

Original article

Acute treatment response among patients with migraine subtypes: A real-world study in Thailand

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Abstract

Background: Migraines with and without aura may have distinct etiologies. Aura can vary in complexity (from simple to complex), which potentially reflects differences in cortical involvement and influences acute treatment response.

Objective: This study aimed to compare the acute treatment responses between patients with migraine with and without aura, as well as aura complexity levels, in Thailand.

Methods: A retrospective cohort study was conducted from January 3, 2007, to June 30, 2022, at the Chulalongkorn Comprehensive Headache Center, King Chulalongkorn Memorial Hospital, Thai Red Cross Society. Baseline data were retrieved from the baseline case-record forms, while clinical data were obtained from paper headache diaries and follow-up case-record forms. The primary outcome was a 2 h pain-free response; secondary outcomes included pain scores and associated symptoms.

Results: Among the 358 patients (110 with aura, 248 without aura), baseline characteristics were largely similar, except for differences in the associated symptoms (photophobia and phonophobia) and the use of antiepileptic drugs for migraine prevention. No significant differences in acute treatment response were found between the groups. However, patients with complex auras exhibited a trend toward better outcomes, with higher 2 h pain-free rates (44.5% vs. 23.9%) and greater improvement in pain duration (33.3% vs. 22.8%) compared with patients with simple auras.

Conclusion: Acute treatment responses did not differ significantly across migraine types, although patients with complex aura may respond better.

Keywords: Acute treatment, aura subtypes, migraine disorders, migraine with aura, migraine with complex aura, treatment response.

Migraine is a common neurological disorder that consists of four phases: the premonitory, aura, headache, and postdrome phases; however, not all patients experience all four phases. ^(1,2) During the aura phase, cortical spreading depression involves different parts of the cerebral cortex and contributes to different aura symptoms, known as aura subtypes. Stimulation of the visual or occipital cortex contributes to visual symptoms, referred to as “visual aura;” ⁽¹⁻³⁾ stimulation of the sensory cortex may contribute to somatosensory symptoms, referred to as “sensory aura;” ⁽⁴⁾ and stimulation of the parietal cortex may

contribute to language or speech disturbances, referred to as “language/speech aura.” ⁽⁵⁾ These three common subtypes are collectively known as typical aura. ⁽⁶⁾ Other aura subtypes are less common and may include motor, brainstem, and retinal auras. ⁽⁶⁾

Because migraine aura has heterogeneous manifestations, a scale to assess aura complexity has been proposed and developed. ⁽⁷⁾ The scale categorizes aura into three groups: simple aura, moderately complex aura, and complex aura, which may reflect differences in cortical thickness. ⁽⁸⁾ However, in clinical practice, migraine with aura can be divided into two subtypes, a simple or complex aura, according to the classification proposed by Petrušić I, *et al.* ⁽⁷⁾

A simple visual aura may include flashing or flickering lights, stars, zigzags, visual snow, or blind spots. In contrast, a complex visual aura includes the perception of disfigurement in the size or shape of objects, discoloration, or a cracked vision. Simple sensory aura includes prickling, paresthesia, or

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numbness, whereas complex sensory aura includes unusual sensations affecting one side of the hand, arm, face, or tongue. Language/speech aura (dysphasic disturbance), which includes difficulty speaking or conversing, uncoordinated speech, word-finding difficulty, impaired memory, apraxia, or ideational agnosia, is categorized as a complex aura. In addition, a simple visual aura followed by a sensory aura, or a visual or sensory aura followed by a language/speech aura, is categorized as a complex aura.

