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Effect of Oral and Inhaled Sodium Cromoglycate in Exercise-Induced Asthma

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Ten patients with bronchial asthma reacting with bronchoconstriction after exercise were studied to compare the effect of oral sodium cromoglycate against sodium cromoglycate inhalation and placebo. Only sodium cromoglycate inhalations protected against exercise-induced asthma. The effect of sodium cromoglycate seems to be a local action of mucosal surfaces.

Key words: bronchoconstriction – exercise-induced asthma – sodium cromoglycate.

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Patients with bronchial asthma may after physical exercise develop bronchoconstriction i.e. exercise-induced asthma (EIA) (7). Pretreatment with inhalation of sodium cromoglycate (SCG) (Lomudal®, Intal®) as a powder (6) or a nebulised solution (3) may prevent EIA. In the present study the protective effect of orally administered SCG (Nalcrom®) on EIA has been examined.

PATIENTS AND METHODS

Ten patients with bronchial asthma without severe chronic obstruction were studied. The basis for selection was that they demonstrated a fall in peak expiratory flow rate (PEFR) of at least 15% after exercise. There were five males and five females and the age range was 13–40 years, mean age 27.9 years.

All patients were skin tested and those suspected of having an IgE-mediated disease were given an inhalation challenge.

In eight patients allergen-induced reactions played a patho-genetic role in their disease and in two patients no IgE-mediated precipitating causes could be detected.

Exercise tests were performed as ergometer cycling. The maximal working capacity was determined on a separate day. The exercise challenge test consisted of bicycling for 6 min with a working load adjusted individually to 70% of the maximal working capacity. PEFR was measured immediately before exercise, after 2, 4 and 6 min of exercise and 1, 3, 5, 10, 15, 20 and 30 min after exercise.

An initial control test was made without prior drug administration. Patients were then tested under double blind conditions in random order with a capsule of 20mg SCG and 20 mg lactose, a placebo capsule (40 mg lactose) both given by spinhaler 5 min before exercise, enterosoluble capsules containing 100 mg of SCG and placebo oral capsules (lactose), both given in doses of two capsules four times daily the day before and two capsules 1 h before the exercise test. Each test was carried out on a different day and tests were always performed at the same time of day. All medical treatment was discontinued at least 12 h before tests.

It was decided to give the oral doses in this way as a preliminary study of six patients showed that a single dose of 200 mg or 400 mg of SCG given orally 1 h before the test did not protect against EIA. Also in oral challenges in

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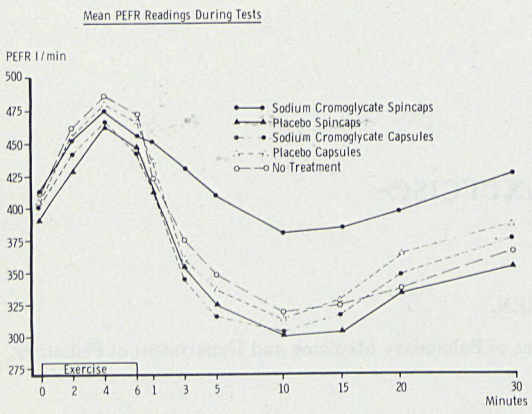

Fig. 1. Mean values of peak expiratory flow rate (PEFR) readings during tests.

patients with food allergy, a pretreatment with a single dose of orally given SCG did not protect against allergic reactions, whereas multiple oral doses as in the present study protected the patients (4).

The statistical evaluation was an analysis of variance on maximal falls in PEFR from baseline.

RESULTS

Fig. 1 is a graphical illustration of mean PEFR readings throughout the trial. Protection was given by SCG inhalation and a significantly ($P < 0.001$) smaller fall in PEFR was seen after exercise with this treatment compared with oral SCG, placeboes or with no treatment.

Table 1 shows the results as mean PEFR values for baseline reading before exercise, the maximum increase during exercise (usually occurring after 4 min) and the maximum decrease from baseline occurring after exercise (usually occurring 10 or 15 min after exercise).

A similar increase in PEFR during exercise was seen after all treatments.

An analysis of variance was made on maximum falls in PEFR from baseline and a significant difference ($P < 0.001$) was detected between treatments. Least significant differences were computed to find which treatments were contributing to the significance. SCG spincaps were found to give a significantly smaller fall in PEFR than the other treatments. There was no difference in results between the other treatments.

Table 1.
Mean value of PEFR readings before exercise (baseline reading), the maximum increase during exercise and the maximum fall from baseline after exercise. Standard deviations are the residual variation from analysis of variance

Treatment	Mean value for :		
	Baseline Reading	Maximum Increase During Exercise	Maximum Fall After Exercise
No treatment	409	81	114
Sodium Cromoglycate Spincaps	411	71	27
Placebo Spincaps	392	74	108
Sodium Cromoglycate Oral	399	71	116
Placebo Oral	403	81	110
Standard Deviation	29.6	23.9	39.2
Degrees af Freedom	36	36	36
Significance	NS	NS	P < 0.001
LSD (P < 0.05)			36
LSD (P < 0.001)			63

LSD: Least significant difference between two treatment means is calculated from estimate of pooled variation obtained in the analyses of variance.
NS: Not significant, $P > 0.05$.

DISCUSSION

It is well established that inhalation of SCG before exercise prevents EIA (1). This study shows that oral administration of SCG does not protect against EIA.

The systemic absorption of SCG after inhalation is 7.6% and after oral administration 0.8–1.0% (8). By giving higher oral doses than inhaled doses, similar amounts of the drug would be present in the body.

Pretreatment with oral SCG both as single or multiple doses did not protect against EIA and it is therefore the local effects of inhaled SCG on the bronchial mucosa that play a role.

In patients with food allergy and asthmatic reactions after ingestion of the specific food, inhalation of SCG did not give any protection whereas orally administered SCG prevented the reactions (2). Also in food allergies the effect of SCG seems to be a local protection on

the gastro-intestinal mucosa and not a result of systemic absorption of the drug.

The present study supports the suggestion that the effect of SCG in allergic reactions is an effect on structures in or on mucosal surfaces. In food allergy SCG may prevent allergic reactions on the gastro-intestinal mucosa and possibly prevent absorption of antigen (5). In inhalation allergies and EIA the protection given by SCG also seems to depend on a surface action. This could be an action on superficially situated mast cells or mast cells in the bronchial lumen.

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