Migraine-preventive prescription patterns by physician specialty in ambulatory care settings in the United States

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ABSTRACT

Many adults with migraine who require preventive therapy are often not prescribed the proper medications. The most likely reason is that primary care physicians are unacquainted with preventive medications for migraine. The present study assessed the migraine-preventive prescription patterns in office visits using data from the National Ambulatory Medical Care Survey from 2006 to 2009 in the United States. Patients who were 18 years or older and diagnosed with migraine were included in the analysis. In accordance with the recommendations of the headache guidelines, we included beta-blockers, antidepressants, triptans for short-term prevention of menstrual migraine, and other triptans for acute treatment. Weighted visits of adults with migraine prescribed with preventive medication ranged from 32.8% in 2006 to 38.6% in 2009. Visits to primary care physicians accounted for 72.6% of the analyzed adult migraine visits. Anticonvulsants (odds ratio [OR] 0.29, 95% confidence interval [CI] 0.14–0.57, $p < 0.001$) and triptans for menstrual migraine (OR 0.50, 95% CI 0.28–0.91, $p = 0.025$) were less frequently prescribed by primary care physicians compared with specialty care physicians, such as neurologists and psychiatrists. There were no significant differences in the prescription patterns of antidepressants and beta-blockers between primary and specialty care physicians. Beta-blockers were prescribed to patients with comorbidity of hypertension, and antidepressants were used by patients with comorbidity of depression. There are differences in the prescription patterns of certain type of preventive medications between primary care physicians and specialty care physicians.

1. Introduction

Migraine is a common, chronic, and disabling disease characterized by attacks of severe headaches (Loder et al., 2012; Silberstein et al., 2012). In the U.S. population, the prevalence of migraine has been estimated to be approximately 18% and 6% in women and men, respectively (Lipton et al., 2001). In survey studies, patients with migraine reported the need for bed rest during headaches, absenteeism from school or work, activity limitations, and impaired health related quality of life (D'Amico et al., 2006; Linde and Dahlöf, 2004; Lipton et al., 2007). Migraine was also the fourth leading cause of visits to the emergency department next to stomach pain, chest pain, and fever, accounting for 3.1% of all the emergency visits from 2009 to 2010 (Burch et al., 2015). Furthermore, migraine is linked to increased financial burdens to patients, their families, and society (Hazard et al.,

2009). Most adults with migraine have often used acute medications such as non-steroidal anti-inflammatory drugs, triptans, and opioids. However, these acute medications induce adverse events and cause medication-overuse headaches (Minen et al., 2016a). Therefore, preventive medications for migraine are recommended according to the headache guidelines (Loder et al., 2012).

The aims of preventive medications are to decrease the frequency, duration, or severity of attacks, enhance the response to acute treatments, prevent progression to chronic migraine, and reduce the overall treatment costs (Dodick and Silberstein, 2007). Preventive medications have been shown to improve the health-related quality of life and the associated health-outcome decrease (D'Amico et al., 2006). The use of preventive medications increased from 8.5% to 15.9% between 1999 and 2010 in the U.S. alone (Mafi et al., 2015). However, it has also been reported that, while approximately 26% of adults with migraine require

preventive treatment considering monthly headache frequencies and attack-related impairments, only 13% of adults with migraine actually receive such treatment (Lipton et al., 2007). Furthermore, a large lapse between migraine diagnosis and start of preventive treatment has been reported, indicating that a limited number of patients are current users of preventive treatments (Dekker et al., 2013).

Low use of preventive medications may be attributed to the primary care physicians (PCPs) who are unfamiliar with preventive medications for migraine, and the reluctance of patients to accept the use of preventive medication. The majority of patients with migraine typically consult family practice physicians (73.5%), followed by neurologists (24.6%) (Bigal et al., 2008). Despite the frequent patient visits, PCPs seem to belief that preventive medication does not work (53.0%), or are afraid of adverse reactions (15.8%) (Minen et al., 2016b). A survey assessing the knowledge and needs of PCPs regarding migraine diagnosis and management indicated that only 28% of PCPs were familiar with the American Headache Society (AHS) and the American Academy of Neurology (AAN) guidelines on preventive treatments (Minen et al., 2016a). Moreover, patients who were against use of preventive medication had fears of adverse reactions (38.1%), experienced minimal attacks (44.0%), or felt emotionally unhealthier because by using daily medication they felt they had a chronic disease (23.8%) (Kol et al., 2008). A survey also reported that patients with migraine have a lower level of expectations for efficacy, concern about drug dependency, and low assessments of their own capacity for compliance (Dekker et al., 2012a).

