

Effects of orally administered sodium cromoglycate in asthma and urticaria due to foods

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Summary

Out of twenty patients with a history of asthma or urticaria attributed to food substances, ten reacted on oral challenge: seven with asthma, one with asthma and urticaria and two with urticaria alone. In five of the eight asthmatic reactors, the symptoms developed within a few sec and there was no associated rise in free venous plasma histamine. In those remaining, two with asthma, two with urticaria and one with both, the symptoms developed only after 20–30 min. A rise in free plasma histamine occurred only in the two subjects with urticaria alone. The third with urticaria and asthma did not have blood estimations performed.

Sodium cromoglycate in a dosage of 800 mg a day for 1 week, or a single dose of 1.0 g by mouth, did not block any of the reactions. By inhalation it blocked the asthmatic reactions which developed within a few sec of challenge.

Introduction

During anaphylaxis, a number of agents are released into the blood, including histamine and slow-reacting substance of anaphylaxis (SRS-A) (Piper & Vane, 1969, 1971). In patients with asthma due to aspirin sensitivity, a rise in free plasma histamine has been shown to coincide with the development of symptoms in proportion to the severity of the attack (Stevenson *et al.*, 1976).

Evidence of specific IgE antibody to foods from skin testing and RAST is well recognized, especially in children (Chua *et al.*, 1976). The effect of sodium cromoglycate on IgE-mediated release of histamine and slow-reacting substance has raised the possibility that symptoms induced by food substances may be blocked by the orally administered drug. There are several reports suggesting that this may occur (Dannaeus, Foucard & Johansson, 1977; Frier & Berger, 1973; Kingsly, 1974; Kuzemko & Simpson, 1975; Werthenschlag, 1975).

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The object of this study was to assess the effects of sodium cromoglycate by mouth and by inhalation on reactions induced in sensitive subjects challenged with specific food substances.

Patients and methods

Twenty patients, sixteen female and four male, ranging in age from 20 to 43 years, were studied. All claimed that asthma or urticaria developed within a short time of taking certain substances by mouth. The materials tested were: port wine, Baccardi, tartrazine, coconut, chocolate, aspirin, bran, cod fish and dried apricots. The patients were admitted for challenge to a day care unit under constant supervision. All were asked to take nothing by mouth after midnight on the day before challenge. Peripheral venous blood samples for histamine estimation and for cell counts were drawn through a 19 Butterfly needle into heparinized 5.0 ml aliquots. Unless the patient gave a history of anaphylactic reactions, customary portions of the test material were given. Only one challenge was made on any one day, with only one test a week. The patients showing no reaction to the initial challenge were finally given either a larger portion of the food or an alternative preparation. Asthmatic attacks were measured with a dry spirometer, and a fall in FEV₁ of greater than 15% was regarded as a significant asthmatic reaction.

The following treatment regimens were used: (a) 200 mg of pure DSCG or lactose placebo in plain capsules, given by mouth four times daily for 1 week, with challenge on the last day of treatment; (b) 1.0 g of pure DSCG or sodium bicarbonate placebo dissolved in warm water and swallowed 30 min prior to challenge; and (c) 40 mg of plain DSCG in lactose by inhalation given 10 min prior to challenge, but not matched with placebo.

Free venous plasma histamine was assayed using an automated fluorimetric method (Siraganian, 1975).

Table 1. Comparison of the different treatment regimens of sodium cromoglycate on symptoms induced by oral challenge in ten sensitive subjects

Patient	Test substance	Treatment regimen			Onset of symptoms (min)	Rise in free plasma histamine (ng/ml)
		(a)	(b)	(c)		
1	Coconut	n.d.	—	+	1	0
2	Port	n.d.	—	+	1	0
3	Tartrazine	—	—	+	1	0
4	Baccardi	—	—	+	1	0
5	Bran	—	n.d.	n.d.	1	n.d.
6	Aspirin	—	n.d.	n.d.	40	n.d.
7	Apricots	—	n.d.	—	75	0
8	Cod fish	n.d.	n.d.	—	40	n.d.
9*	Aspirin	—	n.d.	n.d.	45	32
10*	Chocolate	—	—	n.d.	45	6

n.d. = Not done; (—) no blocking effect; (+) reaction blocked.

* Urticaria only.

Results

Of the twenty patients tested, only ten developed symptoms related to challenge, and of them all but one was atopic. The patients fell into two groups, depending upon the speed with which symptoms developed following challenge (Table 1).

In five subjects (group 1), asthma developed very rapidly, usually within 1 min of the test material being placed in the mouth, was maximal after about 30 min and

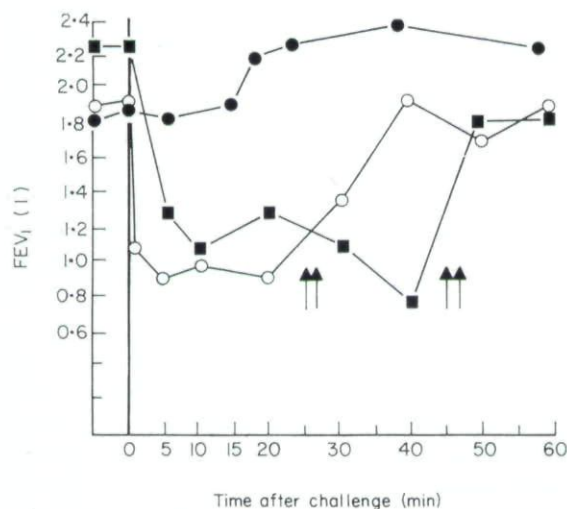


Fig. 1. Oral challenge: tartrazine, 1.0 mg sublingual. Double arrows show inhalation of salbutamol, 200 μ g. (○) DSCG placebo; (●) DSCG, 40 mg by inhalation; (■) DSCG, 800 mg by mouth daily for 1 week.

