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Original Article

TO EVALUATE THE EFFICACY, SAFETY AND TOLERABILITY OF ORAL PROPRANOLOL COMPARISON WITH ORAL AMITRIPTYLINE FOR MIGRAINE PROPHYLAXIS

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ABSTRACT

Objective: Treatment of migraine is both therapeutic and prophylactic. Prophylactic therapy is used to prevent further attacks. Amitriptyline and Propranolol are the most commonly used drugs for prophylactic therapy. The main objective of the study is to compare the efficacy, safety, and tolerability of Amitriptyline and Propranolol.

Methods: A Prospective, Comparative, open-label study was taken up in the department of neurology, Osmania General Hospital, Hyderabad. 80 patients were randomly allocated into two groups. GROUP A with 40 patients received Tab. Amitriptyline 10 mg once daily, GROUP B with 40 patients received Tab. Propranolol 20 mg once daily at night for a period of 3 mo. The severity of the headache was measured by a 4-point pain scale and patients self–assessment migraine diary at the end of the 4th, 8th, and 12th weeks to assess treatment efficacy.

Results: The mean number of attacks in the Amitriptyline and Propranolol group decreased as the duration of treatment increased. The decrease was markedly significant in the Amitriptyline group. There was a significant reduction in the severity of attacks among the Amitriptyline group (P=<0.0000001).

Conclusion: In this study, the mean number of migraine attacks in the Amitriptyline and the Propranolol group decreased as the duration of treatment increased. The decrease was markedly significant in the Amitriptyline group. Thus, Amitriptyline is more effective in decreasing Amitriptyline is more effective than Propranolol in decreasing the number, duration, and severity of attacks.

Keywords: Migraine, Amitriptyline, Propranolol, Migraine prophylaxis

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INTRODUCTION

Migraine is a type of headache and can cause severe throbbing pain or a pulsating sensation, usually on one side of the head. It's often accompanied by nausea, vomiting, sensitivity to light (photophobia), sound (phonophobia), and blurred vision [1]. Migraine is characterized by recurrent headaches present with aura or without aura [2]. Migraine attacks can last for hours–days and the pain can be severe that it interferes with daily activities.

Migraine can affect every aspect of a patient's life, including work, school, job and social activities. Person with migraine may not be able to participate in family roles and responsibilities; this can affect everything from daily household activities and impact every family member. The moderate-severe attack has a negative effect on the quality of life, including physical, social and emotional aspects of daily life such as family, work, and social relationships. An attack may cause the development of psychological disorders like depression, anxiety and bipolar.

The causes include genetic and environmental factors [3], and imbalance in the neurotransmitters of the brain, especially serotonin and calcitonin gene-related peptides (CGRP). The triggers that may act as inciting agents of migraine are hormonal changes in women, drinking and stress, sleep changes or disturbances, some medications, and foods. The risk factors include family history and female gender [4].

Treatment of migraine is both therapeutic and prophylactic [5]. Treatment is used during the attack and prophylactic therapy is used to prevent further attacks. Patients with frequent attacks and/or severe attacks of migraine need therapy for a longer duration of time [6]. The most commonly used drugs for this purpose are Amitriptyline (tricyclic antidepressants), topiramate, valproate anticonvulsants and, methysergide (serotonergic drugs) [7, 8].

Amitriptyline and Propranolol are the most commonly used drugs for prophylactic therapy. Many studies have compared the efficacy of above-said drugs in combination with other drugs. The present study was taken up to compare the efficacy of Amitriptyline over Propranolol when used as immunotherapy. The objective of the study was to evaluate efficacy in terms of reduction in frequency, duration and severity of migraine attacks and to compare adverse drug reactions between 2 groups.

MATERIALS AND METHODS

A prospective, comparative, open-label study was taken up in the department of neurology, Osmania General Hospital, Hyderabad. A total of 80 patients who were diagnosed with migraine were included in the study. Patients in the age group of 15-60 y, both genders with H/O of attack without aura for at least 6months, with 2-6 attacks/month, with pain-free intervals of at least 48 h in between 2 attacks before evaluation, and who can fill headache diary were included in the study. Children of age less than 15 y and who cannot fill the headache dairy were excluded from the study.

