Original Article

Comparison of the efficacy of propranolol versus amitriptyline as monotherapy for prophylaxis of migraine

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Abstract

Background: Approximately 15% of migraine sufferers need preventative medicine because they have more than two episodes each month. Migraine is a regular, persistent condition that frequently makes victims helpless. Numerous drugs from various classes have so far been used in migraine prophylaxis. Their effectiveness is recurrently overshadowed by their side effects because they must be used for a long time, which occasionally necessitates stopping the drug. **Materials and Methods:** In the tertiary care teaching hospital's department of medicine, a prospective, comparative, open-label study was initiated. Two groups of 80 patients were randomly chosen. For 3 months, the 40 patients in Group A were given a tablet of amitriptyline 10 mg once daily, whereas the 40 patients in Group B were given a tablet of propranolol 20 mg once a day. At the conclusion of the fourth, eighth, and twelfth weeks, the patients' own self-assessment migraine diary and a 4-point pain scale were used to grade the intensity of the headaches. **Results:** As a result, in Group A, the mean migraine attack severity in periods 1 and 2 was 5.88 2.69 and 5.41 2.48, respectively. In Group B, the mean was 5.15 2.75 in period 1 and 5.66 2.78 in period 2, respectively. The average length of a migraine attack in Group A was 20.30 5.61 h in period 1 and 16.75 5.23 h in period 2. In Group B, the mean was 16.59 3.21 in period 1 and 18.78 5.14 in period 2. Between groups A and B, there was a statistically significant difference. **Conclusion:** The average number of migraine attacks reduced in the amitriptyline and propranolol groups as the treatment duration increased. Amitriptyline is a popular medication with established effectiveness and manageable levels of negative side effects. It is the tricyclic antidepressant that is most frequently used to prevent headaches. When administered for migraine prevention, it generates a quick response within 3 months. Propranolol is less effective than amitriptyline at reducing the frequency, length, and severity of episodes.

Keywords: Amitriptyline, headache prevention, migraine, tricyclic antidepressants

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Introduction

A migraine, a neurologic disorder, typically causes a strong headache. The headache comes in spurts, and occasionally, it may also be accompanied by light sensitivity, nausea, and vomiting.[1]

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About 15% of migraine sufferers need preventative medicine because they have more than two episodes each month. Migraine is a regular, persistent condition that frequently makes victims helpless. Many different drugs from many different classes have been used in migraine prophylaxis thus far.[2] Their effectiveness is typically outweighed by their side effects because they need to be administered for a long time, which occasionally necessitates stopping the drug.[3]

It is critical to identify the frequency, length, and intensity of headaches as well as any potential triggers. To track the frequency, severity, and length of their headaches, all migraine patients should keep a headache diary.[4] It aids in locating any triggers that can result in a migraine headache. Environmental elements like noise and odor, pharmaceuticals like oral contraceptives, hormone replacement therapy (HRT), and histamine-2 (H2)-receptor blockers, dietary elements like cheese, wine, and chocolate, and behavioral elements like inadequate or excessive sleep are a few examples of typical triggers.[5] If triggers can be found and altered, preventive medication therapy might not be required.

The most popular and efficient first-line treatment for migraine prevention is propranolol.[6] The recommended dosage ranges from 40–320 mg per day. The therapeutic effects may not be felt for up to 12 weeks at a sufficient dose. Timolol, atenolol, and metoprolol are three more beta-blockers that may be employed.[7] Patients with underlying cardiovascular illness must take them into account. Fatigue, nausea, dizziness, poor exercise tolerance, and depression are typical adverse effects of this class of drugs. Heart blockages, severe bradycardia, peripheral vascular disease, and severe asthma are examples of contraindications.[8]

It has been proven that amitriptyline is helpful in preventing migraines. In headaches that include migraine and tension, it could be more beneficial than propranolol. Compared to beta-blockers, the response of therapy can be noticed in as little as 4 weeks. The dosage ranges from 25–150 mg per day. Venlafaxine is a different antidepressant that is probably useful in preventing migraines.[9,10] It works about as well as amitriptyline. The daily dosage is 150 mg. The prevention of migraines has also been treated with fluoxetine. Weight gain, sleepiness, dry mouth, and urine retention are typical adverse effects. Use in conjunction with monoamine oxidase inhibitors (MAOIs) is prohibited.[11] In order to treat migraine headaches, we evaluated the effectiveness and tolerability of propranolol and amitriptyline.

