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Treatment Patterns and Persistence Among Patients Newly Diagnosed With Migraine in South Korea: A Retrospective Analysis of Health Claims Data

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Background and Purpose Migraine is one of the most common chronic neurological diseases worldwide. Although diverse treatment regimens have been recommended, there is insufficient evidence for which treatment patterns to apply in routine clinical settings.

Methods We used nationwide claims data from South Korea for 2015–2021 to identify incident migraine patients with at least one prescription for migraine. Patients were categorized according to their initial treatment classes and followed up from the date of treatment initiation. Treatment regimens included prophylactic treatments (antidepressants, anticonvulsants, beta blockers, calcium-channel blockers, and renin-angiotensin-aldosterone system [RAAS] inhibitors) and acute treatments (acetaminophen, antiemetics, aspirin, ergotamine, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, and triptans). The treatment patterns of migraine were evaluated until the end of the study period, including the secular trends, prevalence, persistence, and changes in migraine treatment.

Results Among the 761,350 included patients who received migraine treatment, the most frequently prescribed acute treatment was an NSAID (69.9%), followed by acetaminophen (50.0%). The most-prescribed prophylactic treatment was flunarizine (36.9%), followed by propranolol (24.4%). Among the patients, 54.8% received acute treatment, 13.5% received prophylactic treatment, and 31.6% received both treatment types. However, 65.7% of the patients discontinued their treatment within 3 months. The 3-month persistence rate was highest for triptans (25.2%) among the acute treatments and for RAAS inhibitors (62.0%) among the prophylactic treatments.

Conclusions While the prevalence rates of medication use were found to align with current migraine guidelines, frequent switching and rapid discontinuation of drugs were observed in routine clinical settings.

Keywords migraine; treatment adherence; South Korea; acute pain.

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INTRODUCTION

Effective migraine management is crucial given that migraine affects more than 1 billion people worldwide.[1,2] Symptoms during migraine attacks such as the headache worsening with activity and being coupled with nausea and vomiting substantially disrupt the daily routines of patients.[3,4] It is also known that migraine is associated with several medical comorbidities including cardiovascular disease[5] and psychiatric and sleep disorders.[6]

The purpose of migraine treatments to relieve pain, restore function, reduce headaches, and prevent progression to chronic migraine, and so they are commonly divided into acute and prophylactic treatments.[7] The acute treatments aim to minimize suffering during a migraine attack, and include serotonin (5-hydroxytryptamine) receptor agonists (triptans),

ergotamine, and analgesics. Prophylactic treatments aim to reduce the severity, frequency, and duration of migraines, and include antihypertensives, antidepressants, and anticonvulsants.[8-10] Various novel therapies such as botulinum toxin A and medications targeting calcitonin-gene-related peptide (CGRP) have recently emerged for the treatment of prophylactic migraine.[11-13]

While various medications are recommended, the rates of utilization and adherence to migraine-specific treatment are relatively low in Asia, including South Korea, which might be due to a low awareness of migraine. A large proportion of individuals with migraine remain underdiagnosed and undertreated.[10,14,15] Accordingly, appropriate treatments for these patients can be determined by identifying treatment patterns for migraine in routine clinical settings. However, treatment patterns in real-world practice have not been evaluated previously.

METHODS

Data sources

This population-based study aimed to determine the treatment patterns of migraine using the claims data from the Health Insurance Review and Assessment Service (HIRA) from January 1, 2015 to December 31, 2021. Since South Korea has a universal health coverage system, the HIRA manages 46 million people, corresponding to approximately 98% of the total population. The claims data for each anonymized identifier consist of general information (i.e., age, sex, and medical aid program), diagnostic information (i.e., inpatient/outpatient diagnosis and major/secondary diagnosis), prescriptions and procedure information (i.e., active ingredients, dosage, and days of supply), and information about healthcare providers (i.e., primary, secondary, and tertiary care).[16,17]

Participants

Incident migraine patients who met the following eligibility criteria between January 1, 2016 and December 31, 2021 were included: 1) at least one inpatient or two outpatient diagnoses of migraine (ICD-10 [International Classification of Diseases, 10th Revision] code G43) within 1 year, and 2) prescription of any migraine treatment regimen associated with a record of a migraine diagnosis. The date of the first diagnosis of migraine was defined as the cohort entry date, and the date of the first prescription for migraine treatment was defined as the index date.

