

Comparison in the Affectivity of Riboflavin against Propranolol for Migraine Prophylaxis.

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ABSTRACT

Background: The objective of this study was to assess the efficacy of Riboflavin as a prophylactic agent for migraine in comparison to the established agent, a beta blocker, Propranolol. **Methods:** 120 patients were grouped randomly into 3 groups after taking demographic details. One group (Group I) was given 80mg/day of Propranolol, second group (Group II) was given 100mg/day riboflavin and the third group (Group III) was given placebo. Frequency and duration of headaches, Visual Analogue scale (VAS) and Migraine disability assessment (MIDAS) score were taken at base line of treatment and at 1st month, 3rd month and 6th month of follow up. **Results:** The mean age of the patients in the study was 35.1 years \pm 3.5 years. There was not much difference in the age of the patients and gender between the 3 groups. Neither was the incidence of family history in the three groups. The frequency of headaches reduced in one month from 3.9 to 3.1 with propranolol compared to riboflavin(3.8-3.2) but in the 3rd month and 6th month riboflavin showed a better effect than propranolol though propranolol was almost as effective (2.7 and 2.4 respectively). In the Riboflavin group, the duration of headaches reduced from 3.2 days at base line to 2.5 at the first month to 2 days in the 6th month, while in propranolol group, the reduction was from 3.1 at base line to 2.6 in the first month to 2 days in the 6th month. VAS and MIDAS were comparable in both the groups. There were more side effects like dizziness and fatigue in th Propranolol group while only orange coloured urine was the complication in the Riboflavin group. **Conclusion:** Riboflavin is comparable to Propranolol in the prophylaxis of migraine. Since it is cost effective as well as non toxic, it can be used instead of Propranolol which has quite a few side effects.

Keywords: MIDAS, Migraine, Propranolol, Riboflavin, VAS.

INTRODUCTION

Migraine is a neurological disorder which results in disability and impaired quality of life. This effects the normal physical activity and work related productivity.^[1-4] In the developed countries more than 11% of the people suffer from migraine.^[5,6] Many of these patients do not consult a doctor for treatment but use over the counter painkillers to reduce the pain. They also require bed rest further debilitating them and affective the life style.^[5]

However, migraines can often be successfully controlled by the avoidance of triggers, lifestyle changes, and abortive treatment.^[7] The goal of preventive medications is to help to reduce the frequency, severity and duration of headaches, thereby improving the quality of life. This also help them from excessive use of drugs and response of acute migraine to treatment.^[8]

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Beta blockers like propranolol was used for a long time for migraine prophylaxis.^[9] There were a few studies which compared propranolol to placebo and

were reported to be a very useful in migraine prophylaxis.^[10] The 2002 American Academy of Family Physicians–American Society of Internal Medicine guidelines for migraine prophylaxis identifies propranolol as one of the first line agents. The known side effects of this agent are fatigue, dizziness, insomnia and depression.^[9]

Riboflavin, a Vitamin B, also is very useful in preventing headaches especially in high doses. The basis for the use of riboflavin is its effect on the mitochondrial dysfunction which may e involved in migraine. One trial compared a high dose of vitamin B2 (400 mg) against placebo. A significant benefit was observed three and four months following initiation of treatment. Riboflavin is also cost effective with less toxicity and side effects.^[11-14]

There are very few studies performed on the affectivity of riboflavin as a useful preventive medicine for migraine especially in India. Thus, we have performed this study to compare the affectivity of riboflavin against beta blocker propranolol and placebo.

MATERIALS AND METHODS

This randomized control trial was conducted on patients with migraine at MNR Medical college over a period of two years.120 patients between the Ages 18–70 years with a history of migraine for > 1 year diagnosed according to the HIS criteria were included

into the study. All these patients were suffering from more than 2 attacks per month. Patients who were using other prophylactic medications for 3 months prior to the study, anemic, pregnant or lactating using of other vitamin supplements, alcoholics, or those patients with abnormal LFT/RFT were excluded from the study.

Informed consent was acquired from all patients. Those who refused to give informed consent were not included in the study. All patients were counseled regarding migraine preventive therapy and the importance of taking treatment for at least 3 months. The patients were assigned to three groups using randomized table.

The 3 groups consisted of 40 patients each. Group I consisted of patients taking tablet Propranolol 80mg once daily and Group II consisted of patients taking Tablet Riboflavin 100mg once daily, and Group III were given placebo once daily.

All the patients were given a diary where in they were instructed to record the number and duration of the attacks, severity of migraine headaches according to the visual analogue scale (VAS) and disability score using migraine disability questionnaire (MIDAS questionnaire). Detailed procedure of how

to maintain the diary was explained to all the patients. Follow up was done regularly at the end of 1st, 3rd and 6th month. During this time the migraine diary was checked for severity and compliance to the drug. Patients were allowed to use medication if needed to abort the migraine attacks. This was also noted in the diary.