The lifetime prevalence of migraine with aura in a population-based study was 15.9%,⁽⁹⁾ whereas the one-year prevalence ranged from 31.0% to 40.8%, depending on the study.⁽¹⁰⁾ In the literature, migraine with aura may respond differently from migraine without aura because of distinct underlying etiologies,⁽¹¹⁾ thus providing a rationale for selecting different medications for the two types. Several studies have demonstrated that migraine without aura has a greater response to triptans than migraine with aura.^(12 - 14) However, a randomized controlled study found no significant difference between the two groups.⁽¹⁵⁾ Previous systematic reviews found insufficient data to compare the efficacy of sumatriptan between migraine with and without aura.^(16 - 18) Moreover, a narrative review suggested that the same treatment should be used for migraine with and without aura.⁽¹⁹⁾

A recent randomized controlled study with subgroup analysis revealed that patients with a history of migraine with aura who received 50 mg of lasmiditan, a new migraine-specific acute treatment, had a higher proportion of pain freedom (50.0%) than the overall population, with and without aura (23.5%).⁽²⁰⁾ A real-world study of ubrogepant, another new migraine-specific acute treatment, revealed that migraine with aura was a predictive factor for a positive response to ubrogepant, with an odds ratio of 2.27.⁽²¹⁾

To date, previous studies have not clearly demonstrated whether acute treatment should differ between migraine with and without aura. Therefore, a gap in evidence on acute treatment between the two groups persists. This study was conducted to address this gap and may have important clinical implications.

In a clinical trial, it is feasible to assess the efficacy of the acute treatment for migraine with and without aura. However, in real clinical practice, this is challenging to apply during an acute attack. Patients

experiencing a severe headache may be distressed, may not distinguish between migraine with or without aura, and often do not have time to consider the most appropriate medicine because of their urgency to relieve pain immediately.

To evaluate the hypothesis that medications acting on the trigeminal system via serotonin 1B/D receptors may also benefit aura, which is cortical in origin and protected by the blood-brain barrier. It is more practical to evaluate the overall acute treatment response in patients with and without aura, as well as between those with simple and complex auras, rather than assessing every individual attack across the migraine subtypes.

Therefore, a retrospective cohort study was conducted at a headache clinic in a tertiary-referral university teaching hospital to evaluate the effectiveness of acute treatment in patients with migraine, with and without aura, as well as those with simple or complex auras.

Materials and methods

Ethics statement

The present study was reviewed and approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB no. 0644/65). All methods were performed in accordance with relevant guidelines and regulations. The institutional committee granted a waiver of informed consent.

Study design and setting

This retrospective cohort study was conducted at the Chulalongkorn Comprehensive Headache Center, King Chulalongkorn Memorial Hospital, a tertiary-referral university teaching hospital in Bangkok, Thailand.

The center has maintained a registry and developed a case-record form to collect patient information at the first and follow-up visits for all patients since January 3, 2007. The first-visit case-record form, referred to as the baseline form, includes patients' demographic and socioeconomic data as well as headache-related information.

To monitor headache treatment outcomes at the center, patients are provided with a paper headache diary and are instructed to complete it in real time to minimize recall bias. The paper headache diary records the time of headache onset, the time that painkillers were taken, the name of the painkillers used, and the

time that pain relief and pain freedom occurred. It also includes pain scores, pain severity, associated symptoms, and any side effects of the painkillers. At each visit, patients bring their paper headache diary to their attending physician to evaluate the response to acute treatment and, if applicable, preventive therapy.

Management was tailored to individual patients. The raw data in the paper headache diary were carefully reviewed, tallied, and transcribed into another case-record form, referred to as the follow-up case-record form. This includes, for example, calculating the total number of headaches per follow-up period and the total number of headache days achieving complete resolution (pain freedom) within 1, 2, 4, or more than 4 h after acute treatment. This also included the total number of headache days associated with symptoms such as nausea, vomiting, photophobia, phonophobia, dizziness, or vertigo relative to the total number of headache days with and without associated symptoms during each follow-up period.

The goal of acute treatment is to achieve headache relief within 2 h after taking acute medications. The general approach to selecting acute treatments follows either a step-care approach within an attack, a step-care approach across attacks, or a stratified care approach. Patients are advised to take acute medications as early as possible when the pain is mild, rather than waiting for the pain to become more severe or expecting it to resolve spontaneously.

