Rhinology, XV, 97-102, 1977

Report on a trial of SCG 2% nasal solution (metered dose) in hayfever

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SUMMARY

An analysis has been performed on the results from 18 patients treated with SCG and 14 patients treated with placebo in a double-blind placebo-controlled group comparative trial of SCG 2% nasal solution (metered dose) in hayfever.
The two treatment groups were found to be similar with respect to relevant characteristics and pre-trial symptomatology.
Analysis of clinician's symptom scorings demonstrated statistically significant differences in favour of SCG for the symptoms Sneezing, Running and Itching.
No significant differences between the treatments were found in the statistical analysis of patient diary card total scores.
Five assessments of overall response made at the end of treatment gave results highly significantly in favour of SCG.

INTRODUCTION

This was a double-blind between-patient (group comparative) trial in which one group of patients took the SCG solution and the second group took a matching placebo. Patients were assigned to the treatments at random and the duration of trial treatment was to be 4 weeks.
Some patient characteristics and disease history details were taken at entry to the trial. At the end of treatment the clinician and patient made overall assessments of treatment efficacy and acceptability; at the same time, side effect complaints were recorded.
Throughout the trial patients assessed their own symptoms on diary cards, which were also used to record the use of antihistamines and any other treatments.
A total of 40 patients were entered in the study, 20 on each treatment. The results for 8 patients have not been included in the analysis because they did not take treatment according to the instructions. There remained for analysis 18 sets of results from the SCG group and 14 from the placebo group.

PATIENT CHARACTERISTICS AND INITIAL SYMPTOM SEVERITY

Table 1 summarises some characteristics of the patients; the two treatment groups were similar with respect to all the characteristics shown. The number of males

Table 1. Patient characteristics

Variable		Frequency or value for: SCG group	Placebo group
Sex:	Male	11	8
	Female	7	6
Age in years:	Mean	29.4	27.4
	Range	10 - 60	7 - 45
Most troublesome symptom:	Sneezing	10	9
	Blocking	2	1
	Running	2	2
	Itching	1	2
	Eye running	1	0
	Sneezing/Itching eyes	1	0
	Sneezing/Itching nose/Itching eyes	1	0
Symptom severity:	Moderate	6	4
	Moderate/Severe	1	0
	Severe	9	7
Seasonality in previous year:	April	1	4
	May	14	9
	June	18	14
	July	18	13
	August	9	7
	September	1	0
Skin test positive to:	Pollen	18	14
	Other vegetable allergens	12	9
	House dust or house dust mite	8	10
	Other animal allergens	16	10
	Fungi	6	4
	Foodstuffs	1	0
Nasal provocation test positive to:	Pollen	9	7
	Animal allergens	2	0
	Test not performed	9	7
Hyposensitisation in last 4 years:	1972	7	4
	1973	10	7
	1974	15	11
	1975	16	12
	None	1	1
Eosinophils in nasal smear:	+	9	4
	++	8	8
	+++	1	1

exceeded the number of females by a small amount in each treatment group; the mean ages of both groups were under 30. The symptom most often named as the most troublesome was Sneezing, and the severity of symptoms was always either Moderate or Severe. In the previous year patients experienced symptoms

chiefly in the months of May, June, July and August, with the peak of the season occurring in June, when all patients in both groups had had symptoms. All patients showed a positive reaction to skin testing with pollen extract; only half the patients in each group had the results of nasal provocation tests recorded, but for all these patients sensitivity to pollen was also demonstrated by this method.

With the exceptions of one patient in each treatment group, all patients had received a course or courses of hyposensitisation injections at some time in the last 4 years; 16 out of the 18 patients in the SCG group and 12 out of the 14 patients in the placebo group had had such a course in 1975. All but one patient in the placebo group showed some degree of eosinophilia in nasal secretions.

The results of the clinician's initial assessments of symptoms are summarised in Table 2. Again, the two treatment groups were found to be similar. The tables confirm that Sneezing was the worst affected symptom.

CLINICIAN'S ASSESSMENTS

The differences between the clinician's scoring of symptoms at the beginning

Table 2. Initial symptom severity as assessed by the clinician

Symptom	Severity	Frequency for: SCG	placebo
Sneezing	None	0	0
	Mild	1	2
	Moderate	8	6
	Severe	9	6
Blocking	None	0	1
	Mild	8	8
	Moderate	6	4
	Severe	4	1
Running	None	0	1
	Mild	3	2
	Moderate	8	8
	Severe	7	3
Itching	None	0	1
	Mild	7	6
	Moderate	5	5
	Severe	6	2
Eye Itching	None	2	1
	Mild	10	11
	Moderate	3	2
	Severe	3	0
Eye Running	None	6	10
	Mild	8	4
	Moderate	2	0
	Severe	2	0

