The Effectiveness between Propanolol and Flunarizine in Migraine Treatment

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Abstract	Original Research Article

Objective: In this study our main goal is to evaluate the effectiveness between propanolol and flunarizine in migraine treatment. *Methods:* This randomized single blind cross over clinical trial was conducted at Department of Pharmacology, Dhaka medical college, Dhaka from July 2016 to June 2017. During the study, adult 64 migraine sufferers (without aura) attending in the Out Patient Department of neurology (Headache clinic), Dhaka Medical College Hospital, Dhaka. All data were recorded systematically in data collection form. One half of the samples were randomly allocated for group A and the other half to group B. Group A: 32 patients will be allocated for the prophylaxis of propranolol. Group B: 32 patients will be allocated for the prophylaxis of flunarizine. *Results:* During the study, the different commonest sites of the headache of both groups. Other than both temple and right back of the scalp, all presenting sites of headache of both groups showed statistically non-significant differences. The most common presenting site of both groups were behind the right eye, behind the left eye, right temple, left temple, back of the scalp on right and left and back of scalp on both sides. Factors Stress (50% vs. 53.12%), bright light (75% vs. 75%), loud noise (68.75% vs. 71.87%), and weather change (40.62% vs. 34.37%), were the most common precipitating factors of both groups. *Conclusion:* From our study we can say that, Migraine is a disabling and costly disorder. There is no cure, but preventive treatment to decrease the number and severity of headache attacks improves health outcomes and quality of life. The patients who received Propranolol had better outcome than those who were under flunarizine both in 1st and 2nd phase the trial. Further study is needed for better outcome.
Keywords: Flunarizine, migraine, propranolol.

INTRODUCTION

The word migraine is French in origin and comes from the Greek hemicranias, as does the old English term megrim. Literally, hemicranias means "half (the) head ", which reflects the long history of the disease [1].

Epidemiological studies have documented its high prevalence and high socio-economic and personal impacts. In the Global Burden of Disease Survey 2010, it was ranked as the third most prevalent disorder and seventh-highest specific cause of disability worldwide [2].

It is usually an episodic headache associated with certain features such as sensitivity to light, sound, or movement; nausea and vomiting [1].

Migraine frequency is divided into episodic and chronic [2]. Episodic migraine is characterized by <15 migraine days and chronic migraine by ≥15 headache days per month. Sometimes migraine may be described as chronic simply because the attacks recur over long periods of time. Chronic migraine affects 1.4 to 2.2 percent of adults [3]. All migraine types significantly affect the physical, psychological, and social well-being of patients, and can impose serious lifestyle restrictions. Each year lost work time and diminished productivity from migraine costs American employers about 225.8 bilion[4].

Propanolol and flunarizine are two most common drugs used in the prophylaxis treatment. Both drugs are cheap, easily available and have well defined side effects which can be easily studied.

In this study our main goal is to evaluate the effectiveness between propanolol and flunarizine in migraine treatment.

OBJECTIVE

General objective
- To estimate the effectiveness between propanolol and flunarizine in migraine treatment.

Type of study	Randomized single blind cross over clinical trial.
Place of study	Department of Pharmacology, Dhaka medical college, Dhaka.
Study period	July 2016 to June 2017.
Study population	Adult 64 migraine sufferers (without aura) attending in the Out Patient Department of neurology (Headache clinic), Dhaka Medical College Hospital, Dhaka.
Sampling technique	Purposive

INCLUSION CRITERIA
- Migraine attacks occurring more than twice a month.
- One attack a month with sufficient severity or disability (for pain or associated symptoms) to warrant the cost and inconvenience of daily medication.

METHOD
- In this study, one half of the samples were randomly allocated for group a and the other half to group B. Group A: 32 patients will be allocated for the prophylaxis of propranolol. Group B: 32 patients will be allocated for the prophylaxis of flunarizine. Data was collect at the Out Patient Department of Neurology (headache clinic), Dhaka Medical College Hospital, and Dhaka. The samples were interviewed with a questionnaire. Pain intensity was assessed with a pain scale. All patients gave their informed consent before entering the study and the protocol of this study was approved by Local Ethical Committee of Dhaka Medical College. Each patient had a complete physical and neurological examination before the study.Patient suffering from migraine without aura according to International Headache Society criteria were randomly assigned to treatment.

DATA ANALYSIS
- All data were recorded systematically in data collection form. Quantitative data were express as mean and standard deviation and qualitative data as frequency distribution and percentage. Data were edited prior to computer entry and analysis. Simple frequencies were calculated and multivariate analysis was done using SPSS software to determine the relationship among the different variables.