Data from the study included all patients registered between January 3, 2007, and June 30, 2022. The reporting followed the STROBE statement⁽²²⁾ and the RECORD extension of the STROBE statement.⁽²³⁾

Study population

In the present study, data were included from patients diagnosed with migraine according to the International Classification of Headache Disorders, 2nd edition,⁽²⁴⁾ 3rd edition (beta version),⁽²⁵⁾ and 3rd edition.⁽⁶⁾ The diagnostic criteria from the different editions have been previously described.⁽²⁶⁾ In brief, the diagnostic criteria for migraine with aura, in the 2nd edition, are classified into six subforms but do not include retinal migraine. The beta version of the 3rd edition combined all migraine aura types and added the criterion of unilateral aura symptoms. In addition, the 3rd edition further included the criterion of positive aura symptoms in the beta version.

The inclusion criteria were as follows: patients aged 15–80 years; at least one migraine attack per month; use of medication for acute attacks; a first follow-up visit within 6 weeks if preventive medications were taken, to minimize the effect of preventive treatment on acute attack characteristics; or no restriction on the timing of the first follow-up visit if no preventive treatment was used.

In clinical practice, migraine preventive medications are typically initiated at a low dose and gradually titrated every 2–4 weeks until an effective dose is achieved. Full therapeutic benefit may take 2–6 months.⁽²⁷⁾ Therefore, only patients who had a follow-up visit within 6 weeks of starting preventive treatment were included to minimize the influence of preventive medications.

The exclusion criteria were other primary or secondary headache disorders (except medication-overuse headache) and the absence of follow-up visits. Patients with migraine who also had other primary headache disorders were included in the study.

Sample size calculation

The sample size was calculated based on the proportion of patients with migraine who achieved pain relief within 2 h after treatment during the first follow-up period, compared with those with and without aura. A medium effect size (relative risk) of 1.8 was assumed, with a type I error of 0.05 and a type II error of 20.0%. The anticipated proportion of patients achieving 2 h pain relief in the migraine with aura group was 24.0%, based on a study of sumatriptan effectiveness.⁽¹²⁾ The ratio of patients with migraine without aura to those with aura was set at 2:1. The required sample size was 96 patients with migraine with aura and 192 patients with migraine without aura.

Measurement of outcomes, study tools, and data collection

Demographic data and baseline headache characteristics were obtained directly from the patients at the first visit. Clinical data at the first follow-up visit were collected prospectively using a paper headache diary.

The primary outcome was the proportion of migraine attacks that were pain-free at 2 h after treatment, defined as the number of attacks achieving pain relief at 2 h divided by the total number of migraine attacks during the first follow-up period, and this was compared between patients with and without aura.

The secondary outcomes were the proportion of migraine attacks that were pain-free at 1 h after treatment and the frequency of associated headache symptoms, including nausea, vomiting, photophobia, phonophobia, dizziness, and vertigo, comparing patients with and without aura.

Additional outcomes included treatment effectiveness between simple and complex auras; differences in pain duration categorized as stable, improved, or worsening; and pain score differences or improvement from baseline after treatment, comparing the migraine subtypes. Raw continuous data on pain duration per attack per patient from the paper headache diary were categorized as pain-free within 1 h, 2 h, or more than 2 h.

The stable condition for pain duration was defined as no change in category (pain-free within 1 h, 2 h, or more than 2 h) between baseline and after treatment. Improved or worsening conditions were defined as a shorter or longer time to pain freedom (1 h, 2 h, or more than 2 h) after treatment compared with baseline. The number of migraine days during the first

follow-up interval was standardized as the number of migraine days per 4 weeks. Headache-associated symptoms, including nausea, vomiting, photophobia, and phonophobia, were summarized for each patient as a percentage by dividing the number of headache attacks with a given associated symptom by the total number of headache attacks and multiplying by 100. These values were then summarized by groups (migraine with or without aura) as medians and interquartile ranges (IQRs).

The pain scores for each attack, ranging from 0 to 10 during the follow-up interval, were summarized as medians. Pain duration changes after treatment compared with baseline were categorized as stable if there was no change, improved if the duration was shorter, and worsened if the duration was longer.

Medications for acute treatment were categorized into two primary groups: the migraine-specific medication group, which included triptans or ergot derivatives, used either as monotherapy or in combination with simple analgesics due to their similar action on serotonin receptors, and the non-migraine-specific medication group, which included simple analgesics, opioids, or their combinations.

