

Oral Disodium Cromoglycate Treatment of Atopic Dermatitis

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Fourteen adults and 10 children with active atopic dermatitis entered this double blind cross-over study of oral disodium cromoglycate (DSCG) (adults 200 mg qid, children 100 mg qid) compared with placebo. Oral DSCG and placebo were given for 6 weeks in random order. According to the investigators' assessments of eczema, significant differences between active and placebo were found after 6 weeks' treatment, DSCG being favoured ($P < 0.05$). No differences were detected in the investigators' assessment of lichenization and overall disease. No significant differences between the two treatments were demonstrated in the patients' assessments. Results from food allergic patients were similar to those from non-food allergic patients. Two patients reported possible side effects of arthralgia and urticaria respectively. There were no treatment effects on serum IgE values or any other laboratory data.

Key words: atopic dermatitis; disodium cromoglycate; double blind cross-over trial; food allergy.

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Recognition of the impeding effect of disodium cromoglycate (Lomudal®, Fisons) on the histamine release of sensitized (IgE-coated) mast cells when exposed, *in vitro*, to the specific antigen, led to the assumption that it might have a beneficial effect on atopic diseases, more specifically on the IgE-mediated histamine and SRS-A release of the allergic Type I reaction.

In 1967 came the first reports of the prophylactic effect of disodium in the treatment of asthma (1). Since then disodium cromoglycate (DSCG) has been used more and more in the treatment of asthma and seasonal rhinitis, showing an effect on the nasal and bronchial mucosa when inhaled. Since 1973 several authors have reported effects of DSCG on gastro-intestinal diseases as well. Given orally DSCG proved to block symptoms to some degree not only from the gastro-intestinal tract, but also from the skin, and the mucosa in the respiratory tract (4, 8).

In this study 24 patients suffering from atopic dermatitis were treated orally with DSCG in a double blind cross-over trial.

MATERIAL AND METHODS

Fourteen adults and 10 children with atopic dermatitis were randomized to a cross-over trial with oral disodium cromoglycate (DSCG) and placebo. After 6 weeks' treatment they crossed over to the other treatment for a further 6 weeks. DSCG and placebo were administered in identical capsules, the contents of which were dissolved in hot water and taken 15-20 min before meals 4 times daily in doses of 200 mg for adults and 100 mg for children. Atopic dermatitis was defined according to Hanifin & Rajka (5). All had severe widespread disease. During the trial the patients were on a basic treatment with moisture cream, oil bath and hydrocortisone butyrate cream. The pa-

tients were examined when entering the study and every 3 weeks. Lichenization was graded on a scale 0–2, eczema on a scale 0–3 and overall disease on a scale 0–4. In all cases 0 referred to "no symptoms".

Patients or their parents recorded the severity of day and night itching and the general severity of eczema on a visual analogue scale (0–5 mm) once a week. Blood samples including serum total IgE were taken for analysis initially and again after each treatment period. IgE were determined at Diagnoselaboratoriet/ALK, Copenhagen by the PRIST technique (Pharmacia Diagnostics, Sweden). Serum specific IgE and skin prick tests were made, after each treatment period, for a number of allergens including foodstuffs. Serum specific IgE were determined at ALK, Copenhagen by the AL-RAST (10). The allergen extracts used for skin prick testing (Soluprick® – SQ) were biologically and immunochemically standardized to have a potency of 1 HEP (histamine equivalent by prick test) by the manufacturer (ALK, Copenhagen).

To define food allergic patients, patients with anamnestic intolerance or positive cutaneous reactions to foodstuffs were submitted to an open challenge before entering the study. If the patients experienced flushing or itching within a few hours of challenge, or aggravation of eczema or itching the following day, the challenge was considered positive.

In statistical tests the paired and unpaired Wilcoxon's test or the paired *t*-test (blood samples except IgE) have been used. Analyses of variance were made on the results from patients' assessments.

