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ORIGINAL RESEARCH

The Relationship Between Treatment Satisfaction and Medication Understanding Among Patients Taking a Novel Oral Pain Reliever: A Questionnaire-Based Cross-Sectional Study

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ABSTRACT

Introduction: Patient satisfaction is important in pain management. Satisfaction with prescribed pain relievers and continued use of these drugs may be affected by a patient's understanding of their efficacy and safety. We investigated the association between patients' satisfaction and understanding of their prescribed medication for three oral pain relievers (lasmiditan, mirogabalin, and tramadol) that recently became available in Japan.

Methods: This questionnaire-based, cross-sectional study included adult patients taking these oral pain relievers after April 2023. The primary endpoint was overall satisfaction (five-point rating) and the secondary endpoint was overall understanding (five-point rating) of the oral pain relievers.

Results: In total, 328 patients (lasmiditan, 36.9%; mirogabalin, 55.5%, tramadol, 8.8%; four patients had been prescribed more than one medication) were included, and 71.6% of patients reported high satisfaction (score 4, 5) with their oral pain relievers (lasmiditan, 62.0%; mirogabalin, 76.1%; tramadol, 85.2%). The proportion of patients in the total population who

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reported a high understanding (score 4, 5) of their oral pain relievers was 68.0% (lasmiditan, 77.7%; mirogabalin, 63.3%; tramadol, 55.6%). In the total population and the lasmiditan and mirogabalin subgroups, the patient satisfaction level was significantly associated with scores on medication understanding (Cochran–Armitage test, $p < 0.0001$ for all). Discontinuation rates were higher in patients who were unsatisfied with their treatment than those who were satisfied (38.7% and 9.8%, respectively).

Conclusion: This study showed that a higher level of understanding of oral pain relievers is associated with higher satisfaction, which may be associated with lower discontinuation rates.

Clinical Trial Registration: UMIN000052629.

Keywords: Lasmiditan; Mirogabalin; Oral pain relievers; Patient understanding; Treatment satisfaction

Key Summary Points

Why carry out this study?

Patients' satisfaction is important for their pain management, but patients may not fully understand the characteristics of the prescribed pain relievers that affect their satisfaction, especially in the case of newer pain relievers.

This study explored the relationship between medication satisfaction and understanding in patients prescribed one or more of three new oral pain relievers recently available in Japan.

What was learned from the study?

Among patients taking new oral pain relievers, higher overall understanding was significantly associated with higher overall satisfaction with the medication.

A level higher satisfaction with oral pain relievers may be associated with lower drug discontinuation rates.

INTRODUCTION

Pain is a subjective symptom that may be influenced by patients' state of mind at the time of its evaluation [1]. Pain severity varies among patients, as do causes of pain and the extent to which pain affects an individual [2]. Unless adequately treated, pain can negatively impact patients' activities of daily living and quality of life [3, 4]. Additionally, multiple factors can influence the effects of treatment including pain improvement and patients' satisfaction [5–7]. Currently, standardized and validated pain assessment scales are available for precise diagnosis and quantification of pain intensity [8, 9]. Beyond these objective measures, however, it is important to measure and improve patients' satisfaction with pain treatment for adequate pain control [10].

Improving patients' satisfaction with pain management requires educating patients about the implications of pain treatment and the types of available medications [11]. Poor understanding of their pain reliever may lead to a decrease in patient satisfaction. Furthermore, patient education may be particularly important when using newer medications. Patients' understanding of medication can be improved through appropriate physician–patient communication. If communication is poor, some patients may not have a sufficient understanding of their pain reliever, including its effectiveness and safety, even if the physician provided a thorough explanation.

Three oral pain relievers have become available in Japan in recent years. Lasmiditan succinate (hereafter, lasmiditan) became available in Japan for migraine treatment in June 2022 [12]. Mirogabalin besylate (hereafter, mirogabalin), an oral gabapentinoid with analgesic effects, was first approved in Japan in 2019 for the treatment of peripheral neuropathic pain [13, 14], with an expanded indication for central neuropathic pain in 2022 [15]. Another oral pain reliever, tramadol hydrochloride, is not new to the market and has been available since 2014; however, a new formulation was released in January 2021

that includes both immediate- and sustained-release components via a bilayer tablet [16].

In clinical practice, treatment adherence is reported to be low for lasmiditan and mirogabalin [17–19]. This may indicate that patients are not satisfied with these oral pain relievers, which in turn may reflect a poor understanding of these medications, although data supporting this hypothesis are limited [11, 20]. Using a web-based questionnaire, we sought to investigate patients' satisfaction with treatment and their understanding of oral pain relievers (lasmiditan, mirogabalin, and sustained-release bilayer tramadol hydrochloride tablets [hereafter, tramadol]). Additionally, we explored the factors influencing patients' treatment satisfaction.

METHODS

Study Design

This was a cross-sectional study using a quantitative one-time web-based survey. Study data were collected between November 2023 and February 2024. The study design, data collection, and data management are described in detail in the Supplementary Methods (see Supplementary Text S1 in the electronic supplementary material).

The study protocol was approved by the Medical Corporation Toukeikai Kitamachi Clinic Ethics Review Board on October 25, 2023. All study procedures were conducted in accordance with local and institutional ethical standards, the 1964 Declaration of Helsinki and its later amendments, the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects [21], the Japanese Act on the Protection of Personal Information, and the revised Personal Information Protection Act. The study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000052629). All patients provided electronic informed consent to participate in the study.