The characteristics of migraine aura were collected through semi-structured interviews with the following questions. “Do you experience any warning symptoms 5–60 minutes before or during a migraine

headache? If yes, please describe.” The responses were recorded in the case record. If the answer was no, the following questions were asked: “Do you experience any abnormal visual symptoms, abnormal sensations in the fingers, hands, arms, face, or around the mouth, or abnormal speech, such as slurred speech, difficulty speaking, or trouble finding words? If yes, please describe.”

Migraine with aura is categorized into two subtypes: simple and complex auras, according to the classification by Petrušić I, *et al.*⁽⁷⁾ The details of aura subtypes have been previously reported.⁽²⁴⁾ In brief, migraine aura subtypes are classified as simple or complex, according to Petrušić I, *et al.*⁽⁷⁾ A simple aura includes a single simple visual or sensory aura. In contrast, a complex aura includes a complex visual or sensory aura; a language/speech aura; or a simple visual aura followed by a simple sensory aura, or by a simple visual aura followed by a simple sensory aura followed by a language/speech aura.

Statistical analysis

Descriptive statistics are used to summarize the data as follows: percentages for categorical variables; means and standard deviations (SD) for continuous variables with normal distribution; and medians and IQRs for ordinal or continuous variables without normal distribution. Inferential statistics were used to compare differences between the two groups as follows: the chi-square test or Fisher’s exact test for dichotomous variables, the unpaired *t*-test for differences in means, and the Mann–Whitney *U* test for differences in medians. Multiple comparisons were adjusted using the Bonferroni correction. Missing data were excluded from the analysis.

Results

A total of 681 patients were registered at the headache center from January 3, 2007, to June 30, 2022. Of these, 109 had other primary or secondary headache disorders, and 572 were diagnosed with migraine. Among the 572 patients with migraine, 171 had a lifetime history of migraine with aura, accounting for 29.9% of the cohort, whereas 401 had migraine without aura. Of the 171 patients with aura, 149 (87.1%) had simple aura, and 22 experienced complex aura (**Figure 1**).

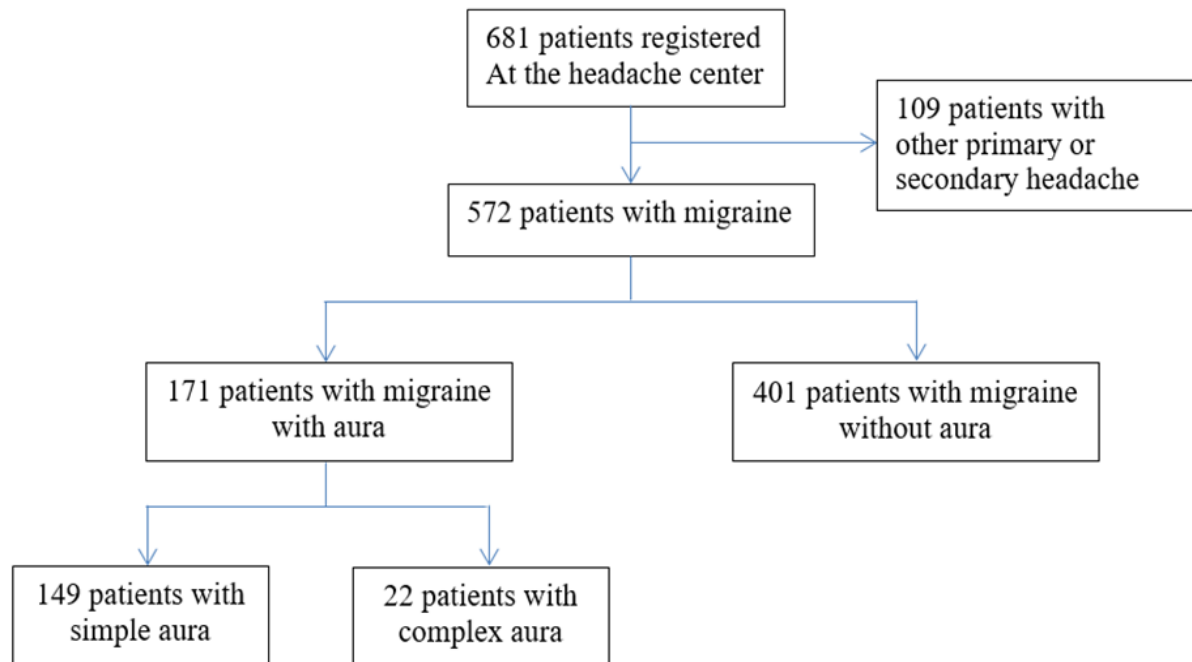


Figure 1. Flow chart for patient recruitment.

