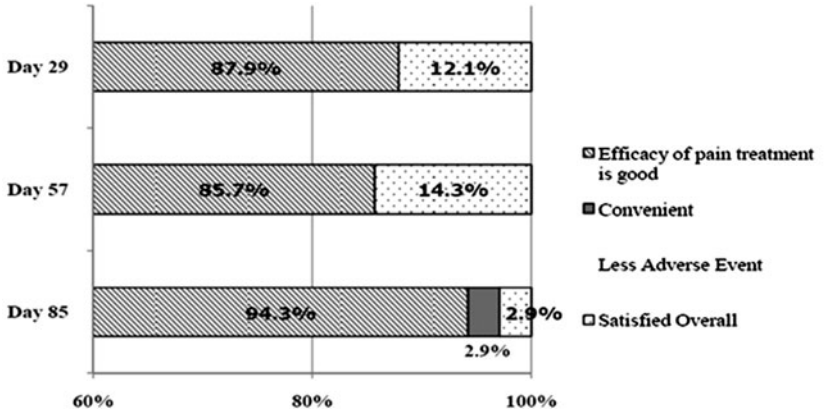

Fig. 7 Reason for patient's satisfaction

($p<0.001$). In the evaluation of the patients' sleep, the frequency of sleep disturbances due to pain was measured (Fig. 5). Patients were divided into a group whose sleep was not disturbed by pain and a group whose sleep was disturbed by pain on more than one occasion. As a result of this analysis, the rate of patients whose sleep was not disturbed increased from 32.6% in the 1st evaluation to 86.1% in the 5th evaluation, which was a statistically significant increase (ITT $p < 0.0001$, PP $p<0.0001$).

Satisfaction with pain treatment on the part of patient and investigator

Satisfaction with pain treatment on the part of patients was evaluated using a five-point scale (very satisfied, satisfied, average, dissatisfied, and very dissatisfied) in the 4th, 8th, and 12th weeks after the administration of the study drug. In these visits, the sum of patients who answered "very satisfied" or "satisfied" was 76.8%, 83.7%, and 93.0%, respectively (Fig. 6). In particular, differences in the sums of the rate of "very satisfied" and "satisfied" measured on the 4th week and the rate of very satisfied and satisfied on the last visit constituted a statistically significant increase ($p<0.05$). The determinants of the patients' satisfaction with pain treatment were (in order of frequency): efficacy of pain treatment is good, satisfied overall, and convenient (Fig. 7). Investigators' satisfaction with the pain treatment was also evaluated on a five-point scale in the 4th, 8th, and 12th weeks, and the sum of the rate very satisfied and satisfied on each of these visits was 83.7%, 83.7%, and 86.0%, respectively (Fig. 8).

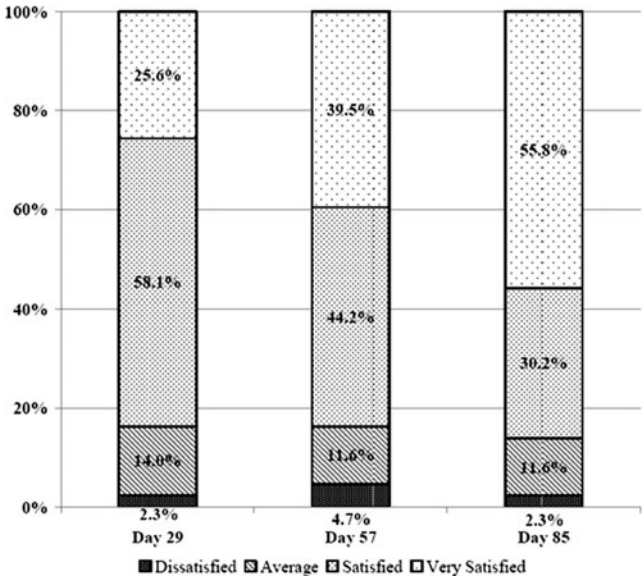

Fig. 8 Clinician's satisfaction (satisfied group; sum of very satisfied group and satisfied group, $p>0.05$, McNemar's text)

Study drug dosage

The average dose administration was 13.95 μg/h upon initial administration and 42.59 μg/h at the termination of the trial, which was statistically high (Table 2, $p<0.001$).

