

Title

Navigating the Acute Migraine Treatment Landscape: Real-World Insights from the Headache Assessment via a Digital platform in United States (HeAD-US) Study

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One sentence summary: This study using 2023 HeAD-US data revealed diverse treatment patterns in individuals with migraine, highlighting gepants' notable effectiveness, especially in patients who use prescription monotherapy.

Background: Individuals with migraine are commonly treated with a combination of acute and/or preventive therapies, and the success of these treatments can vary. Acute treatment has been transformed by the introduction of new classes of pharmacologic agents, particularly gepants. Data on current patterns of acute treatment are limited and often based on electronic health record, medical claims, and pharmacy data, which do not capture the patient voice. This study aims to assess treatment patterns and the efficacy of acute treatments in individuals with episodic migraine (EM, 3 groups based on monthly headache days (MHDs): 0-3, 4-7, 8-14) and chronic migraine (CM, ≥ 15 MHDs) using data collected directly from people living with migraine through a digital platform.

Methods: We used the cross-sectional 2023 data collected as part of the Headache Assessment via a Digital Platform in the United States (HeAD-US) Study. The HeAD-US is a cohort of adults with migraine surveyed through the Migraine Buddy application. Eligible participants self-reported a migraine diagnosis and met modified ICHD-3 criteria for migraine. All participants at baseline assessment were surveyed for sociodemographic information, headache features including severity and frequency, and use of acute and preventive treatments. The Migraine Treatment Optimization Questionnaire (mTOQ-4) was used to evaluate the effectiveness of acute treatment. Effective treatment was defined as moderate or maximum treatment efficacy score based on mTOQ-4 scores.

Results:

A total of 6810 participants were eligible for this study. Participants had an average age of 42.0 years (SD=13, range 18-88), 89.9% were female, 4317 (63.4%) met criteria for EM and 2493 (36.6%) met criteria for CM (Table 1). Of the participants, 52.1% were using acute over-the-counter (OTC) medications, 73.2% were using acute prescription medications, 2.3% were using medical devices, and 59.7% were on preventive treatments. There was no significant difference in treatment effectiveness between participants on polytherapy with two or more types of treatments (39.0%) and those on monotherapy (41.1%, $p=0.105$). Among the 2649 patients on monotherapy with acute medications, the most common categories were triptans (42.4%), OTCs (30.2%), and gepants (23.1%). For patients on prescription monotherapy, individuals using gepants reported the highest rate of effective treatment (55.3%) in head-to-head comparison with triptans (49.2%, $p=0.015$), barbiturates (31.6%, $p<0.001$), and opioids (18.8%, $p<0.001$) but not with ergots (37.5%, $p=0.085$). After classifying participants into EM and CM categories, gepants consistently demonstrated the highest rate of effective treatment in each category.

Conclusion: The HeAD-US study presents an opportunity to examine real-world treatment patterns and the effectiveness of each treatment, when used independently and in combination with other treatments. Patients

relying on monotherapy with treatments that are not migraine-specific may face an elevated risk of inadequate treatment.

Table 1. Sample characteristics for the entire sample and by episodic (EM) and chronic (CM) migraine groups.

