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Original Article

The effectiveness of patches containing Loxoprofen Sodium Hydrate (LX-P) in the conservative therapy of muscular back pain – Clinical results using the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ)

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ABSTRACT

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Objectives: We investigated the analgesic effect, degree of patient satisfaction, and QOL improvement provided by patches containing loxoprofen sodium hydrate (LX-P) using a questionnaire based on the evaluation criteria of the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ).

Methods: In this study of 53 patients (18 men, 35 women) with muscular back pain, LX-P 100mg was applied once per day for four weeks. Patients provided subjective feedback by answering a questionnaire.

Results: After one week of LX-P application, Visual Analogue Scale (VAS) scores were significantly lower and in the fourth week over 50% of the patients who had switched from other NSAIDs reported improved satisfaction over the drug previously used. The JOABPEQ Severity of Illness Index (for all patients) was significantly higher after one week for pain-related disability and lower back functional disorder, and was significantly higher after two weeks for daily life disability. The rate of effectiveness of LX-P against pain-related disabilities in the fourth week was 62.2%.

Conclusion: LX-P showed satisfactory analgesic effect and QOL improvement. We believe it is effective for clinical practice.

Keywords: loxoprofen sodium, JOABPEQ, VAS, QOL, muscular back pain

Introduction

According to the Ministry of Health, Labour and Welfare's Comprehensive Survey of Living Conditions (several surveys conducted in fiscal 2004, 2007, 2010), pain in the locomotive organs, including "lower back pain," "stiff shoulders," and "joint pain," is one of the most common subjective symptoms reported. These surveys also revealed that approximately 30% of those with Certification of Needed Long-Term Care (under the Japanese health insurance system) report the reason they require nursing care as "joint pain" or "bone fracture/falling down" [1−3]. In addition, since health care and nursing care costs are rising every year, medical professionals now need to create treatment evaluation standards that are convincing to third parties and provide medical care that is based on scientific grounds and these standards.

In the past the Japan Orthopaedic Association's lower back pain treatment evaluation score (JOA score) was commonly used in Japan. However, the JOA score had several problems, including the fact that, compared to international evaluation criteria, it did not include patient assessments regarding pain, numbness, and general health condition, and the validity of the evaluation categories as well as the points assigned to each were never verified. Thus, the Japan Orthopaedic Association Back Pain Evaluation

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Questionnaire (JOABPEQ) was released in 2007 as a method of evaluation specific to patients suffering from lower back pain.

JOABPEQ is a new, patient-based evaluation criterion that overcomes the problems associated with the JOA score. It includes in its evaluation categories pain, bodily functions, activities, and psychosocial elements and is considered an effective criterion whose reliability and validity have been verified.

In general, muscular back pain is managed through the use of non-steroidal anti-inflammatory drugs (NSAIDs), but in many cases long-term treatment is necessary and transdermal patches, which are less likely to cause gastrointestinal problems than oral drugs, are commonly used. Loxoprofen sodium hydrate (LX) is known to have strong anti-inflammatory, analgesic, and antipyretic effects when administered orally, and studies have shown that PAP (hydrogel patch) containing loxoprofen (LX-A) has the same degree of efficacy and safety as oral drugs [4−6]. In addition, patches containing loxoprofen (LX-P) have been approved on the basis that they have been confirmed to be the bioequivalent of LX-A and have been shown in animal experiments to have excellent anti-inflammatory and analgesic actions [7].

In this study of patients with muscular back pain, we investigated the analgesic effect and degree of satisfaction, and assessed QOL using a questionnaire that incorporated JOABPEQ evaluation categories. We also surveyed (using patient questionnaires) and investigated the clinical effectiveness of LX-P.

Methods

1. Subjects

The subjects were inpatients and outpatients treated between August 2008 and March 2012 at Saga University Hospital and related facilities within Saga Prefecture who were 20 years of age or older, suffered from muscular back pain, and were prescribed LX-P. Those who met any of the exclusion criteria listed below were not included. The back pain suffered by the subjects in this study was myofascial low back pain, commonly referred to as "lower back pain." Back pain is defined in the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), published by the World Health Organization (WHO), as pain anywhere from the back to the lumbar region. It is diagnosed when the patient presents spontaneous pain, kinesalgia, and pain on palpation in the back or lumbar region when not accompanied by neurologic manifestations and when the cause cannot be attributed to any clearly definable organic injury.

