

The effect of sodium cromoglycate on analgesic-induced asthmatic reactions

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Summary

The onset of increased airways obstruction after analgesic ingestion by asthmatics with analgesic idiosyncrasy suggests an immediate type 1 allergic response. The effect of sodium cromoglycate (DSCG) on this response was assessed in nineteen patients with this syndrome. DSCG prevented asthmatic attacks in only three patients, all non-atopic, suggesting that analgesic idiosyncrasy is not an allergic disorder. The effectiveness of DSCG in preventing asthmatic attacks in some patients with analgesic idiosyncrasy would suggest that a trial of this preparation should be undertaken before commencing continuous corticosteroid therapy.

Introduction

Sodium cromoglycate (DSCG), by stabilizing the mast cell membrane, inhibits degranulation of sensitized mast cells and therefore the release of spasmogens including histamine, 5-hydroxytryptamine and slow reacting substance concerned in anaphylaxis (SRS-A) (*British Medical Journal*, 1972). It is generally accepted that DSCG has an important place in the prevention of episodic bronchial obstruction in patients with extrinsic asthma. Relatively few patients with intrinsic asthma benefit from the drug (Mathison *et al.*, 1971).

Asthmatic patients with aspirin 'allergy' form a sub-group of intrinsic asthma. Giraldo, Blumenthal & Spink (1969) reviewed the literature and concluded that there was no satisfactory evidence that immunological factors were involved in the condition. The structural dissimilarity between the analgesics which will induce asthmatic reactions in patients sensitive to aspirin would tend to confirm this view (Smith, 1971). However, the rapidity of onset of the symptoms of asthma and urticaria after analgesic ingestion in these patients bears a similarity to an immediate (Type 1) allergic response.

In this study the effect of DSCG inhalation prior to analgesic challenge was assessed in patients with analgesic idiosyncrasy. It was demonstrated that only a few patients derived any protective effect from this preparation.

Materials and methods

Nineteen patients with aspirin idiosyncrasy and asthma were tested for the effects of DSCG on analgesic challenge. The patients had previously been challenged and found to be sensitive to paracetamol or small doses of aspirin (Delaney, 1976). In the present study, thirteen patients were challenged with aspirin and six with paracetamol. There were five males and fourteen females aged between 17 and 61 years (mean 43.8 years). Three patients were atopic on the basis of positive reactions to skin prick tests with common allergens.

Measurements of the 1 sec forced expiratory volume (FEV₁), forced vital capacity (FVC) and peak expiratory flow rate (PEFR), were made before oral challenge and repeated at half-hourly intervals for 2 hr after challenge. The FEV₁ and FVC were measured on a dry spirometer (Vitalograph®) and the PEFR on a Wright's Peak flow meter; the recorded measurement being the best of three readings.

Only one challenge was performed each day and in the following order.

- (1) Control challenge (25 mg lactose in plain capsule).
- (2) Analgesic challenge (aspirin or paracetamol in plain capsule).
- (3) Analgesic challenge after DSCG (in Spinhaler®).
- (4) Analgesic challenge after placebo (lactose via Spinhaler®).

Twenty milligrams of DSCG was given by means of a Spinhaler 20 min before analgesic challenge. Lactose placebo was made up in identical capsules to the DSCG and administered by Spinhaler in a similar way.

Results

FEV₁ measurements made at similar times each day before challenge with control or analgesic showed slight variations.

Falls in the FEV₁ > 15% after analgesic challenge indicated attacks of asthma and occurred in all nineteen patients (Table 1). In the majority of cases maximum falls in the FEV₁ occurred 15–30 min after challenge and returned to pre-challenge levels by 2–3 hr.

In only three cases was the reaction inhibited by prior inhalation of DSCG. Lactose placebo inhalation had no effect on these reactions. All three patients were non-atopic on the basis of negative skin tests and normal serum immunoglobulin E (IgE) levels (Table 2). Figure 1 shows the effect of DSCG on analgesic challenge in one of these patients.

In the remaining sixteen patients (including three with positive skin tests to common allergens) DSCG had no effect on analgesic induced asthmatic reactions.

