

The effect of orally administered sodium cromoglycate on allergic reactions caused by food allergens

R. DAHL and O. ZETTERSTRÖM

*Medical Department II, Aarhus Amtssygehus, Aarhus, Denmark, and
Department of Lung Medicine, Akademiska Sjukhuset, Uppsala, Sweden*

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Summary

In five patients who exhibited allergic reactions, four with asthma and one with angioneurotic oedema, to orally administered soybean flour, the protective effect of orally administered sodium cromoglycate has been investigated. Protection from reactions in soybean provocation tests has been achieved with doses ranging from 400 mg to 600 mg given four times daily.

Introduction

The ingestion of specific foods can cause allergic reactions in sensitized patients. The reactions may appear as urticaria, bronchial asthma, rhinitis, angioneurotic oedema or nausea, vomiting, diarrhoea and abdominal pain. The symptoms may appear singly or in combination.

Inhalation of sodium cromoglycate (Lomudal, Intal) may block the asthmatic reaction caused by ingested allergens (Hargreave, 1970). Orally administered sodium cromoglycate may prevent both gastrointestinal and skin reaction after challenge with ingested allergens (Freier & Berger, 1973; Kingsley, 1974). In this study the protective effect of orally administered sodium cromoglycate has been examined in provocation tests in patients with food allergy who react with asthma or angioneurotic oedema after the ingestion of soy protein.

Materials and methods

Ten patients with a history of allergy to soybean flour and with a positive skin prick test or a positive IgE RAST test to soya were challenged by oral administration of soya flour (Danpro-H, Aarhus Oliemolle). The following doses were given at 30 min intervals: 0.1 mg, 1.0 mg, 10 mg, 100 mg, 1.0 g, 5.0 g and 10 g. Five patients gave no reaction, four patients had an asthmatic reaction and one developed angioneurotic oedema. The effect of orally administered sodium cromoglycate was examined in the

Correspondence: Dr Ronald Dahl, Medical Department II, Aarhus Amtssygehus, 8000 Aarhus C, Denmark.

five patients who gave a positive reaction. The drug was administered as gelatine capsules, each containing 100 mg of sodium cromoglycate (Nalcrom).

In a preliminary study it was determined that a single dose of the drug had no protective effect in these challenge conditions. Subsequently the protective effect of a 1 day pretreatment with four doses of drug or placebo, 200 mg, 400 mg, 600 mg and, in one case, 1.0 g, was examined. Further doses were given on the day of challenge 2 hr and 15 min before the antigen.

Provocation tests were performed using the smallest amount of antigen which caused a reaction and at intervals of 7 days. Each test was started at the same time of day and the patients were under constant supervision during the period of the reaction. Any other drug treatment was discontinued at least 24 hr before the test. None of the patients had been treated with corticosteroids.

Patients and results

Patient No. 1

Male, aged 57 years, with perennial allergic asthma since childhood. Numerous commercial foods were shown to cause asthmatic reactions and specifically soybean protein. He had a positive skin test to soya, a doubtfully positive IgE RAST to soya and a total serum of IgE of 5500 u/ml. Oral challenge with 10 g of soybean flour administered via an intragastric tube produced an asthmatic reaction lasting up to 6 hr. This reaction could be prevented by pretreatment with oral sodium cromoglycate in doses of 400 mg. Pretreatment with a similar number of placebo capsules gave no protection.

Patient No. 2

Male, aged 32 years, with bronchial asthma since childhood. Attacks of asthma and slight diarrhoea occurred after ingestion of peas, beans, chocolate, toast and certain canned meats. Status asthmaticus occurred on one occasion after ingestion of a single canned meat ball.

He had a positive skin test to soya, a positive IgE RAST (class four) to soya and a total serum IgE of 950 u/ml. Oral provocation with 100 mg of soybean flour caused a moderate to severe asthmatic reaction. Oral sodium cromoglycate in doses of 200 mg and 400 mg gave no protection, whereas doses of 600 mg prevented both the asthmatic reaction and the diarrhoea.

Patient No. 3

Male, aged 45 years. During the last 12 years he had attacks of swelling of the face and neck occurring once or twice a year. He noticed that the attacks usually followed the ingestion of split peas. He was admitted to hospital on one occasion with severe angioneurotic oedema following the ingestion of two boiled sausages.