In the AHS/AAN guidelines, preventive medications have been categorized into the following five groups: medications with established efficacy as Level A, medications with probable efficacy as Level B, medications with possible efficacy as Level C, medications with inadequate or conflicting data as Level U, and medications established as ineffective as other (Silberstein et al., 2012). A preventive medication is generally chosen on the basis of comorbidity co-treatment, avoidance of adverse events or drug interactions, convenience of formulation, therapy cost, and patient preference (Shapiro, 2012). However, most physicians, especially PCPs, may not necessarily select preventive medications appropriately, because various groups of medications are used as preventive therapies. Furthermore, PCPs may hesitate to use a certain group of medications due to a lack of understanding about their efficacy, adverse events, and contraindications (Dekker et al., 2012b; Minen et al., 2016b). To our knowledge, there is no study comparing the migraine-preventive prescription patterns between PCPs and specialty care physicians.

Appropriate and affirmative uses of preventive medications are required in primary care settings where most patients with frequent severe migraine visit. Therefore, this study attempted to describe the features of adult patients with migraine, assess the association between preventive medications, patient characteristics, and comorbid diseases, and identify differences in migraine-preventive prescription patterns between PCPs and specialty care physicians using data from the 2006 − 2009 National Ambulatory Medical Care Survey (NAMCS).

2. Methods

2.1. Data source

We used data from the NAMCS from 2006 to 2009 (ICPSR 28403, 28,521, 29,921, and 31,482), administered by the Centers for Disease Control and Preventive, National Center for Health Statistics (NCHS) (McCaig and Burt, 2012). The NAMCS is a national, annual survey on patient visits to non-federally employed physicians principally engaged in outpatient care activities. The NAMCS utilizes a multistage sampling design that involves probability samples of primary sampling (PSUs), physician practices within PSUs, and patient visits within practices (Centers for Disease Control and Prevention, 2012). For the final stage of selection, the physician randomly selected a visit during an assigned

week. Each visit was assigned a weight to account for the complex sampling design and also for nonresponse. Sampling weights were used to provide national estimates about the use of ambulatory medical care services in the U.S. For each visit, the demographic data, physicians' diagnoses, and information on medications used or prescribed were included. This study was exempted from the need for ethical approval by the institutional review board because the NAMCS is approved annually by the Ethics Review Board of the NCHS and individual patients are not identified from the data.

2.2. Study population

Physicians could enter up to three diagnostic fields in the patient record form using the International Classification of Diseases, Ninth Revision (ICD-9). Patients who were 18 years or older and have a diagnosis of migraine (ICD-9 code 346) among the three physicians' diagnosis fields were included in the analysis dataset.

2.3. Physician specialty

The NAMCS survey design stratified the physician specialty into the following 15 specialty groups based on information from the American Osteopathic Association and the American Medical Association: General and family practice, internal medicine, pediatrics, general surgery, obstetrics and gynecology, orthopedic surgery, cardiovascular diseases, dermatology, urology, psychiatry, neurology, ophthalmology, otolaryngology, other specialties, and oncology. Physicians specializing in anesthesiology, pathology, and radiology were excluded (Centers for Disease Control and Prevention, 2012). We limited our analyses to visits to general and family practice, internal medicine, psychiatry, and neurology, because it was more likely that migraine was not the main reason for the visits to other medical care specialties; thus, preventive medications were not necessary in these cases. We defined physicians in general and family practices and internal medicine as PCPs, and physicians in the psychiatry and neurology as specialty care physicians.

2.4. Medications

Medications were coded in terms of their generic components using Lexicon Plus®, a proprietary database of Cerner Multum, Inc. (Denver, CO). This medication classification system was implemented in 2006. The Lexicon Plus is a comprehensive database of all prescription and some nonprescription medication products available in the U.S. drug market. Up to 8 medications could be recorded for each visit. We defined the preventive medications for migraine based on the AHS/AAN guidelines (Silberstein, 2000; Silberstein et al., 2012). In accordance with the recommendations of 2012 updated guidelines, we included the following medication groups: anticonvulsants (divalproex sodium; Level A, topiramate; Level A, and carbamazepine; Level C), beta-blockers (propranolol; Level A, atenolol; Level B, metoprolol; Level A, timolol; Level A, nadolol; Level B, nebivolol; Level C, and pindolol; Level C), antidepressants (amitriptyline; Level B and venlafaxine; Level B), and triptans for short-term prevention of menstrual migraine (MM) (frovatriptan; Level A, naratriptan; Level B, and zolmitriptan; Level B). Other triptans for acute treatment (sumatriptan, rizatriptan, and eletriptan) were included as a control group. An antihypertensive group (lisinopril, candesartan, clonidine, and guanfacine), which had been recommended by the AHS/AAN, was excluded from the analyses because the relative standard error was over 30%.