Exclusion Criteria

1. Those suffering from bronchial asthma (due to the risk that their condition may worsen)
2. Those with a history of sensitivity to any of the ingredients of LX-P
3. Those who were pregnant, nursing, may have been pregnant, or those trying to get pregnant during the testing period
4. Those with a history of drug sensitivity to loxoprofen
5. Those from whom written consent could not be obtained
6. Those determined by their attending physicians as unsuitable for this study for any other reason

2. Methods

The study was conducted after providing the subjects with a detailed explanation of the outline of the study and obtaining their consent to participate in the study of their own free will.

In principle, the subjects were administered LX-P 100mg (one application per day) for a period of four weeks. The subjects were asked to fill in questionnaires before the first administration and again in the first, second, and fourth weeks. We did not have any particular standard regarding their use of other NSAIDs prior to the first administration of LX-P. During the study period, we prohibited the subjects from using other NSAIDs or beginning any new type of physiotherapy. However, we allowed them to continue using steroids, muscle relaxants, and other analgesics and anti-inflammatory drugs that they had been using before the start of the study.

3. Evaluation

We evaluated the effect on QOL and the analgesic effect using the JOABPEQ Severity of Illness Score (five categories: pain-related disability, functional disorder of the lumbar vertebrae, walking disorder, daily life disability, psychological disability) based on the length of time LX-P was affixed to the skin and the administration of LX-P (Table. 1). We also assessed the degree of satisfaction reported by patients who were switched from another NSAID tape. The length of time LX-P was affixed, the analgesic effect, the subjects' degree of satisfaction, and the improvement in QOL were assessed using the criteria below. Statistical processing was done using the paired *t*-test and the Wilcoxon signed-rank test, and statistical significance was set at $p<0.05$.

1) Length of time LX-P was affixed

The average length of time (score) LX-P was affixed was calculated for the first, second, and fourth weeks. The length of time corresponding to this average score was set as the length of time LX-P was affixed.

2) Analgesic effect

The analgesic effect was assessed by observing changes in the Visual Analogue Scale (VAS) score.

3) Degree of satisfaction

The degree of satisfaction with having switched to LX-P was assessed using a 5-step assessment scale (large improvement, slight improvement, not sure, not

Table 1. JOABPEQ evaluation.

The following questions were self-administered and answered by the patients. Their answers were assigned points on a scale of 1 to 5 according to a predetermined formula (see 1 below).

Q1-1	You change your body position many times in order to relieve your low back pain	Q3-4	Do you feel it is difficult to go up to the next step on the stairs because you don't feel well?
Q1-2	You lie down more than usual due to low back pain	Q3-5	Do you feel it is difficult to walk more than 15 minutes because you don't feel well?
Q1-3	You have low back pain almost all the time	Q4-1	You don't do any of the housework you normally do due to low back pain
Q1-4	You almost never sleep well due to low back pain	Q4-2	Have you ever felt that you couldn't do as much work or normal activities that you thought you could because you don't feel well?
Q2-1	You ask for assistance when you do something due to low back pain	Q4-3	How much of your normal work has been hindered due to pain?
Q2-2	You try not to bend down or kneel down due to low back pain	Q5-1	You are more impatient with or become more angry at people than normal due to low back pain
Q2-3	You cannot easily get up from a chair due to low back pain	Q5-2	Answer these questions about your current state of health
Q2-4	It is difficult to turn in your sleep due to low back pain	Q5-3	Do you feel down and depressed?
Q2-5	You find it difficult to put on socks or stockings due to low back pain	Q5-4	Do you feel exhausted?
Q2-6	Do you find it difficult to bend forward, kneel down, or lean over because you don't feel well?	Q5-5	Are you in a pleasant mood?
Q3-1	You try to walk only short distances due to low back pain	Q5-6	Do you think you are of average health?
Q3-2	You spend the majority of the day sitting due to low back pain	Q5-7	Do you think your health will worsen?
Q3-3	You take longer to walk up the stairs than normal due to low back pain		

1: Pain-related disability

$$(Q1\text{-}1 \times 20 + Q1\text{-}2 \times 20 + Q1\text{-}3 \times 20 + Q1\text{-}4 \times 10 - 70) \times 100 \div 70$$

Lumbar vertebrae functional disorder

$$(Q2\text{-}1 \times 10 + Q2\text{-}2 \times 10 + Q2\text{-}3 \times 20 + Q2\text{-}4 \times 10 + Q2\text{-}5 \times 30 + Q2\text{-}6 \times 20 - 100) \times 100 \div 120$$

