

Inhibition of human allergic skin reactions *in vivo* by pretreatment with cromolyn (disodium cromoglycate)

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The effect of cromolyn on allergen-induced allergic skin reactions was studied. Two patients with allergic rhinitis, two patients with bronchial asthma and atopic dermatitis and two patients with allergic rhinitis and atopic dermatitis were included in this study. They were allergic to cedar pollen, house dust mite and house dust, respectively. Scratching with allergen induced wheal and erythema reactions in each patient. Simultaneous application of allergen and cromolyn solution did not modulate allergic reactions; however, pretreatment with cromolyn solution inhibited allergen-induced wheal and erythema reactions significantly.

Key words: allergen; allergic patients; allergic skin reactions; cromolyn.

Accepted for publication 9 February 1990

CLINICAL ASPECTS

We recently reported that in children atopic dermatitis improved with topical cromolyn solution. This study shows that pretreatment with cromolyn directly inhibited allergic skin reactions, suggesting the therapeutic mechanisms of cromolyn solution in atopic dermatitis.

MATERIAL AND METHODS

Two men with allergic rhinitis, two woman with asthma and atopic dermatitis and two woman with allergic rhinitis and atopic dermatitis aged 31-46 years (mean age 36.7 years) were studied. They were allergic to cedar pollen, house dust mite (*Dermatophagoides pteronyssinus*) and house dust, respectively. They were without any medication for 72 h prior to the experiments.

A control solution (water) or cromolyn nebulizer solution (Fujisawa Fisons) was applied to the forearms of the patients. After 0 min (immediately after cromolyn pretreatment) and after 5 min allergen (Toril & Co.) was applied and the skin was scratched. Allergen, cromolyn or con-

The effect of cromolyn (disodium cromoglycate) ointment on atopic dermatitis is controversial (2, 4). It has also been reported that cromolyn did not modulate human allergic skin reactions directly *in vivo* (1, 7). In contrast to those reports, Nagano has reported that pretreatment by a cromolyn nebulizer solution (1% cromolyn solution) inhibited contact dermatitis, from house dust mite allergen, in patients with atopic dermatitis who were allergic to house dust mite (5). We found that topical cromolyn solution had a beneficial effect on atopic dermatitis in children (3). Accordingly, we have studied the effects of cromolyn pretreatment on allergen-induced wheal and erythema reactions.

Table 1
Effect of cromolyn on allergen-induced erythema and wheal

Patient (Allergen)	Size (mm) of wheal erythema		
	Allergen alone	Allergen + cromolyn pretreatment (time)	
		0 min	5 min
# 1 Cedar pollen	6 × 6 21 × 23	5 × 6 22 × 23	1 × 1 10 × 9
# 2 Cedar pollen	6 × 7 22 × 23	5 × 6 21 × 22	0 3 × 3
# 3 Mite *	11 × 11 27 × 26	9 × 10 31 × 30	1 × 1 3 × 3
# 4 Mite *	12 × 11 30 × 28	8 × 10 31 × 32	4 × 4 12 × 11
# 5 House dust	6 × 8 22 × 20	8 × 7 20 × 21	2 × 2 12 × 13
# 6 House dust	7 × 8 20 × 21	8 × 7 20 × 20	2 × 1 13 × 13

Patients # 1 and # 2: allergic rhinitis; # 3 and # 4: bronchial asthma and atopic dermatitis; # 5 and # 6: allergic rhinitis and atopic dermatitis. **Dermatophagoides pteronyssinus*.

trol solution were also applied individually and separately to unpretreated skin, and the skin was then scratched; 15 min later, wheal and erythema were measured.

RESULTS

The table shows that simultaneous application of cromolyn solution did not modulate allergic response. However, pretreatment with the cromolyn solution for 5 min inhibited allergic response significantly ($P < 0.01$, Student's t test).

Pretreatment with a control solution, i.e. water, did not modulate skin reactions (not shown). None of the patients showed an allergic response to cromolyn.

DISCUSSION

Our results indicate that cromolyn directly inhibited human allergic skin reactions *in vivo*. However, cromolyn must be applied to the skin before the allergen, since simultaneous application (0 min) did not modulate the allergic response, a result correlating with previous results (1, 7). However, previous researchers did not test the effect of cromolyn pretreatment. It has been reported recently that preincubation of neutrophils or eosinophils with cromolyn selectively inhibits antibody-dependent granulocyte-mediated cytotoxicity (4). Therefore, to accurately study the effect of cromolyn both *in vitro* and *in vivo*, targets should be pretreated with cromolyn.

We recently reported that application of cromolyn solution to atopic skin directly improved atopic dermatitis in children (3). The exact therapeutic mechanisms of cromolyn solution on atopic dermatitis remains to be elucidated. The mechanisms of atopic dermatitis are also unclear. However, the fact that cromolyn solution directly inhibits immediate skin reactions regardless of the allergens suggests the possible role of immediate allergic reactions in atopic dermatitis.

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