2.5. Comorbid diseases

Epilepsy (ICD-9 code 345), hypertension, and depression, for which preventive medications have been used as treatment medications, were included. Arthritis, asthma, and hyperlipidemia were also included because those diseases have been known to be associated with migraine

(Chen et al., 2012; Wang et al., 2017). The diagnoses of chronic co-morbidities other than epilepsy, such as hypertension, depression, arthritis, athma, and heperlipidemia, included all of cases because the diagnoses were independently reported regardless of whether they were included in the three main diagnostic fields (*e.g.*, Does the patient now have hypertension?). Affective psychoses (ICD-9 code 296), schizophrenic psychoses (ICD-9 code 295), paranoid states (ICD-9 code 297), and heart diseases (ICD-9 code $410 - 414$ and $420 - 429$), for which preventive medications have been used as main treatment medications, were not included because the relative standard error was over 30%.

2.6. Patient characteristics

We described the patient characteristics according to the following factors: age groups ($18 - 29$, $30 - 39$, $40 - 49$, $50 - 59$, and ≥ 60 years), sex (female and male), race/ethnicity (non-Hispanic white and others [non-Hispanic black, Hispanic, and non-Hispanic others]), and insurance (private and others [Medicare, Medicaid, Worker's compensation, self-pay, no charge, and unknown]).

2.7. Statistical analysis

All analyses accounted for the complex survey design using the variables provided in the NAMCS. We used the R (R Development Core Team, 2011) and R package Survey ver. 3.3. 2. (Lumley, 2017) for all analyses. Probability values < 0.05 were considered statistically significant. We did not include any variable with an estimate based on fewer than 30 records or that had $> 30\%$ of the relative standard errors, which is a measure of the sampling variability and is calculated by dividing the standard error of the estimate by the estimate itself, because the NCHS considers such estimates to be unreliable.

Patient characteristics, comorbid diseases, and preventive medication groups in adult patients with migraine were calculated in weighted percentages and standard errors. Those according to the physician specialty were also calculated. The associations of physician specialty with patient characteristics, comorbid diseases, and preventive medications were assessed using the Rao-Scott χ^2 tests.

Multivariate logistic regression models were constructed to evaluate multivariate associations among physician specialty, preventive medication groups, patient characteristics, and comorbid diseases. Multivariate logistic regression models with preventive medication groups as the dependent variables were constructed to clarify the features of patients prescribed each preventive medication group. Odds ratios (OR) with 95% confidence intervals (CIs) and *P* values were reported.

3. Results

The 2006–2009 NAMCS samples included 13,678 physicians. A total of 9186 physicians met the following inclusion criteria: office-based, principally engaged in patient care activities, and not in specialties of anesthesiology, pathology, and radiology. Of the eligible physicians, 4080 were excluded for nonresponse ($N = 3283$) and for no patient encounter during the study period ($N = 797$). A total of 5106 physicians have been included in the NAMCS. Each physician completed a maximum of up to 30 Patient Record forms, which was determined based on the estimated number of visits to the physician. The 2006–2009 unweighted response rates were 58.9%, 61.6%, 59.1%, and 62.1%, respectively. Among the 127,229 unweighted visits included in the NAMCS data set, a total of 102,050 were visits of adult patients, and 1252 of them had migraine (Table 1). Weighting and clustering were accounted for to reflect the national estimates in all of the following results. Of the 27,120,104 weighted number of adult visits with migraine, 12,330,600 primary or specialty care visits were used for the analysis in this study and ranged from 4,457,908 in 2006 to 7,746,559 in 2009 (Table 1). The number of prescribed preventive medications

following primary or specialty care visits in adults with migraine increased from 1,460,010 (32.8%) in 2006 to 2,989,066 (38.6%) in 2009.

