A comparative Study between Cyproheptadine and Amitriptyline in the Treatment of Tension Type Headache

The objective of this prospective study of patients with Tension Type Headache in Neurology Clinic in a tertiary referral hospital in Nepal was to compare the efficacy of the drug Cyproheptadine with Amitriptyline in the treatment prophylaxis of Tension Type Headache.

Of the total 66 cases selected for the study, 32 cases were randomly selected to be treated with the antihistamine Cyproheptadine, and 34 were randomly assigned to be treated with tricyclic antidepressant Amitriptyline.

In the Cyproheptadine group, a significant improvement of headache was seen in 25%, mild improvement in 38%, and no improvement in 38%. In the Tension Type Headache group treated with the Amitriptyline, a comparable result of significant improvement was seen in 24%, mild improvement seen in 42%, and 35% showed no change.

In the treatment of tension type headache, Cyproheptadine is comparable to Amitriptyline in terms of efficacy.

Key words: Amitriptyline, Cyproheptadine, Tension Type Headache

Amitriptyline is a commonly used drug for the prophylaxis of Tension Type Headache. Cyproheptadine is relatively less commonly used. Cyproheptadine has been mostly used for prophylaxis for cluster headache. In this study, we have used Cyproheptadine alone as prophylactic treatment for Tension Type Headache in order to see its efficacy; and efforts have been made for comparison with the frequently used tricyclic antidepressant (Amitriptyline) with a view of using Cyproheptadine as the first line preventive therapy, especially since it is a much safer drug.

Materials and Methods

In all patients with headache presenting to the Out Patient Department, secondary headache was excluded by taking detailed history, examination, ENT and dental examination (in selected cases). X ray PNS and CT scan head were done in selected cases. Routine investigations were done in all cases.

All the patients presenting with primary headache were short listed in the Tension Type Headache category if they fulfilled the criteria of Tension Type Headache.

The patients selected were then randomly assigned into two groups. The first group (32 patients) was given Cyproheptadine 4 mg daily; the second group (34 patients) was given Amitriptyline 25 mg daily.

Headache intensity was graded and categorized into 1 to 10. For example, grade 10 was considered to be the worst and the most severe headache for the patient.

Significant improvement was considered to be improvement of 5 grades or more. Improvement less than 5 grades were considered to be mild improvement.

Follow up cases was done at not less than 2 weeks apart. The data analysis was done using SPSS 13.0 version.

The results were displayed in percentages. Significant differences between the two groups were tested with Chi-Square tests or Fisher’s Exact test whichever applicable. The difference was considered significant if p- value was <0.05.
Female patients were disproportionately high (70%) in both groups). The majority (64%) of the patients were in the prime of their life—11-30 years. And 90% of the patients were seen to be between 11 years and 50 years.

It was also noted that the majority of the patients had duration of headache between 13 months and 5 years (42%). Nearly 80% of the patients had headache ranging between four months to five years.

Nearly a quarter of the patients showed significant improvement in their headache after treatment; and nearly 65% showed some improvement after treatment. Both the patients taking Cyproheptadine and Amitriptyline were comparable.

It was noted that the longer the duration of headache, the poorer the response with the drugs.

Discussion

Many studies show that the prevalence of TTH (Tension Type Headache) is more than 70%. But the lifetime prevalence of any primary headache is seen to be even more – 90% in men and 95% in women.

We observe that the prevalence of TTH is disproportionately large in the females (70%); and this is true in all primary headaches where females outnumber males.

TTH catches mostly in the prime of their youth – 65% in 11-30 years. This emphasizes the need in preventing the headache as it can be a loss of huge number of working hours in youth.

Medical help is sought only when the headache becomes sufficiently frequent and chronic to interfere with the patients’ lifestyle. We see in our study that most of the patients — (36%) — present only after four months and within one year of headache.

For prophylaxis of TTH, Amitriptyline in the dose of 5-150 mg a day has been seen to be most effective. We have used 25 mg which is a much smaller dose; this dose seems adequate in patients of our region as seen in one of my previous study as well.

Cyproheptadine has been used mostly for cluster headache; and a very few study exists in which this drug was used for TTH. I had showed in my previous study that Cyproheptadine with Propanolol is equally effective preventive measure compared to Amitriptyline 25 mg daily. Here we have gone a further step to use Cyproheptadine 4 mg alone and showed that it is equally effective and a combination with Propanolol my not really be required, after all. There are other studies which show botulinium toxin and muscle relaxant Baclofen as preventive drugs; but both of these drugs are complex and the former is very expensive requiring subcutaneous injection and possibly also hospitalization.

Most TTH respond well when treated within one year of onset of headache—more than 70% response as seen in this study.

Our study to use Cyproheptadine alone in 4 mg daily doses is efficacious in prevention of TTH and in all respects, comparable to using Amitriptyline 25 mg a day.

In some patients presenting with severe headache, Sodium Valproate 200 mg was given for 10 days along with Naproxen 250-500 mg(SOS) together with Cyproheptadine or Amitriptyline 25 mg daily. Subsequently, Sodium Valproate was stopped (after 10-15 days) and Cyproheptadine or Amitriptyline was continued; and the study completed accordingly.

Conclusions

Cyproheptadine even when used alone in 4 mg daily is effective in preventing TTH; and it is comparable to Amitriptyline 25 mg a day. Since Cyproheptadine is cheap with minimal side effects, Cyproheptadine 4 mg a

<table>
<thead>
<tr>
<th>Drug</th>
<th>&lt; 3 months</th>
<th>4 months-1 yr</th>
<th>13 months to 5yrs</th>
<th>&gt; 5 yrs</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyproheptadine</td>
<td>2</td>
<td>10</td>
<td>20</td>
<td>0</td>
<td>32</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>6</td>
<td>14</td>
<td>28 (42%)</td>
<td>6 (9%)</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>8(12%)</td>
<td>24(36%)</td>
<td>28 (42%)</td>
<td>6(9%)</td>
<td>66(100%)</td>
</tr>
</tbody>
</table>

P Value: 0.522

Table 2. Duration of Headache

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number (Cyproheptadine)</th>
<th>Number (Amitriptyline)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>8</td>
<td>12</td>
<td>20(30%)</td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
<td>22</td>
<td>46(70%)</td>
</tr>
<tr>
<td>Grand Total</td>
<td>32</td>
<td>34</td>
<td>66(100%)</td>
</tr>
</tbody>
</table>
day may be used as the first line drug for prevention of TTH in the developing countries.

Acknowledgements
We thank Dr. Avinav Baidya, Lecturer, Department of Preventive and Social Medicine for help in statistical analysis.

References
10. Freitag FG: Preventative treatment for migraine and tension-type headaches: do drugs having effects on muscle spasm and tone have a role? CNS Drugs 17: 378-81, 2003

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Significant improvement (&gt;50%)</th>
<th>Mild improvement (&lt;50%)</th>
<th>Total improvement</th>
<th>No Change</th>
<th>Worse</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyproheptadine</td>
<td>8(25%)</td>
<td>12 (37.5%)</td>
<td>20(63%)</td>
<td>12(37.5%)</td>
<td>0</td>
<td>32</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>8(23.5%)</td>
<td>14(42%)</td>
<td>22(65%)</td>
<td>12(35%)</td>
<td>0</td>
<td>34</td>
</tr>
<tr>
<td>Grand Total</td>
<td>16(24%)</td>
<td>26(39%)</td>
<td>42(64%)</td>
<td>24(36.3%)</td>
<td>0</td>
<td>66</td>
</tr>
</tbody>
</table>

P Value 0.782. Majority (65%) improve on treatment

Table 3. Improvement gradation.