Materials and Methods

The tertiary care teaching hospital's department of medicine began a prospective, comparative, open-label research. The research comprised a total of 80 participants with a diagnosis of migraine. Patients having a history of (H/O) episodes without aura for at least 6 months, both genders. The study required 2–6 episodes per month, pain-free intervals of at least 48 h between 2 attacks prior to assessment, and the capacity to complete a headache diary. The study excluded participants who were younger than 15 or who were unable to complete the headache diary.

A thorough history was obtained, detailing the present, past, family, and food, and a thorough and systematic evaluation was performed. Everyone who participated gave their free and informed permission. Eighty patients were divided into two groups at random. Group A: Over the course of 3 months, 40 people received amitriptyline 10 mg pills. For 3 months, 40 patients in Group B got a tablet of propranolol 20 mg once daily at night. Participants' self-assessment migraine diaries and a 4-point pain scale were used to determine the severity of their migraines at the end of the fourth, eighth, and twelfth weeks. On a scale of 0 to 3, the absence of pain was represented by a score of 0, slight discomfort by 1, moderate discomfort by 2, and severe discomfort by 3. Self-assessment by the patient: Pain was rated as mild if it did not interfere with daily activities, moderate if it did but did not require bed rest, and severe if it did and did.

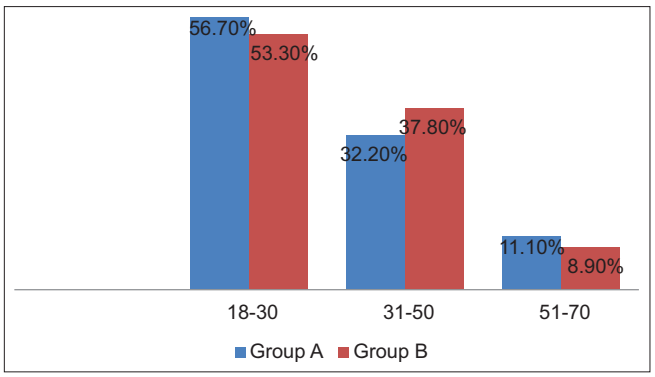
Data entry and analysis

Microsoft Excel 2021 was used to enter the data. The data was analyzed using Microsoft Excel 2021 and Statistical Package for the Social Sciences (SPSS) version 25. Both descriptive and inferential statistical methods were used in the current investigation. For continuous data, the results were presented as mean, standard deviation (SD), and range (Min–Max), and for categorical measurements as the number (%). A 5% limit was used to define the significance level. For continuous variables, the Student *t*-test was employed to compare the intergroup variance.

Results

The majority of patients in both groups were between the ages of 18 and 30, whereas the minority of patients were between the ages of 51 and 70. Patients in Group A had a mean age of 33.49 ± 11.41, while those in Group B had a mean age of 32.33 ± 11.84. The mean age of patients in groups 1 and 2 did not differ statistically significantly from one another.

In our study, in Group A: 18-30 years were 56.70% and Group B were 53.30%. Moreover, in Group A: 31-50 years were 32.20%



Graph 1: Comparison between two groups of age

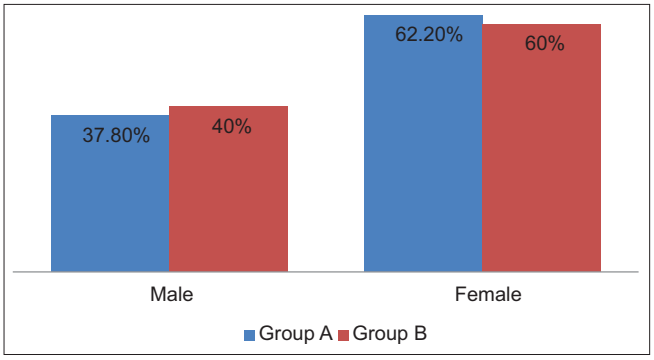
and Group B were 37.80%. In addition, in Group A: 51-70 years were 11.10% and Group B were 8.90%. [Graph 1]

Graph 2 shows that 160 people with migraines in Group A: 56 patients were female (62.2%) compared to 34 male (37.8%) individuals. Thirty-six male patients (40%) and 54 female patients (60%) made up Group B. When we used the Chi-square test, there was no statistically significant difference between the number of patients in Group A and Group B ($P = 0.225$).