Walking disability

$$(Q3\text{-}1 \times 30 + Q3\text{-}2 \times 20 + Q3\text{-}3 \times 10 + Q3\text{-}4 \times 10 + Q3\text{-}5 \times 30 - 100) \times 100 \div 140$$

Daily life disability

$$(Q3\text{-}5 \times 4 + Q4\text{-}1 \times 2 + Q4\text{-}2 \times 6 + Q4\text{-}3 \times 10 - 22) \times 100 \div 74$$

Psychological disability

$$(Q5\text{-}1 \times 3 + Q5\text{-}2 \times 4 + Q5\text{-}3 \times 6 + Q5\text{-}4 \times 6 + Q5\text{-}5 \times 3 + Q5\text{-}6 \times 3 + Q5\text{-}7 \times 3 - 28) \times 100 \div 103$$

much improvement, no improvement at all) for the following categories: effectiveness (analgesic effect), refreshing feeling (cool sensation, cooling sensation), little to no skin irritation, does not easily come off (strong adhesive), easy to affix. Those who said they had a large or slight improvement were considered to have experienced improvement. In the "Other" category, we recorded other reasons for satisfaction with LX-P.

4) Improvement in QOL

We obtained an illness severity score for all of the JOABPEQ categories. From these we excluded from our analysis those who scored 90 points or more before treatment began and those who scored 90 points or more after the treatment. We determined that those whose scores after the treatment showed an increase of at least 20 points compared to their scores before treatment began or those who scored less than 90 points before treatment began and scored at least 90 points after treatment began were cases that indicated the drug was effective (effective cases). The rate of effectiveness was then calculated using the formula: number of effective cases / (number of cases for analysis – cases excluded from analysis).

Results

1. Case particulars and basic patient data

There were 53 patients subject to analysis (18 men, 35 women, average age of 63.6: 22−87 years old). This number included 22 new patients (5 men, 17 women, average age of 54.4: 22−87 years old; the new patient

Table 2. Length of time LX-P was affixed.

	A. All Patients (52 patients: 1 patient not listed)	B. Effective (39 patients)	C. Non-effective (13 patients)
Less than 8 hrs.	25.0%	20.5%	38.5%
8 hrs.–11 hrs. 59 mins.	28.8%	30.8%	23.1%
12 hrs.–23 hrs. 59 mins.	26.9%	30.8%	15.4%
24 hrs. or more	19.2%	17.9%	23.1%

Data for the length of time LX-P was affixed was obtained from the questionnaires for weeks 1, 2, and 4 for all patients. This data was scored according to the score assignments listed below. The average scores were rounded to the first decimal point (rounding up from 5) and the result was used as the evaluation score. The lengths of time 1 to 4 that were applied to these evaluation scores were used as the lengths of time LX-P was affixed during this study. The scores for the lengths of time were as follows:
1. Less than 8 hrs. (score: 1), 2. 8 hrs.–11 hrs. 59 mins. (score: 2), 3. 12 hrs.–23 hrs. 59 mins. (score: 3), 4. 24 hours or more (score: 4).

group), and 31 patients for whom other NSAID tapes were judged to have had insufficient effect and who were switched to LX-P (13 men, 18 women, average age of 68.8: 44–87 years old; the switched group). The drugs used by those in the switched group included 25 who used ketoprofen (13 used tape, 12 used PAP), 5 who used flurbiprofen (tape), and 1 who used methyl salicylate and red pepper extract (tape).

2. Analysis of the questionnaires

1) Length of time LX-P was affixed

We were able to confirm the length of time LX-P was affixed each week for 52 of the 53 subjects. One subject did not record this data. We found that the highest percentage (28.8%) of subjects kept the LX-P affixed for between 8 and 12 hours (Table 2A). We divided the 52 subjects into an effective group (39 subjects) and an ineffective group (13 subjects) and compared the length of time LX-P was affixed. This revealed that the highest percentages (both 30.8%) of subjects in the effective group either kept the LX-P affixed between 8 and 12 hours or between 12 and 24 hours (Table 2B). The highest percentage of subjects in the ineffective group (38.5%) kept the LX-P affixed for less than 8 hours (Table 2C).