Specific objective
- To detect respondent's migraine headache
- To identify precipitating factors

METHODOLOGY

RESULTS

In figure-1 shows distribution of the respondent's age by group where in group A 46.87% respondents were within 14 to 24 years age group which was followed by 31.25% within 25 to 34 years. In group B, 43.75% patients were within 15 to 24 years age group followed by 37.50% within 25 to 34 years. The following figure is given below in detail:
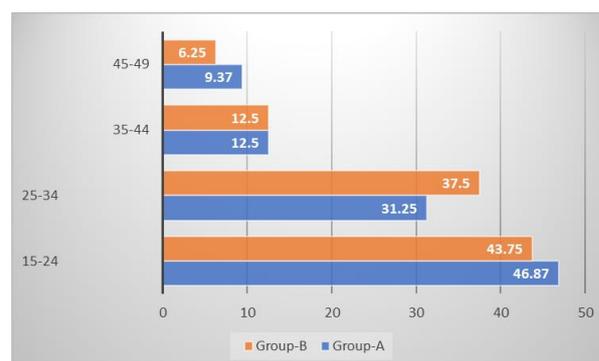

Fig-1: Distribution of the respondent's age by group.

In table-1 shows gender distribution of the patients were out of all patients of group A 37.50% were male and 62.50% were female (male: female= 1:1.66) and in group B were 34.37% were male and 65.62% were female (male: female=1: 1.90). The following figure is given below in detail:out of all patients of group A 37.50% were male and 62.50% were female (male: female= 1:1.66) and in group B were 34.37% were male and 65.62% were female (male: female=1: 1.90). The following table is given below in detail:

Table 1: Distribution of the respondent's gender by group

Gender	Group A (n=32)	Group B (n=32)
Male	12(37.50)	11(34.37)
Female	20(62.50)	21(65.62)

In figure-2 shows distribution of the respondent's educational level by group where the highest proportion (37.5%) of headache patients was found among the HSC in group A. In group B the highest proportion (31.25%) was observed among those who had HSC level education. The following figure is given below in detail:
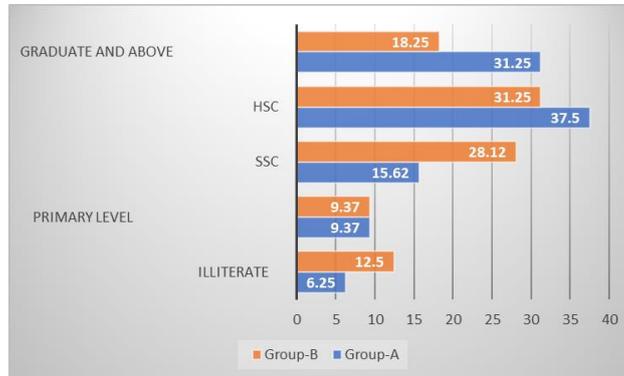

Fig-2: Distribution of the respondent's educational level by group

In table-2 shows distribution of the respondent's migraine headache usually located by group where the different commonest sites of the headache of both groups. Other than both temple and right back of the scalp, all presenting sites of headache of both groups showed statistically non-significant differences. The most common presenting site of both groups were behind the right eye, behind the left eye, right temple, left temple, back of the scalp on right and left and back of scalp on both sides. The following table is given below in detail:

Table-2: Distribution of the respondent's migraine headache usually located by group

Location of headache value*	Group A (n=32)	Group B (n=32)	P
Behind right eye	12(37.5)	16(50)	0.068
Behind left eye	14(43.75)	12(37.5)	0.218
Behind both eye	6(18.75)	5(15.62)	0.578
Right temple	13(40.62)	15(46.87)	0.315
Left temple	12(37.5)	10(31.25)	0.242
Both temple	6(18.75)	2(6.25)	0.009
Above right eyebrow	1(3.12)	2(6.25)	0.307
Above left eyebrow	1(3.12)	1(3.12)	0.561
Above both eyebrows	1(3.12)	1(3.12)	0.195
Back of the head on right	12(37.5)	17(53.12)	0.035
Back of the head on left	13(40.62)	12(37.5)	0.566
Back of the head on both sides	7(21.87)	4(12.5)	0.095

In table-3 shows distribution of the respondents by precipitating factors Stress (50%) vs. 53.12%), bright light (75% vs. 75%), loud noise (68.75% vs. 71.87%), and weather change (40.62% vs. 34.37%), were the most common precipitating factors of both groups. No statistically significant differences were observed in term of precipitating factors in both the groups. The following table is given below in detail:

Table-3: Distribution of the respondents by precipitating factors

Precipitating factors	Group A (n=32)	Group B (n=32)	P value*
Stress (worry, anger)	16 (50)	17 (53.12)	0.486
Bright light	24 (75)	24 (75)	0.872
Weather change	13 (40.62)	11(34.37)	0.311
Loud noise	22 (68.75)	23 (71.87)	0.647
Fatigue	1 (3.12)	2 (6.25)	1.000
Certain smells or perfume	5 (15.62)	3 (9.37)	
Missed meals	2 (6.25)	1 (3.12)	0.552
Sexual activity	1 (3.12)	0 (0)	1.000
Sleep disturbance	8 (25)	9 (28.12)	0.875
Journey	7 (21.87)	5 (15.62)	0.109

chi-square test was done to measure the level of significant.
Parenthesis indicated in column percentage.