Adverse event

In 55 patients (84.6%), more than one adverse event was observed during the trial. Nausea was observed in 32 patients (49.2%), dizziness in 28 (43.1%), drowsiness in 20 (30.8%), constipation in 11 (16.9%), and vomiting in 10 (15.4%). These can be classified, mainly, as mild adverse events (Table 3). There were 18 patients who discontinued the trial due to adverse events (27.7%).

Table 2 Dose of the fentanyl patch

Variable	Mean	SD
Dose (μg/h)		
Day 1	13.95	4.89
Day 8	26.31	2.33
Day 29	33.14	17.01
Day 57	39.71	18.18
Day 85	42.59	20.06
p-Value (day 1 vs. day 85)	<0.001	

Table 3 Adverse event

Adverse event	Severity			No. of patients (%)
	Mild	Moderate	Severe	
Nausea	22	9	1	32 (49%)
Dizziness	22	4	2	28 (43%)
Drowsiness	15	5	–	20 (31%)
Constipation	10	1	–	11 (17%)
Vomiting	4	5	1	10 (15%)
Skin itching	8	–	–	8 (12%)
Edema	3	1	–	4 (6%)
Anorexia	1	1	–	2 (3%)
Dry mouth	–	1	–	1 (2%)

Discussions

This study is a prospective open trial, with a study group only and no control group. Its value is in observing the treatment efficacy of a fentanyl patch for different types of noncancer pain in patients with chronic pain (more than moderate) who have not responded to drug therapies for a period of more than 3 months. We think that the mechanisms of neuropathic pain development in failed back surgery syndrome (FBSS) are either nerve injury during surgery or central sensitization due to persistent chronic pain [7, 17]. In degenerative spinal disease, nerve root injury or irritation due to foraminal stenosis as well as central sensitization due to persistent chronic pain can cause neuropathic pain. The neuropathic pain developed from these mechanisms as well as combined pain commonly can be located in spine and limbs.

This kind of trial, without a control group, has been tried many times in studies examining the efficacy of numerous analgesics [1, 18, 24, 25], and it is appropriate as a way to investigate changes of pain intensity and improvement/impairment in performing daily activities, as linked to the control of drugs.

In some studies, it has been mentioned that hospitalization is necessary for dose optimization when changing to a fentanyl patch in a patient using opioids. However, only 1 (1.5%) patient in this study was administered with potent oral opioids prior to the study, and the transition to the fentanyl patch was safe and efficacious. Many in the study group were administrated with mild oral opioids, such as tramadol HCl/acetaminophen (24, 36.9%). If the previously administered analgesic was used as a rescue dose for the initial administration, transition to the fentanyl patch was considered possible without hospitalization for dose optimization. The initial dose for patients, according to previous analgesics, was set as follows in this study: 59 patients (90.8%) received 12.5 μg/h, 5 patients (7.7%) received 25 μg/h, and 1 patient (1.5%) received 37.5 μg/h.

The dose increase of the study drug administered in 3 weeks for patient pain management demonstrated a similar pattern to the results of previous studies [25]. This is because this study targeted mild pain, and if more pain was experienced, then the goal was to regulate the dose of the drug. Through this active pain control, not only can the pain intensity experienced by the patient be lessened but there can also be improvements to the patient's quality of life, sleep interference, and overall satisfaction. However, drug therapy is just one part of chronic pain treatment; it is recommended as an important factor along with behavioral therapy, physical therapy, and other approaches [23]. In clinical practice, this regimen has been observed to lower the severity of pain from severe to moderate and to improve patients' satisfaction in daily life by encouraging other aerobic exercises.

