Nebulized sodium cromoglycate in young asthmatic children

Double-blind trial

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SUMMARY Seventeen asthmatic children under 5 years of age took part in a double-blind controlled trial of nebulized sodium cromoglycate solution. Daily symptom scores kept by the parents showed improvement in 11 children during active treatment, and a significant improvement in scores for cough by day and night was obtained for the group as a whole.

Sodium cromoglycate is now well established as an effective prophylactic in childhood asthma (Silverman et al., 1972). It is unusual, however, for a child under 5 years of age to be able to use the spinhaler efficiently. This problem can be overcome by administering the drug as a nebulized mist which the child inhales from a face mask. Short reports from Australia (Gale, 1972; Williams and Phelan, 1973; Phelan, 1974) indicate that the regular inhalation of a solution of sodium cromoglycate, made by dissolving the contents of a capsule in water or saline, can be effective in reducing the frequency and severity of wheezing episodes in children between 1 and 4 years of age. Orciprenaline was usually added to the solution to be inhaled. The encouraging response of a few patients treated in this way led us to undertake a double-blind trial of nebulized sodium cromoglycate solution, without added bronchodilators, in a group of young children with frequent troublesome asthma despite the difficulty of objective assessment in this age group.

Patients
Seventeen children (14 boys, 3 girls) took part in the trial. Mean age at the start of the trial was 3 years 5 months (range 2 years 3 months–4 years 6 months). All had frequent troublesome asthma which had led to hospital admission in 16 cases; 6 children had been admitted five or more times, despite treatment with oral salbutamol 2 mg tds (15 patients) or orciprenaline 10 mg tds (2 patients), which was given regularly if the child had persistent symptoms. Those over 3 years of age had tried to use a spinhaler but without success, despite practice at home.

The age of onset of wheezing ranged from 1 month to 2·5 years, 9 children starting under 1 year of age. Known precipitating factors included upper respiratory tract infections 17, exercise 15, excitement and upset 10, and contact with specific allergens 7. 11 of 13 children tested had positive prick tests which were usually multiple (mite 10, house dust 7, dog/cat 7, grass 6). 10 children had eczema and 6 allergic rhinitis. There was a family history of asthma, eczema, or hay fever in 15 cases.

Methods

Trial. The trial was double blind and involved 2 months' treatment with sodium cromoglycate and 2 months' placebo, in random order according to a predetermined design, after a one-week 'trial run' using placebo solution. Sodium cromoglycate was given as Intal nebulizer solution (20 mg in 2 ml). The contents of one 2 ml ampoule was given by inhalation three times a day, using a Pari nebulizer and face mask. The placebo preparation was packed in identical ampoules, which were coded by the manufacturers, and was given in the same dosage. Bronchodilators could be given in addition as required.

Assessment. The mother of each child completed a daily record card of the child's symptoms (wheeze and cough) both by day and by night. Possible scores for wheezing ranged from 1 (‘terrible’) to 6 (‘very well’), and for cough from 1 (frequent, distressing) to 4 (none). Bronchodilator dosage was also recorded.
The children were seen every 4 weeks, when a clinical assessment was made and peak flow was measured wherever possible, using a Junior Wright peak flow meter. Statistical analysis was applied to the diary card symptom scores, use of bronchodilators, peak flow measurements, and parents’ preferences. To avoid carry-over effects the symptom totals for the second month of each treatment period were compared.

Results

All the children completed the trial. The parents had no problem using the nebulizer, and the children accepted this form of treatment very well though some found it tedious. It took about 10 minutes to give each inhalation, and the child could watch television or be read a story while it was given.

Eleven children had higher symptom scores (i.e. fewer symptoms) on active treatment, 5 on placebo, and 1 showed no difference. A carry-over effect of sodium cromoglycate into the placebo period was not apparent in most records but there seemed to be a tendency for the scores on the drug to improve over the first 7 to 10 days. For the group as a whole, a significant difference was found in the scores for cough but not for wheezing, comparing the second month of each treatment period (Table).

<table>
<thead>
<tr>
<th></th>
<th>Mean 28-day totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sodium cromoglycate</td>
</tr>
<tr>
<td>Night</td>
<td></td>
</tr>
<tr>
<td>Wheeze</td>
<td>157</td>
</tr>
<tr>
<td>Cough</td>
<td>100</td>
</tr>
<tr>
<td>Day</td>
<td></td>
</tr>
<tr>
<td>Wheeze</td>
<td>153</td>
</tr>
<tr>
<td>Cough</td>
<td>98</td>
</tr>
<tr>
<td>Maximum scores possible  (i.e. no symptoms):</td>
<td>Wheeze 168</td>
</tr>
</tbody>
</table>

No significant difference was found in oral bronchodilator usage in the different treatment periods, but the 5 children on salbutamol by inhalation all needed fewer doses when on sodium cromoglycate. 10 patients had antibiotics during the trial and 4 required one or more short courses of steroids. Peak flow measurements were obtained in 13 patients at the end of each treatment period. The mean (±SD) value at the end of the period on sodium cromoglycate was 100 (±22) and 96 (±34) at the end of the placebo period. This difference is not significant.

Eleven parents thought that the child was better during the period on the drug, 4 during the placebo period, and 2 had no preference. In 6 cases their preference was not in fact supported by the symptom scores.

Discussion

We have shown that sodium cromoglycate can be given effectively by nebulization to young children, and that this is a practical method of treatment though its widespread use will be limited by the availability of cheap nebulizing systems.

It is interesting that a significant improvement was seen in symptom scores for cough rather than wheeze. Cough is often the symptom which parents complain of most, especially at night, whereas wheezing will only be appreciated when it is noisy or limiting the child’s activity. Some parents commented on improvement in the child’s general well-being while on sodium cromoglycate, perhaps because of better nights. Objective assessment by regular peak flow measurements at home would have given more useful information than monthly measurements, but was impractical in these young children. The increase in peak flow was small after active treatment and did not reach significance, but isolated readings are of limited value in the assessment of asthma. Asthma in young children can be a frightening condition for both child and parents and we felt that the nebulizer itself had a strong placebo effect as many of the children had fewer symptoms during the whole of the trial period than in the preceding few months.

References


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