Original Investigations

Lithium Carbonate in the Treatment of Cluster Headaches

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Summary. Twenty-one patients with cluster headaches participated in an open trial to assess the effectiveness of lithium carbonate in the acute treatment and prevention of cluster headaches. Three women and 18 men ranging from 28 to 70 years of age were divided into episodic cluster [8] and chronic cluster [12]. One patient was in his first cluster. The chronic cluster group was further subdivided into primary chronic (5 patients) and secondary chronic (5 patients). In 11 patients there was absolute improvement, in 5 patients there was partial improvement and in 5 patients there was either no response or the improvement was not sustained. Beneficial results were obtained with dosages lower than those used for effective treatment of bipolar illness. It appears that lithium can be a useful drug in the treatment of cluster headaches provided drug levels and renal function are carefully monitored. No serious side effects were noted.

Key words: Lithium carbonate – Cluster headaches – Migraine.

Prompted by the success of lithium in the treatment of manic-depressive illness and by the fact that cluster headaches also have a cyclic, recurrent pattern, Ekbom used lithium in cluster headaches, and noted its effectiveness [1]. Later Kudrow obtained similar results [2, 3] but suggested that the usefulness of lithium was possibly limited to the chronic type of cluster headaches. More recently Mathew [4] found the substance to be effective both in chronic and episodic types of cluster headaches. Stimulated by those reports we thought it would be useful to attempt further replication of such results and to address the following questions: (1) Is lithium effective only for treatment of the acute cluster, or does it also act as a preventative agent? (2) Are the characteristics of the cluster headache patient identifiable for those who will respond positively to the drug? (3) What dosages can be recommended, on a preliminary basis, and (4) what side-effects should be sought? Considering the severity of pain in cluster headache, a double-blind study was not considered justifiable and an open design was chosen. The following is a report on the results obtained in a preliminary series of 21 patients.

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Materials and Methods

Patients were selected for the study if they presented during a cluster period, and if they either had not been treated previously, or had been treated unsuccessfully and were refractory to other medications. Patients in whom lithium was potentially contraindicated were not included. No patient with known renal, cardiovascular or thyroid dysfunction was treated with this preparation. Preliminary study of the patients included a comprehensive medical and neurological examination as well as routine haematological and biochemical investigations.

The trial was started in 1977 and since then 21 patients have been entered, 19 men and 3 women, with ages ranging from 25 to 70 years. Patients were classified as episodic cluster if they had clear periods of remission between periods of typical cluster headaches, and chronic cluster, if there were no periods of complete remission. The latter group was further subdivided into primary chronic cluster, if the patient had been in a continuous cluster since the first headache appeared, and secondary chronic cluster, if the patient experienced at least one period of complete remission since the first manifestation of the syndrome and if, at the time of classification, the duration of the cluster had clearly exceeded the one previously experienced.

The classification of subjects conformed to the definition of cluster headaches of the World Federation of Neurology [5] and to Ekbom's [6] definition of chronic clusters. Seven patients had primary chronic clusters, 5 had secondary chronic clusters and the remaining 9 had episodic cluster headaches. One patient was in his first cluster. Patients were experiencing typical cluster headaches when the medication was started and were on no other preventive medication during the period of trial.

Lithium was started at 300 mg/day and titrated at a rate of 300 mg every week, provided side effects were absent and blood levels of lithium were not in the toxic range, up to a dosage which produced improvement. However, since no side effects were noted in the first three patients with the initial dosage, it was decided to use 600 mg per day as the initial dosage, increasing by 300 mg each week, as permitted by side effects and indicated by the clinical response.

The results of the intervention were noted as follows: (1) absolute success, if the cluster was interrupted and the patient became symptom free; (b) partial success, if the patient did not become symptom free but experienced a marked decrease in both the frequency and severity of individual headaches and judged them to be at a tolerable level; (c) therapeutic failure, if no improvement was achieved or if, after an initial improvement, the headaches recurred while on the medication and failed to be further affected by it. Improvement was also classified as immediate or delayed, the latter if more than one week elapsed before maximal effect was achieved.

Results

Sixteen patients improved, 2 had to discontinue the medication because of side effects and 5 were unchanged. In the improved group, 11 were absolute successes and 5 were partial. The 5 failures included 3 patients who noted initial

<table>
<thead>
<tr>
<th>Cluster Headache Type</th>
<th>Absolute Improvement</th>
<th>Partial Improvement</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Secondary</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 1. Outcome of trial according to cluster headache type