A detailed history, including present, past, family and diet history, was taken and a general and systemic examination was done. Informed consent was obtained from all participants. 80 patients were randomly allocated into 2 groups.

GROUP A: 40 patients received Tab. Amitriptyline 10 mg once daily at night for a period of 3 mo.

GROUP B: 40 patients received Tab. Propranolol 20 mg once daily at night for a period of 3 mo.

The severity of headache was measured by a 4-point pain scale and patients' self–assessment migraine diary at the end of the 4th, 8th, and 12th weeks to assess treatment efficacy. A 4-point pain scale was used–0 for no pain, 1 for mild pain, 2 for moderate pain, and 3 for severe pain.

Patient self-assessment: It was categorized as mild if pain without consequences on normal activity, moderate if the pain is restricting normal activity without the need to go to, bed, and severe if the pain is preventing activity and requires bed rest.

Data entry and analysis

The data were entered in Microsoft Excel 2010 version. Data were analyzed using Microsoft Excel 2010 and Epi Info 7.2.0. Descriptive and inferential statistical analyses were used in the present study. Results on continuous measurements were presented on mean±SD [Min-Max] and results on categorical measurements were presented in Number [%]. Significance was assessed at a 5% level of significance. Student T-test was used to compare the inter-group variation for continuous variables.

Ethical clearance

Ethical clearance was obtained from the Institutional Ethical Committee, Department of Pharmacology, Osmania Medical College, Koti, Hyderabad bearing the number Ref. No. IEC/OMC/2021/M. No(02)/Acad-22

RESULTS AND DISCUSSION

The age and gender distribution of the study population are given below:

Table 1: Shows the age distribution of the study population

Age group	Amitriptyline	Percentage	Propranolol	Percentage
20-29 y	0	0	10	25
30-39 y	8	20	24	60
40-49 y	22	55	4	10
50 and above	10	25	2	5
Total	40	100	40	100

Among the Amitriptyline group, 55% belonged to the age group of 40-49 y, 25% belonged to the age group of 50 and above and 20% belonged to the age group of 30-39 y.

Among the Propranolol group, 60% belonged to the 30-39 y, 25% belonged to the 20-29 y, 10% belonged to the 40-49 y and 5% belonged to the age>50 y.

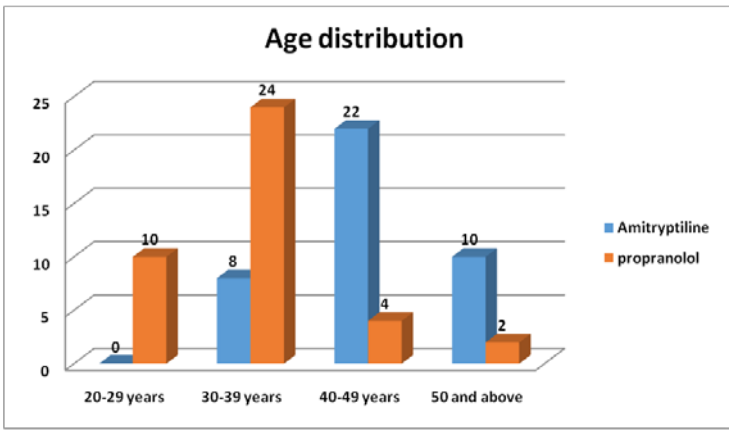

Fig. 1: Showing the age distribution

Table 2: Showing the gender distribution

Gender	Amitriptyline	Percentage	Propranolol	Percentage
Male	16	40	20	50
Female	24	60	20	50
Total	40	100	40	100

