

Treatment of Seasonal Allergic Rhinitis with Budesonide and Disodium Cromoglycate

A Double-Blind Clinical Comparison between Budesonide and Disodium Cromoglycate

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The aim of this study was to compare the efficacy and side effects of budesonide and disodium cromoglycate (DSCG) in seasonal allergic rhinitis. In a double-blind, double-dummy comparative study, 43 patients with seasonal allergic rhinitis were either treated with budesonide (200 µg b.d.) or DSCG (5.2 mg 5 times daily). After a 1 week run-in period treatment was given for 3 weeks. The patient scorings for nasal secretion, nasal itching, sneezing bouts and total nasal symptoms were significantly different between the treatment groups during the whole treatment period. The scorings for nasal blockage were significantly different during the last 2 weeks of treatment. All differences were in favour of budesonide treatment. The patients' assessment of the treatment favoured budesonide ($P < 0.02$). Side effects were few and mild, but one patient from the budesonide group stopped treatment because of headache.

Key words: nasal airway resistance; nasal eosinophilia; seasonal allergic rhinitis.

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CLINICAL ASPECTS

In a double-blind, double-dummy study budesonide nasal aerosol was compared with disodium cromoglycate nasal spray. 42 patients completed the study and received daily either budesonide 400 µg or disodium cromoglycate 26 mg. The clinical effect on nasal secretion, nasal itching and sneezing was significantly different during the whole treatment period and, during the last 2 weeks, on nasal blockage. All differences were in favour of budesonide treatment. Nasal airway resistance was not significantly reduced in any of the two groups. Eosinophilia in nasal smears was not significantly reduced.

Budesonide (Rhinocort®) is a new potent non-halogenated glucocorticoid, which is efficiently inactivated in the liver (1), administered as a pressurized aerosol. Disodium cromoglycate (DSCG), (Lomudal®) is a mast cell stabilizing drug available as a 2% solution for the treatment of allergic rhinitis. Clinical trials with budesonide have shown it to be significantly more effective than placebo in treating allergic and vasomotoric rhinitis when administered intranasally in daily dosages of 200–400 µg (1, 8, 9, 10). DSCG has also been shown to be effective

in the treatment of hay fever in daily dosages of 6×5.6 mg (2, 7). However, few studies comparing the clinical efficacy of intranasal steroids with DSCG in perennial or seasonal rhinitis have been published, and results have been contradictory. In perennial rhinitis beclomethasone dipropionate (BDP) was shown to be significantly more effective than DSCG (6) and in seasonal rhinitis betamethasone valerate was found to be more effective than DSCG (5). In contrast, in another study, BDP was reported to be no more effective than

DSCG in alleviating the symptoms in patients with either perennial or seasonal rhinitis (4).

The aim of this study was to compare the efficacy and short-term side effects of intra-nasal use of budesonide and DSCG in patients suffering from seasonal allergic rhinitis.

MATERIAL AND METHODS

Forty-five patients (23 male, 22 female) entered the trial. There were three withdrawals from the study, two from the group receiving budesonide and one from the group receiving DSCG. One from each group did not return to the clinic for unknown reasons after the first control visit, and one from the budesonide group stopped treatment on day 18 because of headache. The mean age was 29, ranging from 15 to 55 years. Inclusion criteria were: 1) seasonal allergic rhinitis for more than 2 years, 2) positive skin prick test to grass pollen, 3) gave informed consent and 4) stayed in the same environment during the course of the trial.