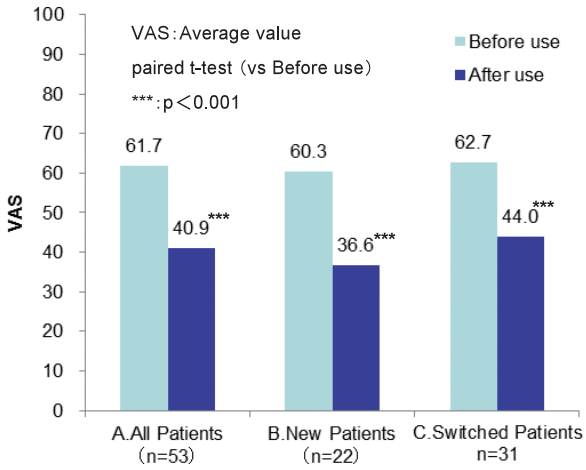

Figure 1. Comparison of VAS before and after use of LX-P.

2) Analgesic effect

We compared the analgesic effect of the 53 subjects before and after administration of LX-P using VAS. The VAS before administration was 61.7 (average in millimeters: same below). The VAS after administration decreased significantly (p<0.001) to 40.9 (Fig. 1). This result was confirmed after the first week (Fig. 2A). We then divided the 53 subjects into a group of 22 new patients and a group of 31 switched patients. In both groups the VAS decreased significantly (both p<0.001, Figs. 1B and 1C). These results were confirmed after the first week (Figs. 2B and 2C).

3) Degree of satisfaction

We investigated the degree of satisfaction for those among the 31 switched subjects who answered the degree of satisfaction questionnaire using the following categories: effect (analgesic effect), refreshing feeling (cool sensation, cooling sensation), little to no skin irritation, does not easily come off (strong adhesive), easy to affix. The results showed that the percentage of patients who reported improvement in the first week was, for each category respectively, 53.6% (15 out of 28 cases), 60.7% (17 out of 28 cases), 63.0% (17 out of 27 cases), 64.3% (18 out of 28 cases, and 42.9% (12 out of 28 cases). In the fourth week, at least 50% of the cases reported improvement in all categories (Fig. 3).

4) Improvement in QOL

We used JOABPEQ to investigate the changes in the Illness Severity Index for the 52 patients who provided answers to the questionnaire. The results showed that for all patients the pain-related disability and lumbar vertebrae functional disorder scores both rose significantly (both p<0.05) after the first week. This improvement continued until the fourth week. The daily life disability score rose significantly

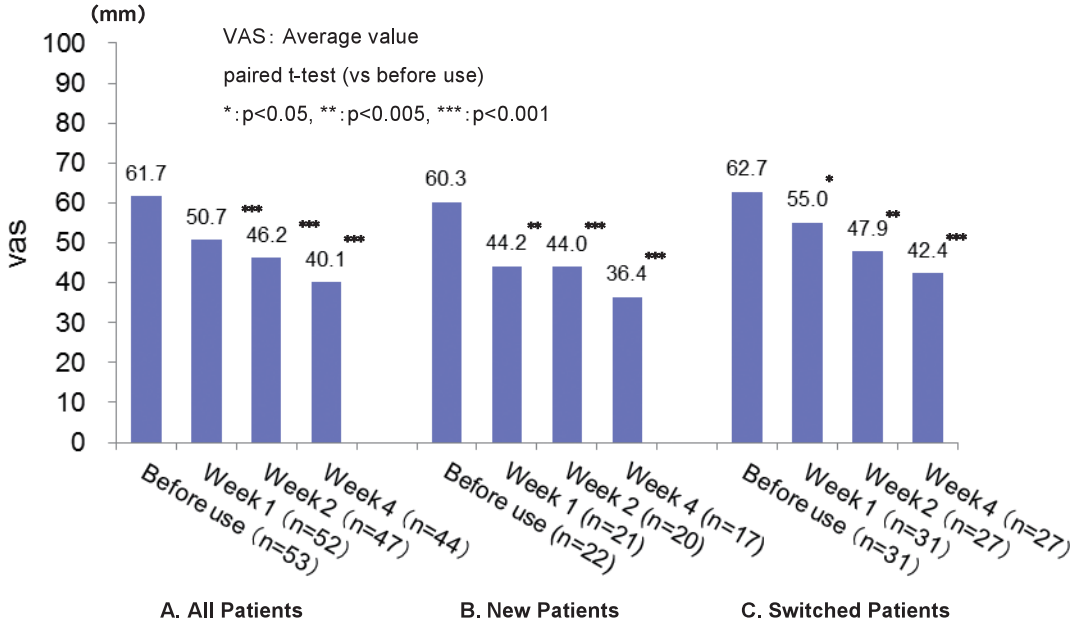

Figure 2. Changes in VAS.