Among patients with simple aura, 96 (64.4%) had simple visual aura, and 53 had sensory aura. The presentations of complex aura included visual aura followed by sensory aura, sensory aura followed by dysphasic aura, and visual aura followed by dysphasic aura and motor aura.

Of the 572 patients with migraine, data from 214 patients were excluded because they did not attend a follow-up visit, had a first follow-up interval longer than 6 weeks while taking preventive medications, experienced no headache during the first follow-up period, did not take any acute pain medication, or had missing data. The remaining 358 patients had eligible data for subsequent analysis.

The baseline characteristics of patients with migraine without ($n = 248$), with aura ($n = 110$), with simple aura ($n = 92$), and with complex aura ($n = 18$) are presented in **Table 1**. The median age of patients without aura was slightly higher than that of patients with aura. A similar pattern was observed when comparing patients with complex and simple auras.

The proportion of comorbidities and the mean or median number of monthly migraine days were similar between patients with and without aura. However, comorbidities and monthly migraine days were both higher in patients with complex aura than in those with simple aura. The proportion of chronic migraine with

medication-overuse headache was nearly twice as high in patients with complex than simple auras.

Medication overuse involving migraine-specific medications was more common in patients without aura than in those with aura, and more common in patients with simple than complex auras. However, these differences were not significant (**Table 1**).

According to the International Classification of Headache Disorders criteria for the overuse of acute medications, 16 patients overused simple analgesics, including nonselective cyclooxygenase-2 (COX2) inhibitors (56.3%), selective COX2 inhibitors (12.5%), and acetaminophen (31.2%). Moreover, 38 patients overused migraine-specific medications, including ergot derivatives (92.1%), triptans (5.3%), and combination therapies (2.6%).

Migraine preventive medications included antiepileptic drugs used either as monotherapy or in combination with other agents, including antidepressants, beta-blockers, muscle relaxants, nutraceuticals, or onabotulinumtoxin A; antidepressants used alone or in combination with calcium channel blockers, beta-blockers, muscle relaxants, or nutraceuticals; and other treatments, including beta-blockers, calcium channel blockers, anti-calcitonin gene-related peptide monoclonal antibodies, and nutraceuticals.

Table 1. Baseline data of patients with simple and complex aura and without aura.