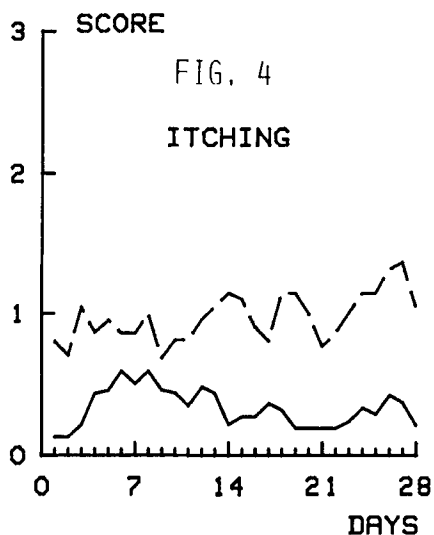
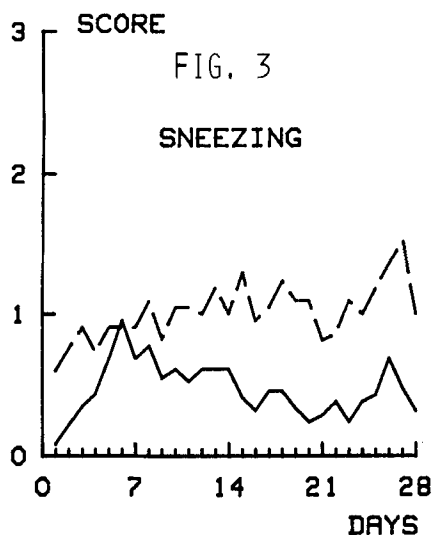
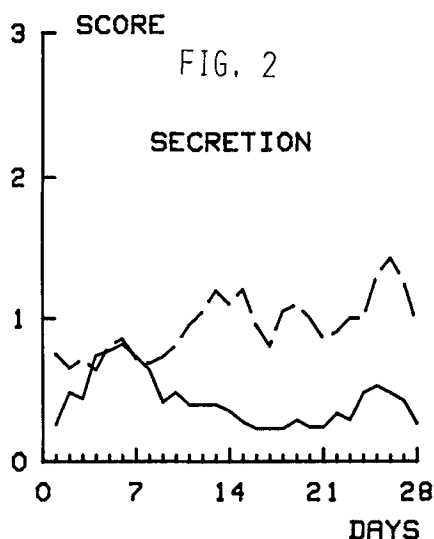
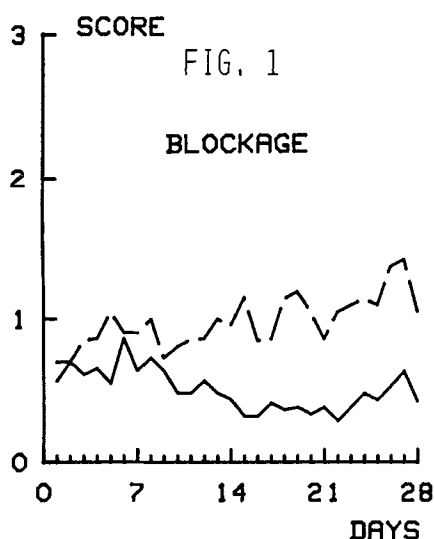
Excluded were patients with: a) nasal stenosis caused by septum deviation or nasal polyps, b) infectious rhinosinusitis, c) patients receiving oral corticosteroid or treatment for asthma, and d) patients who were pregnant. Budesonide (active or placebo) was given as 2 puffs from a pressurized aerosol in each nostril morning and evening (1 puff active substance delivers 50 µg budesonide, total daily dosage 400 µg). The dosage of DSCG (active or placebo) was given as nebulogenum, 1 spray in each nostril 5 times daily. (1 spray active substance delivers 2.6 mg DSCG, total daily dosage 26 mg).

The study was started on May 24th, with a 7-day run-in period followed by a treatment period of 21 days. The patients were randomized into two parallel groups. All patients received both a coded aerosol and a coded nebulogenum, containing either active aerosol and placebo nebulogenum or vice versa. The trial was thus undertaken with a double-blind, double-dummy design.

Table 1

The mean symptom score during the run-in period and treatment periods. *P*-values obtained by Wilcoxon's test (run-in) or stratified Wilcoxon's test

		Blockage	Secretion	Sneezing	Itching	Total nasal symptoms
Run-in	Budesonide	0.59	0.60	0.47	0.33	1.99
	DSCG	0.88	0.76	0.81	0.84	3.29
	<i>P</i>	NS	NS	NS	NS	< 0.05
Week 1	Budesonide	0.51	0.40	0.59	0.44	1.94
	DSCG	0.89	0.95	1.00	0.89	3.73
	<i>P</i>	NS	NS	NS	NS	< 0.05
Week 2	Budesonide	0.37	0.25	0.37	0.27	1.26
	DSCG	1.01	1.00	1.09	0.99	4.09
	<i>P</i>	< 0.05	< 0.001	< 0.01	< 0.001	< 0.001
Week 3	Budesonide	0.44	0.43	0.41	0.31	1.59
	DSCG	1.14	1.10	1.13	1.13	4.50
	<i>P</i>	< 0.05	< 0.02	< 0.02	< 0.01	< 0.001
Weeks 1-3	Budesonide	0.44	0.36	0.46	0.34	1.60
	DSCG	1.01	1.01	1.07	1.00	4.09
	<i>P</i>	NS	< 0.05	< 0.02	< 0.02	< 0.01



Figs. 1-4. The daily mean score of the nasal symptoms: blockage, secretion, itching and sneezing.

Concomitant medication was avoided when possible, but if necessary patients were allowed to take an antihistamine and patients were also allowed to control eye symptoms by eye drops.

A complete history was taken at the first visit and a full ENT-examination was made at the first visit, after 1 week and at the end of the trial. Symptoms evaluated from the nose were sneezing, blockage, secretion and itching, and from the eyes itching and running. Symptoms

were recorded daily on diary cards. The following scale was used: 0 = none, 1 = mild, 2 = moderate, 3 = severe. Any concomitant medication was recorded on the diary card as well as any untoward effects.

