International Journal of Law, Justice & Statutory Affairs
Volume 2, Issue 1, 2026

A low-dose comparison of propranolol and amitriptyline for the prevention of episodic migraine in a tertiary care facility

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Research Article

Date of Submission: 15-01-2026 **Date of Acceptance: 26-02-2026** **Date of Publication: 19-03-2026**

ABSTRACT

Background: The purpose of this research was to evaluate the tolerance and effectiveness of propranolol against amitriptyline at low doses for the prevention of episodic migraine in an Indian population sample.
Methods: Patients with episodic migraines between the ages of 18 and 55 who were not receiving any preventative therapy were randomized to receive either amitriptyline (10 mg/day) or propranolol (80 mg/day). The mean monthly change in migraine attack frequency after three months of therapy was the main effectiveness outcome. Adverse events and other secondary efficacy outcomes were also evaluated.

Results: At three months, both trial groups demonstrated a decrease in migraine frequency, headache intensity, and migraine-related impairment. When compared to amitriptyline at three months, propranolol substantially decreased the frequency of headaches (51.6% vs. 43.6%, p=0.03) and the quantity of rescue drugs (53.1% vs. 43.3%, p=0.01). The propranolol group had a considerably higher percentage of respondents with ≥50% improvement than the amitriptyline group (60% vs. 43.3%, p=0.02). The incidence of adverse events did not significantly vary between the two groups.

Conclusions: At three months, propranolol (80 mg/day) was more effective than amitriptyline (10 mg/day) in considerably lowering headache frequency and rescue medication use. The safety profiles of the two medications were similar.

INTRODUCTION

Migraine is a prevalent neurological disorder that significantly burdens individuals and their families by interfering with everyday functioning and production. It is one of the most common and crippling illnesses in the world, causing financial hardship for both individuals and society as a whole. The primary management approach is prevention, for which a variety of therapies with differing safety and effectiveness profiles are available. Compared to other more recent therapies, amitriptyline and propranolol are extremely ancient medications with a recognized safety profile. Scientific organizations such as the American Headache Society (AHS)/American Academy of Neurology (AAN) guidelines, the National Institute for Health and Care Excellence (NICE) guidelines, the Canadian Headache Society (CHS) guidelines, and the Scottish Intercollegiate Guidelines Network (SIGN) recommend both medications in different doses for migraine prophylaxis. Propranolol and amitriptyline have suggested dosage ranges of 40–240 mg and 10–150 mg, respectively. The majority of research on these medications for migraines has been conducted in Western populations, where high doses within the guideline range have been administered. The effective dosage for Indian patients is much lower, according to the clinician's experience.5 If shown to be effective, low dosages will lessen the medication's negative effects. Studies evaluating the effectiveness of amitriptyline and propranolol at low dosages in the Indian population are few. Therefore, the purpose of this research was to evaluate their safety profile and effectiveness at modest dosages.

METHODS

From February 2023 to October 2023, the research was carried out at the Department of Pharmacology at Rohilkhand Medical College and Hospital, Bareilly, in cooperation with the Department of Medicine.Following clearance from Rohilkhand Medical College's Institutional Ethics Committee (IEC) and Departmental Scientific Review Board, the research was carried out. Every participant in the research provided written informed permission.

Study design

A single-center, parallel, randomized, open-label, prospective trial. During a one-month screening period, all patients were requested to keep a headache diary in which they recorded the frequency, intensity, presence, and type of aura, as well as the daily dosage of rescue medication. The following oral drugs were administered for acute therapy during the screening phase in accordance with the treating doctors' standard of care: naproxen sodium (500–1000 mg), paracetamol (500–1000 mg), or naproxen+domperidone (500+10 mg). Hemograms (blood counts, hemoglobin, ESR), liver function tests (bilirubin, transaminases), kidney function tests (blood urea, serum electrolytes, serum creatinine), random blood sugar, and urinalysis were performed on patients who met the criteria for episodic migraine (4–14 headache days per month). Patients who reported abnormal baseline examinations were not allowed to participate in the trial. Using computer-generated random number tables, the remaining patients were divided into two groups using the block randomization approach. Propranolol tablets were given to Group A at a beginning dosage of 20 mg twice daily for two weeks, then 40 mg twice daily for an additional ten weeks. Amitriptyline tablets were given to Group B at a dosage of 5 mg once daily for the first two weeks, then 10 mg once daily for the next ten. Patients were permitted to withdraw from the research if the doctor determined that the medications were neither safe nor effective.

Study participants

In all, sixty patients of both sexes in the 18–55 age range who met the ICHD-3 diagnostic criteria for episodic migraine (with or without aura) and were not receiving any preventative treatment were included. Patients with a history of asthma, chronic obstructive pulmonary disease, atrioventricular conduction defects, bradycardia, peripheral vascular disease, uncontrolled diabetes mellitus, uncontrolled hypertension, glaucoma, seizure disorders, cardiac diseases, severe depression, anxiety disorders, or a three-month history of antipsychotic, antidepressant, or antianxiety medication were all excluded from the study.