Details of patient characteristics are shown in Table 1. Ten children and 14 adults entered the trial, two boys and eight girls in the child group and 10 men and four women in the adult group. Seven children and nine adults were considered to be food allergic according to a positive food challenge. Mean baseline IgE values in children were 1166 (range 26–8760, normal range < 350) and in adults 2535 (range 191–12,780, normal range < 150). In adults the placebo-DSCG (P-D) patients had significantly higher IgE than the D-P patients ($P < 0.01$).

RESULTS

Patients' assessments

Table 2 shows the results of the analysis of the patients' and their parents' assessment of day and night itching and severity of eczema.

Repeated measure analyses of variance were made on the results with treatment order and adult/child group as factors in the analysis. Mean results were calculated for the first and last of 3 weeks of each treatment period and

Table 1
Patient characteristics

	Treatment order	Male	Female	Age mean (range)	Age at onset mean (range)	Family history of atopy	Other atopic diseases	Food allergy	Serum IgE mean (range)
Children	D-P	1	4	8 (4–11)	1 (0–4)	2	3	4	436 (26–1900)
Children	P-D	1	4	7 (5–9)	0 (0–1)	4	3	3	1896 (59–8760)
Adults	D-P	5	1	28 (24–33)	5 (0–22)	4	6	3	2268 (191–5050)
Adults	P-D	5	3	26 (16–37)	2 (0–13)	5	6	6	3957 (1700–12,780)

Table 2

Analysis of patients' assessments. Mean scores from first and second "3-week period" of active treatment compared with mean scores from corresponding weeks of placebo treatment

		Itching during the day		Itching during the night		General severity of eczema	
		Analysis after		Analysis after		Analysis after	
		3 weeks	6 weeks	3 weeks	6 weeks	3 weeks	6 weeks
Children	D-P	NTS	NTS	NTS	NTS	NTS	NTS
	P-D	NTS	NTS	NTS	NTS	NTS	NTS
	All	NS	NS	NS	NS	NS	NS
Adults	D-P	NS	NS	NS	**	NS	NTS
	P-D	NS	NS	*	NS	NTS	NS
	All	NS	NS	NS	NS	NS	NS
All patients		NS	NS	NS	NS	NS	NS

D-P = DSCG-Placebo group; P-D = Placebo-DSCG group; NS = Not significant ($P < 0.05$); NTS = Numbers too small for statistical tests; * $P < 0.05$ in favour of DSCG; ** $P < 0.05$ in favour of placebo.

Table 3

Analysis of clinical assessments. Scores after first and second "3-week period" of active treatment compared with scores after corresponding period of placebo treatment

		Lichenization		Eczema		Areas of skin involved		Total impression	
		Analysis after		Analysis after		Analysis after		Analysis after	
		3 weeks	6 weeks	3 weeks	6 weeks	3 weeks	6 weeks	3 weeks	6 weeks
Children	D-P	NTS	NTS	NTS	NTS	NTS	NTS	NTS	NTS
	P-D	NTS	NTS	NTS	NTS	NTS	NTS	NTS	NTS
	All	NS	NS	NS	NS	NS	NS	NS	NS
Adults	D-P	NTS	NTS	NTS	NTS	NTS	NTS	NTS	NTS
	P-D	NTS	NTS	NS	NTS	NTS	NS	NS	NS
	All	NTS	NS	NS	NS	NS	NS	NS	NS
All patients		NS	NS	NS	*	NS	NS	NS	NS

D-P = DSCG-Placebo group; P-D = Placebo-DSCG group; NS = Not significant ($P < 0.05$); NTS = Numbers too small for statistical tests; * $P < 0.05$ in favour of DSCG.

DSCG and placebo treatments were compared during the first and last 3 weeks of treatment. No significant differences between the DSCG treatment and the placebo treatment were detected for daytime itching or severity of eczema. In adults who opened the study with placebo, itching during the night was significantly diminished ($P < 0.05$) within the first 3 weeks of DSCG treatment compared with the corresponding period of placebo treatment. In

adults who opened the study with DSCG, itching during the night was significantly diminished ($P < 0.05$) within the second 3 weeks of placebo treatment compared with DSCG treatment.

