American Journal of Psychiatric Rehabilitation

Expert Opinion Article

Compare the safety and efficacy of Propranolol versus Nortriptyline as Monotherapy for Migraine Prophylaxis.

Dr. Vikas Chaudhary[1*], Dr. Suruchi Prakash[2], Dr. Anubhuti Shukla[3]

[1*](Junior Resident) Department of Pharmacology, Sarojini Naidu Medical College, Agra. Email: vkscdy@gmail.com
[2] (Assistant Professor) Department of Pharmacology, Autonomous State Medical College, Firozabad. Email: suruchiprakash21@gmail.com
[3] (Assistant Professor) Department of Pharmacology, Dr. B.S. Kushwah Medical College, Kanpur Email: anubhuti.kgmu008@gmail.com

***Corresponding Author:** Dr. Vikas Chaudhary
* (Junior Resident) Department of Pharmacology, Sarojini Naidu Medical College, Agra. Email: vkscdy@gmail.com

Abstract:
Objective: To compare the safety and efficacy of Propranolol and Nortriptyline as monotherapy in the prophylactic treatment of migraine.
Methods: This study evaluated patients diagnosed with migraine who were treated with either Propranolol or Nortriptyline. The primary endpoints included reduction in frequency, severity, and duration of migraine attacks. Secondary outcomes assessed the tolerability and side effect profile of each medication.
Results: Nortriptyline demonstrated superior efficacy compared to Propranolol, significantly reducing the frequency, intensity, and duration of migraine episodes. However, Propranolol was better tolerated, with fewer and less severe side effects reported.
Conclusion: In This study indicates that Nortriptyline is more effective than Propranolol in migraine prevention, particularly in reducing the frequency, severity, and duration of attacks. However, Propranolol demonstrates better tolerability with fewer side effects. While Nortriptyline appears to be the more efficacious option for migraine prophylaxis, Propranolol may be preferred in patients who prioritize minimal adverse effects.

Introduction: Migraine may be considered as a prolonged neurological condition with periodic exacerbations. It is highly prevalent, with the symptoms of pain and disability. [1] Pain is associated with autonomic symptoms, the mostly common being nausea, vomiting, phonophobia and photophobia, (the International Classification of Headache Disorders (ICHD), third edition, published in 2013). [2]

The complaint is categorized by events of moderate to severe cranium pain, which is frequently one-sided and throbbing, and characteristically aggravated by monotonous physical activities. The period of unprocessed migraine occurrences is slightly long, from 4 hours to 3 days (median duration 18 hours). [3] Other indications, such as osmophobia, fatigue, pallor, difficult in attentiveness, blurry vision, or diarrhea, may be existent. [4]

In numerous patients, the headache stage is headed by predictive symptoms (or prodromes) which can last from a few hours to 24 hours, and are categorised by yawning, fatigue, fluid retention, sensory hypersensitivity, mood changes, food cravings, or increased thirst. Similar psychological, overall and autonomic symptoms can also describe the determination phase of an attack (postdrome). [5]

The prevalence of migraine varies from country to country. In Europe, the 1-year prevalence of migraine was estimated to be 14% with the peak incidence occurring between the age range of 20 and 50 years. [6] In USA, the 3-month overall prevalence of migraine was 14.2%, with the maximum incidence occurring in subjects aged between 18 and 44 years. [11]

Material and Methods: A 12-month Study was conducted in the of department of General Medicine in collaboration with department of Pharmacology and Therapeutics during a period from January 2023- January 2024 at S.N. Medical college and associated hospital, Agra (U.P.).

The study was approved by the scientific review board and institutional ethics committee.

Study design: This study was prospective, comparative, observational.

Inclusion criteria:

- Patient were taken as per International Headache Society Criteria for Migraine with Aura.
- Patient were taken as per International Headache Society Criteria for Migraine without Aura.
- Patients aged between18-65 years were taken.
- Both male and female gender patients were taken

Exclusion criteria:

- Patients <18 years & >65 years.

- Patient having chronic incapacitating illness eg. AIDS, cancer, TB.
- Patient whose primary headaches were other than migraine headaches
- e.g. With a clinical history of stroke or Transient Ischemic Attack (TIA).

