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A New Aerosol Formulation of Sodium Cromoglycate Compared with Conventional Powder in the Treatment of Asthma

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Sodium cromoglycate formulated as a pressurised aerosol was compared with the conventional powder for a period of 12 weeks in a double-blind group comparison trial involving 48 patients. A double dummy technique was used; the dose of sodium cromoglycate was 2 mg four times daily by aerosol, and 20 mg four times daily by Spinhaler®. Patients were able to use the correct technique for both aerosol and dry powder inhalation. Patients recorded the severity of their asthma symptoms, their morning and evening peak flow rate, and the amount of other asthma therapy used, on a daily diary card. They also attended the clinic every 4 weeks for assessment. A statistical comparison of the efficacy of the powder and aerosol forms found no significant differences in clinical assessment of severity, diary card symptom scores, morning and evening peak flow readings, or aerosol bronchodilator usage. Thirty-four patients considered that the aerosol was more convenient and easier to use than the dry powder inhaler.

Key words: aerosol; asthma; powder; sodium cromoglycate.

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CLINICAL ASPECTS

The results of this double-blind study suggest that sodium cromoglycate delivered by pressurised aerosol is a convenient and effective therapy, and should prove especially useful to patients who dislike dry powder inhalation.

Sodium cromoglycate has now been formulated as a pressurised aerosol. Preliminary studies (1, 2, 6) indicated that an aerosol dose of two puffs four times daily (total 8 mg) could maintain patients formerly stabilised on powder (Intal/Lomudal®) therapy. Double-blind comparisons of aerosol and powder forms for periods of 4 weeks (2, 3, 6, 7) and 8 weeks (4, 5) showed that patients responded similarly to both forms.

The objective of this study was to assess the efficacy of the new aerosol relative to the standard powder, when given for 12 weeks to patients who respond to sodium cromoglycate powder therapy.

PATIENTS AND METHODS

A total of 56 patients entered the trial. Two patients withdrew from the study during the first month – one from the aerosol group because of bronchitis, the other from the powder group because of exacerbation of asthma. The first patient and a further seven patients were excluded from the analysis either because they used prednisone extensively during the trial, or were using prednisone continuously before the trial, in contravention of the protocol.

The patient characteristics are shown in Table 1. All patients were perennial asthmatics

Table 1

Patient characteristics

Variable	Frequency value	
	Aerosol	Powder
Age (years):		
Mean	27.0	31.2
Range	9–55	8–60
Type of asthma:		
extrinsic	1	2
extrinsic + intrinsic	22	18
intrinsic	1	3
not stated	1	0
Peak flow (l min):		
Mean (± SD)	366 (± 111.6)	383 (± 159.3)
% of predicted normal	68 (19)	70 (20)
Present therapy:		
sodium cromoglycate powder	25	23
bronchodilator aerosol	19	20
oral bronchodilator	1	2
antihistamine	8	11
theophylline	4	7
ketotifen	0	1
inhaled steroid	0	3
nasal steroid	1	1
nasal sodium cromoglycate	6	5

ranging in age from 8–60 years; there were 31 males and 17 females. They mostly had extrinsic asthma with or without an intrinsic component with a proven response to sodium cromoglycate in a previous challenge test.

All were maintained on sodium cromoglycate powder, and most also used a bronchodilator aerosol; only three patients used a steroid aerosol and none took oral steroids. Patients could use both a pressurised aerosol and a dry powder inhaler (Spinhaler®) correctly.

After a 1 week baseline period, during which Lomudal therapy was continued, 25 patients received the aerosol (2 × 1 mg four times daily) and placebo powder, and 23 patients the powder (20 mg four times daily) and placebo aerosol, for 12 weeks. Treatments were allocated randomly in double-blind fashion.

Patients made a daily record on a diary card of asthma severity during the day and night (0–10 scale), morning and evening PEF (best of three readings using a Mini-Wright peak flow meter), bronchodilator usage, and the dosage of test medication and other therapy taken. At the beginning and end of the baseline week, and subsequently every 4 weeks, asthma severity was assessed at the clinic (0–3 scale).