Patients

Patients who were ≥ 18 years of age; were being treated by a physician member of the Plamed Inc. (Tokyo, Japan) panel; had a history of a new oral pain reliever (defined as an oral pain reliever launched as a drug on the market in Japan after January 2018, excluding generic medication approvals) consisting of one or more of lasmiditan, mirogabalin, or tramadol (sustained-release bilayer tramadol hydrochloride tablets) after April 2023; and were able to both provide consent for study participation and electronically access and respond to questions in Japanese without assistance were eligible for study participation. There were no exclusion criteria for this study.

Questionnaire

The study questionnaire included 32 questions and comprehensive instructions on how each question should be answered (see Supplementary Text S2 in the electronic supplementary material). Patients independently completed the web-based questionnaire, which included questions about the following: patient characteristics, duration of new oral pain reliever use, previous oral pain relievers, concomitant pain relievers, patients' understanding of different aspects of their oral pain relievers (efficacy, safety, and dosing), level of satisfaction with current oral pain relievers, information related to how the oral pain reliever was explained to the patient by healthcare providers (HCPs), and information related to discontinuation of oral pain relievers. Regarding medication understanding, individual efficacy factors included the type of targeted pain and the timing and duration of drug effectiveness. Individual safety factors included side effects, timing of onset, and duration of side effects. Individual dosing factors included the number of tablets taken per day, total daily dose, and possibility of dose adjustment. On the questionnaire,

oral pain relievers were listed by their commercial names instead of their generic names (Reyvow® [lasmiditan], Tarlige® [mirogabalin], and Twotram® [tramadol]). Patients who had taken more than one of the three drugs were randomly assigned to one drug when answering Q1–Q32.

Study Endpoints

The primary endpoint was overall satisfaction with oral pain relievers (Q15). Secondary endpoints included overall understanding of the oral pain relievers (Q10); understanding of efficacy (Q1–Q3), safety (Q4–Q6), and dosing (Q7–Q9) of the oral pain relievers; and satisfaction with the efficacy (Q11), safety (Q12), cost (Q13), and explanation of medication by HCPs (Q14).

Scoring of Endpoints

Scoring for questions related to satisfaction with oral pain relievers was based on a five-point scale: 1, very unsatisfied; 2, unsatisfied; 3, neither; 4, satisfied; 5, very satisfied. Scoring for overall understanding of oral pain relievers was based on the following five-point scale: 1, do not understand at all; 2, understand a little; 3, neither; 4, understand well; 5, understand very well. The score for the overall understanding of efficacy, safety, and dosing was the sum of the relevant individual questionnaire scores. The level of understanding for efficacy, safety, and dosing was then categorized as one of three levels (low, 1–6 points; moderate, 7–9 points; or high, 10–15 points).

Statistical Methods

Taking feasibility into consideration, the target sample size was set to 300 patients. Potential patterns of overall understanding and overall satisfaction were assumed by varying the percentage of patients satisfied at each understanding level and the corresponding number of patients. Applying the Cochran–Armitage test with a one-sided significance level of 2.5%, statistical power ranged from 61 to ≤ 99% under the assumption of 300 patients using the potential patterns identified.

All patients who met the eligibility criteria and provided electronic informed consent were included in the full analysis set (FAS). For the primary endpoint, the percentage of patients who were satisfied with their oral pain reliever was calculated as follows: (number of patients who responded with a score of 5 + number of patients with a score of 4)/(number of patients analyzed) × 100. The Cochran–Armitage test was used for cross-sectional analysis of the trend between overall treatment satisfaction and understanding of the medication; 95% confidence intervals (CIs) were calculated, and the one-sided significance level was set at 2.5%. Subgroup analyses by oral pain reliever (lasmiditan, mirogabalin, and tramadol) were also conducted.

Univariate and multivariate analyses for factors associated with oral pain reliever satisfaction were performed using logistic regression models to calculate odds ratios and 95% CIs. Additional details of the statistical methods are provided in the Supplementary Methods (see Supplementary Text S1 in the electronic supplementary material).

The survey design did not allow patients to submit their answers electronically unless the questionnaire was completed in a specific order so that there were no missing data. "Do not know/ Do not remember" was included as a response option, and this response was not treated as a missing value. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Patients

Of the 354 patients who provided electronic informed consent, 328 met the eligibility criteria, responded to the questionnaire, and were included in the FAS, meeting the target sample size of 300 patients (Fig. 1). In total, 121 (36.9%), 182 (55.5%), and 29 (8.8%) patients

