

Objective

- Prior work has identified associations between cutaneous allodynia, increased migraine day frequency and inadequate acute treatment response.
- The objectives of this study were to:
 1. Estimate rates of allodynia in migraineurs who met ICHD-3beta medication overuse (MO) criteria compared with those who did not (nonMO)
 2. Determine the influence of headache day frequency and other relevant covariates on the presence of allodynia

Methods

- Participants in the MAST Study were recruited from a nationwide online research panel.
- Stratified random sampling identified a representative cohort of individuals aged ≥18.
- A validated migraine diagnostic screen using modified ICHD-3β criteria identified individuals with migraine.
- Those averaging at least 1 headache day per month over the previous 3 months who reported the use of acute migraine medication(s) were eligible to participate.
- The presence of cutaneous allodynia on days with headache was identified using the Allodynia Symptom Checklist (ASC-12, score ≥3).
- ICHD-3β criteria were used to identify MO and nonMO respondents based on usage frequency of acute medications.
- In addition to headache frequency, a pain intensity measure (0-10 intensity rating) and the migraine symptom severity score (MSSS) sum, the binary logistic regression modeling included sociodemographics (age, gender, race, income, BMI, smoking) and depression and anxiety symptomology (PHQ-4, sum score ≥6).
- Allodynia was treated as a dichotomous outcome and covariates were added to the model in a hierarchal manner and retained if significant.
- Odds ratios (OR) and 95% confidence intervals (CI) are provided for models and Chi-square tests ($P < .05$) for group comparisons.

Results

- A total 14,396 acute medication users met inclusion criteria.
- Mean age was 43.4 years, 73.1% were women, 81.5% were white, 70.8% were employed full- or part-time and 40.1% met criteria for allodynia.
- Among MO respondents 50.3% met criteria for allodynia compared to 37.5% of non MO response $P < .001$.
- Give the importance of medication overuse we ran and binary logistic model to explore this relationship
- An initial unadjusted logistic model indicated that MO respondents were 68% more likely to report cutaneous allodynia (OR 1.68, CI 1.55, 1.83).
- In the full adjusted model persons with MO were 15% more likely to have allodynia (OR 1.15, CI 1.04, 1.27). Other significant factors associated with allodynia included being female (OR 1.71, CI 1.57, 1.87) and being white (OR 1.16, CI 1.05, 1.27). The presence of depression and anxiety symptoms (PHQ-4)(OR 1.83, CI 1.68, 2.00), having frequent (≥15 days/month) headache (OR 1.41, CI 1.23, 1.61 versus 1-4 headache days/month reference group), increasing MSSS (1.17, CI 1.15, 1.19) and pain intensity (OR 1.11, CI 1.08, 1.14) were also associated with greater odds of having allodynia.
- The following sociodemographics were not significant predictors of allodynia and were not included in the final model: marital status, BMI, presence of health insurance and education.

Table 1. Allodynia Rates Among Respondents Taking Medication to Treat Headaches

	No Allodynia Present N=8,627 (59.9%)	Allodynia Present N=5,769 (40.1%)	Total N=14,396	Chi	P Value
Gender					
Males	2724 (70.4%)	1148 (29.9%)	3872	239.70	<.001
Females	5903 (56.1%)	4621 (43.9%)	10524		
Marital Status					
Not married	3792 (57.8%)	2767 (42.2%)	6559	22.39	<.001
Married	4835 (61.7%)	3002 (38.3%)	7837		
Education					
Less than 4 year degree	3443 (57.6%)	2534 (42.4%)	5977	22.95	<.001
Four-year degree or higher	5184 (61.6%)	3235 (38.4%)	8419		
Race					
White	6979 (59.9%)	4676 (40.1%)	11655	0.18	.673
Non-White	1592 (60.3%)	1047 (39.7%)	2639		
Personal Income					
Did not work for pay	1024 (54.7%)	847 (45.3%)	1871	78.88	<.001
Less than \$25,000	1619 (55.2%)	1314 (44.8%)	2933		
\$25,000 to \$49,000	2357 (60.5%)	1536 (39.5%)	3893		
\$50,000 to \$74,999	1656 (63%)	974 (37%)	2630		
\$75,000 to \$99,000	913 (63.6%)	522 (36.4%)	1435		
≥ \$100,000	874 (64.5%)	481 (35.5%)	1355		
Current Smoker					
Yes	804 (49.1%)	835 (50.9%)	1639	91.04	<.001
No	7823 (61.3%)	4934 (38.7%)	12757		
Depression and Anxiety Symptoms (PHQ-4) Binary					
No	7153 (65%)	3854 (35%)	11007	498.41	<.001
Yes	1474 (43.5%)	1915 (56.5%)	3389		
Medication Overuse					
No	7208 (62.5%)	4334 (37.5%)	11542	154.40	<.001
Yes	1419 (49.7%)	1435 (50.3%)	2854		
	Mean (Sd)	Mean (Sd)	Mean (Sd)	T test	P Value
Age	44.50 (13.85)	41.65 (13.01)	43.36 (13.62)	12.37	<.001
Pain Intensity Rating	6.42 (1.66)	7.08 (1.55)	6.68 (1.65)	23.95	<.001
MSSS	15.93 (3.00)	17.65 (2.65)	16.63 (2.99)	35.22	<.001

Table 2. Predictors of Allodynia: Results from a Binary Logistic Regression

		Sig
Medication Overuse	1.15 (1.04, 1.27)	.006
Age	0.99 (0.99, 0.99)	<.001
Gender (Ref = Males)	1.71 (1.57, 1.87)	<.001
White (Ref = Non-White)	1.16 (1.05, 1.27)	<.01
Personal Income	0.98 (0.95, 1.00)	.096
Current Smoker (Ref = Smoker)	0.75 (0.67, 0.83)	<.001
Depression and Anxiety Symptoms (PHQ-4) Binary	1.83 (1.68, 2.00)	<.001
Pain Intensity Rating	1.11 (1.08, 1.14)	<.001
Monthly HA Days 5-9 (Ref = 1-4 days)	1.23 (1.12, 1.35)	<.001
Monthly HA Days 10-14 days	1.21 (1.05, 1.39)	<.01
Monthly HA ≥15 days	1.41 (1.23, 1.61)	<.001
Migraine Symptom Severity Score (MSSS)	1.17 (1.15, 1.19)	<.001

Conclusions

- Cutaneous allodynia and MO are strongly associated even after adjusting for covariates, which supports the clinical approach of minimizing the overuse of acute medications.
- Other factors associated with the presence of allodynia included symptoms of depression and anxiety, headache frequency, headache intensity, increasing MSSS being female, being white and smoking.