

From the E.N.T. Department, University Hospital, Lund, Sweden.

AN OPEN ASSESSMENT OF LOMUDAL®
(DISODIUM CROMOGLYCAT) (2 PER CENT)
NASAL SPRAY IN SEASONAL ALLERGIC
RHINITIS

By

THORVALD LÖFKVIST & GUNNAR SVENSSON

The effect of D.S.C.G. (disodium cromoglycate = Lomudal® = Intal) in allergic airways disease has been well documented since the first report appeared in 1967 (1). In most instances, patients suffering from bronchial asthma have been investigated (8). Among the reports concerning the use of D.S.C.G. in seasonal allergic rhinitis those of Engström et al. (4), Holopainen et al. (5) and Taylor & Shivalkar (9) are of particular significance. Engström and Holopainen showed, in their respective double-blind studies of tree-pollen allergics, that the use of D.S.C.G. (in powder form, in a dose of 10 mg to each nostril four times daily) was effective in controlling symptoms and markedly reduced the need for antihistamines. Taylor & Shivalkar investigated firstly the capacity of D.S.C.G. to block allergic reactions in provocation tests using grass pollen; and secondly, the effect of D.S.C.G. in allergic subjects during the grass pollen season (10 mg of the substance in powder form being insufflated into each nostril four times daily). The study was of the double-blind, crossover type. They found that in the provocation tests D.S.C.G. in a dose of 10 mg had a protective effect for 6 hours; whilst in the clinical trial, although results were not significant over the whole duration of the trial, during the period that the pollen count

was known to be high, the effect of the drug on upper airways symptoms was significantly better than that of placebo. In previous trials in which D.S.C.G. has been insufflated as a powder (2, 3, 5, 7), local but no systemic side effects have been observed. Thus some patients have noticed itching and a feeling of dryness in the mucosa of the nose, headache and sore throat. One of the intentions with this trial was to reveal if a solution of D.S.C.G. gave fewer side effects. There was also the possibility of a more effective treatment since the blockage of the nasal mucosa might more easily be overcome by a solution than by a powder. It seems that a simultaneous study by Illum et al. (6) in Denmark was initiated for the same reason.

MATERIAL AND METHODS

The trial was conducted over a 4-week period between mid-June and mid-July during the summer of 1972, i.e. at the time when the pollen count in the south of Sweden would be at its maximum.

In all, 23 patients (14 male and 9 female), aged between 14 and 46 years (average 26 years) were entered into the trial. All of them were sensitive to grass pollen (as shown by positive provocation tests), and had suffered from hay fever during at least the last two seasons. Any patient exhibiting asthmatic symptoms was excluded. No subject currently on a hyposensitization course was included. It was ascertained that all patients would be remaining at home in a constant environment throughout the period of the trial.

D.S.C.G. was administered by nasal spray as an aqueous solution of Disodium cromoglycate 2 per cent with a preservative and E.D.T.A. The dose was two squeezes of the spray into each nostril every 3 h throughout the day, i.e. 1.6 mg D.S.C.G. $\times$ 6 = about 10 mg D.S.C.G./day to each nostril. A supply of antihistamine tablets (chlorphenoxamin—Systral-coffein®) was issued to each patient with instructions to take them only if symptoms were so severe as to make that medication indispensable.

Each subject recorded the following symptoms on a daily diary card: sneezing, running, blocking and itching, on a 0-3 scale (0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe). The presence or absence of eye symptoms and the all-over general condition were also recorded. If it was necessary to take antihistamines (Systral-coffein), the number of tablets taken was also entered on the diary card.

Each patient was interviewed and examined medically before entry to the trial and again after 4 weeks of treatment. The condition of the nose was recorded as to the presence of oedema and mucus, again on a 0-3 scale, as above. Full haematological analysis and bacteriological examination of the nasal secretions were

carried out. The data obtained from the diary cards and medical examinations were subjected to statistical analysis.