A statistically significant reduction in the degree of sleep disturbances of patients owing to pain was observed during the course of trial in this study (Fig. 5). This can be interpreted as a reduction of sleep impairment due to an increase in daily activities due to reduction of the patients' pain [1], or as a steady analgesic effect provided during sleep due to the maintenance of a regular blood concentration of the drug, which could be possible because of the enhanced pharmacokinetics of the delivery of the study drug.

In contrast to the findings of Payne et al. [28] in 1998, in which patients stated that their major reason for their preference of the fentanyl patch over oral morphine was because of fewer adverse events linked to its use, the patients in this study responded that they preferred the fentanyl patch over other analgesics administered prior to the study due to its excellence in the treatment of pain (Fig. 7).

Fifty-five patients complained of adverse events at least once (85%), and the study was designed to evaluate patients' pain and adverse events (even slight/mild) accurately by conducting consistent phone inquiries with the patient at intervals of 3 days. However, most of the adverse events reported were mild, and the percentage of moderate and severe adverse events was 10–15%. This is not so very different from the results of previous studies [1, 2, 12, 18, 24, 25]. In particular, constipation, which was known to decrease the quality of patients' lives significantly, was found in 17% of patients. However, in this study, constipation was mild and did not interfere with daily life (Table 3). Therefore, the pharmacological merits of the fentanyl patch were observed in terms of a decrease in the rate of constipation by not acting on μ-opioid receptors of gastrointestinal tract because it did not pass through digestive systems.

In reality, the unconcern of medical professionals toward patients with chronic pain, and the fact that clinicians tend to hesitate to use to potent opioid analgesics for patients

whose analgesic effects were insufficient after administration of NSAIDs and mild opioid analgesics, are still major issues. Some of the suspected causes for this phenomenon are the fact that patients tend not to express their pain actively, medical doctors are still anxious about the use of opioid analgesics, and there are national regulatory restrictions on their usage [21].

Previously, the use of potent opioid analgesics for patients with chronic pain was controversial, but opioid analgesics have become a crucial treatment modality because of their potent analgesic effects in the treatment of cancer pain. Recently, diverse research findings on the efficacy of opioid analgesics in chronic pain treatment have played a part in inducing the implementation of standards in pain treatment through the recommendations of government organizations worldwide [4, 8, 13, 32].

However, there is recently a case report that shows increased deaths due to prescription itself or abuse of fentanyl transdermal patch [16]. Although the matrix type of fentanyl transdermal patch is considered safer than the gel-type, cautious administration and close medical observations such as slow titration, daily contact by phone in the first week, and monthly visit in the outpatient setting, are always required for the safety of patients.

Conclusions

In this prospective study, the efficacy and safety of a fentanyl transdermal patch-type delivery system (Durogesic® D-TRANS) in patients with moderate to severe pain of the spine and limbs, which represents a significant portion of patients with chronic pain, were examined by evaluating the clinical usefulness for nociceptive pain, neuropathic pain, or complex patterns of pain in terms of pain relief and for improvement in the performance of daily activities and sleep disturbance. Based on our results, the pain could be decreased down to mild pain by increasing dosages of fentanyl patch in relatively short period. The side effect of gastrointestinal system could be prevented with small dose of antiemetics. Therefore, the fentanyl patch monotherapy should be considered before other invasive intervention procedures in chronic moderate to severe noncancer pain, which includes nociceptive, neuropathic, or combined pain originated from underlying spinal disorders.

Acknowledgements The authors express their gratitude to Sun Keun Huh for his assistance in the collection of data. This research was financially supported by a grant (protocol number FEN-KOR-10) from Janssen Korea, Seoul, South Korea, whose role was restricted to providing assistance to the investigators in the conception, conduct, and analysis of this study.

Conflicts of interest None

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