Result: In both the groups, maximum number of patients were in the age group of 18-25 years and least number of patients were 46-65 years of age. Mean age in group 1 patients were **27.21±7.71** and in Group 2 patients were **28.01±7.65**. There was no statistically significant difference in mean age of patient from Group 1 and Group 2 patients with

Table 1: Comparison of Mean Age in Groups:

Age-Group	Group 1		Group 2	
	No	Percentage	No	Percentage
18-25 years	37	61.6%	34	56.6%
26-45	20	33.3%	25	41.6%
46—65	3	5.0%	1	1.6%
Total	60	100	60	100
Mean±SD	27.21±7.71 years		28.01±7.65 years	
p-value	0.609			

Figure 1: Comparison of Mean Age in Groups:

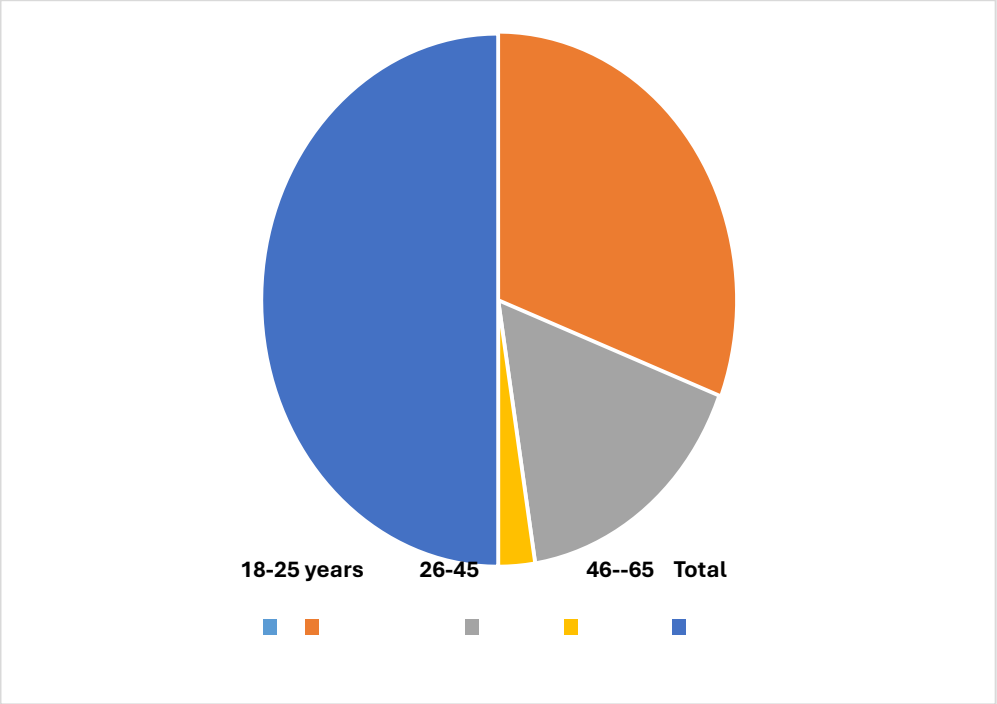


Table 2: Gender difference between Group-1 and Group-2

	Group 1		Group 2		Chi-square test P=value
	n=60	(%)	N=60	(%)	
Male	19	31.6	21	35.0	0.112
Female	41	68.3	39	65.0	
Total	60	100	60	100	

The table 3 reflects that 120 migraine patients in Group 1: 19 were male (31.6%) while 41 were female patients (68.3%). In Group 1 consisted of 21 male patients (35%) and 39 female patients (65%). There was no statistically significant difference in number of patients from Group 1and Group 1 patients (0.112) when we applied with Chi-square test.