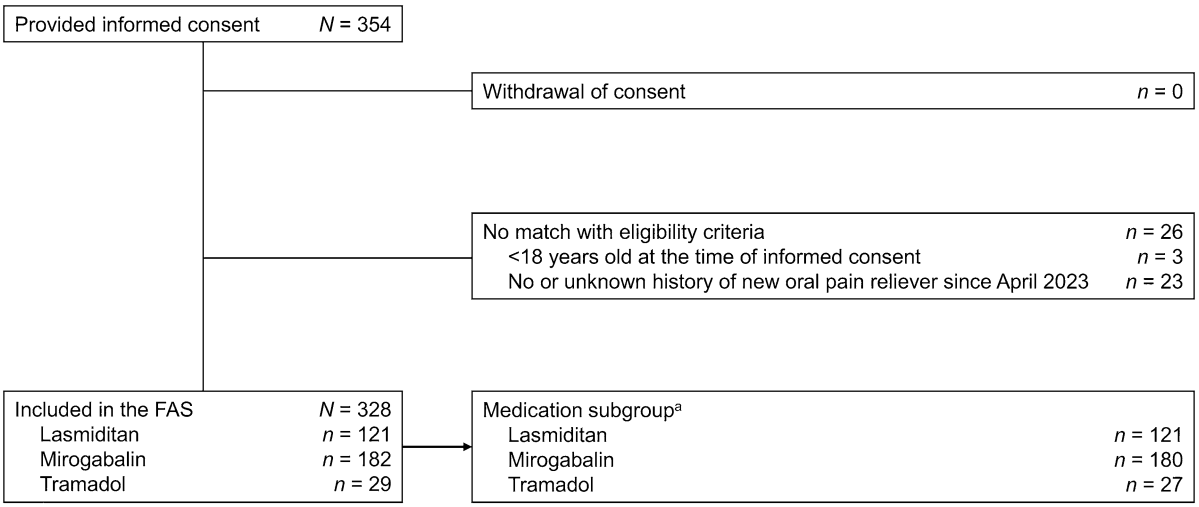

Fig. 1 Patient disposition. Duplicate tabulation of drugs was used. [a]Patients who reported taking more than one oral pain reliever were randomly assigned to one subgroup. *EAS*, full analysis set

were prescribed lasmiditan, mirogabalin, and tramadol, respectively. Four patients had been prescribed more than one medication. Information on whether these medications were taken concurrently or whether the patient switched from one to the other was not collected.

Patients' characteristics are shown in Table 1. The mean age of the patients enrolled was 53.4 years, 66.2% of patients were female, 52.1% had been prescribed oral pain relievers by general physicians, and 68.0% had been taking new oral pain relievers for at least 1 month. Patients prescribed lasmiditan tended to be younger (mean age, 42.7 years) and the proportion of women was higher (79.3%) compared with patients prescribed mirogabalin (59.8 years, 58.9% female) or tramadol (58.6 years, 55.6% female). The proportion of patients who had used oral pain relievers for ≥ 1 month was higher for the mirogabalin recipients (75.6%) than for lasmiditan (59.5%) and tramadol (55.6%) recipients.

Relationship Between Satisfaction and Understanding of Oral Pain Relievers

The percentage of patients who were highly satisfied (score of 4 or 5) with their oral pain reliever (primary endpoint) was 71.6% (Fig. 2a). By subgroup, high overall satisfaction was reported by 62.0%, 76.1%, and 85.2% of patients taking lasmiditan, mirogabalin, and tramadol, respectively (Fig. 2b–d). The results of the five-point rating for satisfaction are presented in Table S1 in the electronic supplementary material.

Most patients reported a high understanding (score of 4 or 5) of their oral pain reliever (68.0%; $n = 223$) (Fig. 3a), whereas a moderate (score of 3) or low (score of 1 or 2) understanding was reported for 25.0% ($n = 82$) and 7.0% ($n = 23$) of patients, respectively. Subgroup analysis showed that high understanding was reported for 77.7%, 63.3%, and 55.6% of patients in the lasmiditan, mirogabalin, and tramadol groups, respectively (Fig. 3b–d). The results of the five-point rating for understanding are presented in Table S2 in the electronic supplementary material.

Understanding was significantly associated with overall satisfaction (Cochran–Armitage test, $p < 0.0001$). Among patients who reported a high understanding, 83.4% ($n = 186/223$) were satisfied with their medication (Fig. 3a). Among those with a moderate understanding, 47.6% ($n = 39/82$) were satisfied, and for those with a low understanding, 43.5% ($n = 10/23$) were satisfied. A significant association between satisfaction and understanding was observed

Table 1 Patient characteristics

	Total (*N* = 328)	**Lasmiditan (*n* = 121)**	**Mirogabalin (*n* = 180)**	**Tramadol (*n* = 27)**
Age (years), mean (SD)	53.4 (16.2)	42.7 (12.4)	59.8 (15.1)	58.6 (12.9)
18–19	1 (0.3)	0	1 (0.6)	0
20–29	28 (8.5)	21 (17.4)	6 (3.3)	1 (3.7)
30–39	46 (14.0)	32 (26.4)	13 (7.2)	1 (3.7)
40–49	57 (17.4)	33 (27.3)	22 (12.2)	2 (7.4)
50–59	81 (24.7)	28 (23.1)	46 (25.6)	7 (25.9)
60–69	56 (17.1)	2 (1.7)	43 (23.9)	11 (40.7)
70–79	41 (12.5)	4 (3.3)	33 (18.3)	4 (14.8)
≥ 80	18 (5.5)	1 (0.8)	16 (8.9)	1 (3.7)
Sex				
Female	217 (66.2)	96 (79.3)	106 (58.9)	15 (55.6)
Department of prescribing physician				
General physician	171 (52.1)	31 (25.6)	122 (67.8)	18 (66.7)
Neurology	57 (17.4)	38 (31.4)	17 (9.4)	2 (7.4)
Psychiatry	8 (2.4)	6 (5.0)	2 (1.1)	0
Neurosurgery	70 (21.3)	42 (34.7)	23 (12.8)	5 (18.5)
Pain clinic/pain medicine	11 (3.4)	4 (3.3)	6 (3.3)	1 (3.7)
Other departments	7 (2.1)	0	6 (3.3)	1 (3.7)
Do not know/do not remember	4 (1.2)	0	4 (2.2)	0
Duration of oral pain reliever use				
< 1 week	38 (11.6)	22 (18.2)	13 (7.2)	3 (11.1)
1 week to < 2 weeks	25 (7.6)	14 (11.6)	7 (3.9)	4 (14.8)
2 weeks to < 3 weeks	14 (4.3)	4 (3.3)	10 (5.6)	0
3 weeks to < 1 month	28 (8.5)	9 (7.4)	14 (7.8)	5 (18.5)
≥ 1 month	223 (68.0)	72 (59.5)	136 (75.6)	15 (55.6)