To retrieve incident patients with migraine, patients diagnosed with migraine 1 year prior to cohort entry were excluded. In addition, to allow treatment patterns to be observed for at least 1 year, we excluded patients who could not be followed up for that period. To focus on medications for the treatment of migraine, we excluded patients who were prescribed the drug of interest (defined in detail below) as a treatment regimen for conditions other than migraine (Supplementary Table 1 in the online-only Data Supplement).

Variables

Treatment regimens

Based on the treatment guidelines for pharmacological therapy for migraine in South Korea in 2021, we defined the following medications to observe the treatment patterns of migraine: prophylactic treatments (antidepressants, anticonvulsants, and antihypertensives: beta blockers, calcium-channel blockers [CCBs], and renin-angiotensin-aldosterone system [RAAS] inhibitors) and acute treatments (ergotamine, triptans, aspirin, acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antiemetics, and opioids).[18] The treatment classes for each treatment class are listed in Supplementary Table 2 (in the online-only Data Supplement). The probability of misclassifying medications for the indication of migraine treatment was reduced by only including medications for which there was a migraine diagnosis record in the same prescription.

Patient characteristics

Demographic characteristics such as age, sex, insurance type, and region of residence were assessed on the cohort entry date. Clinical characteristics including comorbidities (allergies, neuropsychiatric disorders, cardiovascular diseases, and digestive system diseases), Charlson Comorbidity Index, and proxies for the overall health status were measured within 1 year prior to the cohort entry date.

Outcomes

The clinical outcomes were assessed in a stepwise manner. First, we assessed secular trends in migraine medication use from 2016 to 2021. Second, the migraine medications prescribed on the index date that were used during the study period were categorized according to treatment classes. Third, changes in the treatment regimens for patients with migraine were measured over time, with the patients categorized into prophylactic, acute, and both (prophylactic and acute) treatment groups. Fourth, the persistence of the initial treatment for migraine was assessed, which was defined as the absence of discontinuation (no prescription of the initial treatment for more than 60 days) and switching of the initial treatment. Finally, switching and additional patterns of migraine-specific acute treatment were explored by examining the use of other acute treatments among patients treated with triptans.

Statistical analyses

Categorical variables are presented as proportions, and continuous variables are presented as mean±standard-deviation values or medians and interquartile ranges. The following statistical analyses were performed:

1) To estimate the secular trends (i.e., changes in the number of prescriptions for each migraine treatment during the study period) in migraine medication use, we calculated the number of quarterly prescriptions for each treatment class from 2016 to 2021.

2) To measure the prevalence rates of the different treatment regimens, we calculated the number of patients with at least one prescription per regimen class during the study period.

3) To quantify treatment changes over time, each patient was categorized into the acute, prophylactic, or both-treatments group based on their initial treatment. The number of patients in each category was calculated every 3 months using a Sankey diagram, which consisted of nodes positioned along the vertical axis and another dimension arranged horizontally, where the height of each node corresponded to the number of patients associated with it, and the flows illustrated the probabilities of transitioning between states (treatment categories) during different time periods (days 0, 90, 180, 270, and 360).

4) To assess the persistence of the initial migraine treatment, we calculated the number of patients who were still receiving the medication without discontinuation or switching (i.e., the survival probability). Additionally, survival curves of discontinuation and switching of the entire study population were depicted as a Kaplan–Meier plot. As a time-to-event analysis, the y-axis of the Kaplan–Meier plot represented the survival probability, with curves starting at 1 and moving downwards when the event (discontinuation or switching) occurred as time (x-axis) progressed.

5) To examine acute treatment patterns among patients who were prescribed triptans as an initiation medication for acute migraine, we stratified patients according to whether a triptan prescription was repeated within 12 months after the index date.