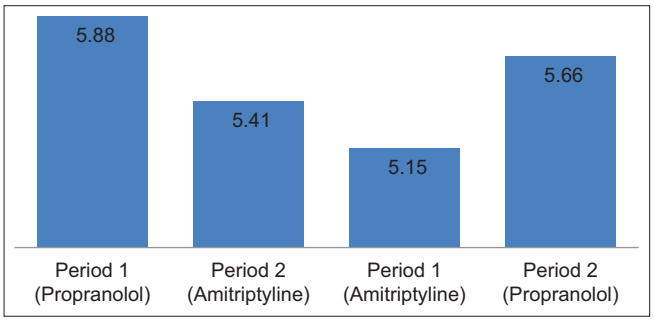
According to Graph 3, For Group A, the mean number of assaults each session was 7.73, with an SD of 4.19, and 7.14, with an SD of 2.99. Group B's mean and SD for periods 1 and 2 were 6.74 and 2.89, respectively, and 7.71 and 4.18, respectively. A statistically significant difference between groups 1 and 2 was found using the unpaired *t*-test ($P = 0.024$).

In Graph 4, in Group A, across periods 1 and 2, the mean migraine episode intensity was 5.88 with an SD of 2.69 and 5.41 with an SD of 2.48. For Group B, the mean and SD for periods 1 and 2 were 5.15 and 2.75 and 5.66 and 2.78, respectively. The unpaired *t*-test revealed a statistically significant difference between groups 1 and 2 between them ($P = 0.044$).

According to Graph 5, the average length of a migraine attack in Group A was 20.30 h with an SD of 5.61 in period 1 and 16.75 h with an SD of 5.23 in period 2. Group B's mean for periods 1 and 2 was 16.59 h with an SD of 3.21 and 18.78 h with an SD of 5.14, respectively. A statistically significant difference between groups 1 and 2 was found using the unpaired *t*-test ($P = 0.030$).



Graph 2: Distribution of gender between two group

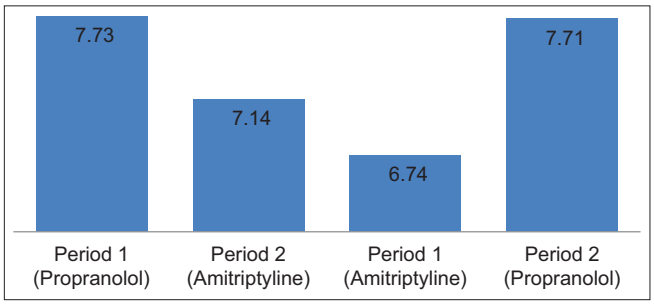


Graph 4: Comparison between two groups for severity of attack of migraine

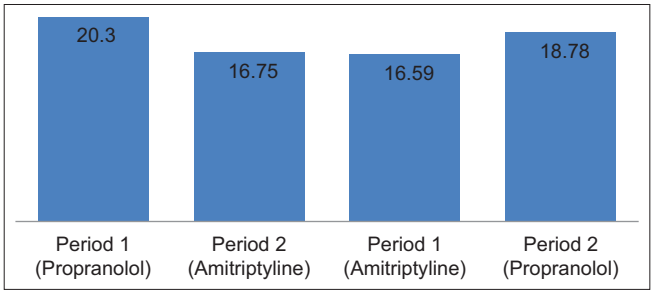
Discussion

Migraines are usually seen in females, often preceded by aura, nausea, vomiting, photophobia, or phonophobia. The pain usually lasts for 2–3 days. It is often presented as a pulsating, unilateral, disabling pain. The identified triggers for acute migraine attacks are increasing amount of stress, irregular menstrual cycle, and loss of appetite. The auras that precede migraine attacks are often visual and presented as dark, bright spots in the central vision, that is, scintillating scotoma. The sensory auras include tingling in the limb or face and rarely affect the speech. The physiology behind pain in the Migraine attacks is due to the activation of cranial nerve V, that is, trigeminal nerve, leading to the irritation of the meninges and also the release of vasoactive neuropeptides like substance P, neurokinin A, and calcitonin gene-related peptide (CGRP).