He had a positive skin test to soya, a positive IgE RAST (class three) to soya and a total serum IgE of 100 u/ml. Provocation with 10 g of soybean flour administered via an intragastric tube caused oedema of the lips. Pretreatment with oral sodium cromoglycate in doses of 400 mg prevented this reaction, whereas pretreatment with doses of 200 mg or with placebo capsules gave no protection.

Patient No. 4

Male, aged 32 years, with bronchial asthma since childhood. Asthma attacks occurred after eating green peas, beans and peanuts.

He had a positive skin test to soya, a positive IgE RAST (class one) to soya and a total serum IgE of 270 u/ml. Provocation with 1.0 g of soybean flour produced an asthmatic reaction. Oral sodium cromoglycate in doses of 200 mg and 400 mg were ineffective, but doses of 600 mg were effective in preventing the reaction.

Patient No. 5

Male, aged 23 years, with intermittent attacks of asthma since childhood. Attacks of asthma occurred after ingestion of green peas. Ingestion of beer always resulted in abdominal pain and diarrhoea.

He had a positive skin test to soya, a negative IgE RAST to soya and a total serum IgE of 100 u/ml. Provocation with 5.0 g of soybean flour administered orally caused an asthma attack. Pretreatment with placebo or oral sodium cromoglycate in doses of 200 mg had no effect, whereas doses of 400 mg and 1000 mg prevented the asthmatic reaction. These doses also prevented the gastrointestinal reaction to beer for a period of 2 days.

Discussion

Soybeans are the seed of the plant *Glycine max*, a member of the Leguminosae family. They are used as a major source of protein in oriental countries and, in western society, soya flour is a constituent of bakery foods, ice cream, cows' milk substitutes, infant foods, sausages and dietetic foods. Other edible members of the same family include peas, beans, lentils and peanuts, which explains some of the cross-sensitivities described in these patients.

The soybean flour used in the challenge tests has, during manufacturing, gone through different extraction procedures and may thereby have a reduced allergen content. This could be the reason for the negative challenge tests in some patients.

Soybean flour as a provoking agent in these experiments has been used as a model for food allergy. However, it also illustrates that sensitivity of this type is not uncommon and may be a factor in perennial asthma. Because of the extensive use of soya as a protein substitute and additive it is difficult for sensitive patients to protect themselves by avoidance.

The amount of sodium cromoglycate absorbed systemically is known to be 0.8–1.0% after oral administration and 7.6% after inhalation (Moss *et al.*, 1971). In patient No. 1, pretreatment with inhaled sodium cromoglycate given 20 mg four times the day before and 20 mg every 30 min before and during an oral provocation did not give any protection. Therefore, it seems unlikely that it is a local effect in the lung from systemic absorption of the drug that is effective in the oral administration of the drug (Dahl, 1978).

Orally administered sodium cromoglycate may possibly act in these circumstances by reducing or preventing an allergic reaction in the gastrointestinal mucosa. Whether it is chemical mediators released from the gastrointestinal mucosa which cause the asthmatic reaction or because the resultant mucosal oedema allows antigen absorption is unknown.

Present treatment of food allergy is based on an elimination diet, symptomatically effective drugs and hyposensitization. In patients who are allergic to multiple foods it is sometimes difficult or impossible to maintain a strict elimination diet and maintain adequate nutrition. Such patients often have chronic allergic symptoms. Treatment with oral sodium cromoglycate in some selected cases of food allergy may possibly provide an effective and alternative form of treatment.

References

- DAHL, R. (1978) Disodium cromoglycate and food allergy. *Allergy* (In press).
- FREIER, S. & BERGER, H. (1973) Disodium cromoglycate in gastrointestinal protein intolerance. *Lancet*, i, 913.
- HARGREAVE, F.E. (1970) Effect of disodium cromoglycate on inhalation tests in man. *Disodium Cromoglycate in Allergic Airways Disease* (eds J. Pepys and A.W. Frankland), p. 27. Butterworths, London.
- KINGSLEY, P.J. (1974) Oral sodium cromoglycate in gastrointestinal allergy. *Lancet*, ii, 1011.
- MOSS, G.F., JONES, K.M., RITCHIE, J.T. & COX, J.S.G. (1971) Plasma levels and urinary excretion of disodium cromoglycate after inhalation by human volunteers. *Toxicology and Applied Pharmacology*, 20, 147.

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