Given that both the migraine burden and prevalence peak in females of reproductive age, we conducted a subgroup analysis among females of reproductive age (15 years to 49 years) to assess differences in treatment patterns. We also conducted a sensitivity analysis assessing treatment patterns during the period of the coronavirus disease 2019 (COVID-19) pandemic (defined as from January 20, 2020, which was the date of the first COVID-19 confirmed case in South Korea, to December 31, 2021) considering potential differences in treatment patterns during the lockdown period.

All statistical analyses were conducted using SAS software (version 9.4, SAS Institute, Cary, NC, USA). This study was approved by the Institutional Review Board of Sungkyunkwan University (SKKU 2022-09-007). Since this study analyzed anonymized administrative claims data, the requirement to obtained informed consent was waived.

RESULTS

The eligibility criteria were met by 761,350 patients (Supplementary Fig. 1 in the online-only Data Supplement). They were aged 48.8±17.1 years, most of them were female (*n*=552,218, 72.5%), and they included some children (*n*=15,109, 2.0%), females of reproductive age (*n*=282,109, 37.1%), and those diagnosed with migraine in the clinic (*n*=487,052, 64.0%) and residing in rural areas (*n*=400,078, 52.6%). Some of the patients also had acute upper respiratory infections (*n*=426,566, 56.0%), acute bronchitis (*n*=380,114, 49.9%), and acute rhinitis (*n*=372,051, 48.9%) (Supplementary Table 1 in the online-only Data Supplement).

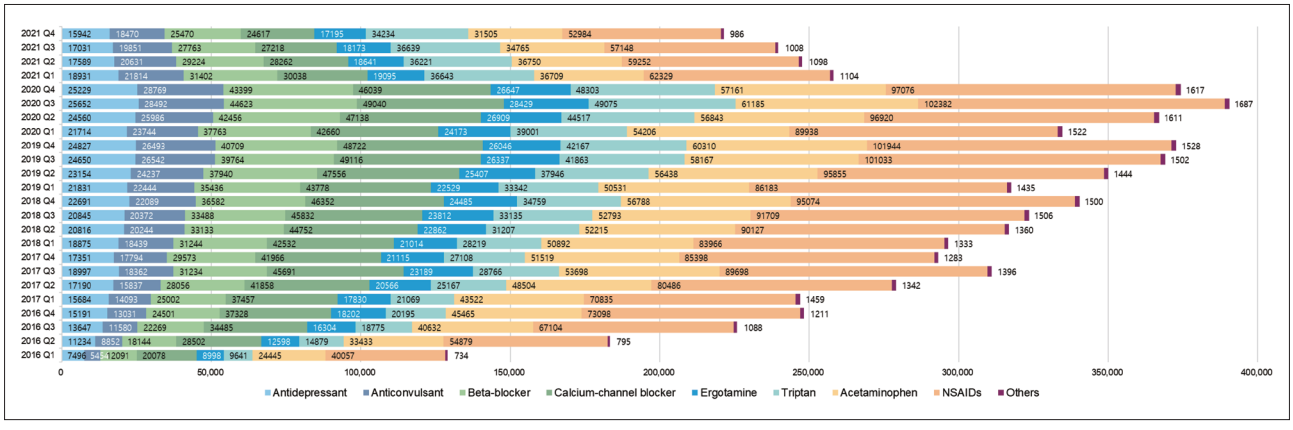

Fig. 1. Secular trends in the frequency of medication use for migraine according to treatment classes between 2016 and 2021. Others include renin-angiotensin-aldosterone system inhibitors, aspirin, antiemetics, and opioids. NSAIDs, nonsteroidal anti-inflammatory drugs; Q, quarter.