Data are *n* (%) unless otherwise noted

Four patients had concomitant oral pain reliever use

SD, standard deviation

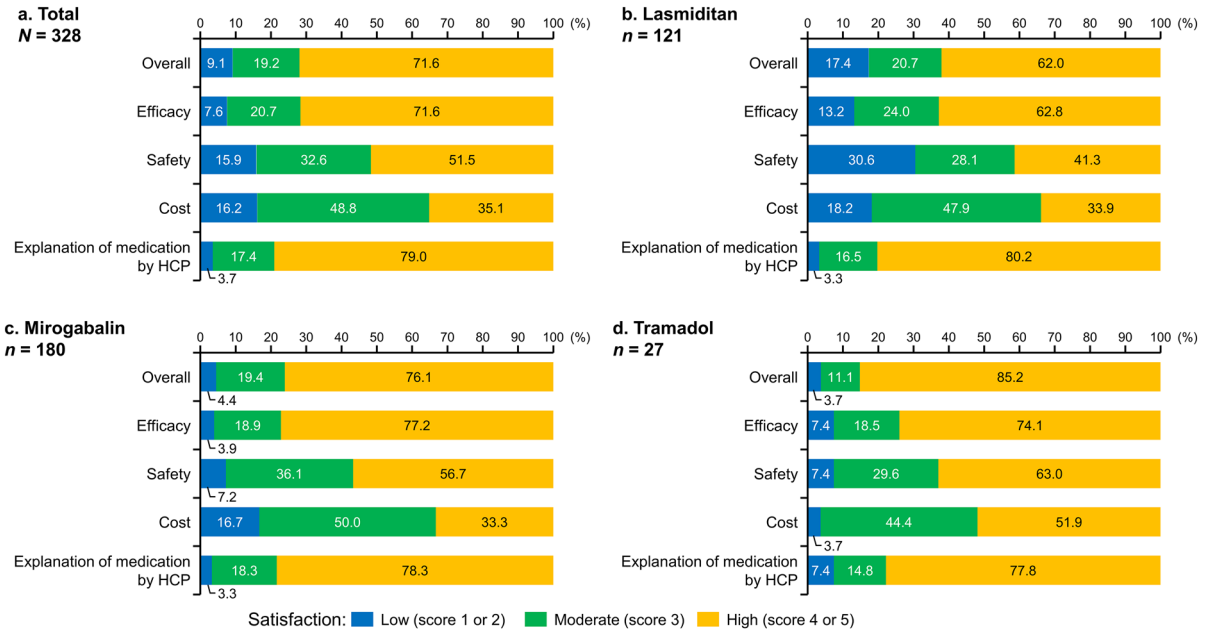

Fig. 2 Summary of overall satisfaction (%) (low, moderate, high) for the total population (FAS) (**a**), lasmiditan subgroup (**b**), mirogabalin subgroup (**c**), and tramadol subgroup (**d**). The overall satisfaction rate is the percentage of patients with scores of 4 or 5. *EAS*, full analysis set; *HCP*, healthcare provider

for the lasmiditan and mirogabalin subgroups ($p<0.0001$ for both) (Fig. 3b, c), but not for the tramadol subgroup ($p=0.3419$) (Fig. 3d).

Subitems for Oral Pain Reliever Understanding and Satisfaction

Over 50% of patients reported an understanding of each efficacy domain evaluation item, with a higher proportion understanding the type of pain targeted (86.3%), followed by the timing (60.1%) and duration (50.6%) of effect (Fig. S1a); similar tendencies were reported for each oral pain reliever subgroup (Fig. S1b–d). Understanding of the safety domain was relatively high for main side effects (63.1%) but lower for timing of onset of side effects (33.2%) and duration of side effects (24.7%) (Fig. S1a); subgroup findings were similar (Fig. S1b–d). Understanding of dosing was high overall, with 89.6% understanding when to take the drug, 80.8% understanding the daily dose, and 76.2% understanding that the dose could be adjusted (Fig. S1a).

Factors Associated with Satisfaction

Multivariate analysis showed that factors significantly associated with high satisfaction (score of 4 or 5) included duration of medication (≥3 months), a high level of efficacy understanding (score of 4 or 5), and a high level of dosing understanding (score of 4 or 5) (see Fig. S2 in the electronic supplementary material). The results of univariate analysis for factors associated with satisfaction in the lasmiditan and mirogabalin subgroups are shown in Table S3 in the electronic supplementary material. Among factors other than satisfaction domains (safety, efficacy, cost, and explanation of medication by HCP), the identified significant factor for lasmiditan was a high level of overall and efficacy understanding, and those for mirogabalin were a high level of overall, efficacy, safety, and dosing understanding; no factors were identified for tramadol (data not shown).

