

Predictors of Acute Treatment Response in Migraine: The Headache Assessment Via Digital Platform in United States (Head-US) study

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OBJECTIVE

To examine predictors of effective acute migraine treatment in the HeAD-US cohort and compare effectiveness of medication classes (Opioid/Barbiturates, Gepants, and Triptans) in achieving 2-hour pain freedom and 24-hour pain relief.

Conclusions

Gepants and triptans show comparable efficacy for 2-hour pain freedom. However, gepants were more effective at 24-hour pain relief, contradicting prior meta-analyses favoring triptans.

Predictors of poor treatment response were consistent across 2-hr and 24-hr outcomes, with higher migraine disability, pain intensity, and pain frequency per month predicting worse responses.

Patient profile-based models may improve personalized migraine therapy. Frequent attacks, severe pain, and high disability scores may help guide treatment selection and support the use of gepants for more sustained relief.



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INTRODUCTION

Burden: Migraine affects >1 billion people and ranks 2nd in global disability.¹
Current therapies: Triptans relieve attacks but carry vasoconstrictive risks; gepants offer non-vasoconstrictive, well-tolerated alternatives.²
Evidence gap: Few head-to-head comparisons exist, and predictors of real-world response to triptans vs gepants remain unclear.

RESULTS

Table 1. Demographics by Medication Class

Variable	Triptans (N =1018)	Gepants (N = 570)	Opioids/ Barbiturates (N = 81)
Age, mean (SD)	43.92 (13.41)	42.32 (12.29)	49.91 (13.78)
Sex			
<i>Female (%)</i>	902 (88.6%)	530 (93.0%)	74 (91.4%)
<i>Male (%)</i>	101 (9.9%)	37 (6.5%)	6 (7.4%)
<i>Other (%)</i>	15 (1.5%)	3 (0.5%)	1 (1.2%)
Marital Status			
<i>Married (%)</i>	569 (55.9%)	290 (50.9%)	44 (54.3%)
<i>Unmarried (%)</i>	449 (44.1%)	280 (49.1%)	37 (45.7%)
Pain Frequency per month, mean (SD)	10.16 (7.47)	12.05 (8.41)	14.17 (8.70)
Pain Intensity, mean (SD)	8.20 (1.38)	7.76 (1.66)	7.66 (1.68)
Cutaneous Allodynia			
<i>< Half of the time</i>	742 (72.9%)	379 (66.5%)	54 (66.7%)
<i>Half or more of the time</i>	276 (27.1%)	191 (33.5%)	27 (33.3%)
Depression			
<i>Not Depressed (%)</i>	924 (90.8%)	508 (89.1%)	68 (84.0%)
<i>Depressed (%)</i>	94 (9.2%)	62 (10.9%)	13 (16.0%)
Disability (MIDAS)			
<i>MIDAS – None (%)</i>	48 (4.7%)	16 (2.8%)	1 (1.2%)
<i>MIDAS – Mild (%)</i>	61 (6.0%)	32 (5.6%)	4 (4.9%)
<i>MIDAS – Moderate (%)</i>	137 (13.5%)	63 (11.1%)	5 (6.2)
<i>MIDAS – Severe (%)</i>	772 (75.8%)	459 (80.5%)	71 (87.7%)
Interictal Burden (MIBS)			
<i>MIBS –No Burden (%)</i>	44 (4.3%)	26 (4.6%)	4 (4.9%)
<i>MIBS – Mild (%)</i>	92 (9.0%)	34 (6.0%)	3 (3.7%)
<i>MIBS – Moderate (%)</i>	151 (14.8%)	80 (14.0%)	11 (13.6%)
<i>MIBS – Severe (%)</i>	731 (71.8%)	430 (75.4%)	63 (77.8%)
Preventive Medication			
<i>On Preventive Medication (%)</i>	725 (71.2%)	467 (81.9%)	53 (65.4%)
<i>Not on Preventive Medication (%)</i>	293 (28.8%)	103 (18.1%)	28 (34.6%)
Aberrant Sleep (≤6h or ≥9h)			
<i>Normal Sleep</i>	660 (64.8%)	368 (64.6%)	43 (53.1%)
<i>Aberrant Sleep</i>	358 (35.2%)	202 (35.4%)	38 (46.9%)

