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TREATMENT OF VASOMOTOR RHINITIS* WITH INTRANASAL DISODIUM CROMOGLYCAT (SCG)

Results from a Double-Blind Cross-Over Study

By

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The role of disodium cromoglycate (Intal®, Lomudal®) in the prophylactic management of bronchial asthma has now been firmly established for several years (2). In the upper airways, the efficacy of the drug in seasonal allergic rhinitis (hay fever) has been demonstrated both as a dry powder and a 2 per cent aqueous solution (2). Trials with the drug have also shown a considerable degree of success in patients suffering from perennial rhinitis in whom allergic factors have been demonstrable. So far, however, no studies to our knowledge, have been done solely in patients with perennial rhinitis in whom allergy has *not* been demonstrated, i.e. patients with vasomotor rhinitis. Considering the refractoriness of this condition to various therapies, and with the beneficial effect of disodium cromoglycate in asthma bronchiale of non-allergic aetiology in mind (9), we felt a trial of this drug in vasomotor rhinitis would be of interest.

* In this article the term *vasomotor rhinitis* is used in agreement with the definition of Hansel (5), i.e. symptoms simulating allergic rhinitis but with negative findings in allergological examinations.

MATERIAL AND METHODS

The study comprised 49 patients aged 16-65 years (average 34 years) with vasomotor rhinitis for many years. The symptoms were of a perennial type with varying degrees of obstruction, running, sneezing and nasal itching. Allergological examination in the form of intracutaneous tests with different extracts (six dust, two mould, eight animal epithelium and ten pollen extracts) proved negative. Pretreatment analysis of IgE/serum with RIST and estimates of eosinophils in nasal secretion, according to the classification of Koch (7), were carried out (cf. Table 1). Patients with nasal polyposis, obvious septum deviation and bronchial asthma were excluded.

TABLE 1
Pretreatment Analysis of IgE/Serum with RIST, and Estimates of Eosinophils in Nasal Secretion in 49 Patients with Vasomotor Rhinitis.*

Eosinophils	IgE/serum ng/ml					
	<100	100-200	201-300	301-400	401-500	>500
0	12	1				1 (760)
±		1				
+	7	2				
++	3	2		1 (380)		
+++	8	2				
++++	4	2				1 (520)

* IgE is lacking in two subjects with no eosinophils.

The trial was a double-blind cross-over and took place for 13 weeks during January-April 1973. Twenty-four patients started with a 6-week treatment period with SCG followed by 1 week without medication and finished with 6 weeks' placebo treatment. The other 25 patients were treated in reverse order.

SCG and placebo were presented in identical gelatin capsules and were administered as nasal powder. A specially designed insufflator was used for this. The dosage during the SCG period was 10 mg of disodium cromoglycate plus 10 mg lactose, equally distributed in both nostrils four times a day, i.e. total dose of 40 mg SCG in 24 h. The placebo capsule contained 20 mg lactose. Each subject recorded on a daily diary card the following symptoms: blocking, running, sneezing and itching on a scale 0-3 (0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe) during all 13 weeks.

Each patient was interviewed and medically examined before entry into the trial and on the last day both in the SCG and the placebo period. The condition of the nose was recorded as to the severity of redness, oedema and purulent discharge, on a 0-3 scale as above. Haematological analysis (haemoglobin, leuco-

cyte count, differential leucocyte count and sedimentation rate) and bacteriological examination (ordinary cultivation) of the naso-pharyngeal secretion were also carried out on these occasions.

On the last day of both treatment periods, the patient's subjective evaluation of the therapeutic effect was recorded as follows: no symptoms, improved, unchanged, deteriorated, and at the last examination, their opinion as to which of the treatment periods had been most effective in controlling nasal symptoms, or whether no difference existed. The data obtained from the diary cards and medical examinations were subjected to statistical analysis.

RESULTS

In all, 49 cases were entered into the study, but full data were not obtained in all cases. The results for each treatment, based on subjective evaluation, are given in Table 2. It is apparent that the results differed little. As far as patients' preferences are concerned, the figures are shown in Table 3. Again there is no statistical evidence of any advantage in either form of treatment. This is in agreement with the findings at physical examination, in which the condition of the nasal mucosa was found unchanged in relation to treatment.

TABLE 2
Condition After Each Treatment.