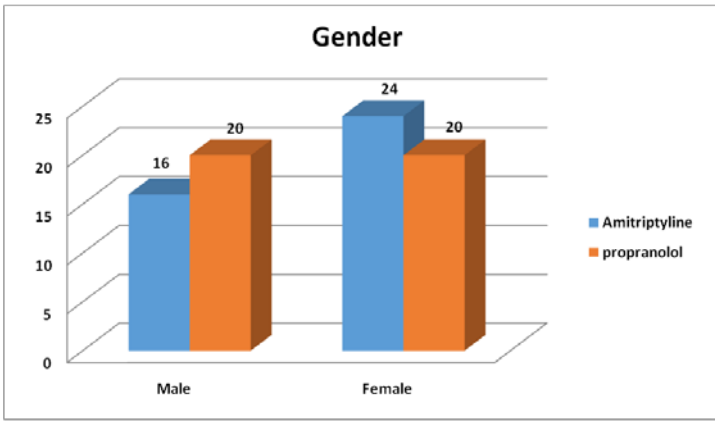

Fig. 2: Showing the gender distribution

Table 3: Showing the number of attacks

No. of attacks	4 w	P value	8 w	P value	12 w	P value
Amitriptyline	2.45±1.05	0.02*	0.95±0.94	0.003*	0.05±0.22	<0.0000001*
Propranolol	2.95±0.94		1.5±0.64		0.8±0.64	

The mean no. of attacks in the Amitriptyline and the Propranolol group decreased as the duration of treatment increased. The decrease was markedly significant in the Amitriptyline group. Thus, Amitriptyline is more effective in decreasing the number of attacks and severity of attacks among migraine patients when compared to propranolol.

Table 4: Shows the severity of attacks among the Amitriptyline group

Severity	4 w	Percentage	8 w	Percentage	12 w	Percentage
No	2	5	18	45	38	95
Mild	16	40	22	55	2	5
Moderate	22	55	0	0	0	0
Total	40	100	40	100	40	100

P=<0.0000001 (Statistically significant P value)

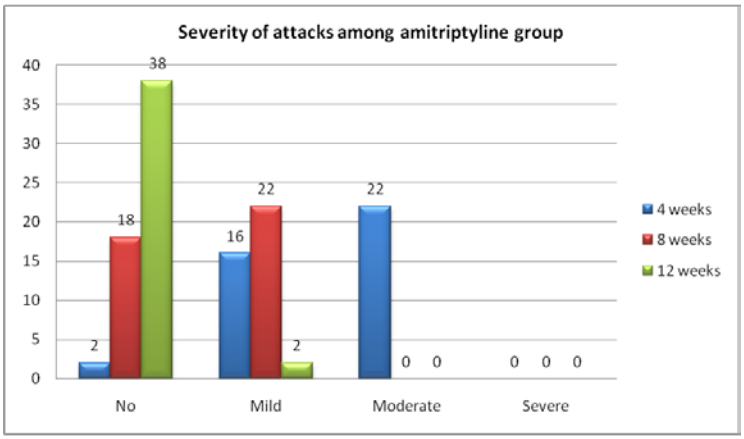

Fig. 3: Showing the severity of attacks among the amitriptyline group

Table 5: Showing the severity of attacks among the propranolol group

Severity	4 w	Percentage	8 w	Percentage	12 w	Percentage
No	12	30	8	20	8	20
Mild	18	45	20	50	22	55
Moderate	10	25	12	30	10	25
Total	40	100	40	100	40	100

P=0.77

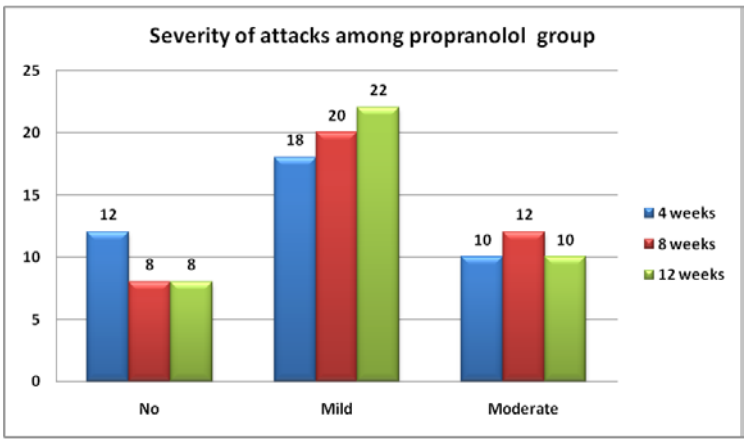

Fig. 4: Shows the severity of attacks among the propranolol group

Table 6: Shows the duration of attacks in minutes

No. of attacks	4 w	P value	8 w	P value	12 w	P value
Amitriptyline	10.5±4.55	<0.0000001*	3±2.99	<0.0000001*	0.25±1.11	<0.0000001*
Propranolol	12.95±6.55		11.86±7.42		10.99±6.46	