At the final examination, answers were recorded to the following questions:

- a) Were your nasal symptoms adequately controlled?
- b) Were your nasal symptoms less marked than during last summer?
- c) Would you use the spray next summer if it were available?
- d) Do you wish to continue treatment with the spray for the rest of the summer?
- e) Do you regard the treatment with the spray as a success or a failure?

In addition, the trialists also recorded their opinion as to the success or failure of the treatment.

RESULTS

Records of the subjective symptoms suffered during the trial period were completed by all 23 participants in such a form that statistical analysis was possible. An assessment by the trialists as to the efficacy of the treatment in the terms "success" or "failure" was recorded in all patients. Owing to insufficient data in one subject as to the nasal condition before starting treatment, the records of the appearance of the nasal mucosa included only 22 subjects.

Table 1 shows the variations in subjective symptom scores and antihistamine usage throughout the period of the trial. For nearly all local symptoms a gradual improvement was apparent throughout the 4 weeks. The only exception in this respect was the symptom, nasal obstruction, which increased during the first 2 weeks but was thereafter reduced. The opinion of patients as to their general condition paralleled the degree of nasal blockage, i.e. it was worse with increasing nasal obstruction. The usage of antihistamines was highest during the first week.

Table 2 shows the changes in the condition of the mucosa with regard to oedema and mucus secretion, as assessed by anterior and posterior rhinoscopy at the beginning and at the end of the trial. A statistically significant improvement was noted.

A summary of the results of the treatment based on the answers to the questions put to the patients and the opinion of

TABLE 1

Subjective Symptoms and Antihistamine Tablet Usage from Diary Card Data in 23 Hay Fever Patients Treated with Disodium Cromoglycate.*

Symptom response and tablet usage*	Gradation	At day of entry**	Mean value			
			week 1	week 2	week 3	week 4
Sneezing	0-3	7.28	5.87	5.78	4.57	4.77
Nasal catarrh	0-3	7.00	5.26	5.26	5.04	4.09
Blockage	0-3	5.18	5.74	7.13	5.13	4.68
Itching	0-3	4.90	3.26	2.26	1.91	1.36
Eye symptoms	0-3	2.73	2.52	2.26	1.96	1.73
Tablets	n/day	0.93	1.74	1.65	1.57	0.82
General condition	0-3	8.19	8.29	8.41	8.05	8.33
(good-bad)						

* Systral-coffein®.

** Mean value at day of entry $\times 7$.

TABLE 2

Oedema and Mucous Production in the Nasal Mucosa—Statistical Analysis in 22 Hay Fever Patients Treated for 4 Weeks with Disodium Cromoglycate.

Symptoms	Mean value*		Wilcoxon T-value	Significance
	start	end		
Oedema	0.9	0.5	13	$P < 0.02$
Mucous	0.8	0.4	15	$P < 0.02$

* Registration after scale 0-3.

the trialists is given in Table 3. Although nasal symptoms were neither controlled nor less pronounced in five subjects, only three of them were so dissatisfied with the treatment that they did not want to continue it for the rest of the summer. Twenty subjects (80 per cent) regarded the trial as successful, which was in accord with the opinion of the trialists. From Table 3 it can be seen that five patients did not find the treatment fully acceptable because of the short intervals between doses during the day. Of these five persons, however, four were satisfied with the effect of the treatment.

No side effects were noted with this form of treatment.

TABLE 3

Evaluation of Patients and Trialists after 4 Weeks of Treatment with Disodium Cromoglycate.