	EM	CM	Total
N (%)	4317	2493	6810
Age, Mean (SD)	41.4 (12.9)	42.4 (13.5)	41.7 (13.1)
Female, Sex (%)	3861 (89.4%)	2258 (90.6%)	6119 (89.9%)
Race, Whites (%)	3664 (84.9%)	2104 (84.4%)	5768 (84.7%)
Using Preventive therapy, N (%)	2254 (52.2%)	1812 (72.7%)	4066 (59.7%)
Not using acute RX/OTC or Preventive medications	452 (10.5%)	185 (7.4%)	637 (9.4%)
Not using any acute Rx/OTC medication	654 (15.1%)	372 (14.9%)	1026 (15.1%)
Acute medications use			
Any Acute Medication Treatment	3663 (84.9%)	2121 (81.1%)	5784 (84.9%)
Acute Medication Mono Therapy	1813 (42%)	836 (33.5%)	2649 (38.9%)
2 or more acute medications	1850 (42.9%)	1285 (51.5%)	3135 (46%)
Total Acute Medication Use			
OTCs (sold without prescription), such as Aspirin, Acetaminophen, ibuprofen, Excedrin	2202 (51%)	1349 (54.1%)	3551 (52.1%)
Opioids, such as Hydrocodone, Vicodin, Oxycodone, OxyContin.	154 (3.6%)	194 (7.8%)	348 (5.1%)
Barbiturates, such as Butalbital, Fiorinal	198 (4.6%)	189 (7.6%)	387 (5.7%)
Ergots, derivative, e.g., (Dihydro)Ergotamine, Migergot, Cafergot, Migranal	43 (1%)	50 (2%)	93 (1.4%)
Gepants, such as Ubrelvy or Nurtec	1108 (25.7%)	855 (34.3%)	1963 (28.8%)
Triptans, such as Zomig, Imitrex, Maxalt, Amerge, Relpax, Axert	2216 (51.3%)	1191 (47.8%)	3407 (50%)
Mono Acute Medication Use			
Only OTC	564 (31.1%)	237 (28.3%)	801 (30.2%)
Only Opioid	12 (0.7%)	20 (2.4%)	32 (1.2%)
Only Barbiturate	33 (1.8%)	24 (2.9%)	57 (2.2%)
Only Ergot	12 (0.7%)	12 (1.4%)	24 (0.9%)
Only Triptan	813 (44.8%)	311 (37.2%)	1124 (42.4%)
Only Gepant	379 (20.9%)	232 (27.8%)	611 (23.1%)
Medical Device Use			
Total Medical Device	61 (1.4%)	98 (3.9%)	159 (2.3%)
Cefaly	39 (0.9%)	63 (2.5%)	102 (1.5%)
electroCore noninvasive vagus nerve stimulator (nVS))	2 (0%)	4 (0.2%)	6 (0.1%)
eNeura transcranial magnetic stimulation device (TMS)	6 (0.1%)	8 (0.3%)	14 (0.2%)
Nerivio Armband	22 (0.5%)	32 (1.3%)	54 (0.8%)

Table 2. Headache Characteristics, Comorbidities, & Outcomes in Patients on Monotherapy for Migraine by Acute Medication Class

		OTC	Opioids/ Barbiturate	Triptans	Gepants	ANOVA	
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	F	Sig.
Monthly Headache Days		10.2 (7.9)	14.3 (8.8)	10.8 (7.6)	13 (8.2)	46.652	<0.001
Migraine Symptom Severity Score		17.3 (3)	18 (2.6)	17.6 (2.8)	17.8 (2.6)	8.675	<0.001
		N (%)	N (%)	N (%)	N (%)	Chi-Square	P
Disability (MIDAS)	None to Mild	80 (9.9%)	14 (6.7%)	266 (9.6%)	135 (6.9%)	13.408	0.004
	Moderate to Severe	732 (90.1%)	195 (93.3%)	2510 (90.4%)	1828 (93.1%)		
Anxiety (PHQ-4)	Absent	429 (52.8%)	130 (62.2%)	1648 (59.4%)	1183 (60.3%)	15.039	0.002
	Present	383 (47.2%)	79 (37.8%)	1128 (40.6%)	780 (39.7%)		
Depression (PHQ-4)	Absent	561 (69.1%)	132 (63.2%)	2002 (72.1%)	1423 (72.5%)	10.92	0.012
	Present	251 (30.9%)	77 (36.8%)	774 (27.9%)	540 (27.5%)		
Monthly Headache Day Frequency	0-3	180 (22.2%)	21 (10%)	434 (15.6%)	226 (11.5%)	146.285	<0.001
	4-7	217 (26.7%)	45 (21.5%)	745 (26.8%)	398 (20.3%)		
	8-14	174 (21.4%)	32 (15.3%)	695 (25%)	484 (24.7%)		
	≥15	241 (29.7%)	111 (53.1%)	902 (32.5%)	855 (43.6%)		
Treatment efficacy - based on MTOQ-4	Very Poor	107 (13.2%)	20 (9.6%)	179 (6.4%)	127 (6.5%)	123.092	<0.001
	Poor	483 (59.5%)	136 (65.1%)	1403 (50.5%)	986 (50.2%)		
	Moderate	153 (18.8%)	35 (16.7%)	738 (26.6%)	496 (25.3%)		
	Maximum	69 (8.5%)	18 (8.6%)	456 (16.4%)	354 (18%)		
Note. OTC = Over the counter; MIDAS = Migraine Disability Assessment, Grades 3 and 4 are categorized as moderate to severe disability; PHQ: Patient Health Questionnaire; MTOQ = Medication Treatment Questionnaire.							