The mean duration of attacks in the Amitriptyline group decreased as the duration of treatment increased. The decrease was markedly significant in the Amitriptyline group. The decrease was only marginal in the Propranolol group. Thus, Amitriptyline is more effective in decreasing the number of attacks and severity among migraine patients when compared to propranolol.

Table 7: Shows the nature of ADR observed in the study

Type of ADR	Amitriptyline	Percentage	Propranolol	Percentage
Nausea and vomiting	8	20	6	15
Tremors	0	0	4	10
None	32	80	30	75
Total	40	100	40	100

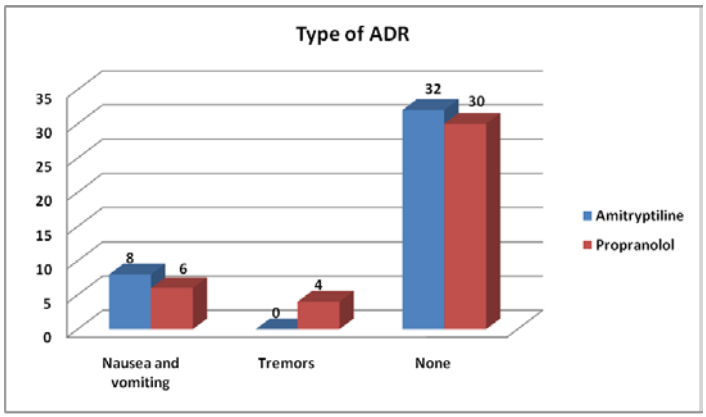

Fig. 5: Showing the type of ADR

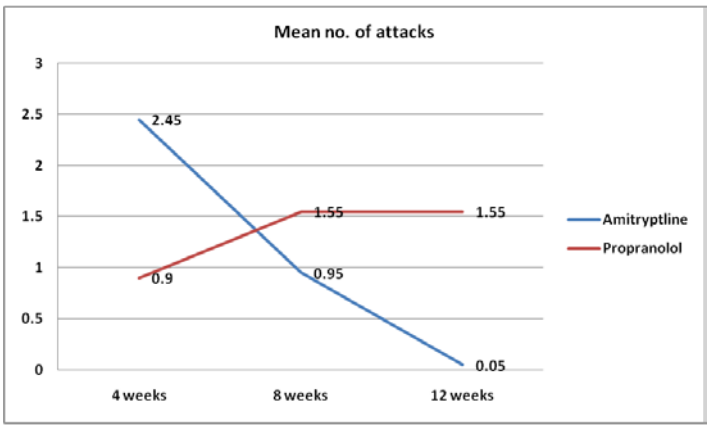

Fig. 6: Showing the mean VAS score among the groups

DISCUSSION

The present prospective, comparative, open-label study was taken up in the department of neurology, Osmania General Hospital, Hyderabad, to evaluate the efficacy, safety, and tolerability of Amitriptyline over Propranolol for migraine prophylaxis.

In the present study, Among the Amitriptyline group, 55% belonged to the age group of 40-49 y, 25% belonged to the age group of 50 and above and 20% belonged to the age group of 30-39 y. Among the propranolol group, 60% belonged to the 30-39 y, 25% belonged to 20-29 y, 10% belonged to 40-49 y and 5% belonged to the age>50 y. The findings of the present study can be compared with the following studies. In the study done by Ismail MA *et al.* [9] In group A, 16-25 age group were 24 (60.0%), 26-35 age group were 14 (35.0%), 36 and above age group were 2 (5.0%). In group B, 16-25 age group were 20 (50.0%), 26-35 age group were 15 (37.5%), 36 and above age group were 5 (12.5%).