RESULTS

The mean age of the patients in the study was 35.1 years ± 3.5 years. There was not much difference in the age of the patients and gender between the 3 groups. Neither was the incidence of family history in the three groups. The incidence was 27.5% in Propranolol (group I), 32.5% in Riboflavin (Group II) and 30% in placebo (Group III). The demographic details of the patients are given in Table 1. The type of migraine was similar between the two groups with majority of them diagnosed to have migraine without aura. Values of frequency, duration of headache, VAS (Visual analogue score) and MIDAS (Migraine disability score) were statistically similar in both the groups at base line [Table 2].

Table 1: General characteristics in patients

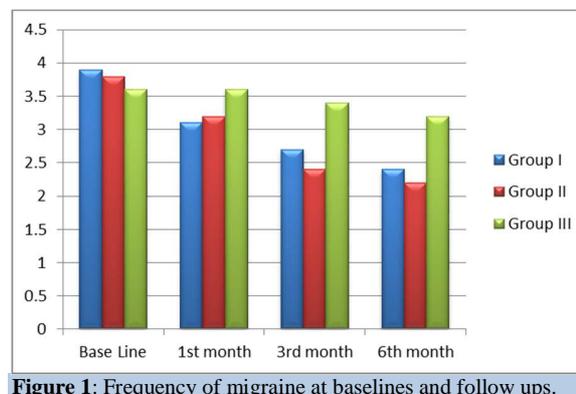
Particulars	Group I (Propranolol) N=40	Group II (Riboflavin) N=40	Group III (Placebo) N=40
Age	35.2 ± 4.2	33.8 ± 3.5	36.2 ± 2.7
Gender (M/F)	22/18	19/21	17/23
Family history	11 (27.5%)	13 (32.5%)	12 (30%)
Duration of Migraine (in years)	5.7 ± 1.2	6.1 ± 0.9	6.5 ± 1.5
Type of Migraine (with/without aura)	11/29	14/26	12/28

Table 2: Values of frequency, duration of headache, VAS and MIDAS scores

Parameters	Group I (Propranolol) n=40	Group II (Riboflavin) n=40	Group III (placebo) n=40
Frequency of attacks (no of times)	3.9 ± 1.3	3.8 ± 1.1	3.6 ± 1.3
Duration of attacks (in hours)	3.1 ± 0.4	3.2 ± 0.9	3.1 ± 0.7
MIDAS	6.2 ± 1.1	5.9 ± 1.7	5.8 ± 1.2
VAS	5.5 ± 1.3	5.1 ± 1.8	4.9 ± 1.2

The frequency of headaches reduced in one month with propranolol compared to riboflavin but in the 3rd month and 6th month riboflavin showed a better effect than propranolol though propranolol was almost as effective [Figure 1].

The duration of headaches also reduced considerably in both the groups, though there was no significant difference between the two groups. In the Riboflavin group, it reduced from 3.2 days at base line to 2.5 days in the 6th month, while in propranolol group, the reduction was from 3.1 at base line to 2.6 in the first month to 2 days in the 6th month [Figure 2].



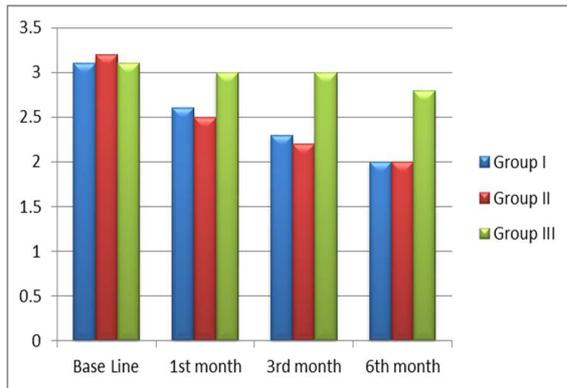


Figure 2: Duration of headaches at base line and follow ups

Similar results were seen in the visual analog score and migraine disability assessment score [Figure 3&4].

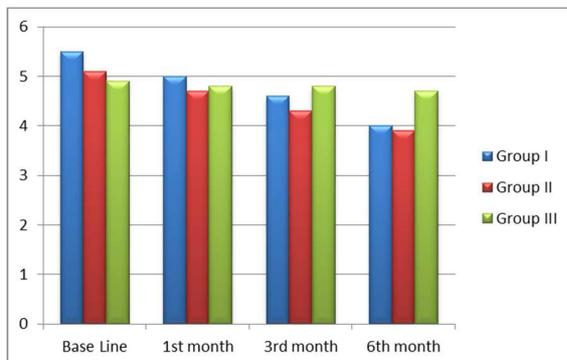


Figure 3: VAS at base line and follow ups

Among the side effects, 85% of the group II with riboflavin and 58 % of the propranolol group showed no side effects. The majority was dizziness followed by fatigue in the patients in propranolol group. In the riboflavin the most common side effect was orange discoloration of urine.

