mality, hyaline membrane disease, and pulmonary infection are absent.

Summary

A term infant, born by caesarean section for fetal distress, developed grunting and cyanosis by 15 minutes of age. Ventilation at low pressures was achieved without difficulty but did not improve blood gas levels, and he died at 26 hours. Necropsy examination showed large heart and small lungs; histologically the lungs showed multiple obstructive lesions at medium size pulmonary artery level.

References


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Controlled trial of disodium cromoglycate in prevention of relapse of steroid-responsive nephrotic syndrome of childhood

The aetiology of steroid-responsive nephrotic syndrome (SRNS) is not known, but allergy is implicated: atopic features are more frequent in children with SRNS than in healthy ones, especially if they have tissue type HLA B12 (Thomson et al., 1976). In some patients with nephrotic syndrome associated with atopy, relapses are precipitated by episodes of hay fever (Hardwicke et al., 1959; Reeves et al., 1975). Disodium cromoglycate (DSCG) prevents bronchial, nasal, and perhaps gastrointestinal atopic symptoms. In one atopic patient with SRNS described below, DSCG appeared to prevent relapse during the hay fever season. We therefore studied a possible preventative role of this drug in SRNS by a double-blind trial.

Case report

A 12½-year-old boy presented with nephrotic syndrome in July 1972, associated with upper respiratory tract symptoms. There was no history of atopic disease but skin prick testing was strongly positive for mixed grass pollens and spring flower pollens. Remission of the nephrotic syndrome was induced with prednisolone 2 mg/kg per day. Relapses occurred in June 1973 and May 1974, the latter associated with the onset of hay fever. His HLA type was A2 A3 B7 B12. Serum total IgE was 52 IU/ml (normal <150 IU/ml), but specific IgE antibody to Timothy grass pollen allergen was raised as measured by the radioallergosorbent test (RAST).

Remission of the nephrotic syndrome was again induced with prednisolone and the hay fever treated with intranasal DSCG. Prophylactic DSCG was given four times daily for 6 months from March 1975 as oral inhalation 20 mg by spinhaler, nasal insufflation 10 mg to each nostril, and oral capsules 40 mg with meals. The hay fever occurred in June 1975 and he was given a single intramuscular injection of methylprednisolone 20 mg. His urine was tested daily with Albustix, and was consistently negative, apart from a trace reaction on one day 3 weeks later. He has been symptom free from both hay fever and nephrotic syndrome throughout the past 2 years without treatment.

Patients and methods

The 21 children studied had at least 3 relapses of the nephrotic syndrome and responded to prednisolone treatment. They were in remission on a maintenance dose of prednisolone for at least 2 weeks before entry into the trial. All were over 4 years of age and capable of co-operating with the methods of drug administration. Diagnostic criteria for nephrotic syndrome and relapse are described elsewhere (Barratt and Soothill, 1970). The children were not selected for atopic features, but were consecutive clinic attenders who fulfilled criteria for entry to the trial.
Fig. Time to relapse (weeks) in 21 children with steroid-responsive nephrotic syndrome allocated into 2 groups. Group A received placebo and Group B disodium cromoglycate. Patients with positive HLA B12, atopic symptoms, and positive skin-prick tests are indicated.
HLA type was determined by a two-stage microtoxicity method (Batchelor, 1973). A questionnaire eliciting atopic symptoms and skin-prick testing was done as previously described (Thomson et al., 1976).

The children were randomly allocated in a double-blind manner to one of 2 regimens, DSCG or placebo (lactose), for 16 weeks. The allocation was arranged so that the frequency of HLA B12 in the two treatment groups was similar. DSCG/placebo administration was four times daily as oral inhalation 20 mg by spinhaler, nasal insufflation 10 mg to each nostril, and oral capsules 20 mg mixed with food. Prednisolone therapy was reduced logarithmically and discontinued at the end of week 8.

The parents tested the urine daily with Albustix and reported if a reaction of 2+ or more was observed on 2 consecutive days. Children were classified as relapsing if relapse criteria were observed on or before week 16.

Results

At 16 weeks 5 out of 10 patients in the placebo group and 9 of 11 in the DSCG-treated group had relapsed (Fig.). The median week of relapse in the control group was 15 and in the DSCG treated group 7 (P > 0.05; rank sum test). No association between results of treatment and atopic history on questionnaire, positive prick test, or HLA B12 was observed.

Discussion

DSCG did not prevent relapse of SRNS. It remains a possibility that a minority of patients would benefit, as suggested by our patient described in the case report. However, his failure to relapse may be explained by a lack of exposure to the allergen, to his outgrowing his allergy, or to some long-term effect from the corticosteroid injection. The latter is unlikely in our experience, but Freier and Berger (1973) have reported that children allergic to milk may lose their symptoms on DSCG, and remain well after its withdrawal.

The failure in the trial may well be due to inadequate dose, as a far higher oral dose is now being used in food allergy and eczema (A. M. Edwards, personal communication, 1977). Studies in man have shown that DSCG is very poorly absorbed from the gastrointestinal tract. The absorption of an orally administered dose amounts to 1%, half of which appears in the urine (Walker et al., 1971).

DSCG acts by inhibiting the degranulation of mast cells, thus blocking the release of biochemical mediators such as histamine and slow reacting substance of anaphylaxis. Higher doses of DSCG or absorbable analogues might be effective, but patients in relapse with SRNS did not respond to doxantrazole (Bluett et al., 1977).

Summary

A controlled trial of disodium cromoglycate treatment of steroid-responsive nephrotic syndrome failed to show a therapeutic effect on the tendency to relapse after withdrawal of corticosteroids.

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References


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