In the present study, the mean number of attacks in the Amitriptyline and the Propranolol group decreased as the duration of treatment increased. The decrease was markedly significant in the Amitriptyline group. Thus, Amitriptyline is more effective in decreasing the number of attacks and severity among migraine patients when compared to propranolol.

The findings were similar to the study done by Ismail MA *et al.* [9], where the mean number of attacks of headache decreased significantly in the Amitriptyline Group.

The findings of the present study can be compared with Ismail MA *et al.* [9]. Were in group A, the duration of pain was 1 to 4 h 1 (2.5.0%), 5

to 8 h 16(13.3%) 9 to 12 h 14(35.0%). Above 13 h 9(22.5%) In group B, the duration of pain from 1 to 4 h 1(2.5), 5 to 8 h 16(13.3%), 9 to 12 h 19(47.5), and above 13 h 4(10.0). The difference was not statistically significant. The duration of pain in the final follow-up was recorded among the patients. In group A, duration of pain 1 to 4 h 24 (60.0%), 5 to 8 h 14 (35.0%), 9 to 12 h 2 (5.0%). In group B, duration of pain 1 to 4 h 20 (50.0%), 5 to 8 h 15 (37.5%), 9 to 12 h 12 (30.0%). The difference was not statistically significant.

In the present study, the severity of attacks decreased significantly in the Amitriptyline group than in the Propranolol group.

In the present study, among the Amitriptyline group, 20% had nausea and vomiting. Among the Propranolol group, 15% had nausea, and vomiting and 10% developed tremors.

The findings of the present study can be compared to Ismail MA *et al.* [9], wherein in group A, no adverse effect was found 26 (65.0%), drowsiness 6 (15.0%), dryness of mouth 6 (15.0%), constipation 2 (5.0%). In group B, no adverse effect was found 29 (72.5%), drowsiness, dryness of mouth, and constipation were not found, fatigue and bradycardia were 7 (17.5%) and 4 (10.0%).

According to Osterhaus JT [10], Migraine is one of the most common disabling disorders worldwide, which compromises the quality of life. Amitriptyline is one of the frontline drugs [11, 12] with proven efficacy and acceptable levels of adverse drug effects. It is the most commonly used tricyclic antidepressant for headache prevention [13]. It produces a rapid response within four weeks when used for prophylaxis of migraine [14]. There is no consensus about the lowest effective dosage of Amitriptyline.

Srinish G *et al.* [15], proved that Amitriptyline at a dose of 10 mg is more efficacious than that at 5 mg in controlling headache and the associated symptoms of Migraine. A minimum dose of 10 mg may be safely used without any increased risk of adverse effects.

A comparison of Amitriptyline 25 mg therapy with placebo by Couch JR *et al.* [16] reported a superior response to Amitriptyline, with an improvement in frequency of headache ≥of50% at eight weeks (25% vs. 5%, p= 0.031) and 16 w (46% vs. 9%, p=0.043).

A controlled trial involving 100 patients determined that the difference between Amitriptyline and placebo response rates was significant [17].

Levinstein B, in a crossover study, reported amitriptyline to be effective in 50%-60% of cases compared with propranolol and cyproheptadine [18].

CONCLUSION

Migraine is one of the most common disabling conditions in the world, which undermines quality of life; the mean number of migraine attacks in the Amitriptyline and the Propranolol group decreased as the duration of treatment increased. Amitriptyline is one of the leading drugs with proven efficacy and acceptable levels of adverse drug effects. It is the most commonly used tricyclic antidepressant for headache prevention. It produces a rapid response within four weeks when used for prophylaxis of migraine. Amitriptyline is more effective than propranolol in decreasing the number, duration, and severity of attacks with significant P values.

LIMITATIONS OF THE STUDY

It is an open-labeled prospective study and hence results cannot be generalized to the entire population. Randomized control trials with larger sample sizes should be taken up to prove the efficacy of one drug over the other.

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AUTHORS CONTRIBUTIONS

All authors have made significant contributions to writing the manuscript, reviewing and editing, and submission.

CONFLICTS OF INTERESTS

None declared

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