The secular trends in the frequency of migraine treatments from 2016 to 2021 are shown in Fig. 1. In the first quarter of 2016, NSAIDs accounted for the largest proportion of prescriptions (31.1%). Among the acute treatments, the proportion of patients using triptans increased from 7.5% in quarter (Q)1 of 2016 to 15.5% in Q4 of 2021, whereas the proportion decreased for NSAIDs (from 31.1% to 24.0%) and acetaminophen (from 19.0% to 14.2%). Among the prophylactic treatments, the proportion of patients using anticonvulsants increased from 2016 4.23% in Q1 of 2016 to 8.34% in Q4 of 2021, while the proportion using CCBs decreased (from 15.6% to 11.1%). The subgroup analysis of female patients of reproductive age produced consistent results (Supplementary Fig. 2 in the online-only Data Supplement).

Table 1 presents the prevalence of migraine medications at the index date during the study period, categorized according to treatment classes. These patients included 556,158 (73.1%) who were prescribed more than 1 migraine medication during the study period. The incidence of receiving migraine medication was 8.0 prescriptions per person-years. During the study period, 442,809 (58.2%) patients were prescribed prophylactic treatments and 702,686 (92.3%) were prescribed acute treatments. The most-prescribed prophylactic treatment was flunarizine (*n*=280,857, 36.9%), followed by propranolol (*n*=185,953, 24.4%) and amitriptyline (*n*=103,130, 13.6%). The most-prescribed acute treatment was an NSAID (*n*=532,194, 69.9%), followed by acetaminophen (*n*=380,675, 50.0%) and triptans (*n*=214,446, 28.2%). During the study period, the prevalence of triptan use was higher in females of reproductive age (41.1%) than in the overall study population (28.2%) (Supplementary Table 3 in the online-only Data Supplement).

Changes in the treatment regimens for patients with migraine over time are shown in Fig. 2. The 761,350 study patients included 417,522 (54.8%) who received acute treatment, 103,035 (13.5%) who received prophylactic treatment, and 240,793 (31.6%) who received both acute and prophylactic treatments. At 3 months after the start of treatment, 65.7% of patients had discontinued treatment, 13.9% were receiving acute treatment, 7.6% were receiving prophylactic treatment, and 12.9% were receiving both treatments. The results are further stratified according to each migraine medication class in Supplementary Figs. 3-6 (in the online-only Data Supplement).

The persistence of initial migraine treatment according to individual medication classes is presented in Table 2. Among acute treatments, the persistence rate at 3 months was highest for triptans (25.2%) and lowest for antiemetics (2.9%) and opioids (10.2%). Among prophylactic treatments, the 3-month persistence rate was highest for RAAS inhibitors (62.0%), followed by anticonvulsants (54.7%), beta blockers (40.7%), antidepressants (39.8%), and CCBs (31.2%). The subgroup analysis of female patients of reproductive age produced consistent results (Supplementary Table 4 in the online-only Data Supplement), as did the sensitivity analysis considering the lockdown period of the COVID-19 pandemic (Supplementary Table 5 in the online-only Data Supplement). The times of discontinuation and switching to other treatments for all patients, regardless of their initial treatment

Table 1. Prevalence of medication use for migraine treatment during the study period in all 761,350 patients

Characteristic	Value
Migraine treatment, prescriptions per person-years	8.04
Combination therapy with >1 distinct migraine medications	556,158 (73.05)
Migraine treatment regimen	
Prophylactic treatment	442,809 (58.16)
Antidepressants	129,581 (17.02)
Amitriptyline	103,130 (13.55)
Venlafaxine	2,191 (0.29)
Nortriptyline	31,696 (4.16)
Anticonvulsants	101,259 (13.30)
Divalproex sodium	24,730 (3.25)
Valproate	8,750 (1.15)
Topiramate	79,760 (10.48)
Beta blockers	195,162 (25.63)
Propranolol	185,953 (24.42)
Atenolol	1,783 (0.23)
Nadolol	12,412 (1.63)
CCBs	
Flunarizine	280,857 (36.89)
RAAS inhibitors	2,288 (0.30)
Candesartan	2,285 (0.30)
Lisinopril	3 (0.00)
Acute treatment	702,686 (92.29)
Ergotamine	149,583 (19.65)
Triptans	214,446 (28.17)
Sumatriptan	104,948 (13.78)
Zolmitriptan	24,776 (3.25)
Almotriptan	44,752 (5.88)
Frovatriptan	34,226 (4.50)
Naratriptan	60,178 (7.90)
Aspirin	1,930 (0.25)
Acetaminophen	380,675 (50.00)
NSAIDs	532,194 (69.90)
Antiemetics	1,110 (0.15)
Opioids	9,645 (1.27)

Data are *n* (%) values.
CCBs, calcium-channel blockers; NSAIDs, nonsteroidal anti-inflammatory drugs; RAAS, renin-angiotensin-aldosterone system.