Data were evaluated using two-tailed t-tests (parametric data) and Mann-Whitney U-tests (non-parametric data). A level of significance of 0.05 was considered significant.

RESULTS

Clinical assessments of asthma severity

Comparison of the changes from the baseline assessments shows no difference in patients' responses to aerosol and powder (Table 2).

Patients and the clinician were asked each month if asthma had improved, not changed, or

Table 2

Clinical assessment of asthma severity

Treatment	Mean score at end of baseline*	Change from baseline		
		Week 4	Week 8	Week 12
Aerosol	1.2 (25)	±0.1 (23)	0.1 (25)	0.0 (22)
Powder	1.1 (23)	0.3 (21)	0.1 (20)	0.1 (22)
2-tail significance**	NS	NS	NS	NS

* Symptom scale: 0–3.

** Mann-Whitney U-test.

worsened during the previous 4 weeks. The results for aerosol and powder were similar.

Diary cards

Diary card data for aerosol and powder were compared for the first, second and third months of the study (Table 3). There were no significant differences at any time in day-time severity, night-time severity, usage of bronchodilators, or morning and evening PEF. Symptoms during the trial were generally mild. Average use of aerosol bronchodilators was between two and four puffs daily.

At the end of the trial, patients' device preferences were 34 for the pressurised aerosol and 11 for the dry powder inhaler ($P < 0.01$ Binomial test). The most frequent reason given was that the aerosol was more convenient and easier to use. However, four patients commented that they preferred aerosol because it caused no throat irritation or coughing as did powder inhalation. On the other hand, three patients preferred powder, because the aerosol irritated their throat or caused them to wheeze. There were no other unusual symptoms attributable to the trial treatments.

DISCUSSION

The results of this study confirm and extend the findings of earlier studies (2–7), and enable some important conclusions to be made on the therapeutic efficacy and acceptability of this new aerosol form of sodium cromoglycate. Since no differences were observed between patients' responses to aerosol and powder therapy in either the first, second, or third month of the trial, it is reasonable to conclude that patients previously maintained by sodium cromoglycate powder continued to benefit for the whole 3 months' period when the drug was

Table 3

Diary card scores (daily means)

Variable	Treatment	Mean during baseline	Difference from baseline ± SD		
			Weeks 1–4	Weeks 5–8	Weeks 9–12
Day-time severity of asthma*	Aerosol	1.6	−0.2	−0.1	−0.1
	Powder	1.7	0.0	−0.3	−0.1
	2-tail significance[a]	NS	NS	NS	NS
Night-time severity of asthma*	Aerosol	1.5	−0.1	0.1	0.1
	Powder	1.9	−0.1	−0.4	−0.6
	2-tail significance[a]	NS	NS	NS	NS
Morning peak flow	Aerosol	379 ± 121.5	8 ± 51.8	11 ± 66.0	9 ± 69.1
	Powder	398 ± 149.9	23 ± 60.4	35 ± 63.0	37 ± 72.8
	2-tail significance[b]	NS	NS	NS	NS
Evening peak flow	Aerosol	407 ± 125.7	6 ± 50.6	3 ± 58.2	0 ± 64.3
	Powder	435 ± 143.3	6 ± 46.2	19 ± 54.3	21 ± 68.7
	2-tail significance[b]	NS	NS	NS	NS
Aerosol bronchodilator	Aerosol	2.5	−0.2	0.0	0.2
	Powder	4.1	0.3	0.2	0.2
	2-tail significance[a]	NS	NS	NS	NS

[a] Mann Withney U-test.

[b] t-test.

NS $P > 0.05$.

* Symptom scale: 0 to 10.

administered by pressurised aerosol. It is possible that a larger proportion of the aerosol dose may be inhaled as fine particles, thus making the difference in dosage between the powder and aerosol rather less than 10:1. Our results also suggest that the majority of patients will find the aerosol convenient and easy to use. The few patients who are troubled by transient throat irritation or cough after inhaling sodium cromoglycate by one method may find the alternative method of administration useful. Hence it may be concluded that this new aerosol form of sodium cromoglycate is an effective asthma therapy and a useful alternative to the standard powder.

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