Clinical assessments

Scores from DSCG and placebo treatments were compared after 3 and 6 weeks (Table 3).

No significant effects were detected except for eczema in all patients after 6 weeks' treatment. DSCG treatment gave significantly better results than placebo ($P < 0.05$).

Relation of response to food allergy

No differences were found between food allergic and non-food allergic patients in the subjective and clinical assessment during the first and second 3 weeks of treatment.

RAST and skin tests

RAST and skin tests were made with a number of foodstuffs and non-foodstuffs after each treatment period. As the number of tests made on each patient varied, a mean score for RAST and skin test results was calculated for each patient. Tests for foodstuffs and non-foodstuffs were kept separate. Results of RAST and skin tests after DSCG and placebo treatments were compared. No significant differences were detected.

Safety data

Possible side effects were reported by two patients. One adult experienced joint pains and one child had an unexplained urticaria during DSCG treatment. Rheuma tests were negative in the adult patient, and the arthralgias disappeared after DSCG was withdrawn. The child had often experienced urticaria before the trial and is still having attacks. Results of blood samples after DSCG and placebo treatments were compared. Thrombocytes were significantly lower after DSCG than after placebo in the children ($P < 0.05$), however, the baseline mean value was lower still. No other significant differences were detected. In particular there were no significant differences in serum IgE or eosinophil count.

DISCUSSION

Dannaus et al. (4) found in a double blind trial on 20 food allergic children a significant effect

of DSCG compared with placebo, particularly on the skin symptoms in some of the children.

In an open trial Molkhou & Waguët (6) treated 35 children with atopic dermatitis with an average DSCG dosis of 200 mg daily for 1 month, and recorded successful outcome in 23 patients (66%) whose lesions had almost disappeared, and four improvements (12%), while Atherton et al. (2) in a double blind study found no effect of oral DSCG on children with eczema.

In the present study the adults evaluated the last 6-week periods as being significantly the best, whether they received active or inactive DSCG and only as far as itching during the night was concerned. In patients who received active DSCG in the last 6-week period the diminished scoring was recorded after only 3 weeks. Apparently this effect on itching was short-lasting and had not been recorded in relation to itching during the day. In patients who received placebo the reduced scoring first appeared after 6 weeks. If a carry over effect is to be expected from the preceding DSCG period it would reduce the symptoms after 3 weeks rather than after 6 weeks. These results therefore may represent a type I error. However, it is notable that only the P-D patients, who had higher IgE levels than D-P patients, found an effect in the DSCG period. This raises the question whether high IgE is associated with a response to DSCG. In support of this Molkhou & Waguët (6) found raised IgE levels in half of the children who benefited from treatment with DSCG while none of the children who failed to respond to DSCG had elevated IgE levels.

According to the clinical assessment, including all 24 patients, DSCG was found to give significantly better results with diminished eczema after 6 weeks' treatment, whether patients were food allergic or not, but no differences were detected between active and placebo in the scores concerning total impression or patients' assessments of eczema and itching during the day.

Side effects in oral DSCG treatment are rare and not serious. The most frequent symptoms are headache and urticaria, but gastro-intestinal symptoms have also been reported (7, 8).

In the present trial there were two cases with possible side effects, arthralgias and urticaria, the latter unlikely to have been connected with the DSCG treatment.

No changes in serum IgE, number of circulating eosinophils or RAST were noticed during the treatment. Regarding the changes in thrombocytes, the values after DSCG did not fall below the starting point. We have found no reports of bone marrow depression with DSCG.

The mechanism of the effect of oral DSCG is unknown, but since less than 1% is absorbed (9) it is reasonable to assume that DSCG exerts its effect on the intestinal mucosa, possibly by impeding the release of chemical mediators, but other as yet unknown mechanisms of effect can not be excluded.

We have not been able to confirm the favourable results of DSCG in atopic dermatitis reported by Molokhou & Waguët (6). Oral DSCG give few side effects, and in our opinion further clinical studies are necessary in order to estimate its priority in the treatment of atopic dermatitis.

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