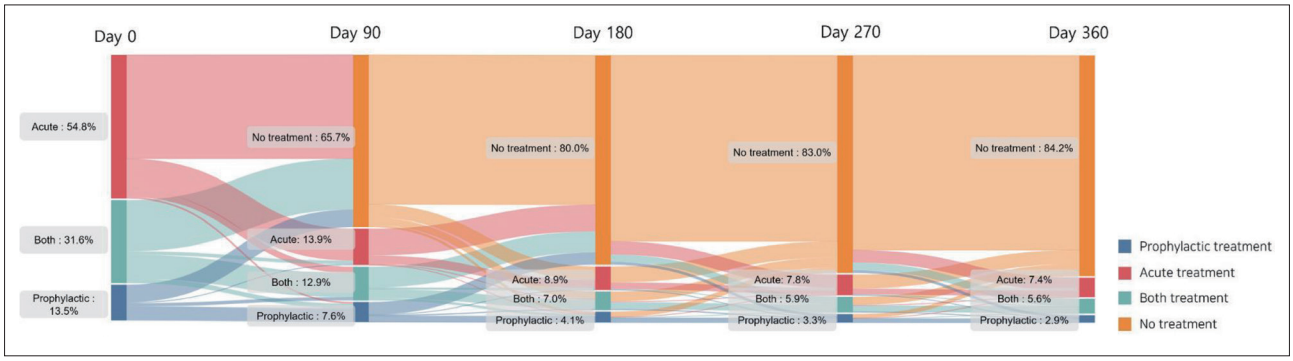

Fig. 2. Sankey diagram of treatment changes across 3-month periods in patients with migraine from the index date. Prophylactic treatments comprised antidepressants, anticonvulsants, and antihypertensives (beta blockers, CCBs, and RAAS inhibitors). Acute treatments comprised ergotamine, triptans, aspirin, acetaminophen, NSAIDs, antiemetics, and opioids. CCBs, calcium-channel blockers; NSAIDs, nonsteroidal anti-inflammatory drugs; RAAS, renin-angiotensin-aldosterone system.

class, are reported in Supplementary Fig. 7 (in the online-only Data Supplement). Half of the patients had switched their initial treatment by 11.9 weeks and discontinued by 9.3 weeks.

The switching and addition patterns of triptans, which are a migraine-specific acute drug, are shown in Fig. 3. Among patients who did not receive a repeat triptan prescription after initiation on the index date, NSAIDs and acetaminophen were the most-used nontriptan acute treatments within the timeframes of 1–6 months (59.3% and 29.6%, respectively) and 1–12 months (62.7% and 32.8%, respectively) (Fig. 3A). A similar trend was observed for patients who received a repeat triptan prescription within the timeframes of 1–6 months (56.6% and 25.9% for NSAIDs and acetaminophen, respectively) and 1–12 months (61.0% and 29.6%, respectively) (Fig. 3B).

DISCUSSION

This study has revealed the treatment patterns of patients with migraine in South Korea. The use of migraine-specific agents increased during the study period. However, most patients either discontinue treatment within a short period or do not adhere to their treatment regimen. By characterizing migraine treatment patterns in routine clinical settings, this study provides real-world evidence for identifying patients with migraine who are less likely to receive sufficient treatment.