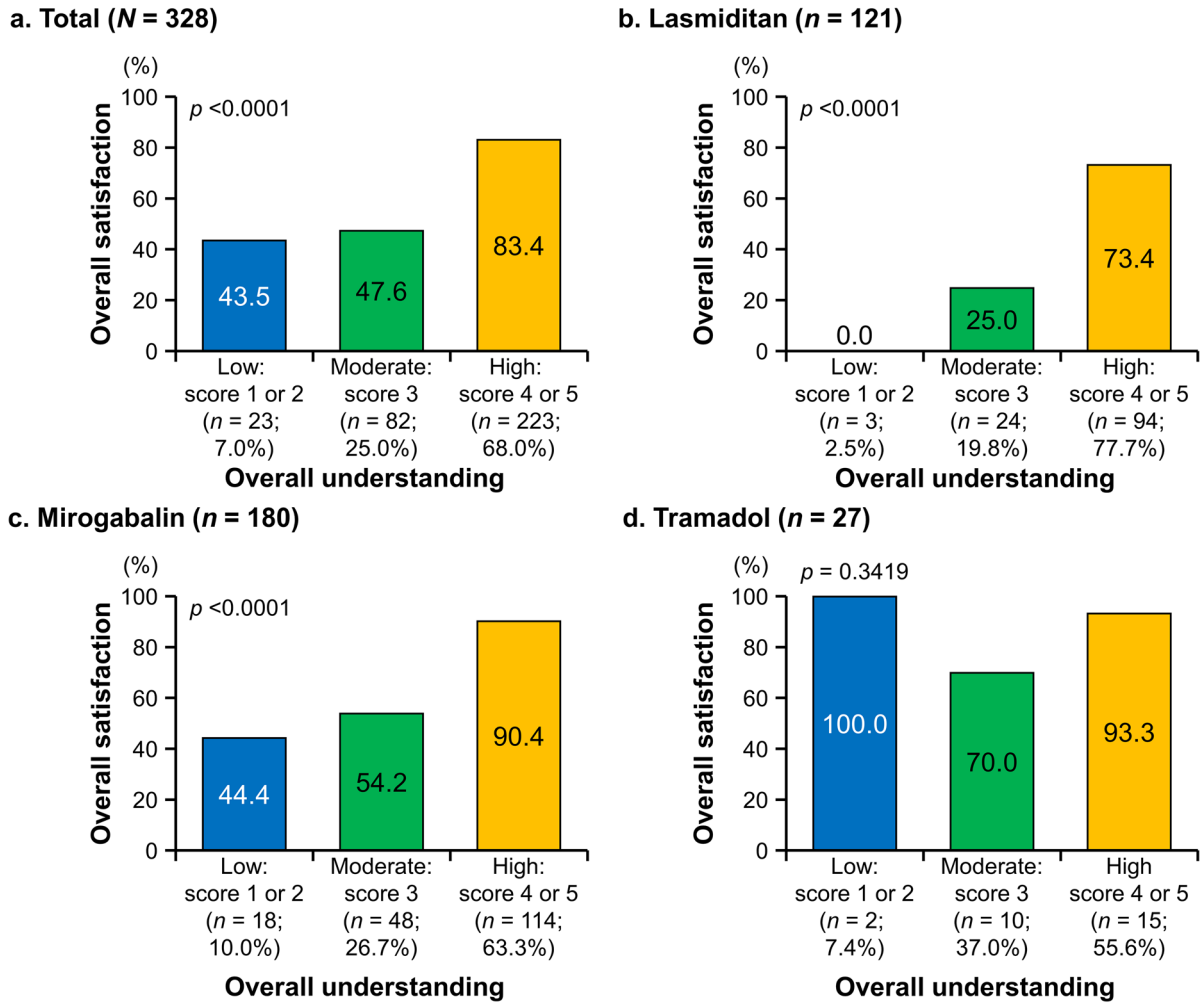

Fig. 3 Relationship between overall satisfaction and overall understanding in the total population (**a**), lasmiditan subgroup (**b**), mirogabalin subgroup (**c**), and tramadol subgroup (**d**). The *n* (%) values below the bars represent the number and percent of patients with low/moderate/high understanding as a fraction of the population of each subgroup. The *p* value was determined using the Cochran–Armitage test.

Oral Pain Reliever Discontinuation

Overall, 18.0% of patients discontinued their oral pain reliever, with the highest rate for lasmiditan (21.5%), followed by mirogabalin (16.7%) and tramadol (11.1%) (Fig. 4a). Patients who were unsatisfied had a higher discontinuation rate than those who were satisfied (38.7% [*n* = 36/93] vs. 9.8% [*n* = 23/235]). The most common reason for discontinuation was symptom improvement (45.8%) followed by lack of efficacy (28.8%) and other reasons (27.1%; no detailed information was collected regarding other reasons) (Fig. 4b–e). In the lasmiditan subgroup, other reasons were most commonly cited for discontinuation (50.0%), followed by lack of efficacy (38.5%). The most common response in the mirogabalin subgroup was symptom improvement (66.7%).