Patient evaluation

For three months, patients were monitored on a monthly basis. The information was gathered using a pretested, validated, and organized

proforma that included family history, triggering and relieving events, and a thorough history of headache features contained in the ICHD-3 criteria for the diagnosis of episodic migraine. Every appointment included a clinical evaluation that included blood pressure and pulse rate measures. Every visit included data on the total number of migraine days, the intensity of the headache, the disability, and the quantity of rescue medications administered. Any adverse effects were also noted.

Primary and secondary outcomes

The decrease in the frequency of migraine headache attacks per month at the end of three months was the main effectiveness result. The percentage of patients with ≥50% fewer migraine headache days per month, a decrease in headache intensity (visual analog scale), a decrease in headache-induced disability (HIT-6), and a decrease in the quantity of rescue medicine used relative to baseline were all considered secondary efficacy outcomes.Six The WHO-UMC scale was used to determine causality, Hartwig's Severity Assessment Scale was used to gage severity, and adverse effects were recorded.7,8

Statistical analysis

A minimum of thirty patients were recruited for each group using a suitable sampling technique. The statistical program SPSS 23.0 and Microsoft Excel were used to input and evaluate the data. The mean plus standard deviation was used to display continuous data. Percentages were used to convey categorical data. Depending on the kind of data, the appropriate statistical tests were used; at a 95% confidence interval, a p value of less than 0.05 was deemed significant.

RESULTS

The research included sixty patients who satisfied the inclusion criteria. Patients in both trial groups had similar demographics. Propranolol and amitriptyline groups had mean ages of 32.8 (±7.9) and 32.7 (±8.1) years, respectively. Women predominated in both categories. The majority of individuals had migraines without aura (Table 1). From baseline (7.1±2.54) to the end of three months (3.43±1.67) ($p<0.0001$), propranolol (80 mg/day) reduced the frequency of headaches (Figure 1). By the end of three months, at least 50% fewer headaches were experienced by 60% of the patients. At the end of three months, the VAS Score for headache intensity dropped considerably from 7.67±0.61 at baseline to 6.82±1.41 ($p<0.0001$) (Figure 2). Disability caused by headaches as determined by the HIT-6 Score dropped

between 66.80±5.95 and 61.33±7.6 ($p<0.0001$) (Figure 3). Rescue medication use dropped along with the frequency of headaches, from 7.1±2.54 at baseline to 3.33±1.34 at the end of three months ($p<0.0001$) (Figure 4). Throughout the research, the improvement persisted without losing effectiveness. The frequency of headaches was progressively reduced with amitriptyline (10 mg/day) from 6.57±2.49 at baseline to 3.7±1.39 at the end of three months ($p<0.0001$) (Figure 1). By the end of three months, at least 50% fewer headaches were experienced by 43% of the patients. At the end of three months, the VAS Score for headache intensity dropped considerably from 7.68±0.67 at baseline to 7.26±0.58 ($p=0.001$) (Figure 2). The HIT-6 Score for headache-induced disability dropped from 66.77±5.65 to 62.73±5.86 ($p<0.0001$) (Figure 3). Rescue medication usage similarly dropped with decreasing headache frequency, from 6.07±2.12 at baseline to 3.43±1.48 at the end of three months ($p<0.0001$) (Figure 4). Throughout the research, the improvement persisted without losing effectiveness.

The propranolol group saw a mean change in headache frequency from baseline to the end of therapy of -3.67±1.47, while the amitriptyline group experienced a mean change of -2.87±1.36 ($p=0.03$). In the propranolol plus amitriptyline group, the percentage of patients with a decrease of at least 50% was 60% compared to 43.3% ($p=0.02$). In both groups, the number of rescue medication intakes dropped from baseline (-3.77±1.79 vs. -2.63±1.50, $p=0.01$).

Both groups had a reduction in headache intensity and headache-related impairment. Table 2 shows that there was no statistically significant difference between the two groups. Nine individuals on propranolol and seven on amitriptyline had mild side effects. Amitriptyline was associated with drowsiness (10%), dry mouth (10%), and constipation (3.3%), while propranolol was associated with tiredness (23.3%) and bradycardia (6.67%) (Table 3). Since side effects were self-limiting, the treatment procedure was not changed.

Table 1:

Demographic characteristics of patients.

Characteristics	Group A (n=30) mg/day (Mean±SE
Age	32.8 (7.90)
Female gender (%)	28 (93.3%)
Type of migraine (%)	
With aura	1 (3.3%)
Without aura	29 (96.7%)
Frequency of migraine/month	7.1±2.54
Headache severity (VAS score)	7.45±0.79
Headache-induced disability (HIT score)	66.80±5.95
Rescue medication/month	6.22±2.11

VAS- Visual Analogue Scale, HIT- Headache Impact Test

Table 2: Comparison of primary and secondary outcomes of efficacy.