Our analysis of the secular trends in migraine medication prescriptions from 2016 to 2021 showed that the use of triptans doubled, while the use of simple analgesics such as NSAIDs and acetaminophen decreased. This increase in triptan use over time can be explained by a stratified-care treatment strategy that uses migraine-specific medications (e.g., triptans) showing better clinical outcomes than a step-care treatment strategy that prescribes simple analgesics for the initial treatment of migraine.[19]

The most commonly used acute treatment regimens for migraine were NSAIDs, acetaminophen, and triptans. Similar results regarding usage patterns by medication class have been observed in several countries, such as triptans (53%) and NSAIDs (31.4%) in Italy,[20] NSAIDs (77.4%) and triptans (59.9%) in the United States,[21] and acetaminophen (68.8%), ergotamine (49.4%), and NSAIDs (38.4%) in Taiwan.[22] However, the results regarding the prevalence of opioid use are inconsistent. Few patients with migraine are prescribed opioids in most countries, including South Korea (1.3%), Italy (1.7%), and Taiwan (0.2%). This contrasts markedly with 77.4% of patients with migraine in the United States who are prescribed prophylactic treatment use opioids for acute migraine management. Discrepancies in the findings of the United States with those of the current study may be explained by heterogeneity in the physicians' preferences for opioid use.[23] Additional research on the use of opioids for migraine treatment in regional clinical settings is therefore needed.

Flunarizine, propranolol, and amitriptyline are the most-prescribed medications for the prophylactic treatment of migraine. This is consistent with the guidelines for prophylactic treatment mostly recommending propranolol, metoprolol, flunarizine, and amitriptyline in each regimen class.[18] A study from Italy found that during the 60-day period from the first diagnosis of migraine, 17.4% were prescribed topiramate; 18.7% were prescribed antidepressants, including amitriptyline; and 8.4% were prescribed beta blockers, including propranolol.[20] A study that sampled Korean claims data found that propranolol (35.0%), flunarizine (32.5%), topiramate (13.7%), and amitriptyline (12.8%) were the most-used prophylactic treatments among patients for migraine prophylaxis.[24] A study from Taiwan produced similar results, with flunarizine (68.9%), propranolol (40.7%), and topiramate

Table 2. Treatment patterns of medication use for migraine according to initial treatment class

Treatment pattern	Prophylactic treatment					Acute treatment					
	Antidepressants (*n*=71,761)	Anticonvulsants (*n*=52,035)	Beta blockers (*n*=121,919)	CCBs (*n*=203,362)	RAAS inhibitors (*n*=587)	Ergotamine (*n*=105,051)	Triptans (*n*=135,510)	Aspirin (*n*=1,214)	Acetaminophen (*n*=266,199)	NSAIDs (*n*=414,277)	Antiemetics (*n*=477)	Opioids (*n*=4,861)
Treatment persistence												
3 months	28,568 (39.81)	28,481 (54.73)	49,567 (40.66)	63,418 (31.18)	364 (62.01)	23,326 (22.20)	34,150 (25.20)	286 (23.56)	60,136 (22.59)	99,686 (24.06)	14 (2.94)	496 (10.20)
6 months	9,300 (12.96)	10,236 (19.67)	16,430 (13.48)	19,846 (9.76)	161 (27.43)	7,756 (7.38)	9,462 (6.98)	125 (10.30)	21,042 (7.90)	32,478 (7.84)	6 (1.26)	114 (2.35)
9 months	5,469 (7.62)	5,881 (11.30)	9,987 (8.19)	12,857 (6.32)	106 (18.06)	5,457 (5.19)	6,052 (4.47)	78 (6.43)	15,163 (5.70)	23,293 (5.62)	5 (1.05)	64 (1.32)
12 months	3,707 (5.17)	3,873 (7.44)	6,970 (5.72)	9,392 (4.62)	75 (12.78)	3,959 (3.77)	4,424 (3.26)	57 (4.70)	11,534 (4.33)	17,978 (4.34)	4 (0.84)	51 (1.05)
Treatment discontinuation (days)												
Mean±SD	133.11±178.68	159.46±199.18	139.16±197.53	126.04±195.65	202.34±259.10	110.79±172.74	110.90±171.93	108.53±134.28	117.66±197.30	119.43±200.43	67.34±37.21	79.61±104.64
Median [IQR]	79 [68–118]	94 [74–152]	81 [68–120]	73 [66–100]	101 [75–199]	68 [64–83]	68 [65–90]	64 [62–86]	68 [64–85]	68 [64–88]	62 [62–62]	62 [62–66]
Treatment switching (days)												
Mean±SD	84.31±192.67	81.76±195.87	85.05±193.18	107.25±213.98	110.13±246.75	112.60±195.38	125.35±239.66	144.33±270.36	123.90±227.34	120.24±231.41	156.04±258.56	162.05±303.23
Median [IQR]	14 [7–65]	14 [7–52]	14 [6–71]	18 [6–125]	21 [8–74]	34 [6–155]	28 [7–142]	30 [6–161]	29 [6–159]	24 [6–146]	39 [9–202]	21 [7–176]