Table 3. Mann-Whitney U-tests of changes in clinicians symptom scores

Symptom	* Mean change for: SCG	placebo	U-statistic	2-tail significance
Sneezing	-0.7 (18)	0.0 (14)	60.0	$P < .05$
Blocking	-05 (18)	-0.1 (14)	75.5	$P > .05$
Running	-1.0 (18)	0.0 (14)	34.5	$P < .01$
Itching	-0.8 (18)	-0.1 (14)	56.0	$P < .05$
Eye Itching	-0.2 (18)	0.0 (14)	112.0	$P > .05$
Eye Running	-0.4 (18)	-0.1 (14)	85.5	$P > .05$

* Figures in brackets are the sample sizes.

and at the end of treatment were calculated and used to compare the two treatment groups. The results of the non-parametric statistical tests used are given in Table 3. The average decreases in scores were greater for SCG than for placebo on all symptoms. Significant differences were detected for Sneezing, Running and Itching.

DIARY CARD SCORES

Patients entered the trial at different times over the period May 1 to June 27, and also completed the trial at different times. To analyse the daily scores it was decided to choose a single fixed interval of time and use only the scores recorded during this time.

The interval chosen was the 4 weeks from June 1 to June 28. There were two reasons: most patients were on treatment during this time, and all patients had said that they experienced symptoms in the month of June in the previous year (see Table 1).

Diary card scores were totalled for this 28 day period symptom by symptom, and the derived totals used to compare the two treatment groups. The results of the non-parametric statistical tests used are given in Table 4; none demonstrated

Table 4. MannWhitney U-tests of diary card mean 28-day totals (for the period 1/6/75 - 28/6/75)

Symptom	* Mean scores for: SCG	placebo	U-statistic	2-tail significance
Blocking	28.1 (11)	26.5 (8)	39.5	$P > 0.05$
Running	26.7 (10)	35.4 (8)	30.0	$P > 0.05$
Sneezing	28.8 (11)	35.9 (8)	32.0	$P > 0.05$
Itching	23.6 (11)	23.0 (8)	42.0	$P > 0.05$
Antihistamine	10.4 (12)	9.9 (8)	41.0	$P > 0.05$
Total Nosedrops	28.6 (12)	32.0 (7)	31.0	$P > 0.05$

* Figures in brackets are the sample sizes.

a significant difference between SCG and placebo. It is of interest that there were large differences between the mean scores of the two groups for the symptoms Sneezing and Running that were in favour of SCG; Sneezing and Running were the two worst affected symptoms initially according to clinician's assessments (see Table 2).

Table 5. Final assessments.

Assessment		Frequency for: SCG	placebo	"Exact" probability
Compared to last year, were symptoms:	Better	15	0	
	No better	2	13	$P < .001$
	Uncertain	1	1	
If drug available next year would patient use it?	Yes	15	0	$P < .001$
	No	3	14	
Would patient continue drug for rest of season?	Yes	15	0	
	No	3	13	$P < .001$
	Uncertain	0	1	
Patient's rating of treatment:	Success	14	0	
	Failure	2	12	$P < .001$
	Uncertain	1	1	
Clinician's rating of treatment:	Success	12	0	
	Failure	3	14	$P < .001$
	Uncertain	3	0	
Was method of application acceptable:	Yes	18	13	$P < .05$
	No	0	1	

FINAL OVERALL ASSESSMENTS

Five such assessments were made at the end of treatment, and at the same time patients were asked whether the method of application of the solutions was acceptable. The results of these assessments are given in Table 5. The responses to the five overall assessments of treatment effect showed a very clear advantage to SCG; the differences between the treatments were statistically very highly significant. ("Uncertain" responses were ignored). All but one patient found the method of application acceptable.

SIDE EFFECTS

Two patients complained of side effects. One patient given SCG complained of dizziness and Sneezing, and one patient given placebo complained of nasal irritation.

RÉSUMÉ

Une analyse a été effectuée sur les résultats de 18 patients traités avec le cromoglycate disodique et 14 patients traités avec placebo pendant la période polinique.

Il s'agit ici d'un essai clinique du type groupes comparatifs en double issues avec contrôle placebo. La substance active était le cromoglycate disodique à 2% en solution aqueuse dosée.
Les deux groupes traités étaient similaires en ce qui concerne les caractéristiques significatifs et le pré-essai clinique symptomatologique.
L'analyse des symptômes marqués par le clinicien démontre des differences statistiques significatives en faveur du cromoglycate disodique pour les symptômes suivants: éternuements, écoulements et démangeaisons.
Des différences significatives dans les traitements n'ont pas été trouvées dans l'analyse statistique des scores totales de la carte d'évaluation journalière du patient.
Cinq évaluations des réactions finales, faites à la fin du traitement, donnaient des résultats extrèmement significatifs en faveur du cromoglycate disodique.

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