Among patients who discontinued treatment in the lasmiditan subgroup, most took the medication once or 2–4 times (34.6% or 38.5%, respectively), and approximately half of the patients took the medication for a short duration (< 1 week, 38.5%; 1 week to < 2 weeks,

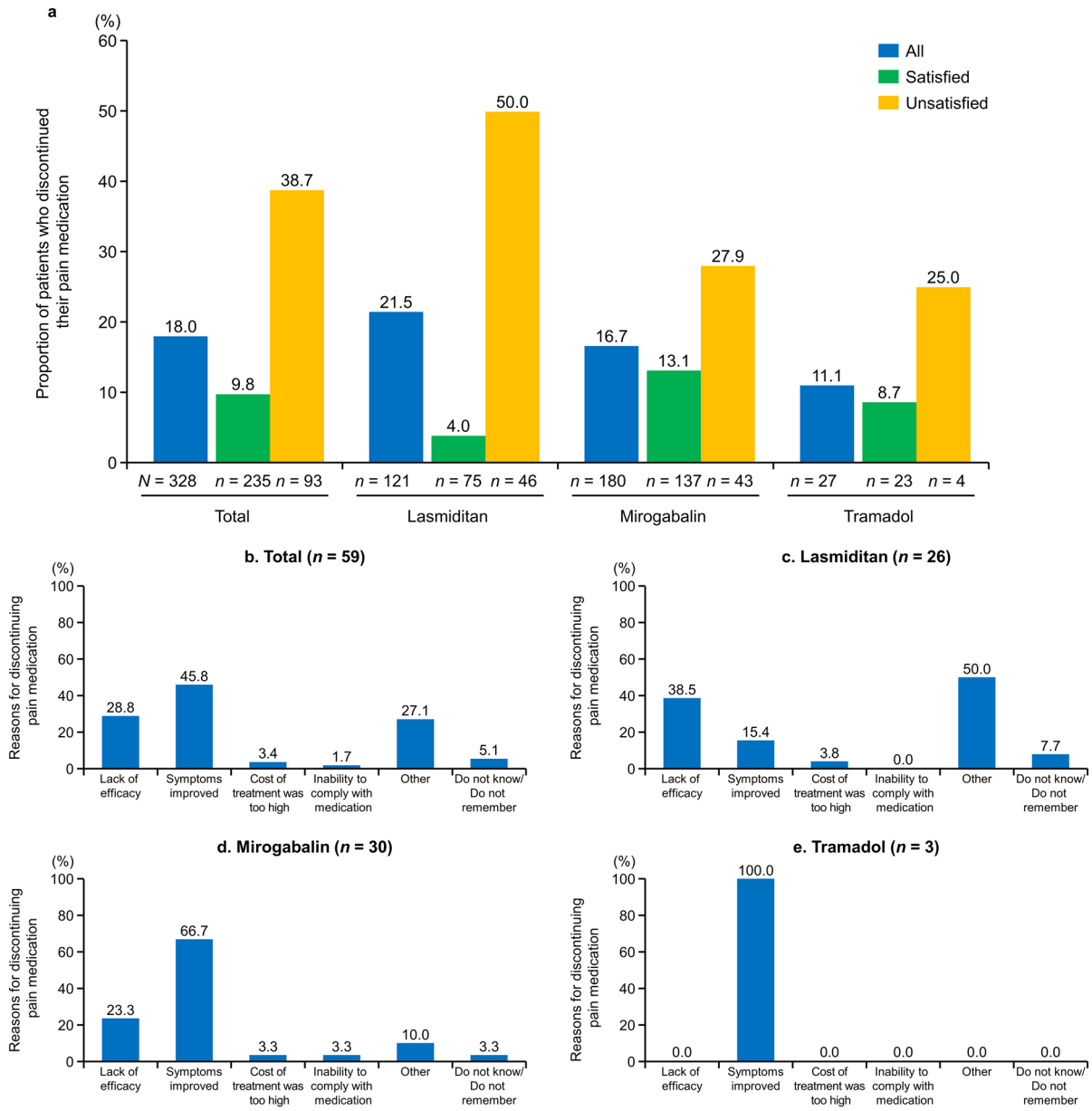

Fig. 4 Proportion of patients who discontinued their oral pain reliever and satisfaction level (**a**) and reasons for discontinuation in the total population (**b**), lasmiditan subgroup (**c**), mirogabalin subgroup (**d**), and tramadol subgroup (**e**). Multiple selections were allowed

15.4%; Fig. S3a and S3b in the electronic supplementary material). Patients in the mirogabalin subgroup who discontinued treatment showed a different trend from those in the lasmiditan subgroup who discontinued; the duration of mirogabalin use was 3 weeks to < 1 month in 20.0% of patients and > 1 month in 50.0% of patients (Fig. S3b).

Overall, 47.5% of patients switched to another medication after discontinuation (Fig. S3c in the electronic supplementary material). The proportion of patients who switched medication was highest in the lasmiditan subgroup and lowest

in the mirogabalin subgroup (88.5% and 13.3%, respectively). In the lasmiditan subgroup, the most common drugs switched to after discontinuation were rizatriptan (39.1%), loxoprofen (21.7%), and others (26.1%) (data not shown).

HCP Explanation of Oral Pain Relievers

Most patients received an explanation of their oral pain reliever from their HCP (89.3%) (see Fig. S4a in the electronic supplementary material). A higher proportion of patients in the lasmiditan subgroup (95.9%) had received an HCP explanation compared with the mirogabalin and tramadol subgroups (86.1% and 81.5%, respectively). Of all patients who received an explanation from an HCP, 84.6% ($n=248$) received the explanation from a physician, 61.4% ($n=180$) from a pharmacist, and 11.6% ($n=34$) from a nurse (Fig. S4b in the electronic supplementary material). By satisfaction level, 67.3% (146/217) of satisfied patients and 44.7% (34/76) of unsatisfied patients received an explanation from a pharmacist, although both satisfied and unsatisfied patients received an explanation from a physician or nurse at a similar rate (satisfied vs. unsatisfied: 84.3% vs.85.5% from physician, 11.5% vs. 11.8% from nurse) (Fig. S4c and S4d in the electronic supplementary material).