Patient characteristics, comorbid diseases, and preventive medications of adult patients with migraine who visited PCPs or specialty care physicians and the results of Rao-Scott χ^2 tests are shown in Table 2. Most of the adult patients with migraine were between $40 - 49$ years of age (25.5%), female (83.7%), white (85.9%), had private insurance (70.5%), and had comorbidity of depression (23.7%). Visits to PCPs accounted for 72.6% of all of the adult migraine visits analyzed. There were no significant differences in the following patient characteristics between primary and specialty care visits: age, sex, race, and insurance. Patients who visited PCPs had significantly more comorbidity with asthma (9.4% *vs* 4.7%, $p = 0.013$) and hyperlipidemia (17.3% *vs* 7.1%, $p = 0.006$) than patients who visited specialty care physicians. Anticonvulsants were less frequently prescribed by PCPs compared with specialty care physicians (12.5% *vs* 34.0%, $p < 0.001$).

The patient characteristics and comorbid diseases for which each preventive medication group was prescribed are shown in Table 3. Anticonvulsants were less frequently prescribed by PCPs compared with specialty care physicians (OR 0.29, 95% CI 0.15–0.57), less frequently prescribed to adult patients with migraine aged 60 years or over (OR 0.39, 95% CI 0.17–0.90), and less frequently prescribed for patients with asthma (OR 0.40, 95% CI 0.21–0.76). Beta-blockers were more significantly prescribed to patients who had hypertension (OR 3.82, 95% CI 2.26–6.45). Antidepressants were more significantly prescribed to patients who had depression (OR 3.38, 95% CI 1.98–5.76), and less frequently used in patients who were of the white race (OR 0.45, 95% CI 0.24–0.84). Triptans for the prevention of MM were less frequently prescribed by PCPs compared with specialty care physicians (OR 0.48, 95% CI 0.26–0.88) and more frequently prescribed to adult patients with migraine aged $40 - 49$ years (OR 3.15, 95% CI 1.07–9.26) and $50 - 59$ years (OR 7.56, 95% CI 2.73–20.88) Other triptans used only for acute treatments were less frequently prescribed to adult patients with migraine aged 60 years or over (OR 0.36, 95% CI 0.15–0.89).

Although limited to visits that were driven due to migraine as a main diagnosis in three diagnostic fields, anticonvulsants (OR 0.36, 95% CI 0.19–0.68) and triptans for MM (OR 0.31, 95% CI 0.13–0.75) were prescribed significantly less often by PCPs compared with specialty care physicians.

4. Discussion

The main finding in the present study is that anticonvulsants and triptans for MM were less frequently prescribed by PCPs compared with specialty care physicians. To the best of our knowledge, this finding is reported here for the first time. There were no significant differences in the prescription patterns of beta-blockers and antidepressants between PCPs and specialty care physicians. Furthermore, beta-blockers were prescribed to patients with hypertension, and antidepressants were prescribed to patients with depression. These findings are consistent with the guidelines that beta-blockers have been recommended to be prescribed for patients with both migraine and hypertension and antidepressants for patients with both migraine and depression (Silberstein et al., 2012). The prescribing rate in the current study was higher than that in past studies. This is likely because all types of preventive medication with the possibility were included in our study. In a survey study, only 12.4% of patients with migraine indicated that they were taking a preventive medication, but 17.2% were using medications with potential antimigraine effects for other medical reasons (*e.g.*, depression) (Diamond et al., 2007) This result indicates that 29.6% patients with migraine were currently or coincidentally using a preventive medication. This value was closely accorded with the prescribing rate (30.1%) recalculated for anticonvulsants, beta-blockers, and antidepressants.

PCPs prescribed anticonvulsants less frequently than medical care specialists. The AHS/AAN guidelines classify topiramate and divalproex

Table 1
Visits of adult patients with migraine prescribed preventive medications, from the National Ambulatory Medical Care Survey (2006–2009).