Discussion

Sodium cromoglycate treatment prior to challenge with analgesics in nineteen patients with analgesic idiosyncrasy inhibited the development of increased airways obstruction in three patients only. The three patients were all non-atopic. On the other hand, DSCG had no effect in preventing airways obstruction after analgesic ingestion in those patients in the series with positive skin tests to common allergens. These findings would support the view that an immunological basis for the syndrome is unlikely. In accordance with this it has been shown that whereas no histamine can be liberated from the basophils of aspirin-intolerant patients with soluble aspirin, aspirin anhydride or aspirin-conjugates, in those aspirin intolerant patients with

Table 1. Analgesic challenge in nineteen patients with analgesic idiosyncrasy

Patient	IgE (u/ml)	Challenge material	Dose (mg)	FEV ₁ (l)	
				Before challenge	After challenge
1	41.4	Paracetamol	1000	2.10	1.65
2	270	Aspirin	100	4.15	3.50
3	121	Aspirin	100	3.20	2.05
4	114.7	Paracetamol	1000	1.70	1.05
5	500	Aspirin	100	2.00	1.60
6	292.5	Aspirin	60	2.90	1.40
7*	2063	Aspirin	30	1.40	0.90
8*	1675	Paracetamol	1000	3.45	1.80
9	92	Aspirin	100	2.85	1.85
10	141.3	Paracetamol	1000	2.85	2.15
11*	1105	Aspirin	100	1.70	1.20
12	370	Paracetamol	1000	1.65	0.90
13	467.5	Aspirin	80	1.75	1.40
14	91.5	Aspirin	100	1.95	1.45
15	247.5	Paracetamol	1000	1.80	1.35
16	92	Aspirin	80	1.45	0.95
17	170	Aspirin	100	4.25	3.60
18	26.1	Aspirin	30	1.50	1.05
19	110.0	Aspirin	30	1.15	0.80

* Atopic patients with positive skin tests (prick method).

Table 2. Effect of DSCG on analgesic challenge in three patients with analgesic idiosyncrasy

Patient	Challenge	FEV ₁ before challenge (l)	Max. % fall in FEV ₁ after challenge			
			Control	Analgesic	DSCG + analgesic	Lactose + analgesic
1	Paracetamol 1000 mg	2.1	4.5	21.4	7.1	16.7
2	Aspirin 100 mg	4.2	3.6	15.7	4.8	16.9
3	Aspirin 100 mg	3.2	6.3	35.9	3.1	34.4

known allergies, e.g. to pollen, histamine can be liberated from the basophils with the specific allergen (Kallós, 1975).

Aspirin and indomethacin will suppress prostaglandin synthesis (Vane, 1971). The development of asthmatic attacks in patients with analgesic idiosyncrasy may be related to the ability of a particular analgesic to suppress prostaglandin synthesis (Szczeklik, Gryglewski & Czerniawska-Mysik, 1975). It has been demonstrated that when prostaglandin synthesis is suppressed the release of SRSA is markedly enhanced (Walker, 1973) and may result in airways obstruction. In some patients

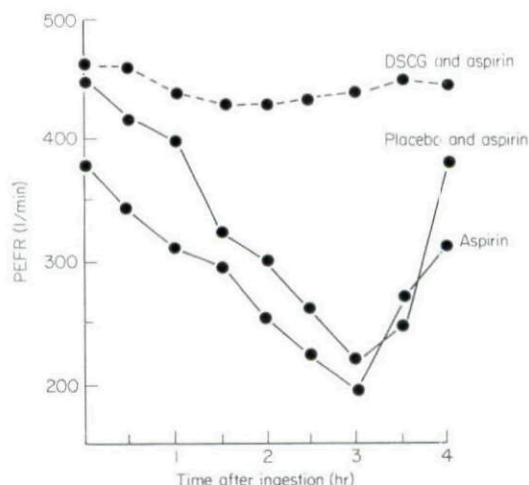


Fig. 1. PFT's after the inhalation of sodium cromoglycate and challenge with soluble aspirin (100 mg) compared with inhalation of placebo and aspirin challenge.

with analgesic idiosyncrasy it appears that DSCG is able to stabilize the mast cell membrane and prevent the release of SRSA.

The asthma and rhinorrhea associated with analgesic idiosyncrasy are usually controlled with continuous corticosteroid therapy. As DSCG appears to benefit some patients with this syndrome a therapeutic trial is justifiable before embarking on long-term corticosteroids.

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