Baseline data	Migraine without aura (n = 248)	Overall (n = 110)	Migraine with aura		P (without vs. with aura)	P (simple vs. complex aura)
			Simple aura (n = 92)	Complex aura (n = 18)		
At baseline						
Median age, years (IQR)	44.0 (33.0–53.0)	39.5 (30.8–52)	37.5 (30–52)	40.5 (34.3–49)	0.057	0.68
Female sex, n (%)	208 (83.9)	95 (86.4)	80 (87.0)	15 (83.3)	0.66	0.92
Comorbidity presence, n (%)	127 (51.2)	63 (57.3)	50 (54.3)	13 (72.2)	0.34	0.25
Median history of migraine headache, years (IQR)	5.0 (1.5–10.0)	4.0 (1.0–10.0)	4.3 (1.0–10.0)	3.0 (1.0–20.0)	0.33	0.49
Mean monthly migraine days, (IQR)	17.9 (9.5)	18.1 (9.4)	17.4 (9.3)	21.7 (9.5)	0.83	0.07
Median monthly migraine days, (IQR)	17.0 (8.0–28.0)	16.0 (8.0–28.0)	16.0 (8.0–28.0)	28.0 (12.0–28.0)	0.76	0.08
Chronic migraine subtype, n (%)	103 (41.5)	47 (42.7)	40 (43.5)	7 (38.9)	0.92	0.92
Chronic migraine with medication overuse headache, n (%)	39 (15.7)	18 (16.4)	13 (14.1)	5 (27.8)	0.99	0.28
Overuse of medications:	10 (25.6)	6 (33.3)	4 (30.8)	2 (40.0)	0.62	0.61
Simple analgesics, n (%)						
Migraine-specific medications, n (%)						
Others, n (%)	28 (71.8)	10 (55.6)	9 (69.2)	1 (20.0)		
Associated nausea symptom, n (%)	1 (2.6)	2 (11.1)	0 (0)	2 (40.0)	0.12	0.21
Associated vomiting symptom, n (%)	165 (66.5)	83 (75.5)	72 (78.3)	11 (61.1)	0.20	0.61
Associated photophobia symptom, n (%)	111 (44.8)	58 (52.7)	50 (54.3)	8 (44.4)	< 0.001	0.95
Associated phonophobia symptom, n (%)	108 (43.5)	71 (64.5)	60 (65.2)	11 (61.1)	< 0.05	0.99
Associated phonophobia symptom, n (%)	100 (40.3)	58 (52.7)	48 (52.2)	10 (55.6)	0.21	0.97
On migraine prevention, n (%)	212 (88.1)	100 (90.9)	83 (90.2)	17 (94.4)	< 0.05	0.96
Antiepileptics or combinations	79 (37.3)	47 (47.0)	39 (42.4)	8 (47.1)		
Antidepressants	72 (34.0)	20 (20.0)	17 (18.5)	3 (17.6)		
Other medications	61 (28.8)	33 (33.0)	27 (29.3)	6 (35.3)		
Median pain duration, h (IQR)	5.0 (3.0–8.0)	4.0 (3.0–8.0)	4.8 (3.0–8.0)	4.0 (1.8–7.3)	0.57	0.14
Median pain score, NRS (IQR)	7.0 (5.0–8.0)	7.0 (6.0–8.0)	7.0 (6.0–8.0)	7.0 (5.0–9.0)	0.066	0.78

IQR, interquartile range; NRS, numerical rating scale.

The proportion of associated symptoms, including photophobia and phonophobia, was approximately 1.5- and 1.3-fold higher in patients with aura than in those without aura, respectively. In addition, preventive treatment with antiepileptic drugs was significantly more common among patients with aura than without aura.

Median pain duration and pain scores were similar between patients without and with aura, as well as between those with simple and complex auras (**Table 1**).

At the first follow-up visit (**Table 2**), which occurred at a median interval of 3 weeks from baseline, the median pain score and median monthly migraine days were generally similar to baseline values across all groups. However, median monthly migraine days were slightly lower than baseline among patients with migraine without aura and those with complex aura. In addition, pain scores at the first follow-up visit were missing for 24 patients, including 19 without aura, 4 with simple aura, and 1 with complex aura.

The proportion of patients achieving pain relief within 2 h after acute treatment was similar between patients with and without aura but was slightly higher among those with complex aura than among those with simple aura. Improvement in pain duration after treatment compared with baseline was slightly more frequent among patients with complex auras than among those with simple auras. In contrast, similar proportions were observed between patients with and without aura (**Table 2**).

The median percentage of patients achieving pain relief at 1 and 2 h, the median pain score after treatment, and the mean or median differences in pain scores between post-treatment and baseline were similar between patients without and with aura, as well as between those with complex and simple auras (**Table 2**).

Regarding the classes of medications used for acute treatment, neither migraine-specific nor non-migraine-specific medications differed significantly between patients with and without aura or between those with simple and complex auras. However, patients with complex aura used migraine-specific medications less frequently than those with simple aura (**Table 2**).

Discussion

In this study, the proportion of patients with migraine with aura was comparable to previous reports, with

most auras being simple, predominantly visual, followed by sensory symptoms, which is consistent with the literature. Migraine is frequently associated with comorbid conditions. In this study, these conditions were more common in patients with complex auras than in those with simple auras. These comorbidities are important to consider when selecting treatment because of any potential contraindications, particularly in patients with vascular risk factors or diseases that may limit the use of migraine-specific medications.

