Bronchodilator effect of disodium cromoglycate administered as a dry powder in exercise induced asthma

C. R. HORN, R. M. JONES*, DENISE LEE & S. R. BRENNAN

Department of Respiratory Medicine, Northern General Hospital, Sheffield

A double-blind, placebo controlled study of the effects of disodium cromoglycate (DSCG), administered as a dry powder via the spinhaler, in established exercise-induced asthma, was carried out. DSCG resulted in an increase in the rate of recovery compared with placebo. The findings confirm that DSCG has bronchodilator properties.

Keywords disodium cromoglycate asthma

Introduction

Disodium cromoglycate (DSCG) has an established place in the prophylactic management of asthma (Davies, 1968). It has been stated to have no bronchodilator properties, but recent evidence suggests that this is not the case (Chung & Jones, 1979; Hasham *et al.*, 1981; Jones *et al.*, 1983). Previous studies all used DSCG as a pressurised aerosol or respiratory solution and we undertook this study to determine if the dry powder, delivered by the spinhaler, possessed similar properties.

Methods

Nine subjects (five male, four female) aged between 17 and 48 (mean 25.4) years were studied. All were asthmatics of long standing and gave a clear history of exercise induced asthma, with a fall in FEV₁ on exercise of at least 20%. All subjects gave informed consent.

All therapy was discontinued for at least 8 h before each study. Spirometry and flow volume loops were recorded prior to exercise and the FEV₁ and flow at 20% of expired vital capacity (FEF₂₀) determined. After two resting measure-

ments (10 min apart) the subjects exercised by running for 7 min in the hospital grounds. Three minutes after the completion of exercise repeat measurements were made.

Following this each subject received 60 mg (three capsules) of dry powder DSCG ('spincaps') or three identical placebo capsules. Spirometry and flow-volume loops were repeated at 20, 30, 40, 50 and 60 min after the beginning of exercise. Fenoterol (540 µg) was then administered and final measurements made 20 min later.

Within 2 weeks of the first study a second exercise test was carried out in broadly similar ambient conditions. Each subject covered an identical distance on the two runs, although the distance covered was not the same for different subjects. A fall in FEV₁ of within 10% of that in the first study was necessary for the study to continue on the second occasion. The subjects then received placebo or active spincaps as on the first study day and the rate of recovery followed. The study was carried out in a randomised, double-blind manner.

Statistical analysis was carried out using paired Student's *t*-tests.

Correspondence and present address: Dr Christopher R. Horn, Department of Respiratory Medicine, 4th Floor Outpatients Department, Guy's Hospital, St Thomas' Street, London SE1 9RT

*Present address: Faculty of Medicine, Congella, South Africa.

Figure 1 The effect of DSCG on recovery on FEV₁ after exercise. •.....• placebo, •——• DSCG.

Results

These are shown in Figures 1 and 2. There was no difference in the parameters in the resting period on the two study days (mean FEV₁ 3.32 vs 3.25 l). Following exercise the FEV₁ fell by a mean of 42.2% on the placebo day and by 40.3% on the DSCG day. The falls in the FEF₂₀ (52.1% vs 53.5%) were also similar on the 2 days.

Twenty minutes after the beginning of exercise (10 min after DSCG or placebo) there had been no significant recovery of any parameter in either group. However by 30 min DSCG had resulted in a small but significant improvement in FEF₂₀ (0.8 to 1.0 l/s; $P < 0.05$). The FEV₁ had also improved but this did not reach significance (1.94 to 2.21 l $P > 0.1$). The placebo group had shown no increase in either parameter and were significantly worse than on the DSCG day (FEF₂₀: $P < 0.05$). At 40 min the FEV₁ had risen by 25.8% in the DSCG group compared to 11.5% in the placebo group ($P < 0.025$). Even at 60 min recovery in the placebo group was significantly worse than in the DSCG group (mean FEV₁ 2.8 vs 2.5 l: $P < 0.025$; FEF₂₀ 1.5 vs 1.1 l/s: $P < 0.025$).

Discussion

This study set out to look at the influence of disodium cromoglycate (DSCG) on established asthma and exercise was chosen as a reproducible and commonly encountered stimulus. Although we did not rigidly control the level of exercise the almost identical fall in spirometry suggests a very similar respiratory heat loss on the 2 study days. Certainly the starting point for administration of the DSCG or placebo was comparable. The results confirm that DSCG has a significant effect on airways tone in established exercise-induced asthma (EIA).

It is not clear why we have been able to demonstrate an acute effect of DSCG on airways tone when others have not. DSCG used prophylactically in EIA is thought to act in small, peripheral airways (Godfrey *et al.*, 1974). Although DSCG has a mass median diameter of 2.6 μ m aggregation results in less than 25% of particles in the dispersed cloud being less than 6 μ m (Bell *et al.*, 1971). In addition Smith *et al.* (1980) showed that an increase in humidity (such as may be experienced in the oropharynx) caused a growth of particle size. The site of deposition of inhaled particles is also influenced

Figure 2 The effect of DSCG on recovery of FEF_{20} after exercise. placebo, —•— DSCG.

by differences in technique of inhalation, tidal breathing tending to distribute aerosols more diffusely throughout the lungs, whilst vital capacity inhalation results in more central deposition (Dolovich *et al.*, 1979). Our subjects inhaled DSCG whilst still breathless following exercise. This resulted in rapid vital capacity breaths into central airways which had been cooled and dried during exercise. These factors may have distributed the DSCG to produce different relative concentrations at central and peripheral receptors compared to those seen following inhalation in the resulting state; this may partly account for our results being at variance with earlier studies. Further work

using radiolabelled DSCG may resolve this problem.

This study does not help to elucidate the mechanism of action of DSCG as a bronchodilator. Although when given after exercise it may act, in part, by preventing on going mast cell degranulation this would not account for its bronchodilator properties when given in the resting state as shown by us and others (Chung & Jones, 1979; Hasham *et al.*, 1981; Corkey *et al.*, 1982; Jones *et al.*, 1983).

Although the magnitude of the bronchodilator effect is not great it may be useful, particularly when given after exercise.

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