Table 3. Changes in the JOABPEQ severity score.

Severity Score: Average value
Wilcoxon signed-rank test (vs. before use)
*, $p<0.05$; **, $p<0.01$; ***$p<0.001$;
†, $p<0.0005$; ‡, $p<0.0001$.

A. Changes in the JOABPEQ Severity Scores for All Patients.

	Before Use	Week 1	Week 2	Week 4
Pain-related disability	39.5	49.1*	56.1***	62.7‡
Lumbar vertebrae functional disorder	52.5	57.5*	62.8†	65.1‡
Walking disability	49.6	52.7	52.3	54.5
Daily life disability	45.0	48.3	52.7**	52.0*
Psychological disability	47.6	47.4	48.6	47.6

B. Changes in the JOABPEQ Severity Scores for New Patients.

	Before Use	Week 1	Week 2	Week 4
Pain-related disability	38.8	55.0***	57.8†	59.6‡
Lumbar vertebrae functional disorder	59.4	67.4*	70.4**	71.5***
Walking disability	66.7	70.7	68.0	73.2
Daily life disability	52.1	56.2	61.7*	62.5
Psychological disability	52.9	53.8	53.7	51.4

C. Changes in the JOABPEQ Severity Scores for Switched Patients.

	Before Use	Week 1	Week 2	Week 4
Pain-related disability	40.0	45.1	54.9	64.8**
Lumbar vertebrae functional disorder	47.5	50.5	57.0	60.9**
Walking disability	37.6	40.7	40.8	43.1
Daily life disability	40.3	43.5	46.4	46.0
Psychological disability	44.5	44.0	45.5	45.6