Medication overuse, particularly migraine-specific medications, was common across the migraine subtypes, including patients with and without aura and those with simple aura, but not those with complex aura. This finding may explain the low proportion of migraine-specific medication use among patients with migraine at the first follow-up visit in this study, especially in settings where certain agents are available over the counter and are prone to overuse.

Due to the high frequency of monthly migraine days, almost all patients were taking preventive medications, particularly antiepileptic drugs, which are generally effective. Most patients with migraine referred from other clinics receive tricyclic antidepressants, beta-blockers, or a combination of both for migraine prevention, as these medications have been previously established for this purpose. However, if referred patients did not respond to the medications they were recently prescribed, they required alternative migraine treatments, including antiepileptic drugs.

At their first follow-up visit, changes in the median monthly migraine days among patients with migraine without aura and those with complex aura were observed over short follow-up periods. The median follow-up period of only 3 weeks may reflect the natural course of the disease rather than the full effect of preventive treatments, as these typically require a longer duration, generally 1 or 2 months, to demonstrate efficacy.

Overall, no clear differences in acute treatment response were observed between migraine with and without aura or across aura complexity levels. However, following acute migraine treatment, pain relief within 2 h tended to be more common in patients with complex aura, who used fewer migraine-specific medications, than in those with simple aura, who used a higher proportion of migraine-specific medications. This trend may reflect differences in the underlying pathophysiology, although the lack of significance may be attributable to the limited sample size.

Table 2 Clinical data on the first follow-up visit.

Clinical data		Migraine without aura (n = 248)	Migraine with aura		P (without vs. with aura)	P (simple vs. complex aura)
			Overall (n = 110)	Simple aura (n = 92)	Complex aura (n = 18)	
At the first follow-up visit						
Median interval of first follow-up visit, weeks (IQR)		3.0 (2.0–4.0)	3.0 (2.0–5.0)	3.0 (2.0–5.0)	3.0 (2.0–4.3)	0.89
Median monthly migraine days (IQR)		11.0 (4.0–24.0)	15.0 (6.0–27.0)	15.0 (6.0–27.0)	16.0 (3.0–28.0)	0.78
Pain duration, n (%)						
≤ 1 h		39 (15.7)	21 (19.1)	16 (15.2)	5 (27.8)	0.48
≤ 2 h		80 (32.2)	36 (32.7)	28 (23.9)	8 (44.5)	0.25
> 2 h		168 (67.8)	74 (67.3)	64 (76.1)	10 (55.5)	0.25
Pain duration difference after treatment and baseline, n (%)						
Stable condition		159 (64.1)	74 (67.3)	65 (70.7)	9 (50.0)	0.17
Improved condition		64 (25.8)	27 (24.5)	21 (22.8)	6 (33.3)	
Worsening condition		25 (10.1)	9 (8.2)	6 (6.5)	3 (16.7)	
Median percent pain-free at 2-h, (IQR)		10.0 (0.0–75.0)	0.0 (0.0–70.5)	0.0 (0.0–50.0)	13.5 (0.0–100.0)	0.40
Median percent pain-free at 1-h, (IQR)		0.0 (0.0–14.5)	0.0 (0.0–29.0)	0.0 (0.0–25.0)	0.0 (0.0–100.0)	0.24
Median pain score, NRS (IQR)		6.0 (5.0–7.0)	6.0 (5.0–7.0)	6.0 (5.0–7.0)	5.0 (4.0–7.0)	0.19
Median pain score difference (improvement) after treatment and baseline (IQR)		–1.0 (–3.0 to 0.0)	–1.0 (–2.0 to 0.0)	–1.0 (–2.0 to 0.0)	–1.0 (–2.5 to 0.0)	0.46
Mean pain score difference (improvement) after treatment and baseline (SD)		–1.1 (2.2)	0.69	–1.0 (2.0)	–1.7 (2.3)	0.2
Median percent nausea, (IQR)		0.0 (0.0–4.8)	0.0 (0.0–17.5)	0.0 (0.0–19.5)	0.0 (0.0–0.0)	0.16
Median percent vomiting, (IQR)		0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.30
Median percent photophobia, (IQR)		0.0 (0.0–0.0)	0.0 (0.0–7.0)	0.0 (0.0–10.0)	0.0 (0.0–0.0)	0.21
Median percent phonophobia, (IQR)		0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.68
Drug class for acute treatment						
Nonmigraine-specific medication group, n (%)		200 (80.6)	92 (83.6)	77 (83.7)	15 (83.3)	0.79
Migraine-specific medication group, n (%)		27 (10.9)	10 (9.1)	9 (9.8)	1 (5.6)	
Others, n (%)		21 (8.5)	8 (7.3)	6 (6.5)	2 (11.1)	