Sleep, Allodynia, Depression, and Preventive Medication Use were coded as binary variables. Aberrant Sleep is defined as ≤6h or ≥9h of sleep per night. Abbreviations MIBS=Migraine Interictal Burden Scale; MIDAS = Migraine Disability Assessment Scale; MSSS= Migraine Symptom Severity Scale

METHODS

- Study Design & Population:**
 - HeAD-US is a U.S. adult migraine cohort recruited via the Migraine Buddy smartphone app (Sept – Nov 2023).
 - Users received an in-app invitation; participation was voluntary with electronic consent (CIRBI #00072897).

- Case Definition & Outcomes:**
 - Migraine classified via AMS/AMPP diagnostic module (ICHD-2/3–aligned; sensitivity 100%, specificity 82%³.)
 - Acute response: 2 h pain freedom and 24 h sustained relief assessed using mTOQ-6 items.
- Inclusion/Exclusion:**
 - Of 6,810 respondents, 6,606 met migraine criteria; **1,669 were current users of triptans, gepants, or opioids/barbiturates.**
- Statistical Analyses**
 - Multivariate logistic regression and estimated marginal means

Logistic Regression Results for 2-Hour and 24-Hour Outcomes

Term	2hr Est.	95% LCL	95% UCL	24hr Est.	95% LCL	95% UCL
(Intercept)	8.35	2.00	35.51	13.261	2.95	61.07
Age	1.01	1.00	1.02	1.01	1.01	1.02
Sex (Reference =Female)	1.09	0.81	1.45	0.96	0.71	1.29
MSSS	0.96	0.91	1.01	0.96	0.92	1.01
Pain Frequency Per month	0.95	0.94	0.96	0.94	0.92	0.95
Aberrant Sleep	0.83	0.67	1.03	0.71	0.57	0.89
Pain Intensity	0.91	0.86	0.98	0.88	0.82	0.94
Migraine Disability Assessment Scale (MIDAS) – Reference = No burden						
MIDAS - Mild	0.58	0.27	1.20	0.51	0.22	1.14
MIDAS - Moderate	0.41	0.21	0.79	0.33	0.15	0.67
MIDAS – Severe	0.39	0.20	0.71	0.34	0.16	0.65
Allodynia	0.97	0.88	1.06	0.96	0.87	1.06
Depression	0.83	0.58	1.19	0.71	0.48	1.03
Migraine Interictal Burden Scale (MIBS) – Reference = No burden						
MIBS-Mild	0.47	0.24	0.88	0.75	0.37	1.48
MIBS-Moderate	0.68	0.37	1.23	0.71	0.37	1.30
MIBS-Severe	0.46	0.26	0.80	0.49	0.27	0.86
Preventive Medication	0.90	0.70	1.14	0.76	0.59	0.97
Medication Class (Reference = opioids/barbiturates)						
Triptans	2.61	1.52	4.66	3.33	1.87	6.25
Gepants	2.80	1.61	5.06	4.61	2.55	8.77

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Pairwise Comparisons of Medication Class (estimated marginal means)

2 hour Pain Relief			
Comparison	Odds Ratio	LCL	UCL
Triptans – Opioids/Barbiturates	2.63	1.33	5.00
Gepants – Opioids/Barbiturates	2.78	1.41	5.56
Gepants - Triptans	1.07	0.83	1.39
24 hour Pain Freedom			
Triptans – Opioids/Barbiturates	3.33	1.61	6.67
Gepants – Opioids/Barbiturates	4.55	2.22	10.00
Gepants - Triptans	1.39	1.05	1.82

^ Estimated using marginal means

* < .05, ** < .01, *** < .001