	2006	2007	2008	2009	Total
Visits of adult patients in all visits, unweighted no.	24,282	27,169	23,561	27,038	102,050
Visits of adult patients with migraine, unweighted no.	317	274	305	356	1252
Visits of adult patients with migraine, weighted no.	6,500,634	6,099,149	5,905,930	8,614,391	27,120,104
Primary or specialty care visits[a] by adults with migraine, weighted no.	4,457,908	5,414,762	5,382,197	7,746,559	12,330,600
Visits of adults with migraine prescribed preventive medications, weighted no.	1,460,010	1,911,941	1,984,655	2,989,066	8,345,672
Visits of adults with migraine prescribed preventive medications, weighted %	32.8	35.3	36.9	38.6	36.3

[a] Primary care visits were defined as visits to physicians in general and family practices and internal medicine. Specialty care visits were defined as visits to physicians in psychiatry and neurology. The following specialty groups were excluded: pediatrics, general surgery, obstetrics and gynecology, orthopedic surgery, cardiovascular diseases, dermatology, urology, ophthalmology, otolaryngology, other specialties, and oncology.

Table 2
Patient characteristics, comorbid diseases, and preventive medications for adult patients with migraine who visited primary or specialty care physicians, from the National Ambulatory Medical Care Survey (2006–2009).

	Total	Primary care physicians	Specialty care physicians	Rao Scott χ^2 tests
	Weighted % (S.E.)	Weighted % (S.E.)	Weighted % (S.E.)	P-value
Physician specialty	100.0	72.6 (3.4)	27.4 (3.4)	
Age (years)				
18–29	19.2 (2.0)	19.8 (2.5)	17.4 (2.2)	0.613
30–39	24.5 (1.8)	24.7 (2.3)	23.8 (2.2)	
40–49	25.5 (2.2)	24.0 (2.9)	29.5 (2.1)	
50–59	20.3 (2.2)	21.1 (2.9)	18.4 (1.9)	
≥ 60	10.5 (2.0)	10.4 (2.7)	10.8 (1.4)	
Sex				
Male	16.3 (2.0)	16.0 (2.7)	17.0 (1.5)	0.758
Female	83.7 (2.0)	84.0 (2.7)	83.0 (1.5)	
Race				
White	85.9 (2.1)	86.6 (2.6)	83.9 (2.4)	0.439
Others	14.1 (2.1)	13.4 (2.6)	16.1 (2.4)	
Insurance				
Private	70.5 (2.3)	69.2 (2.9)	73.8 (3.1)	0.277
Others	29.5 (2.3)	30.8 (2.9)	26.2 (3.1)	
Comorbid diseases				
Epilepsy	0.7 (0.2)	– [a]	2.6 (0.6)	< 0.001
Hypertension	17.4 (1.9)	18.3 (2.5)	14.8 (2.0)	0.255
Depression	23.7 (2.0)	24.7 (2.6)	21.0 (2.5)	0.336
Arthritis	11.2 (1.5)	10.9 (2.0)	11.8 (1.8)	0.749
Asthma	8.1 (1.4)	9.4 (1.9)	4.7 (0.9)	0.013
Hyperlipidemia	14.5 (1.9)	17.3 (2.5)	7.1 (2.1)	0.006
Preventive medications				
Anticonvulsants	18.4 (2.5)	12.5 (3.5)	34.0 (3.1)	< 0.001
Beta-blockers	10.2 (1.9)	9.9 (2.4)	10.8 (1.5)	0.757
Antidepressants	8.4 (1.7)	7.4 (2.2)	11.0 (2.0)	0.232
Triptans for MM	5.5 (1.0)	4.5 (1.2)	8.3 (1.4)	0.318
Other triptans	29.8 (3.2)	29.2 (4.2)	31.4 (3.6)	0.698

MM, menstrual migraine; S.E., standard error.
[a] Fewer than 30 records or > 30% of relative standard error.

sodium as Level-A medications and recommend their prescription to patients with migraine for preventive therapy (Silberstein et al., 2012). Anticonvulsants (late 1980s–2000s) have been considered as preventive medications more recently than tricyclic antidepressants and beta-blockers (late 1960s and 1970s) (Bagnato and Good, 2016). It is possible that many PCPs have yet to perceive anticonvulsants as preventive medications. Furthermore, PCPs might be also be suspicious of the efficiency of anticonvulsants or recognize no need to use them because acute medication or other preventive medication had sufficient efficacy (Minen et al., 2016b). PCPs may also hesitate to use anticonvulsants because they have fears of serious adverse events and contraindications. For example, common adverse events of topiramate are paresthesia, difficulty with concentration and memory, weight loss, metabolic acidosis, and renal calculi (Marmura, 2014). The usage of both topiramate and divalproex sodium should be avoided during pregnancy due

to the risk of teratogenesis (Bagnato and Good, 2016).