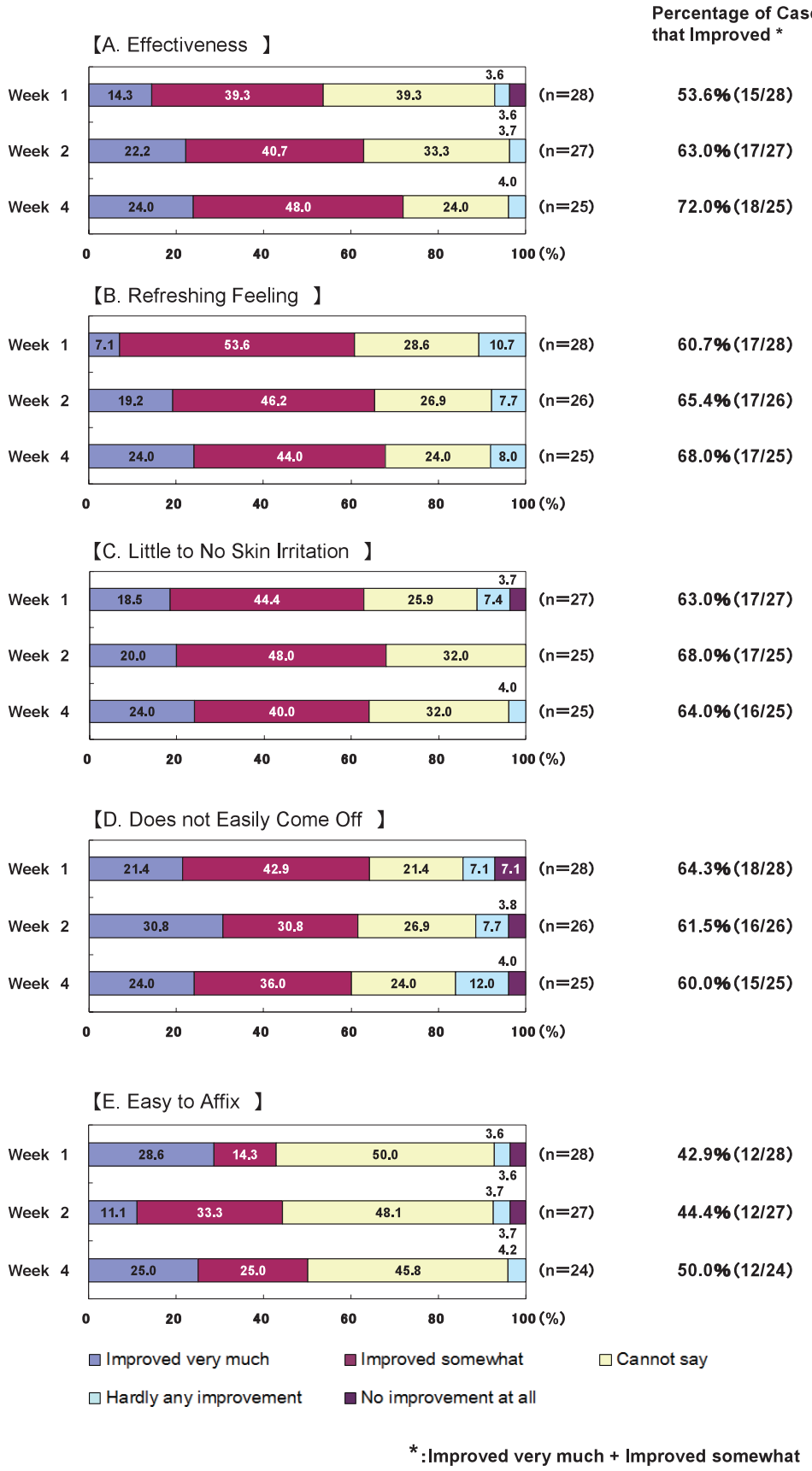

Figure 3. Changes in the degree of satisfaction of switched patients.