In connection with the first and the last examination the nasal secretion was studied for eosinophilia using a semi-quantitative scale from 0 to +++. In addition, posterior bilateral rhinomanometry was done without de-

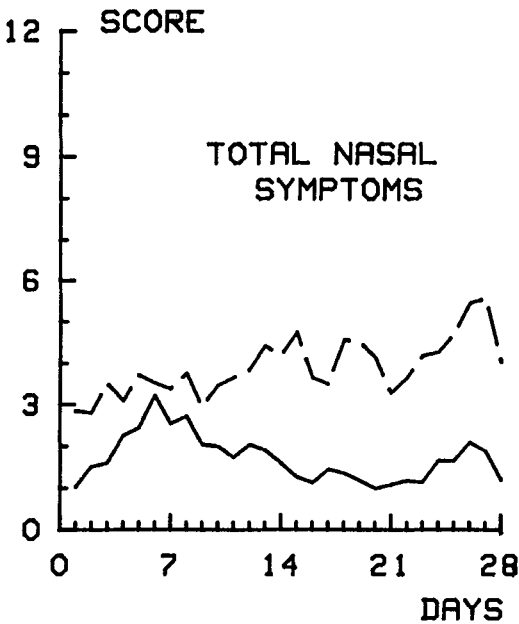


Fig. 5. The daily mean score of total nasal symptoms. DSCG = ----; budesonide = —.

congestion. The equipment used was Mercury Nasal Resistance Meter No. 1. At the end of the trial the patients were asked to give their opinion of the treatment on a 1–4 scale.

Table 2
Adverse effects

	Budesonide	DSCG
Dryness of nose and throat	1	2
Irritation of nose and throat		3
Crusts in the nose	1	2
Headache	2*	

* 1 patient stopped treatment.

Table 3
Patients' opinions of treatment

	Budesonide	DSCG
Very good	6	2
Good	15	13
No effect	0	6

$\chi^2 = 8.14$. $P < 0.02$.

The data obtained from the diary cards were analysed by two-sided stratified Wilcoxon's rank sum test (between groups) and Wilcoxon's signed rank sum test (within groups). A stratification according to the baseline scores during the run-in period was used because of a reference between the scores in the two groups. This implied that only treatment results from patients belonging to the same stratum were compared. The patient material and the patients' subjective assessment of the treatment were analysed by means of a Chi-square test.

RESULTS

Twenty-two patients received budesonide and 21 DSCG. There were no differences in age, familial predisposition, and duration of the disease. There was, however, a considerable difference between the two groups in the symptom scores during the run-in period, being higher in the DSCG group than in the budesonide group. This problem was overcome by the use of a stratified test in the statistic evaluation. 42 patients completed the trial and filled in the score cards correctly.

The results from the analysis of the score cards and the mean score values are seen in Table 1. No statistically significant differences between the two groups were found during the run-in period or the first week of treatment for any nasal symptoms, while a significant difference was found in the second and third week for all nasal symptoms in favour of budesonide (Table 1, Figs. 1–4). The daily score values were increasing in the DSCG group during the whole treatment period, while the score values were stable or slightly decreasing in the budesonide group, being significantly different when pooled for each of the nasal symptoms: secretion, sneezing and itching (Table 1, Figs. 1–4). The total nasal symptom scores for each week were significantly lower in the budesonide group (Table 1, Fig. 5). The eye symptom scores were significantly lower in the budesonide group when pooled ($P < 0.05$).

The adverse effects are listed in Table 2. One patient in the budesonide group stopped treat-

ment on day 18 because of headache for the previous 5 days, with still a slight headache on the following days.

All other adverse effects were mild. The use of eye drops and antihistamine tablets was modest in both groups. The amount of eosinophils in nasal secretion was very slight in both groups before the trial as well as at the end of the treatment. No significant difference in the number of eosinophils was found at any time. Measurements of nasal airway resistance could be done in 85% of the patients. There were no significant differences between treatments, either before the trial or after. The patients' opinions of treatment (Table 3) were significantly in favour of the budesonide treatment.

DISCUSSION

Judging from the low nasal symptom scores during the run-in period the grass pollen season had not yet started. A rise in symptom scores towards the end of the run-in period indicated increasing pollen amounts, just before the start of the treatment.

The result of the therapy for seasonal allergic rhinitis was markedly better in patients treated with budesonide than in patients treated with DSCG. Although the scores for all nasal symptoms were low in the budesonide group already during the run-in, treatment either reduced them or kept them unchanged during the pollen season. In contrast, nasal symptom scores increased during DSCG treatment, although starting from higher run-in values.

Both budesonide and DSCG treatment were well accepted by the patients and the side effects were few.

It is concluded that budesonide, 200 µg b.i.d., is a safe and effective drug in the treatment of seasonal allergic rhinitis, yielding significantly better treatment results than DSCG in the recommended dosage of 5.2 mg 5 times daily. Moreover, patient compliance is likely to be better with budesonide (b.i.d.) than with DSCG (5 times daily).

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