

## Oral Sodium Cromoglycate in Chronic Urticaria

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Fifteen patients were included in a double-blind cross-over trial to investigate the efficacy of oral sodium cromoglycate in the treatment of chronic urticaria. Only patients with positive oral provocation tests were entered into the study. The challenging agents were food additives or antirheumatic agents. Treatments were taken for 4 weeks and the dose of sodium cromoglycate was 200 mg four times daily. No significant differences were found between active and placebo treatment periods for diary card symptom scores. Six patients preferred the active treatment, two preferred placebo and seven had no preference. The clinician showed no preference for either treatment.

*Key words:* chronic urticaria; sodium cromoglycate

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Sodium cromoglycate (SCG) is now recognized as an effective drug in the treatment of allergic asthma, allergic rhinitis, and allergic conjunctivitis. The most important mode of action is supposed to be related to its ability to inhibit mast cell degranulation and mediator release (6). Recently the possibility of using orally administered SCG in patients with food allergies has been proposed and preliminary studies have indicated a therapeutic effect (2, 4). These promising data suggested a trial in patients with chronic urticaria, where dietary factors could be of importance (5).

The present study reports on a trial with oral SCG in patients with chronic urticaria and positive oral provocation tests to azo dyes, preservatives or antirheumatic drugs such as aspirin and indomethacin.

### MATERIAL AND METHODS

Fifteen patients aged 19-58 suffering from chronic urticaria of from 3 months to 35 years duration were entered into the study. All had positive provocation tests to food additives or

antirheumatic agents. All had previously been treated with antihistamines with only temporary relief, six had been on an elimination diet. Four patients also had gastrointestinal complaints. Only one patient had near relatives with atopic history. The ingested agents used for challenge tests during the trial can be seen in Table 1.

The patients were studied by a double-blind cross-over technique. Treatment with either SCG or a placebo was taken for 4 weeks, then the alternative treatment for the next 4 weeks. Doses of sodium cromoglycate were prepared from capsules containing 200 mg SCG dissolved in 15 ml water. The contents of one capsule was taken four times daily at regular intervals.

Patients were challenged with the oral agent they were already known to react against, on 1 day during the active and placebo periods. Clinical assessments were made every 2nd week and scores were given for symptom severity. Diary cards included the patients' evaluation of their symptoms. In statistical tests a 2-tail significance level of 5% has been used.

Table 1  
Agents used for challenge

| Agent           | Dosage (mg) |
|-----------------|-------------|
| Amaranth        | 2           |
| Aspirin*        | 1,000       |
| Indomethacin    | 50          |
| Nyckockin       | 10          |
| Sodium benzoate | 500         |
| Tartrazin       | 10          |

## RESULTS

Mean values for weekly urticaria scores based upon analyses of diary cards were for the active period 5.9 and for the placebo period 6.4. The respective scores for skin irritation were 3.8 and 5.7. No significant differences were found using Wilcoxon's matched pairs test although mean scores were slightly less in the active period.

Thirteen patients underwent a clinical assessment score during the active period, 11 during the placebo period. Twelve of the 13

patients experienced symptoms during the active period, nine of 11 during the placebo period.

The results of provocation tests performed during active and placebo periods appear in Table 2. Score values for symptoms from the day before tests, the day of the test, and the day after the tests are listed. Table 3 shows treatment preference by patients and clinician. Six patients preferred the active treatment whereas two preferred placebo and seven had no preference. The clinician considered the active treatment best in one case, placebo best in one case, and had no preference in 13 cases. The differences recorded were not significant.

Side effects were registered in four patients. One complained of stomach-ache in the active period, another of severe tiredness, and one patient of headache and tiredness. The last had similar complaints together with complaints of nausea, vomiting and diarrhoea in the placebo period. One other patient reported nausea and diarrhoea during placebo.

Table 2  
Average clinical assessment scores before, during, and after oral challenge assessed during active treatment period and placebo period

| Symptoms                      | Active period |             |           | Placebo period |             |           |
|-------------------------------|---------------|-------------|-----------|----------------|-------------|-----------|
|                               | Day before    | Day of test | Day after | Day before     | Day of test | Day after |
| Urticaria (11)                | 1.1           | 1.2         | 1.2       | 0.6            | 1.5         | 1.3       |
| Gastrointestinal symptoms (4) | 0.9           | 1.1         | 0.9       | 1.1            | 0.5         | 1.3       |

Figures in brackets are maximum sample sizes for that symptom.

Table 3  
Patients and clinicians preference for treatments

| Preference by | Treatment order group | Preference for |          |         |
|---------------|-----------------------|----------------|----------|---------|
|               |                       | Active         | No diff. | Placebo |
| Patient       | A-P                   | 3              | 3        | 1       |
| Patient       | P-A                   | 3              | 4        | 1       |
| Clinician     | A-P                   | 1              | 5        | 1       |
| Clinician     | P-A                   | 0              | 8        | 0       |

## DISCUSSION

We may conclude that oral SCG had no significant effect on our patients suffering from chronic urticaria. This is in accordance with the results of Denman (3) on patients with idiopathic chronic urticaria. Denman, however, found that 900 mg oral SCG prevented exacerbation of symptoms in a group of urticaria patients with dietary hypersensitivity. The slight, but not significant, difference between provocations performed during the active period and during the placebo period in our group together with a slightly higher patient preference for the active drug could suggest that a similar but less pronounced effect could be present among our patients but that the oral dose of SCG is not potent enough against urticaria released by a type of agent, where the mode of action is not by allergic hypersensitivity.

Our results are not in accordance with data from an open cross-over trial performed in a similar group of patients (1). Trials on chronic urticaria should, in our experience (7), in order to be of any validity, be performed on a double-blind basis as these patients usually show a pronounced placebo effect.

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