Data are *n* (%) values except where indicated otherwise.
CCBs, calcium-channel blockers; IQR, interquartile range; NSAIDs, nonsteroidal anti-inflammatory drugs; RAAS, renin-angiotensin-aldosterone system; SD, standard deviation.

(16.0%) being the most-used prophylactic treatments in patients with migraine.[22] As new treatments for migraine are released, such as medications targeting CGRP, changes in prophylactic treatment patterns should be carefully monitored.

In the present study, 54.8% of patients with migraine initially received acute treatment, while only 34.4% of migraine patients persisting on their initial treatment for 3 months, and half of the patients discontinuing or switching the initial treatment after 4 months. Most patients were initiated on an acute migraine treatment regimen that was consistent with treatment guidelines, and they received prophylactic treatment after a debilitating migraine attack that occurred despite receiving appropriate acute treatment.[18,25] This was also consistent with a study based on claims data from Japan, in which 63.6% of patients started on acute treatment, 5.4% started on prophylactic treatment, and 9.5% started on both acute and prophylactic treatments.[26] The causes of discontinuation could not be ascertained from the database, but one plausible explanation is that acute treatments are typically prescribed for the rapid relief of migraine pain, which might lead patients to discontinue treatment once their pain has been temporarily relieved.[27]

Fewer than 10% of the present patients persisted with their prophylactic treatment for 12 months, which is a lower rate than in previous studies. The persistence rate of prophylactic treatment in a study from the United States ranged from 13% to 16% at 12 months after initiation.[28] The difference between these results may be explained by differences in the awareness of migraine treatment and the definition of persistence. Asian countries are known to have lower awareness of migraine treatment, which leads to lower adherence.[10] Additionally, our study defined nonpersistence as the discontinuation or switching of the initial treatment, whereas that previous study from the United States defined nonpersistence as an interval of longer than 30 days between two prescriptions for the same medication, and it involved patients with chronic migraine. The persistence rate might therefore have been lower in our study due to more patients being defined as nonpersistent and acute migraine patients also being included.

This study utilized HIRA claims data up to December 31, 2021, which presented challenges in capturing data for the usage of newer monoclonal antibodies targeting the CGRP pathway (anti-CGRP mAb). These medications are recommended as first-line treatments in the latest European Headache Federation guidelines, and have been available in South Korea since 2019, with coverage under National Health Insurance starting in 2021.[29] However, insurance coverage is restricted to a small proportion of all anti-CGRP mAb users in South Korea, since it is only available for chronic migraine

