The Prophylactic Activity of Propranol and Nimodipine on Migraine Headache

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Abstract: Different groups of drug are used for prevention of migraine headaches. However, there are controversies about the efficacy of these drugs. Furthermore, the priority of one to other group is not clear. This study was designed to compare the effects of propranol and nimodipine on severity, duration and frequency of migraine headache. In a randomized clinical trial (RCT), prospective, single blind study, 102 patients with migraine without aura who met the criteria of ICH 2004 entered the study. Patients were randomly divided in two groups, receiving propranol 40 mg/daily and nimodipine 30 mg/daily for 6 month. Data was collected by a questionnaire. Patients were asked to record the severity, duration and frequency of their migraine attacks. Data analysed using t-test and P<0.05 was considered as significant. Results: The duration and severity of migraine attacks in propranol group were less Conclusion: Propranol seems to be more effective than nimodipine in prevention of migraine headache.

Key word: Headache, Migraine, Nimodipine, Propranol

INTRODUCTION

The prevalence of migraine is high; migraine attacks affect 17% of women and 6% of men each year; most common in those aged 30 to 39 [1, 2]. Migraine illness is defined by several episodes of pulsatile headaches, uni / bi-lateral, accompanied or preceded by signs of central and autonomic nervous system dysfunction [3]. Its social and economic repercussions are serious, while considered benign, it can lead to non negligible social and professional handicap [4]. Migraine cause severe impairment or bed rest in more than half (57%) of affected people; impairs quality of life both during and between attacks [5-7].

A number of groups of medications are used for the prophylactic treatment of migraine. Propranolol, non selective B-blocker, which crosses the blood-brain barrier exerting central as well as peripheral effects and been used for migraine prophylaxis since the 1966, when its effectiveness in migraine headache in patients being treated for angina pectoris was proved [8]. Calcium-channel blockers as prophylaxis in migraine headache is another choice, because reduction in cerebral blood flow during the initial phase of migraine symptoms leads to ischemia and hypoxia, result in calcium overload and cellular dysfunction, because calcium-channel blocker selectively inhibit the intracellular influx of calcium ions. The efficacy of these agents for migraine prophylaxis were evaluated [9]. Preventive medications appear to be a cost-effective approach to the management of migraine in the primary care setting compared with the approach of abortive treatment only [10].

MATERIAL AND METHODS

In a randomized clinical trial (RCT), prospective, single-blind study, 102 patients with migraine without aura aged from 20 to 60 who met the defined criteria of ICH 2004 (recurrent headache disorder manifestating in attacks lasting 4-72 hours, with 2 of the following characteristics, unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and /or photophobia and phonophobia) entered the study. Exclusion criteria were diagnosis of probable medication overuse headache according to the international classification of headache disorder criteria, a pain disorder.
other than migraine as the primary presenting problem, 20 or more days with headache a month, contraindication or sensitivity to any study drug, current use of migraine preventive drugs, current physiological treatment, psychiatric disorder needing immediate or priority treatment and inability to read and understand the study materials; for women, current or planned breast feeding or pregnancy or unwillingness to use an established contraceptive method were also exclusion criteria. At the first blosh of study, the frequency, severity and duration of headache and also response to rescue medications were recorded for a period of 4 weeks before initiation of drug prophylaxis and randomly patients were divided into 2 groups of A and B, receiving propranolol and nimodipine, respectively. The patients received prophylaxis for at least 6 months. Participants were evaluated by using a detailed questionnaire including feature of headaches (frequency, duration and intensity of attacks) and general health characteristics. Headache severity was scored on a 1-3 point scale with 1 presenting no effect on daily activity, 2 for partial inhibition of daily activity and 3 for loss of daily activities. Responses to rescue medications 2h after taking an agent of acute therapy, was scored on a 1-4 point scale as clinical impression of effect: 1 for ineffective, 2 for somewhat effective, 3 for effective and 4 for very effective. The drug is considered effective as a prophylactic agent in migraine headache if it could reduce more than 50% the baseline headache frequency per month. Paired sample T test, Z-test and chi-square have been used in statistical analysis. Value of p<0.05 in Z and T test and values of p<0.01 in chi-square were considered significant.

**RESULTS**

A total of 102 patients, 17 men and 85 women, completed the full prophylaxis period. 2 cases of group A were lost to follow up. 83.3% of patients were women and mean average ages was 47. In both groups, demographic characteristics and pre-treatment frequency and intensity had no significant differences.

Propranolol’s side effects like hypotension, cardiac block, bronchospasm and bradycardia were observed in 15% of patients and nimodipine side effects such as hypotension and GI complication were also observed in 17% of patients. Fortunately occasional minor side effects fairly were tolerated by both groups and withdrawal of treatment was not required in any cases due to drug side effects.

### Table 1: To compare numbers, severity, duration of migraine attacks in 2 groups

<table>
<thead>
<tr>
<th>Attack Characteristics</th>
<th>Drug</th>
<th>Numbers</th>
<th>Duration (hours)</th>
<th>Severity (0-5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Propranol</td>
<td>7.03±2.4</td>
<td>13±2.7</td>
<td>1.5±2.1</td>
</tr>
<tr>
<td></td>
<td>Nimodipine</td>
<td>7.11±2.4</td>
<td>17±2.6</td>
<td>2.6±2.3</td>
</tr>
</tbody>
</table>

The mean headache frequency per 6 month was reduced from 15 to 7.03+/-2.4 and 7.11+/-2.4 in group A and group B respectively. (Table 1). Propranolol could reduce more than 50% the baseline headache frequency in 74% of group A patients.

Using paired sample T test with p value <0.05 showed that propranolol and nimodipine both were effective as a preventive migraine prophylaxis.

69% of group A patients showed reduction in headache duration and 50% of them had less severe headache at least for one grade after prophylactic pharmacotherapy with propranolol; these criterias were 32% and 25% in group B respectively.

Further more 21.% of group A became headache free and recorded no pain in their calendar after prophylaxis preventive medication.

**CONCLUSION**

Pharmacological preventive treatment of migraine and chronic migraine is a major challenge. Using paired sample T test with p value <0.05 showed that propranolol and nimodipine both were effective as a preventive migraine prophylaxis. Propranolol showed efficacy in reducing headache duration, severity and better response to medication (chi square with p value <0.01). Although there was statistically significant difference in duration and severity of attacks between group A & B, headache frequency was approximately similar in both groups.

Diener *et al.* study showed that properanol 160 mg daily and also topiramat reduced frequency, severity and duration of migraine attacks [11-13].

In another study, propranol has a effect like pizotifen in reducing the frequency of migraine attacks [14].

Andersson *et al* studies showed that $\beta$-blocker like propranolol and metoprolol reduced frequency of migraine headache. Its effects appeared after 4 weeks of treatment and augmented by increasing the duration of treatment. Calcium channel blocker (CCB) like flunarizin also reduced the frequency of attacks but its effect on reducing severity and duration of headache is unknown [15, 16].

Several studies on the prophylactic effect of nimodipine against migraine headache showed that its effect appears in the short period of time and by discontinuing nimodipine, its effects disappear [17, 18].
While propranol has long-term effect against migraine attacks after discontinuing [19], there are many studies supported the efficacy of propranol as prophylaxis for migraine. In addition to reduce headache frequency as the major effect of a drug used for migraine preventive pharmacotherapy, both of these drugs have shown significant improvement in the severity and duration of headache as well as better response to reduce medications. While in our study propranol seems to be more effective than nimodipine in prevention of migraine headache.

REFERENCES