Patient group	Condition	Treatment	
		SCG	Placebo
SCG-Placebo	Symptom-free	1	1
	Improved	11	9
	Not improved	10	9
	Deteriorated	1	3
Placebo-SCG	Symptom-free	0	3
	Improved	12	9
	Not improved	8	10
	Deteriorated	4	1

The summary of diary card data is given in Table 4. Analysis on the whole material and the subgroups "blockers",

"runners", "blockers and runners", "patients with sneezing and itching" and "patients with high eosinophilic count in nasal smear" gave no significant differences between the two types of treatment independent of drug order. Nevertheless, some patients experienced the same degree of relief with both forms of medication, or had a preference for SCG. In order to exemplify this the following cases are chosen:

TABLE 3
Patients' Preferences.

Patient group	Preference		
	SCG	Placebo	Neither
SCG-Placebo	9	9	3
Placebo-SCG	9	10	5
Total	18	19	8

TABLE 4
Summary of Diary Card Data.

Variable	Group size	Average scores for		Wilcoxon T-value*	Significance
		SCG	Placebo		
Blocking	43	46.4 $\pm$ 40.6	51.4 $\pm$ 38.9	343.0 (38)	$P > 0.10$
Running	43	46.1 $\pm$ 27.8	47.7 $\pm$ 25.9	439.5 (43)	$P > 0.10$
Sneezing	44	36.2 $\pm$ 23.1	38.5 $\pm$ 21.5	471.0 (44)	$P > 0.10$
Itching	42	22.2 $\pm$ 22.7	21.9 $\pm$ 21.4	297.0 (35)	$P > 0.10$

* Figures in brackets are the number of non-tied pairs included in the test; tied pairs are excluded.

E.F. A 22-year-old woman whose main symptoms were blocking and sneezing with some degree of running and itching. She had had symptoms for 5 years. The nasal mucosa was livid and oedematous at every examination. Before the start of treatment there were (+) eosinophilic cells in the nasal secretion. The serum IgE was 170 ng/ml. Previous treatment with antihistamines, cortisone injections and bacterial vaccine had had no effect.

After treatment with SCG no definite effect was seen against running, itching and sneezing, but for the main symptom, blocking, there was considerable im-

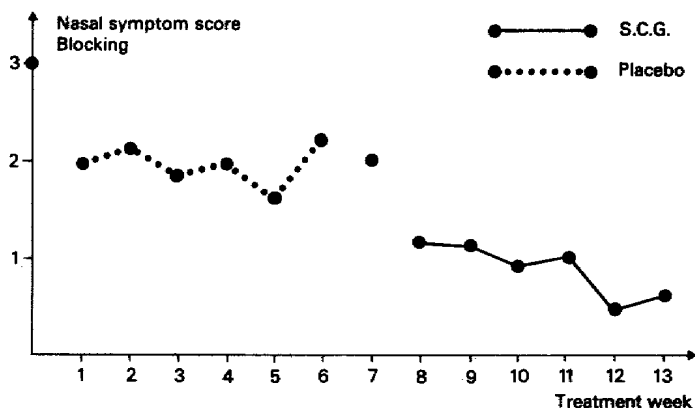


Fig. 1.

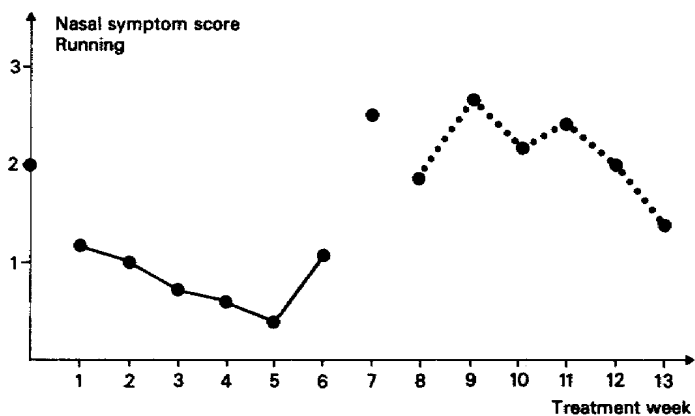


Fig. 2.

Figs. 1 and 2.

Nasal symptom score for two different patients, noted at start, once a week during the treatment with SCG and placebo and the wash-out week in between.

provement (Fig. 1). Placebo had in this respect considerably less (or no) effect and the patient preferred SCG.

I.H. A 31-year-old woman with nasal symptoms for 10 years. The main symptom was running, with the other symptoms to a lesser degree. On examination,

before starting the treatment, oedema and red nasal mucosa and (+++) eosinophilic cells in the nasal secretion were recorded. IgE/serum was 156 ng/ml. Treatment with antihistamine earlier had been without effect, while injections with bacterial vaccines had given some improvement.