According to Verspeelt[12] (1994), migraine is one of the most prevalent incapacitating illnesses that places a special, severe burden on the quality of life. Such incapacitating headaches frequently require immediate pain relief. Prophylaxis may be necessary if the frequency, intensity, or length of these headache episodes increases. Prophylactic treatment is also justified by the requirement for frequent acute pain medicines. One of the first-line medications, amitriptyline, has a track record of effectiveness and manageable levels of side effects. It is the tricyclic antidepressant that is most frequently used to prevent headaches.[13] When administered for migraine



Graph 3: Distribution of frequency of attack of migraine between two groups



Graph 5: Comparison between two groups for the duration of attack of migraine

prevention, it generates a quick response within 4 weeks.[14] The lowest amitriptyline dosage that is still effective is still up for debate. In this study, the effectiveness of amitriptyline at two different doses — 5 mg and 10 mg — was examined throughout a 3-month follow-up period. The findings from the present investigation confirm the finding of Evers S.[15] that migraine prophylaxis may be regarded as helpful if migraine episodes are decreased by at least 50% during a 3-month follow-up period.

A study by Couch[16] contrasting amitriptyline 25 mg medication with a placebo showed that amitriptyline had a better response, with a reduction in headache frequency after 16 weeks (46% vs. 9%, $P = 0.043$) and at 8th weeks (25% vs. 5%, $P = 0.031$), respectively, of 50%. The response rates to amitriptyline were significantly different from placebo ($P = 0.05$), in a controlled experiment including 100 participants.[17] In their meta-analysis of 37 trials, Steiner *et al.*[1] (2013) found that tricyclic antidepressants were more effective over time at preventing migraine attacks than selective serotonin reuptake inhibitors. Amitriptyline was shown to be more efficacious than propranolol and cyproheptadine in 50–60% of instances, according to Martelletti[2] (2013), who conducted a crossover trial. According to Oldenmenger *et al.*[18] (2013), amitriptyline improved approximately 80% of migraine sufferers. However, Cady *et al.*[19] (2011) found that the data on the efficacy of amitriptyline in the treatment of migraine prevention was insufficient after reviewing 166 articles on the topic.

In this trial, two therapy groups with 41 patients each were randomly allocated to 80 consecutive patients. For 3 months, amitriptyline was administered orally in two groups: Group A received 10 mg, while Group B received 5 mg.

At the conclusion of the 3-month follow-up, the headache scores among patients in either group, as measured by a 0–10 numeric pain rating scale, showed a substantial improvement. However, in terms of how severe the attacks were, those in Group A had better headache control.

According to the 9-point Physician Global Assessment Response to Treatment (PGART) scale, the overall improvement in migraine symptoms was scored. Both groups had notable reductions in migraine-related symptoms as well as an improvement in overall well-being. Patients in the 10 mg amitriptyline group, however, experienced better overall symptom management. It was noted that there was a statistically significant difference between the groups.

Couch[20] evaluated the prophylaxis effectiveness of 50 mg of amitriptyline compared to 25 mg of the same drug in lowering the number of migraine attacks per day in an open-label, 6-month prospective research. At 3 or 6 months of follow-up, the researchers were unable to find a statistically significant difference between the two groups. Amitriptyline usually has unpleasant side effects, including sleepiness, gaining weight, dry mouth, a metallic taste in the tongue, and epigastric pain. Amitriptyline's rare adverse effects include constipation, tachycardia, palpitations, impaired vision, urine retention, and orthostatic hypotension.[21] Because of the modest dose used for migraine prophylaxis, the aforementioned side effects are often acceptable. Three participants in Group A and one participant in Group B both exhibited epigastric discomfort. In Group A, one patient experienced nausea. In every case, the observed ill effects were momentary and went away on their own. None of these patients needed their amitriptyline treatment to be stopped. Both groups of patients reported sedation in every case. Given that the majority of these patients had a history of insomnia before starting medication, it was found to be desired in all cases. By lowering sleep latency, amitriptyline helps with migraine-related insomnia.[22]

Conclusion

Migraine, one of the most common incapacitating disorders worldwide, reduces one's quality of life. In the amitriptyline and propranolol groups, the mean number of migraine episodes decreased as the duration of the treatment regimen increased. Amitriptyline is a popular medication with established effectiveness and manageable levels of negative side effects. It is the tricyclic antidepressant that is most frequently used to prevent headaches. When administered for migraine prevention, it generates a quick response within 3 months. Propranolol is less effective than amitriptyline at diminishing the frequency, length, and severity of episodes.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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