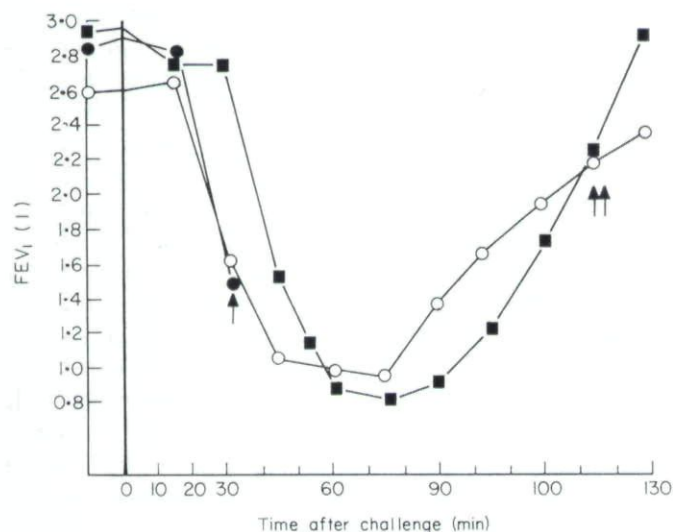


Fig. 2. Oral challenge: dried apricots. Single arrow shows injection of adrenalin; double arrows show inhalation of salbutamol, 200 μ g. (○) DSCG placebo; (●) DSCG, 40 mg by inhalation; (■) DSCG, 800 mg by mouth daily for 1 week.

resolved usually within 1 hr. This was typical of sensitivity to alcoholic beverages, and in one patient who was sensitive to tartrazine, asthma developed within 15 sec of a dose of 1.0 mg placed sublingually (Fig. 1).

In the other five subjects (group 2), the reactions consisted of asthma in two, asthma and urticaria in one and urticaria alone in two, starting about 20–30 min after the challenge, maximal at 1.5–2.5 hr and lasting more than 2 hr (Fig. 2).

Patients in group 1 developing symptoms within 1 min showed no change in free plasma histamine. In group 2, a steep rise in free plasma histamine was seen only in the two subjects with urticaria alone due to aspirin and milk chocolate respectively. In these cases the rise in free plasma histamine coincided with the onset of the urticaria. Neither regimen (a) or (b) of oral sodium cromoglycate had an effect on any of the asthmatic reactions or on the rise in free plasma histamine in the two patients with urticaria. Inhalation of sodium cromoglycate exerted a blocking effect of greater than 70% on the asthmatic reactions of patients in group 1 compared with placebo, but it had no effect on the reactions to aspirin, apricot or milk chocolate, which developed after 20–30 min. Blood estimations were not performed on the patient with both asthma and urticaria.

Discussion

The differing speed with which sensitive subjects react to orally ingested material suggests that the antigen is being absorbed in different ways. In those reacting rapidly it is possible that the allergen is being absorbed from the mouth. In those reacting after 20–30 min, absorption from the gut seems likely. There are other reports on differences in the speed of reactions to food substances (Freedman, 1977). The absence of a detectable rise in free venous plasma histamine, even with the most severe asthmatic reactions, may be due to release of mediators from mast cells in the lung. By contrast, the two patients who developed urticaria alone showed a steep rise in free plasma histamine, developing after 20–30 min and coincident with the symptoms.

It has been suggested that mediators may be released from mast cells and from circulating white cells, as a pharmacological property of the absorbed agent, without the co-operation of IgE or complement. It is possible that asthma induced by analgesics develops in this way (Schlumberger, Lobbecke & Kallos, 1974), and Delaney has demonstrated a poor blocking effect with inhaled sodium cromoglycate in asthma induced by aspirin (Delaney, 1976).

Release of mediators from the gut wall following antigen challenge has been demonstrated in rats sensitized with ovalbumin. Both antihistamines and sodium cromoglycate given by mouth prior to challenge reduced the resulting oedema of the gut wall (Byars & Ferraresi, 1976). Reports in man of relief of symptoms by oral sodium cromoglycate refer mainly to reactions in the gastrointestinal tract, such as abdominal pain, distension and diarrhoea, and to eczema in infants with cows' milk allergy. We have shown that the oral doses of sodium cromoglycate used in our study did not block the asthmatic or urticarial reactions to ingested foods. In a separate study, the symptoms in a patient with abdominal pain resulting from the eating of rice were controlled by 200 mg of sodium cromoglycate taken by mouth four times a day.

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