DISCUSSION

Mitochondrial dysfunction resulting in impaired oxygen metabolism is said to pay an important role in migraine patients.^[14,15] Migraine can be a common feature in patients affected with mitochondrial encephalo-myopathy, lactic acidosis and stroke like symptoms. Since riboflavin is a precursor to flavin mononucleotide and flavin adenine dinucleotide, which are involved in electron transport chain, given in high doses might increase the mitochondrial activity.^[16,17]

Beta blockers like propranolol have been established as effective agents for migraine. In the recent years, evidence that brain stem and cortical dysfunction is

involved in the patho-physiology of migraine. Modified neuronal excitability may be one explanation for preventive pharmacological effects.

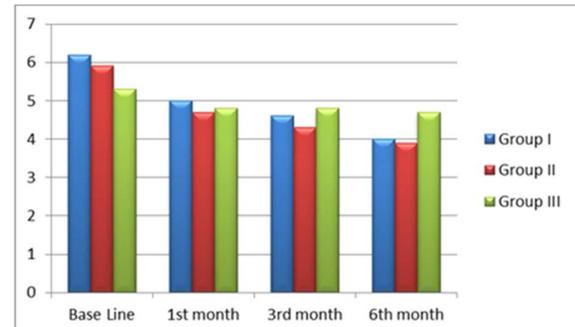


Figure 4: MIDAS at base line and follow ups

The goal of any preventive therapy is to successfully prevent the disease and improve the quality of life of a patient. The prophylaxis for migraine concentrates on not only improving the quality of life but also reducing the frequency, severity and duration, and increasing the responsiveness of migraines to treatment. Therefore, the prophylactic drugs should have a very high level of effectiveness and a low level of toxicity and side effects. The dosage should be low initially and slowly increased over period of time. Normally the duration of therapy would be between 2–6 months depending on the severity¹². The therapy can be discontinued if there is a reduction in the duration and frequency to over 50% for 6-12 months.^[8,13]

In our study we could demonstrate the prophylactic effect of riboflavin which was comparable to the beta blocker Propranolol. There was a significant reduction of frequency of the episodes from nearly 4 at baseline to a little over 3 in the first month in both the groups, though the decrease with propranolol was higher. But thereafter, there was a better decrease in the number of attacks per month with riboflavin group, though propranolol was not far behind with the number of attacks reducing from nearly 4 to less around 3 in the first month and consequently to less than 3 in the 6th month.

This was in concordance with a similar study by Nambiar et al wherein 100 patients in 2 groups were treated with Riboflavin and propranolol. It was found that 100mg/dl of riboflavin was comparable to 80 mg/dl of propranolol in its affectivity against migraine.^[18] Propranolol showed a faster effect than the riboflavin group in the first month. Sandor et al in yet another study on 26 patients, reported that there was considerable clinical improvement with both treatments. In patients in the riboflavin group demonstrated a reduction from 3.5 to 1.7 attacks/month.^[19]

In an open pilot study by Schoenen et al, it was observed that riboflavin was superior to placebo when given at 400mg/day, as with our study.^[11]

There was a significant decrease in the duration of attacks with both riboflavin as well as propranolol in the 1st, 3rd as well as 6th month. There was no significant difference in the severity and duration reduction between riboflavin and propranolol group. This reduction in the intensity of migraine was observed by Boenkhe et al, although it did not reach the significance levels but in a study by Condo et al, there was a significant decrease in the intensity of the headaches.^[20,21]

Similar results were seen in VAS and MIDAS scores. There was a considerable reduction in the two scores in both the groups compared to placebo, where no significant change was observed. The reduction was rapid in the first month but thereto slow till the 6th month.

There was considerable side effects seen in the propranolol group with dizziness and fatigue in more than half of the patients while in the riboflavin group, the most common side effect was orange colored urine. Only one patient suffered from diarrhoea, but this could not be positively attributed to riboflavin.

Sandor et al reported that although majority of the patients showed clinical improvement, the beta-blockers and riboflavin act on two distinct pathophysiological mechanisms.^[19] Therefore, combining both treatments is expected to enhance their efficacy without increasing central nervous system side effects.

CONCLUSION

We conclude that Riboflavin is comparable to Propranolol in the prophylaxis of migraine. Since it is cost effective as well as non toxic, it can be used instead of Propranolol which has quite a few side effects.

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