Parameter	Group A (n=30) 80 mg/day
Change in frequency of headache from baseline (Mean±SE)	-3.67±1.47
≥50% reduction in headache from baseline	19 (60%)
Headache severity: change in VAS score from baseline (Mean±SE)	-0.85±1.28
Headache induced disability: change in HIT Score from baseline (Mean±SE)	-5.8±5.52
Change in rescue medicines intake from baseline (Mean±SE)	-3.77±1.79

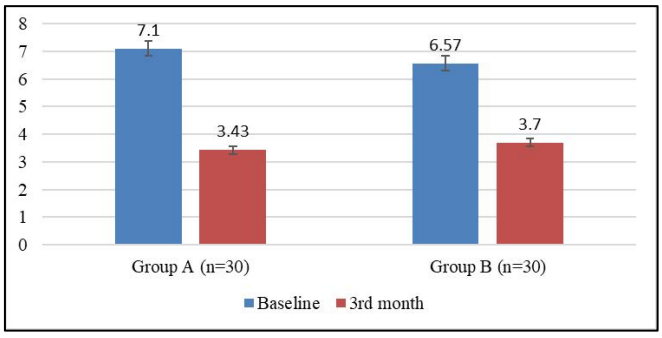

Figure 1: Reduction in migraine headache attack at the end of 3 months from baseline.

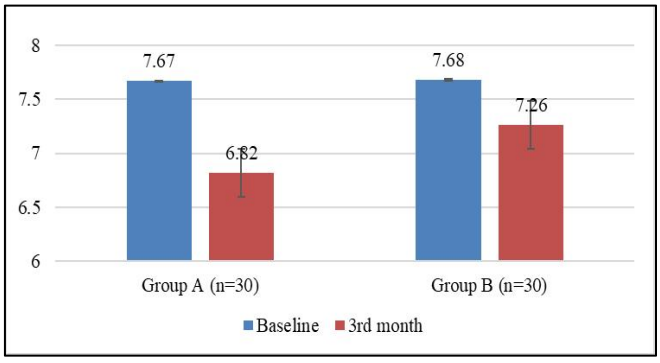

Figure 2: Reduction in headache severity at the end of 3 months from baseline.



Table 3: Comparison of adverse events between patients receiving Propranolol (Group A) and Amitriptyline (Group B).

Adverse events	Group A (n=30) Propranolol 80 mg/day	Group Amitript
	No (%)	**No (%)**
Present	9 (30)	7 (23.3)
Drowsiness	0 (0)	3 (10.0)
Dry mouth	0 (0)	3 (10.0)
Fatigue	7 (23.33)	0 (0)
Constipation	0 (0)	1 (3.33)
Bradycardia	2 (6.67)	0 (0)

DISCUSSION

Figure 3: Reduction in headache induced disability at the end of 3 months from baseline.

When compared to the amitriptyline group at three months, propranolol substantially decreased the frequency of headaches (51.6% vs. 43.6%, P=0.03) and the quantity of rescue drugs (53.1% vs. 43.3%, p=0.01). The propranolol group had a considerably higher percentage of respondents with ≥50% improvement than the amitriptyline group (60% vs. 43.3%, p=0.02). There aren't many research in the literature that compare propranolol and amitriptyline side by side for migraine prevention. The majority of these research were carried out between 1980 and 1995. At the end of six months, 62% of patients on propranolol and 42% of patients on amitriptyline showed improvement in the 1980 Texas trial. In this trial, 50–75 mg of amitriptyline and 120–160 mg of propranolol were administered daily.9 The effectiveness of lower doses in our research might be attributed to genetics, a different metabolic rate, or the smaller body shape of Indians. A recent study comparing the safety and effectiveness of propranolol (80 mg/day) vs amitriptyline (50 mg/day) for migraine prevention in Dhaka, Bangladesh, found a substantial decrease in headache frequency after three months. After three months, amitriptyline substantially decreased headache attacks compared to propranolol (71.24% vs. 63.87%, p=0.0001). The amitriptyline group had significantly more side effects than the propranolol group, although they were still minor.Ten Over a 12-week period, both propranolol and amitriptyline were shown to be safe and well tolerated. The side effects were minor and didn't need a change in therapy. When compared to earlier research, these were comparable.Ten Higher dosages of propranolol and amitriptyline were associated with increased adverse effects in certain trials.11–13 This is the first study in an Indian population sample that demonstrates that low doses of amitriptyline (10 mg/day) and propranolol (80 mg/day) significantly reduce headache frequency, severity, and disability and have a better safety profile than higher doses in patients with episodic migraine.

The study's open label design, limited sample size, and brief follow-up period were its limitations. Because of

Due to methodological limitations, blinding the research was not possible. To draw firm conclusions about the results, a bigger sample size is needed, and a longer follow-up period might provide more insightful findings.

CONCLUSION

Propranolol seems to be more beneficial than amitriptyline in individuals with episodic migraine, despite the fact that both medications are similar, safe, and efficacious.

financing: No sources of financing No declared conflicts of interest

Ethical approval: The Institutional Ethics Committee gave its clearance to the project.

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