Among patients who received an explanation from an HCP, 62.5% considered explanations from physicians to be of high quality, whereas explanations from pharmacists and nurses were considered high quality by 29.0% and 3.4% of patients, respectively (Fig. S5a in the electronic supplementary material). A higher proportion of satisfied patients reported a high-quality explanation from a pharmacist compared with unsatisfied patients (32.3% [$n=70/217$] and 19.7% [$n=15/76$], respectively) (Fig. S5b in the electronic supplementary material).

The most common explanatory method was verbal (90.4%), followed by written (38.6%) and video (0.7%) (see Fig. S6a in the electronic supplementary material). The preferred explanatory method was verbal for 56.4% of patients, written for 39.0%, and video for 1.8% (Fig. S6b in the electronic supplementary material). Fewer patients preferred a verbal explanation among the unsatisfied versus satisfied patients (47.3% vs. 60.0%) and the preference for a written explanation was higher (unsatisfied 46.2% vs. satisfied 36.2%) (data not shown).

Explanations most frequently included information about efficacy (84.6%) followed by dosing (69.3%) and side effects (68.6%) (Fig. S7a in the electronic supplementary material). By oral pain reliever subgroup, most patients in the lasmiditan and mirogabalin subgroups received explanations of efficacy (92.2% and 81.3%, respectively). Regarding specific information to be included in the medication explanation, 56.7% of patients preferred inclusion of information on efficacy; 30.4%, on side effects; and 12.9%, on dosing (Fig. S7b in the electronic supplementary material). Although information on efficacy was preferred by the highest proportion of patients, among unsatisfied patients in the lasmiditan subgroup, 41.9% preferred information on side effects, which was almost as high as that reported for efficacy information (data not shown).

DISCUSSION

The primary goal of this study was to assess the effect of oral pain reliever understanding on treatment satisfaction in patients receiving treatment for pain. We also sought to highlight the important role of HCPs in ensuring that patients understand their oral pain relievers while undergoing treatment. Most of the satisfied patients had a high level of understanding of their oral pain reliever. A statistically significant association between understanding and satisfaction with oral pain relievers was identified in the total patient population, with similar significant associations in the lasmiditan and mirogabalin subgroups. Furthermore, the findings indicate that high-quality explanations of new medications by HCPs may contribute to treatment satisfaction by increasing patients' understanding of their medication.

Patients satisfied with their medication had a higher level of understanding of all domains than unsatisfied patients. The largest difference in understanding between satisfied and

unsatisfied patients was in the efficacy domain; unsatisfied patients had a particularly low level of understanding of the expected timing and duration of drug efficacy. Similar findings were observed by medication subgroup. Multivariate analysis showed that a high level of both efficacy and dosing understanding significantly affected satisfaction. While efficacy understanding greatly affected satisfaction, safety understanding had a lesser effect, except for lasmiditan. The univariate analysis showed that a high level of understanding of dosing was not significantly associated with satisfaction in the lasmiditan subgroup analysis. Overall, few patients had a high understanding of safety. In particular, the timing and duration of adverse drug reactions were not well understood. The level of understanding of safety may have a more positive impact on satisfaction, reiterating the need to improve understanding of safety.

Overall, 18.0% of patients discontinued their oral pain reliever, and similar discontinuation rates were observed for lasmiditan and mirogabalin. There was a large difference between the proportion of satisfied and unsatisfied patients who discontinued. Although there were both positive and negative reasons for discontinuation, positive reasons (e.g., symptom improvement) were more common in satisfied patients, whereas negative reasons (e.g., lack of efficacy) were more common in unsatisfied patients.

In this study, patients discontinued lasmiditan primarily for other reasons (possibly including side effects such as somnolence and dizziness) or lack of efficacy. The percentage of satisfied patients in the lasmiditan group was 62.0%, and patients who discontinued this medication were more likely to discontinue after one or several doses. Although most patients in the CENTURION long-term study were satisfied with lasmiditan treatment for migraines, 29.5% of patients were dissatisfied with treatment, which is in line with our findings [22]. Aside from patient withdrawal, the main reasons for discontinuation in the CENTURION trial were lack of efficacy and/or adverse events. Considering this, lasmiditan discontinuation in the present study may have been due to side effects in the early stages of treatment or low satisfaction due to lack of efficacy. It should be noted that in this study, adverse events/side effects were not included as options for the questions on reasons for discontinuation. If patients are informed in advance by their HCPs about lasmiditan side effects and their appropriate prevention/mitigation management, they might continue taking lasmiditan.

Patients in the mirogabalin subgroup mainly discontinued because of symptom improvement or lack of efficacy. Most of them did not switch to other medications after discontinuing. These results are consistent with those of a previous post-marketing study, in which more than half of the discontinued cases discontinued mirogabalin because of symptom improvement [23]. The discontinuation group taking mirogabalin for a shorter period may have perceived a lack of efficacy before the medication was sufficiently titrated. Indeed, stepwise titration is recommended to reduce the risk of side effects [24] and many patients are prescribed a lower dose rather than the maintenance dose (20–30 mg/day) as specified in the mirogabalin package insert [18, 25]. Thus, it is important to fully inform patients about what to expect with medication efficacy and safety during the titration period.