Triptans for short-term prevention of MM were also less frequently used in primary care specialties compared with medical care specialties. The most likely reason is that preventive treatments for menstrual migraine have not been inconsistent (Brandes, 2006). At least 50% of women with migraine have migraine attacks at the same time as or near the menstrual flow (Martin and Lipton, 2008). A review indicated that triptans for MM provide an effective, short-term, prophylactic strategy for the management of MM (Hu et al., 2013). In particular, frovatriptan, zolmitriptan, and naratriptan are highly effective, and have been recommended as first-line medications for the treatment of moderate to severe migraines, including MM (Allais et al., 2012). We could not distinguish triptans for short-term prevention of MM from other triptans for acute treatment. However, it is certainly likely that triptan for MM was less frequently prescribed by PCPs than specialty care physicians because there was no significant difference in other triptans for acute treatment between PCPs and specialty care physicians.

In the prescription pattern of beta-blockers, there was no difference between the physicians' specialties. Beta-blockers are also the most widely used class of medications in preventive migraine treatments and are reported to have favorable benefit-to-harm ratios (Shamliyan et al., 2013). It is certainly possible that PCPs have a lot of knowledge of beta-blockers because they often prescribed beta-blockers to patients with hypertension (McGill, 2010). Although it has not been determined whether PCPs intended to prescribe beta-blockers for both conditions, these medications have not been necessarily first-line medications for patients with only hypertension (McGill, 2010). Thus, these medications may have been prescribed for patients with both migraine and hypertension, although most beta-blockers were consistently established as effective for patients only migraine with. Contraindications to use of beta-blockers include asthma, chronic obstructive lung disease, and peripheral vascular diseases (Silberstein, 2015). Behavioral adverse events such as drowsiness, fatigue, and nightmares can be caused by all beta-blockers (Silberstein, 2015). Information related to the adverse events or contraindications of beta-blockers should be provided to PCPs even if they are familiar with prescribing beta-blockers.

There was also no significant difference in the prescription pattern of antidepressants between PCPs and specialty care physicians. PCPs may have no feeling of resistance to prescribing antidepressants due to their frequent use in primary care settings (K. Linde et al., 2015). Although antidepressants are useful in preventing migraine regardless of the presence of depression (Xu et al., 2017), they are recommended to be prescribed to patients with both migraine and depression because a significant association between migraine and depression has been supported by many studies (Breslau et al., 1991). In our study, antidepressants were actually prescribed to patients with both migraine and depression. However, it is not easy to treat both depression and migraine appropriately. For example, appropriate management of depression often requires high doses of tricyclic antidepressants, which may be associated with more adverse events (Silberstein, 2015). Although selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors are first-line medications in the

Table 3
Physician specialty and patient characteristics related to preventive medications, from the National Ambulatory Medical Care Survey (2006–2009).

	Anticonvulsants OR (95% CI)	Beta-blockers OR (95% CI)	Antidepressants OR (95% CI)	Triptans for MM OR (95% CI)	Other triptans OR (95% CI)
Physician (primary, 1; specialty, 0)	0.29 (0.15–0.57)	0.82 (0.44–1.51)	0.62 (0.31–1.26)	0.48 (0.26–0.88)	0.85 (0.52–1.41)
Age (years)					
30–39	0.89 (0.41–1.95)	0.60 (0.20–1.78)	0.75 (0.36–1.57)	2.21 (0.64–7.62)	0.55 (0.27–1.11)
40–49	0.97 (0.51–1.87)	0.89 (0.31–2.56)	0.70 (0.34–1.44)	3.15 (1.07–9.26)	0.88 (0.50–1.54)
50–59	0.79 (0.39–1.58)	1.42 (0.56–3.56)	0.37 (0.13–1.04)	7.56 (2.73–20.88)	0.80 (0.49–1.33)
≥ 60	0.39 (0.17–0.90)	0.65 (0.23–1.84)	0.45 (0.16–1.27)	2.27 (0.62–8.41)	0.36 (0.15–0.89)
Sex (female, 1; male, 0)	1.70 (0.89–3.26)	0.78 (0.35–1.72)	1.20 (0.44–3.29)	1.06 (0.46–2.43)	1.64 (0.88–3.06)
Race (white, 1; others, 0)	0.67 (0.37–1.19)	1.92 (0.73–5.07)	0.45 (0.24–0.84)	1.72 (0.73–4.04)	1.17 (0.71–1.92)
Insurance (Private, 1; Others, 0)	1.33 (0.87–2.01)	0.94 (0.46–1.91)	0.94 (0.46–1.99)	2.05 (0.80–5.27)	0.88 (0.58–1.35)
Comorbid diseases (Yes, 1; No, 0)					
Epilepsy	1.59 (0.61–4.09)	– [a]	– [a]	– [a]	– [a]
Hypertension	1.36 (0.76–2.46)	3.82 (2.26–6.45)	– [a]	– [a]	1.08 (0.57–2.03)
Depression	1.42 (0.88–2.29)	0.98 (0.42–2.29)	3.38 (1.98–5.76)	1.82 (0.75–4.40)	0.87 (0.55–1.39)
Arthritis	1.09 (0.63–1.91)	0.68 (0.28–1.64)	– [a]	– [a]	0.73 (0.37–1.46)
Asthma	0.40 (0.21–0.76)	– [a]	– [a]	– [a]	1.13 (0.62–2.07)
Hyperlipidemia	0.74 (0.31–1.75)	1.38 (0.62–3.04)	– [a]	– [a]	1.43 (0.63–3.25)