In this trial SCG had the best effect on the main symptom, "running" (Fig. 2), but also some effect on blocking and itching. The effect of placebo was considered less pronounced and the patient preferred SCG.

G.I. A 26-year-old man, whose main symptoms were blocking and running for many years. On examination, before start of treatment, livid and oedematous nasal mucosa were recorded and (+++) eosinophilic cells in the nasal secretion. IgE/serum was 20 ng/ml.

SCG had no effect on running, but blocking was improved. Symptoms were unchanged during the placebo period and he preferred SCG.

Safety and Side Effects

No bacteriological changes in the nasopharynx were recorded. The haematological analysis also remained normal during both treatment periods. Side effects were reported by nine patients, five on active and four on placebo, and consisted of a feeling of dryness and irritation in the nose and throat.

DISCUSSION

As a condition of obscure aetiology, vasomotor rhinitis has been treated in many different ways, i.e. with drugs, vaccines and surgery (11) and the benefits of these treatments have not always been convincing.

No trial, on the effect of SCG in patients with vasomotor rhinitis alone, had been published when we started our study in the beginning of 1973. A great number of studies, however, were published during 1972-75 on the effect of SCG in perennial rhinitis. In these studies both allergic and vasomotor rhinitis were included. Only in a few studies is it possible to make comparisons with our own trial, as the distinction between allergic and vasomotor rhinitis was poor and the treatment periods throughout were shorter. Our patients were treated for 6 weeks with each preparation with an interval of 1 week. This rather long period of treatment was chosen in view of

the well-known variability of the symptoms of vasomotor rhinitis.

In our study of 49 patients with vasomotor rhinitis, no definite effect from SCG was seen. This result, made on statistical analysis of data concerning subjective parameters and evaluation of the status of the nasal mucosa by physical examination, conforms with that of Mygind et al. (10) in their investigation of 12 patients with vasomotor rhinitis. However, it differs from the results of Fagerberg & Zetterström (4) who studied 23 patients, of which 19 were considered suffering from vasomotor rhinitis. They found a good response to SCG and a clear preference for this drug in comparison with placebo. This was especially the case when the SCG period succeeded the placebo period. When the patients started with SCG, the difference in results was less pronounced, which was supposed to be a consequence of the long-lasting carry-over effect of the active drug, possibly due to the absence of a wash-out period.

Bernstein et al. (1) have argued that SCG could have a carry-over effect for up to 4 weeks. Like Fagerberg & Zetterström (4) we doubt this with regard to "the current opinion of the mode of action of SCG". With the method used by us—longer-treatment period plus wash-out period—the risk for carry-over effect should be reduced. As we moreover had a larger patient material at our disposal, it seems as if our results could have a greater validity.

Holopainen et al. (6) presented in 1975 a trial including 29 patients with vasomotor rhinitis and 11 patients with allergic rhinitis. The authors put together the treatment results for both these patient categories and concluded that "there is no difference in the degree of the response to SCG between intrinsic and extrinsic forms of rhinitis". Our experiences from treatment of an allergic material (8) and results from our existing trial of vasomotor rhinitis, are not in agreement with Holopainen's. Our examination of the allergic clientele showed a more favourable response to SCG. It is true that Holopainen used SCG in a 2 per cent solution while we, in this study of

vasomotor rhinitis, used powder, but we assume that the most probable explanation for the difference in treatment results for Holopainen and us is that Holopainen's patient material comprised more allergic patients than were detected. Bruun (3) has shown that among patients, characterized as vasomotor patients, allergic patients are included, in whom it is very difficult to prove allergy. One may in this connection speculate about Type I and/or Type III reactions initiated by allergens unavailable in ordinary allergological diagnosis of today. A further illustration of the difficulty of diagnosing an allergic condition is shown by our investigation. In spite of the fact that our study has not shown statistical evidence for the therapeutic effect of SCG in vasomotor rhinitis, we could see a dramatic improvement in the symptoms in some patients after treatment with SCG. These patients continued with the drug with good results. We therefore think that SCG is worth trying in cases of vasomotor rhinitis as the drug is completely atoxic (2) and its use, on the whole, is without side effects.

SUMMARY

The effect of SCG powder (Lomudal®, Intal®) intranasally in vasomotor rhinitis has been studied on 49 adult volunteers in a double-blind cross-over study during 13 weeks in January–April 1973. The dose of SCG was 40 mg/day. Although a substantial number of results were obtained, no significant difference between the effects of SCG and placebo treatment, on variables measured, was detected. However, some patients experienced relief with, and preferred, the treatment with SCG. The results from this investigation are discussed in comparison with those from other studies including patients with vasomotor rhinitis.

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