Figure 2: Gender difference between Group 1 and Group 2

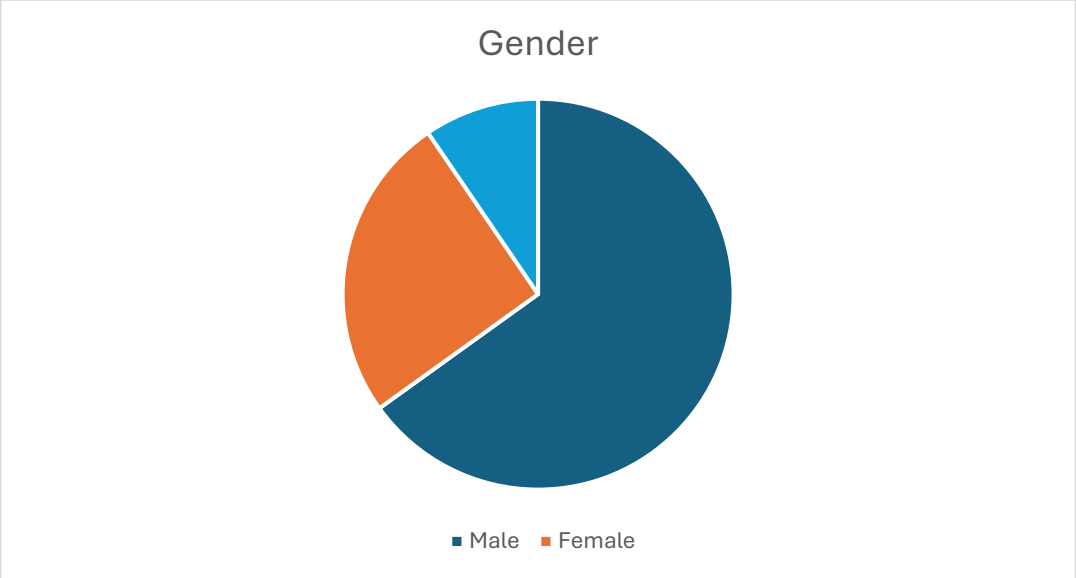


Table 3: Comparison of Frequency of migraine Attack between Group 1 and Group 2

	Group 1 Mean±SD		Group 2 Mean±SD		p-value
Frequency of Attack	Period 1 (Propranolol)	Period 2 (Nortriptyline)	Period 1 (Nortriptyline)	Period 2 (Propranolol)	**P=0.016**
	4.41±1.22	**4.01±0.92**	**3.93±0.97**	**4.21±1.02**	

Table 4, the mean Frequency of Attack of migraine in **Group 1** at period 1 was 4.41 with SD of 1.22 and period 2 was 4.01 with SD 0.92. In **Group 2** during period 1 was 3.93 with SD of 0.97 and in period 2 mean 4.21 with SD 1.02. These was statistically significant difference in **Group 1 and Group 2** (p=0.016) with **Unpaired t test**.