CI, confidence interval; MM, menstrual migraine; OR, odds ratio.
[a] Fewer than 30 records or > 30% of relative standard error.

treatments of depression, there is not enough evidence on their preventive effects against migraine (Banzi et al., 2016). Physicians need to ascertain what symptoms should be treated as a priority for each patient.

Although migraine should be adequately controlled because of its negative effect on the quality of life, a high economic burden, and overuse of acute medications, it has been identified as a suboptimally treated disease in primary care settings (Minen et al., 2016a). Although preventive medications covered by the insurance companies are different among countries, it is a common problem that most patients with migraine who need preventive medications do not actually receive them (Dekker et al., 2013). Differences in the prescription patterns of certain preventive medications in our findings may indicate that PCPs have little detailed knowledge of preventive medications, PCPs feel no necessity for the use of them, or patients hesitate to use some types of preventive medication. PCPs or general physicians may need to acquire more knowledge about these preventive treatments and medications (Minen et al., 2016a). In addition, patient education is recommended to allow the use of preventive medication appropriately (Dekker et al., 2012a). Efficient referral systems to specialists may be useful and beneficial for both PCPs and patients with migraine.

Some limitations of this study should be mentioned. First, the associations between diagnoses and medications have not been determined. Indeed, it is not known when the medications are prescribed for the preventive treatment of migraine. For example, a physician may have prescribed antidepressants to patients only for the treatment of depression. However, most preventive medications in this study were not prescribed as first-line medications, indicating that physicians may have been expecting some effects on migraine. Second, our estimates may have been underestimated due to the limited number of diagnoses and medications. Data from the NAMCS allowed for three diagnoses and eight medications at most. The diagnosis of migraine or medications for migraine treatment may not have been recorded in the limited format. Third, the migraine-preventive prescription patterns are unknown following the update of the AHS/AAN guidelines in 2012. An increase in guideline-recommended preventive treatments for migraine has been observed (Mafi et al., 2015). However, a study conducted in 2016 reported that only 28% of the PCPs were familiar with the AHS/AAN guidelines (Minen et al., 2016a). Most PCPs may still be unfamiliar with these guidelines and the use of preventive medications. Fourth, because the unit of analysis was an office visit rather than an individual patient, it is possible that a patient could have been sampled more than once. However, the period of the NAMCS was a week, which is relatively short, indicating that preventive medications were less likely to

be prescribed multiple times. Fifth, we excluded estimates with > 30% relative standard errors or < 30 records in accordance with the NCHS' instruction (Centers for Disease Control and Prevention, 2010). However, some standard errors ranged from 20% to 30% due to fewer records. We need to validate our findings using a large sample study targeting patients with migraine in the future.

5. Conclusion

The main conclusion of the present study was that anticonvulsants and triptans for prevention of MM were less frequently used by PCPs compared with specialty care physicians. Furthermore, there were no significant differences in the prescription patterns of antidepressants and beta-blockers between PCPs and specialty care physicians. Beta-blockers were more frequently used by patients with a comorbidity of hypertension, and antidepressants were frequently used by patients with a comorbidity of depression. There were differences in the prescription patterns of certain type of preventive medications between PCPs and specialty care physicians. These findings could help address prescription patterns of preventive medications for migraine in primary care settings. Future studies are needed to confirm or reject our findings in a large sample study.

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