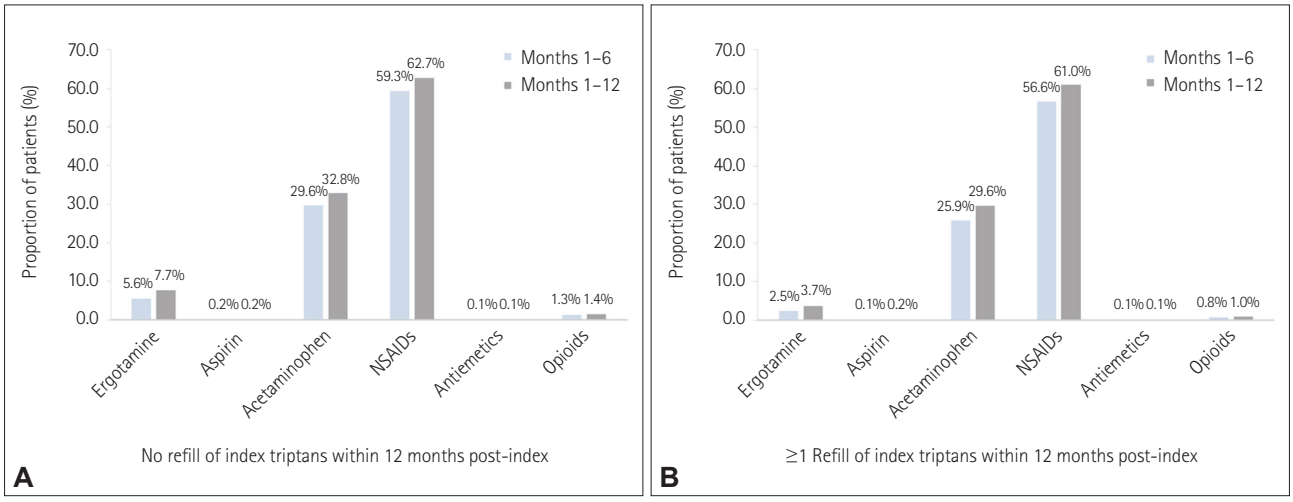

Fig. 3. Use of nontriptan acute treatment at 6 months and 12 months from the index date among patients who did not receive a repeat triptan prescription within 12 months from the index date (A) and patients who received at least one repeat triptan prescription within 12 months from the index date (B). NSAIDs, nonsteroidal anti-inflammatory drugs.

that is refractory to three oral medications taken for at least 6 months. The finding that fewer than 10% of patients persisted with their prophylactic treatments for 12 months in our study suggests insufficient effectiveness or safety concerns as reasons for their discontinuation. Given the high efficacy and good tolerability of anti-CGRP mAb, relaxing reimbursement requirements is essential for ensuring that appropriate treatments are given to migraine patients who require them.

Since triptans are the most frequently used migraine-specific drug for acute treatment, we also examined the treatment pattern after the first prescription of triptans. According to the switching or addition of acute treatments focused on triptans, NSAIDs and acetaminophen were the most-used nontriptan acute treatments. The treatment pattern after triptan use was similar to that in the United States, with analgesics such as NSAIDs and opioids being widely used after the initial treatment with triptans.[30] Furthermore, there was no significant difference in the NSAID prescription rates between patients who received a repeat prescription at least once within 12 months after their first triptan prescription (61.0%) and patients who did not receive such a repeat (62.7%).

This study had several limitations. First, owing to the characteristics of the claims data, we defined patients with migraine using diagnostic codes. Since the claims database did not include symptoms or clinical manifestations, the severity of migraine could not be considered in the analyses. Second, while we identified medications prescribed for migraine based on prescriptions with records of migraine diagnosis codes and additionally applied exclusion criteria, it is possible that some of the treatment regimens were prescribed for indications other than migraine. In particular, the 3-month persistence among prophylactic treatments was highest for RAAS inhibitors, which may have been prescribed to patients with migraine who had hypertension as a comorbidity. Despite patients with a diagnosis of hypertension prior to the index date being excluded in order to minimize such misclassification, it is still possible that the RAAS inhibitors were indicated not only for migraine but also for hypertension after the index date. Third, the over-the-counter (OTC) market is very active in South Korea, which makes it likely that there are patients who experience migraine but do not visit a doctor for a diagnosis and prescription, instead using OTC medications on their own to relieve their pain,[31] which was not captured in this study. Finally, since the reasons for discontinuation and switching were unavailable, further research is required to determine why patients discontinue or switch treatment.

Notwithstanding these limitations, this study has comprehensively outlined real-world treatment patterns, including almost all regimens, using the nationwide claims database of South Korea. The data analyses have revealed that healthcare professionals need to focus on maintaining patient adherence to migraine treatment.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2023.0485.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

Min Kyung Chu, a contributing editor of the *Journal of Clinical Neurology*, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

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