The questionnaire showed that physicians were most likely to provide high-quality explanations of medication compared with other HCPs. The unsatisfied group received fewer explanations by pharmacists than the satisfied group. Thus, it may be necessary to improve explanations of medication efficacy, safety, and dosing not only by physicians but also by pharmacists. Among dissatisfied patients, fewer preferred verbal explanations of their medication and more preferred written materials for this purpose compared with the satisfied group. It is possible that some patients may be unable to fully understand after receiving verbal explanations during a single HCP consultation; in such cases, written explanatory materials with illustrative figures may be useful after the initial consultation to improve patients' understanding. Furthermore, the unsatisfied group tended to take their medication for a shorter period. With inadequate understanding, patients may discontinue treatment when side effects occur or efficacy is not fully achieved in the early stages of administration, leading to dissatisfaction.

Together, this suggests that dissatisfied patients may have preferred more extensive information or to have had the opportunity to increase their own understanding from written materials when initiating the medication, followed by verbal explanations. Thus, in order to improve patient understanding, it may be especially useful to provide an explanation of oral pain relievers from multiple HCPs, either verbally or with written materials (according to each patient's preference), prior to initiating administration, as patients lack experience with the treatment. Digital tools or other innovative methods for enhancing patient education may be useful for improving patient understanding. However, in this study, the number of patients who received video explanations was very small compared with those who received verbal or written explanations, so it was not possible to evaluate the usefulness of digital tools.

The unsatisfied patients taking lasmiditan had a preference for safety and efficacy information, with a higher preference for safety information versus the satisfied patients taking lasmiditan. Thus, their dissatisfaction may have stemmed from a perception that they were not fully informed about safety and efficacy prior to initiating the medication. In particular, as improving patients' understanding of the efficacy, safety, and dosing of oral pain relievers may be important for increasing treatment satisfaction, further longitudinal data are needed to confirm these associations. Lasmiditan discontinuation often occurs within the first few doses, so it may be important to provide patients taking lasmiditan with information on both efficacy and safety at the first prescription. Based on treatment adherence and patient satisfaction, a 100-mg dose/attack has been reported to be optimal for most patients, and continuous administration can reduce the occurrence of adverse events [26]. At the first prescription of lasmiditan, advising patients to take the first dose at night (before bed) or when they are able to take a nap is beneficial to manage central nervous system-related adverse events [27]. Furthermore, the package insert for lasmiditan states that if there are concerns about the tolerability of a 100-mg dose, a 50-mg dose should be considered [28]. In clinical practice, lasmiditan is occasionally started at 50 mg and increased to 100 mg depending on the patient's condition. The results of our study suggest that patient satisfaction can be achieved by explaining the potential side effects and how to manage them as discussed above, ensuring appropriate lasmiditan use, and establishing an effective dose treatment adherence for individual patients.

This study had several limitations that should be considered. The cross-sectional nature of the study means that causal relationships for outcomes cannot be fully clarified. This study did not use multivariate analysis to examine factors related to understanding or to evaluate the impact of satisfaction and understanding on patient outcomes (e.g., pain control). These points, along with the inclusion of efficacy and safety measurements, should be addressed in future research. The questionnaire used in this study was not validated; however, it met the basic principles of item creation as described by Clark and Watson [29]. Information on the type or severity of pain also was not collected. It must be noted that satisfaction is reported to vary depending on the type of pain being treated, the type of drug used for treatment, and the type of pain targeted by each drug [30]. As this survey was administered to each patient only once, the responses were likely affected by the patient's condition at the time of the survey as well as the time period recalled, which probably differed among the patients. This study did not collect information on complications or the specific indication for which each drug was prescribed. Furthermore, patients self-reported their eligibility for study inclusion, and no information was collected on cognitive function or complications that may have influenced cognitive function (e.g., dementia, depression, or schizophrenia). Finally, the questionnaire responses were not verified by a third person, such as the attending physician.

CONCLUSION

The relationships of patients' understanding of the efficacy, safety, and dosing of oral pain relievers with treatment satisfaction and with treatment discontinuation suggest that a higher level of understanding may be associated with higher satisfaction, and higher satisfaction may be associated with lower drug discontinuation rates. Further studies, such as a longitudinal study to identify the causal relationship between understanding and satisfaction, would be of value in the future.

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Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author and Daiichi Sankyo Co., Ltd., a study sponsor, on reasonable request. Data disclosure can be requested for 36 months from article publication.

Declarations

Conflict of Interest. Makio Takahashi received honoraria and consulting fees from Daiichi Sankyo Co., Ltd. Sho Kodama, Maiko Akahane, and Shuhei Yamamoto are employees of Daiichi Sankyo Co., Ltd. Takashi Yonemoto and Haruhiko Seki are employees of INTAGE Healthcare Inc.

Ethical Approval. The study protocol was approved by the Medical Corporation Toukeikai Kitamachi Clinic Ethics Review Board on October 25, 2023; no approval number was issued. All study procedures were conducted in accordance with local and institutional ethical standards, the 1964 Declaration of Helsinki and its later amendments, the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects, the Japanese Act on the Protection of Personal Information, and the revised Personal Information Protection Act. The study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000052629). All patients provided electronic informed consent to participate in the

study; no identifying information is included in the manuscript.

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