IQR, interquartile range; NRS, numerical rating scale; SD, standard deviation.

The generally low response to acute treatment, particularly for achieving pain relief within 2 h, may also be influenced by the timing of medication use. Early treatment after symptom onset is known to improve outcomes, thus highlighting the importance of patient education and timely intervention.

To the author's knowledge, there is insufficient data on the response to acute treatment for patients with migraine with simple auras and those with complex auras. A single study with intravenous magnesium sulfate for the acute treatment of migraine demonstrated a better response in the pain intensity scale in migraine with aura at 30 and 60 min and 4 h after treatment compared to migraine without aura, as well as headache response and pain-free at 60 min after treatment: 50.0% and 36.7% in migraine with aura compared to 33.3% and 23.3% in migraine without aura, respectively.⁽²⁸⁾ Moreover, a study with intravenous dipyrone for the acute treatment of migraine with and without aura revealed no difference in headache response or pain-free response at 30 and 60 min and 24 h after treatment.⁽²⁹⁾ A study on the efficacy of sumatriptan and inhaled dihydroergotamine discovered a lower response rate in pain relief 2 h after treatment in migraine with aura, 24.0% vs. 32.0% in migraine without aura, and 27.2% vs. 29.4% in migraine without aura, respectively.⁽¹²⁾ A study of intravenous magnesium sulfate compared with metoclopramide in the management of acute migraine attacks revealed a significant reduction in pain intensity at 15 and 30 min in patients with migraine with aura who received magnesium vs. metoclopramide, respectively, but no significant difference between treatment arms in all patients with migraine.⁽³⁰⁾ One randomized controlled trial with subgroup analysis found that 50 mg of lasmiditan, a new migraine-specific medication, was associated with a better pain-free response in patients with a history of migraine with aura.⁽²⁰⁾ However, the sample size was small, and no definitive conclusions could be drawn. A real-world study of ubrogepant, a new migraine-specific acute treatment, revealed that migraine with aura was a predictive factor for a good response to ubrogepant.⁽²¹⁾ However, the sample size was small, and no definitive conclusions could be drawn. This limitation warrants further investigations to determine any differences in responses to acute treatment for migraine between patients with simple and complex auras. A larger sample size is required to confirm this tendency. This is particularly relevant for migraine with complex auras, including those involving the brainstem, retina, or motor systems;

treatment with vasoconstrictors such as triptans and ergot derivatives should be used with caution.⁽³¹⁾ Still, for other aura types, they have not made any recommendations.

The present study has some limitations, including its single-site, retrospective design and no direct comparison with medications for individual attacks between migraine with and without aura and between simple and complex auras. The time to take acute pain medications after the onset of pain and the time to record the associated symptoms are other limitations. This retrospective study should be interpreted with caution, as many biases and confounders may introduce errors in the collected data, including recall bias, patients' compliance with self-medication at home, other non-recommended interventions, or drugs used to rapidly terminate headaches.

Conclusion

Specific drugs for the acute treatment of migraine in patients with aura cannot be recommended. In clinical practice, empirical observation of the response to acute treatment may be the best treatment course for migraine with simple or complex aura. More research is required to understand why those with aura benefit from acute treatment.

Author contributions

The author contributed the entire study concept and design; the data acquisition, analysis, and interpretation; drafted, revised, and approved the final version of the submitted manuscript; and approved its publication.

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Conflict of interest statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data sharing statement

All data generated or analyzed in the present study are included in the published article. Further details are available for non-commercial purposes from the corresponding author upon reasonable request.

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