Figure 3: Comparison of Frequency of migraine Attack between Group 1 and Group 2

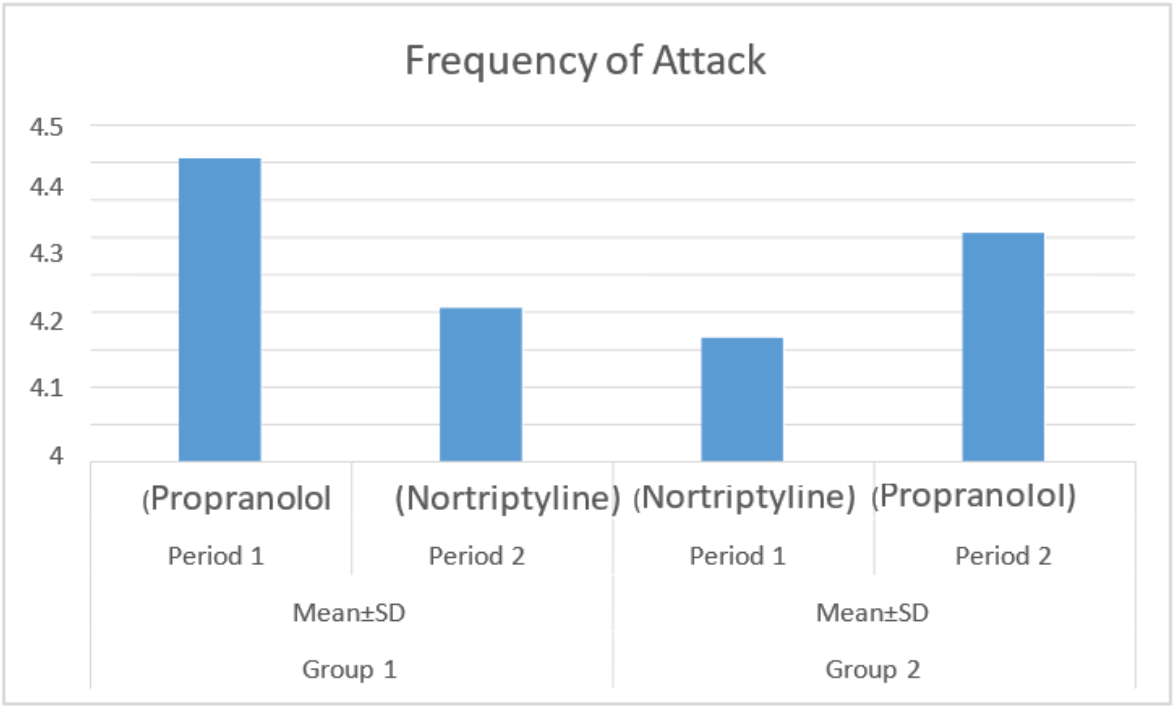
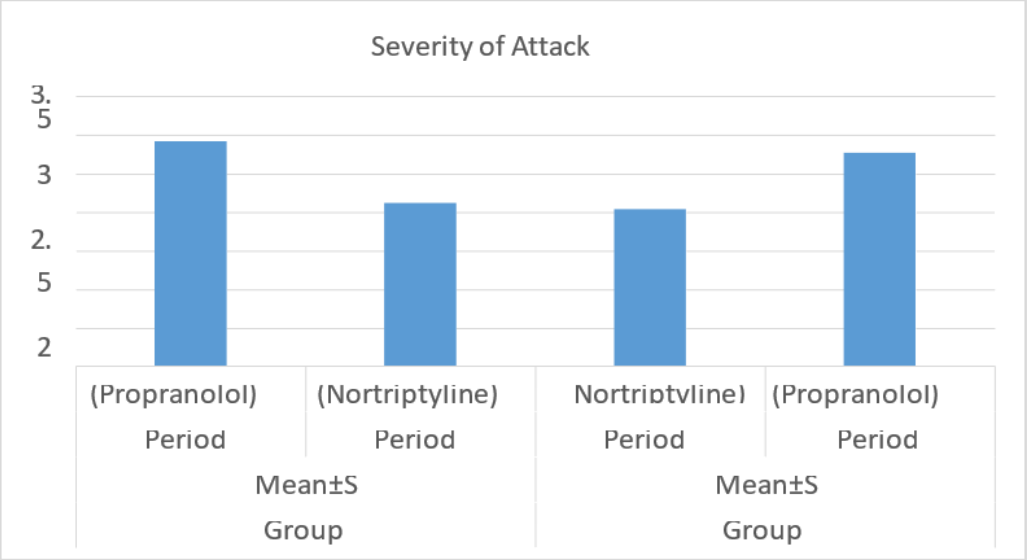


Table 5: Comparison of severity of Attack of migraine between Group 1 and Group 2

	Group 1 Mean±SD		Group 2 Mean±SD		p-value
Severity of Attack	Period 1 (Propranolol)	Period 2 (Nortriptyline)	Period -1 (Nortriptyline)	Period 2 (Propranolol)	P=0.023
	2.91±0.84	2.11±0.64	2.76±0.81	2.76±0.81	

In Table 5, the mean severity of Attack of migraine in Group 1 at period 1 was 2.91 with SD of 0.84 and period 2 was 2.11 with SD 0.64. In Group 2 during period 1 was
2.03 with SD of 0.71 and in period 2 mean 2.76 with SD 0.81. These was statistically significant difference in Group 1 and Group 2 (p=0.023) with Unpaired t test.

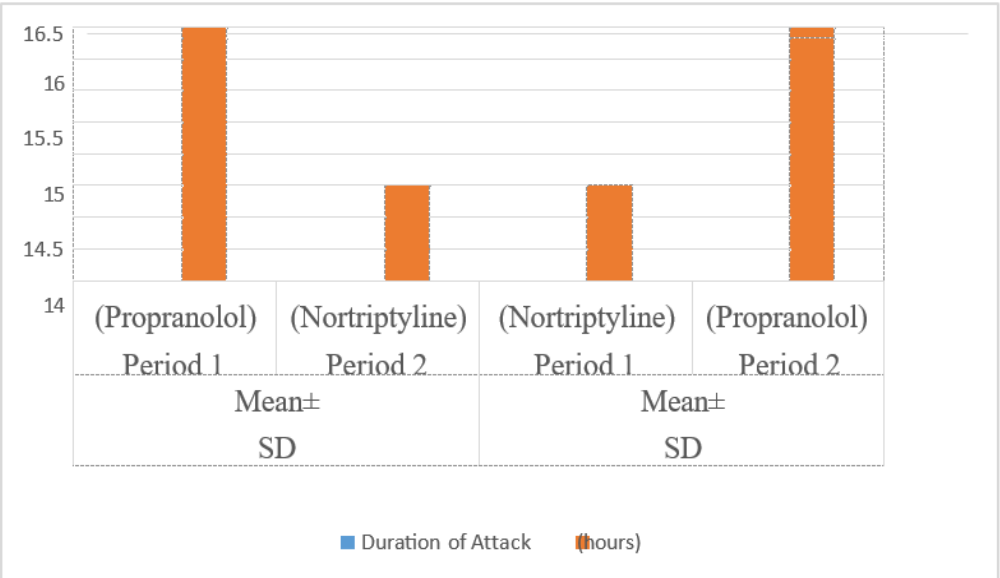
Figure 4: Comparison of severity of Attack of migraine between Group 1 and Group 2