In table-4 shows distribution of the respondent's by intake of drugs for relieve of acute attack of migraine where maximum patients of both groups were taken paracetamol, prochlorperazine, diazepam and cinnarizine as relieving medication for their migrainous pain. The following table is given below in detail:

Table-4: Distribution of the respondent's by intake of drugs for relieve of acute attack of migraine

Medicine	Group A (n=32)	Group B (n=32)
Paracetamol	24(75)	21(65.62)
Prochlorparazine	22(68.75)	23(71.87)
Indomethacin	1(3.12)	3(9.37)
Ibuprofen	4(12.5)	2(6.25)
Diclofenacsodium	2(6.25)	3(9.37)
Diazepam	18(56.25)	20(62.5)
Cinnarizine	24 (75)	21(65.62)
Aspirin	1(3.12)	2(6.25)

In table-5 shows distribution of percentage improvement 0f HUI score of both groups at 8 weeks of two phases where after receiving prophylaxis at the end of 1st and 2nd phase of trial. Significant improvement was observed in group A when they were under trial of propranolol. Similar observation was also elucidated in group B during 2nd phase of treatment when drug was crossed over. The following table is given below in detail:

Table-5: Distribution of percentage improvement 0f HUI score of both groups at 8 weeks of two phases

At 8 weeks	group A	group B	P value
1st phase	64.41	58.43	0.001
2nd phase	32.58	42.76	0.023

DISCUSSION

This clinical trial, single cross over study with a single blind randomized treatment sequence compared and evaluated the effects of Propranolol with that of flunarizine as prophylactic agent who had migraine without aura. Dose level ranged from 40 mg/day for Propranolol and 10 m/day for flunarizine.

Out of all patients of group a 37.5% were male and 62.5% were female and in group B 34.37% were male and 65.63% were female. In the present study a higher ratio of migraine was observed among females and the male – female ratio for group A was 1: 1.66 and for group B was 1: 1.90.

The commonest sites of the migrainous headache in the present study were behind eye, temple and back of the head. Similar findings were also observed by one study [4]. They found over 41% of the subjects had a unilateral onset of migraine headache of which slightly over half had an ocular location of pain at the onset and slightly over one-third had location of pain at the onset in the temporal region.

Stress, bright sunshine, loud noise and weather change were the most common precipitating factors of both groups found in the study. One study noted 62% of the subjects thought weather was a factor but only 51% were sensitive to weather changes [5]. In a Brazilian study 64% responded reported that emotional stress was the triggering factor [6]. Similar to our study another study reported that migraineurs have lower thresholds for light-induced discomfort, noise tolerance and olfactory sensitivity compared to the general population [8].

Most common relieving factors of both groups were rest, quiet and darkness and pressure over migraine area. Other study mentioned similar maneuvers including pressing and applying cold stimuli to the painful site, trying to sleep, changing posture, sitting or reclining in bed (using more pillows than usual to lay down), isolating themselves, using symptomatic medication, inducing vomiting, changing diet and becoming immobile during the attacks[9].

During baseline the mean HUI score in both the groups were almost the same, in Group An it was 0.50±0.11 and in Group B it was 0.53±0.11. After 8 weeks of prophylactic treatment the mean score reduced in both the groups, however, the reduction was more pronounced in group A and the difference of mean scores in Group A and Group B was statistically significant (p<0.001). After cross over during baseline the mean HUI score in both the groups were almost the same (mean scores in Group A and Group B were 0.33±0.13 and 0.35±0.11 respectively). After 8 weeks of prophylactic treatment during cross over the mean score reduced in both the groups, however, the reduction was more pronounced in group B, who received propanolol, and the difference of mean scores in Group A and Group B was statistically significant (p< 0.05). Significant improvement was observed in Group A when they were under trial of Propranolol. Similar observation was also elucidated in Group B during 2nd phase of treatment when drug was crossed over.

CONCLUSION

From our study we can say that, Migraine is a disabling and costly disorder. There is no cure, but preventive treatment to decrease the number and severity of headache attacks improves health outcomes and quality of life. The patients who received Propranolol had better outcome than those who were under flunarizine both in 1st and 2nd phase the trial. Further study is needed for better outcome.

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