Question		Answer	
		n/persons	significance
1. Were nasal symptoms controlled?	yes	18	0.0106
	no	5	
2. Were the nasal symptoms less pronounced than last summer?	yes	18	0.0106
	no	5	
3. Would you use the spray solution next summer (if you could get it)?	yes	20	0.0005
	no	3	
4. Do you want to continue the treatment with the spray solution during the rest of the season?	yes	20	0.0005
	no	3	
5. Do you find the treatment with the spray solution successful?	yes	20	0.0005
	no	3	
6. The trialist's evaluation of success.	yes	20	0.0005
	no	3	

DISCUSSION

The trial carried out here was of the open assessment type. It was originally intended to conduct a double-blind study, but this was not possible because of the limited number of patients, which would have detracted from the value of the trial. A further disadvantage was the lack of information as to the pollen count during the trial period. Despite these deficiencies one may make a positive assessment of the preparation on the basis of the trial carried out. It was conducted during the summer of 1972, which was warm with very little rain, conditions which should have produced a comparatively high pollen count. In these circumstances about 80 per cent of the patients in the trial considered the treatment successful. Comparison is warranted with the results of the trials conducted by Engström, Holopainen and by Taylor & Shivalkar.

The same favourable effect of D.S.C.G. observed by Eng-

ström et al. (4) and Holopainen et al. (5) in tree-pollen allergics has here been observed in grass-pollen allergics. The therapy was more successful than that of Taylor & Shivalkar (9) in their study of patients with grass-pollen rhinitis. Perhaps the fact that D.S.C.G. was given by us as a solution and not as a powder deserves some attention in explaining the difference. Illum et al. (6), who studied the response of grass-pollen allergics to D.S.C.G. (solution) during the same summer when our investigation was carried out, got results which compare well with ours. In their study, however, some patients noticed slight side effects, but none were observed in our group.

SUMMARY

The effect of Disodium cromoglycate (Lomudal, Intal) on allergic rhinitis, given as a solution in a nasal spray, was studied in 23 adult volunteers with grass pollen allergy, none of whom were having hyposensitization therapy. The trial was carried out as an open assessment during the months of June and July, 1972. Two squirts (1.6 mg D.S.C.G.) from the nasal spray were applied to each nostril every 3 h throughout the day. In 80 per cent of subjects the treatment was successful. No side effects were noted, but five patients expressed a preference for a preparation that could be administered at less frequent intervals.

ACKNOWLEDGEMENTS

We wish to thank Fisons Sweden AB for providing the equipment used in this trial, and Dr J. Pearson (Medical Adviser, Fisons Research & Development Laboratories) for his assistance.

REFERENCES

1. Altounyan, R. E. C. (1967): Inhibition of experimental asthma by a new compound—disodium cromoglycate "Intal". *Acta allergol.* 22, 487.
2. Anderson, W. V., Marshall, N. E. V. & Clark, M. C. (1972): A double-blind controlled trial of disodium cromoglycate in seasonal allergic rhinitis. *Practitioner* 208, 676-679.

3. Blair, H. & Herbert, R. L. (1972): The use of disodium cromoglycate in seasonal rhinitis. *Practitioner* 208, 671-676.
4. Engström, I., Oberger, E., Blyckert, A. & Kraepien, S. (1971): Disodium cromoglycate in the treatment of seasonal allergic rhinoconjunctivitis in children. *Ann. Allergy* 29, 505-509.
5. Holopainen, E., Backman, A. & Salo, O. P. (1971): Effect of disodium cromoglycate on seasonal allergic rhinitis. *Lancet* i, 55-57.
6. Illum, P., Meistrup-Larsen, U., Moesner, J., Olesen, K. & Olsen, S. Z. (1973): Disodium cromoglycate (Lomudal®) in the treatment of hay fever. *Acta allergol.* 28, 416-424.
7. Olivier, P. J. (1971): The use of Rynacrom (Disodium cromoglycate) in allergic rhinitis. *Med. Proc.* 17, 392-395.
8. Strandberg, K. (1973): Lomudal®-dinatriumkromoglikat. *Svenska Läk.-Tidn.* 70, 1420-1421.
9. Taylor, G. & Shivalkar, P. R. (1971): Disodium cromoglycate: laboratory studies and clinical trial in allergic rhinitis. *Clin. Allergy* 1, 189-198.

Address of author:

Gunnar Svensson, M.D.
 Department of Otolaryngology
 University Hospital
 S-221 85 Lund
 Sweden

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.