	Group 1 Mean±SD		Group 2 Mean±SD		p-value
Duration of Attack (hours)	Period 1 (Propranolol)	Period 2 (Nortriptyline)	Period 1 (Nortriptyline)	Period 2 (Propranolol)	P=0.038
	16.01±2.60	13.51±2.22	13.63±1.56	15.83±2.00	

Table 6: Comparison of Duration of Attack of migraine between Group 1 and Group 2

Figure 5: Comparison of Duration of Attack of migraine between Group 1 and Group 2



Type of Reaction	Group 1		Group 2		
	Period 1 (Propranolol)	Period 2 (Nortriptyline)	Period 1 (Nortriptyline)	Period 2 (Propranolol)	p=value
Xerostomia	2	6	7	1	0.02
Dizziness	6	3	2	7	0.03
Weight gain	3	4	3	2	0.09
Somnolence	2	7	6	1	0.01
Constipation	1	3	2	1	0.04

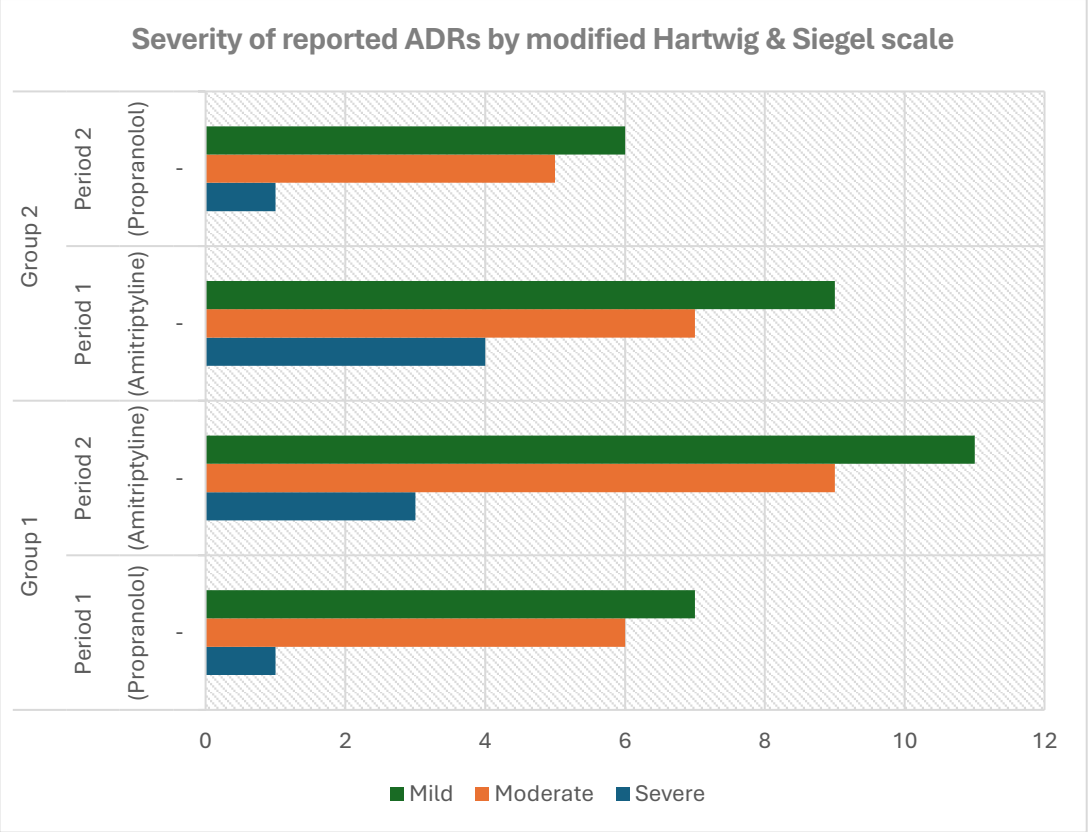
Table 7:

Comparison of ADRs during treatment with Group 1 and Group 2:
The most commonly reported adverse drug reactions (ADRs) varied between the two groups. In Group 1, during Period 1, the most frequent ADR was dizziness, while constipation was the least reported. In Period 2, somnolence became the most common ADR, with dizziness and constipation being the least frequent. In contrast, for Group 2, the highest incidence of ADR in Period 1 was xerostomia, and the least was constipation. During Period 2, dizziness was the most frequently reported ADR, followed by weight gain, xerostomia, somnolence, and constipation.

Table 9: Severity of reported ADRs by modified Hartwig & Siegel scale

Type of reaction	Group 1		Group 2	
	Period 1 (Propranolol)	Period 2 (Amitriptyline)	Period 1 (Amitriptyline)	Period 2 (Propranolol)
Lethal	-	-	-	-
Severe	1	3	4	1
Moderate	6	9	7	5
Mild	7	11	9	6

Bar graph 6: Severity of reported ADRs by modified Hartwig & Siegel scale



Discussion: In this study, we compared two drugs Propranolol and Nortriptyline are first choice drugs use in migraine prophylaxis, and are commonly used Propranolol, a non-selective beta-adrenergic blocker, and nortriptyline, a tricyclic antidepressant (TCA), are both widely used for migraine

prophylaxis. Their mechanisms of action differ significantly—propranolol is believed to reduce migraine frequency by modulating vascular tone and suppressing cortical spreading depression, while nortriptyline influences serotonin and norepinephrine pathways implicated in migraine pathogenesis. Comparing their safety and efficacy profiles is essential for tailoring migraine management to individual patient needs.
The reduction in frequency and severity of migraine attacks was statistically significance when compared to each other. This study shows that Nortriptyline is more effective and well tolerated in migraine prophylaxis.

Conclusion: Preventive pharmacological treatment of migraine and chronic migraine remains a significant challenge. While monotherapy has been extensively researched, combining medications may offer potential benefits by targeting various aspects of migraine pathophysiology. This study demonstrated that Propranolol and Nortriptyline are both effective and well-tolerated.
This study indicates that Nortriptyline is more effective than Propranolol in migraine prevention, particularly in reducing the frequency, severity, and duration of attacks. However, Propranolol demonstrates better tolerability with fewer side effects. While Nortriptyline appears to be the more efficacious option for migraine prophylaxis, Propranolol may be preferred in patients who prioritize minimal adverse effects.

Limitations:
Short study duration – Does not provide information on the long-term efficacy and safety of the drugs.
Single-center study – Reduces the external validity and applicability to other populations or settings.
Lack of blinding (if applicable) – May introduce bias in outcome reporting, especially for subjective symptoms.
Fixed drug dosages – No adjustment based on individual response, which could affect efficacy and tolerability.
Reliance on self-reported data – Potential for recall bias and inconsistency in reporting migraine characteristics.

References:
1. The Global Burden of Migraine: A 30-Year Trend Review and Future Projections by Age, Sex, Country, and Region:2024 Dec 11;14(1):297–315.
2. The International Classification of Headache Disorders, 3rd edition Volume 38, Issue 1 , January 2018, Pages 1-211
3. Britt W. et al Defining migraine days, based on longitudinal E-diary data Volume 43, Issue 5 , May 2023
4. Terrin, A., Mainardi, F., Lisotto, G. (2020). A prospective study on osmophobia in migraine versus tension-type headache in a large series of attacks. Cephalalgia, 40(10), 1063–1070.
5. Roberta M. et al Tracking the evolution of non-headache symptoms through the migraine attack:2022 Nov 23;23(1):149
6. Stovner, L. J., Hagen, K., Jensen, R., T. J. (2022). The global prevalence of headache: An update, with analysis of the influence of methodological factors on prevalence estimates. Journal of Headache and Pain, 23(1), 1–18
7. Rebecca C. The prevalence and burden of migraine and severe headache in the United States:2015 Jan;55(1):21-34.