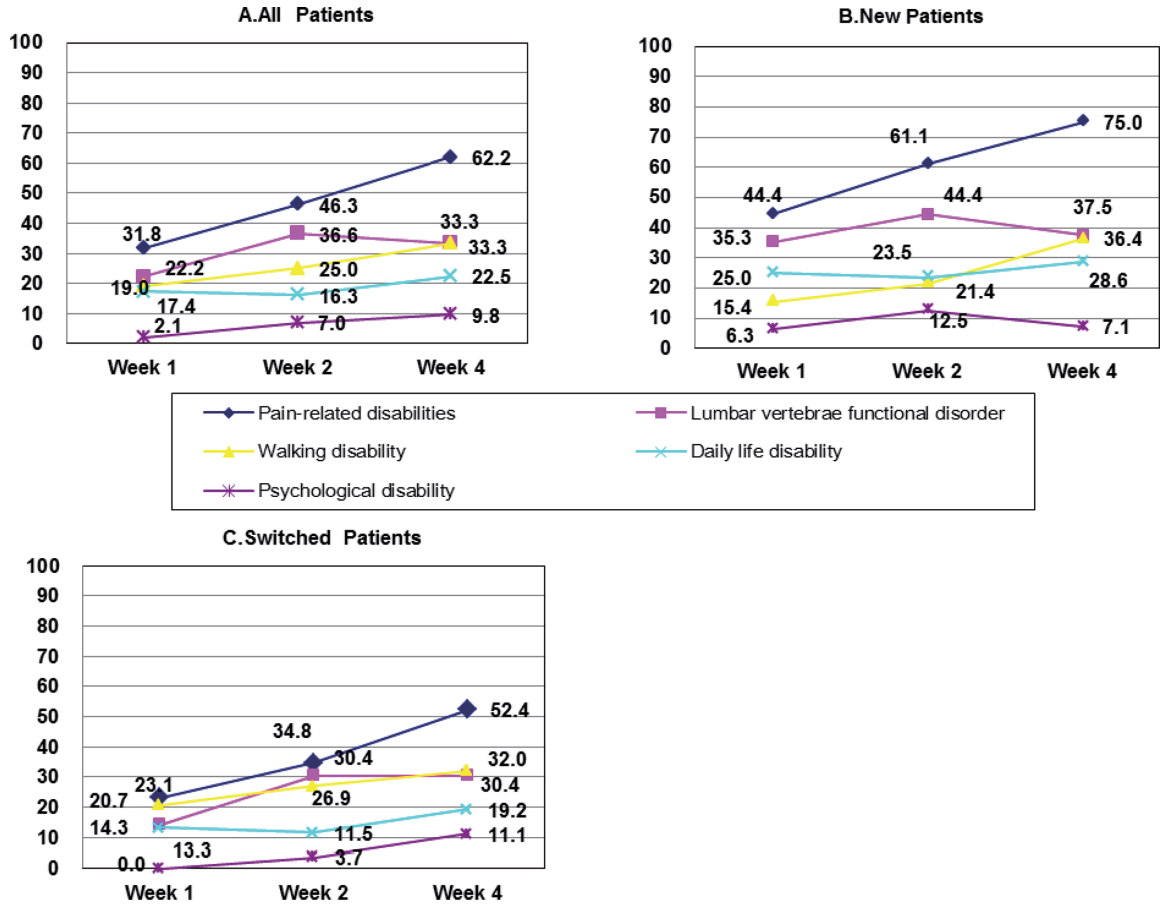

Figure 4. Changes in the rate of effectiveness of LX-P according to JOABPEQ.

(p<0.01) after the second week, and this effect continued until the fourth week. However, no change was observed in any of the other categories (Table 3A). In the new patient group, the pain-related disability and lumbar vertebrae functional disorder scores both rose significantly (p<0.005, p<0.05) after the first week, and this effect was observed until the fourth week. The score for daily life disability rose significantly (p<0.05) in the second week, but no change was observed for any of the other categories (Table 3B). In the switched patient group, the scores for pain-related disability and lumbar vertebrae functional disability both rose significantly (both p<0.01) in the fourth week, but no change was observed for any of the other categories (Table 3C).

We then examined the effectiveness for all categories. All patients as well as the pain-related disability, walking disability, and psychological disability (Figs. 4A and 4C) for the switched patient group and the pain-related disability and walking disability (Fig. 4B) for the new patient group all showed sustained improvement in effectiveness from the first to the fourth weeks. The other categories did not show sustained improvement in effectiveness, but improvements in effectiveness were observed for all categories in the fourth week (Figs. 4A, 4B, and 4C). In particular, over 50% of those in both the new and switched patient groups showed improvement in pain-related disability.

Discussion

In this study we used VAS to investigate analgesic effect and found that VAS significantly decreased in both the new patient and switched patient groups, thus confirming that the administration of LX-P had an analgesic effect. Normally, we would expect that there would be residual anti-inflammatory and analgesic effects of the drugs used by the switched patient group before this study began and that this would make it almost impossible for the patients in the switched patient group to show a significant difference from the new patient group. However, in this study the new patient and switched patient groups showed nearly the same decrease in VAS, suggesting that LX-P may have shown sufficient effectiveness even in those cases in which other NSAIDs were judged to have been insufficiently effective.

We evaluated QOL using a new multi-faceted patient-based method whose validity and reliability we confirmed using JOABPEQ. Our results showed that in all categories except for pain-related disability the pre-administration scores of the switched patient group were lower than those of the new patient group. This suggests that a longer period of time had passed since the onset of illness for the patients in the switched

patient group than for the patients in the new patient group and the symptoms had therefore become chronic. Regarding pain-related disability, the new patient group showed significant improvement from the first week and the switched patient group showed significant improvement from the fourth week. An investigation into this analgesic effect using VAS confirmed that there was marked improvement at an early stage in the new patient group, which is consistent with gradual and definite improvement in the switched patient group. This suggests that administration of LX-P for only one week may have an analgesic effect on acute lower back pain but that for chronic lower back pain administration for four weeks would be effective.

Regarding degree of satisfaction, over 50% of the patients in the switched patient group answered that ultimately LX-P "was more effective than the previously used drug." The degree of satisfaction for "effectiveness," "refreshing feeling," "little to no skin irritation," "does not easily come off", and "easy to affix" was high in each case. Skin irritation and discomfort of the tape influence patient preferences for particular treatments [8,9]. It has been reported that the discomfort caused by a transdermal patch is a factor that has a strong influence on whether or not a patient complies with the usage instructions [8]. Thus, it is important to sufficiently consider this factor when choosing a treatment. The results of this study suggest that LX-P not only has an analgesic effect but also is comfortable to use and therefore may result in improved patient satisfaction even when used on patients who were dissatisfied with other NSAID patches.

Finally, a limitation of this study was the fact that the lack of a control group meant that the effectiveness of LX-P itself could not be verified. However, the fact that our results show that this type of intervention is effective in alleviating the symptoms of muscular back pain and in improving QOL is of clinical significance.

Conclusion

Using JOABPEQ, a new evaluation criterion whose reliability and validity have been verified, this study demonstrated that treatment using LX-P not only has an analgesic effect but also is clinically effective from a QOL standpoint.

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