144 NEBULISED SALBUTAMOL AND IPRATROPIUM BROMIDE IN ACUTE ASTHMA

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Anticholinergic drugs have shown good bronchodilating properties in both adults [1] and children [2] with asthma. When combined with a bronchodilator, a summation effect has sometimes been seen [3]. In a double blind study we have compared the effect of nebulised salbutamd with nebulised salbutamol plus ipratropium bromide in children admitted with an acute attack of asthma. 127 consecutive admissions were studied, each patient being randomly allocated to one of the above treatment groups. Therapy was given 4 hourly for the first 24 hours and then as required thereafter. The number of nebulisations were noted as was the length of hospital stay. Peak Flow rates were measured in those children who were able to use a peak flow meter. There were no overall differneces in rate of improvement between the two treatment groups and the number of nebulisations was not significantly different. Conclusion - From this study there is no evidence that nebulised ipratropium bromide and salbutamol has any benefit over nebulised salbutamol alone in children admitted to hospital with acute asthma.

1. Lightbody et al — Br J Dis Chest 1978; 72:181-6
2. Milner — Arch Dis Child 1981; 56:84-5
3. Petrie et al — Br Med J 1975; 1:430-32

145 INHALATION DEVICES FOR TREATMENT OF ASTHMA; A COMPARISON OF NEBUHALER AND ROTAHALER.

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The use of a standard metered aerosol needs considerable skill and coordination, which is extremely difficult for children. To ensure satisfactory inhalation of drugs several devices have been developed to overcome this problem. A study to compare the clinical and bronchodilator effect of Terbutaline-sulphate administered via a nebuhaler (TN), with that of Salbutamol powder administered via a rotahaler (SR), was carried out in 10 boys with stable moderate asthma; age-range 8-13 years. The effects were measured by means of spirometry and clinical assessment in a double-blind randomized cross-over fashion. With both drugs cumulative dose-response curves were established. With intervals of 20 minutes 0.25 mg of TN or 0.2 mg of SR was administered up to a maximal dose of 1.0 mg of TN and 0.8 mg of SR. Lungfunction-tests (FVC, FEV_1, MMEF, MEF 50%, MEF 75%, PEFR) were performed 15 minutes after each administration of drug.

In all children significant bronchodilatation was seen after 0.5 mg of TN or 0.4 mg of SR. The maximal bronchodilator effect of SR was significantly larger than that of TN, as can be shown for MMEF, MEF 50% and MEF 75%; this could not be shown for FEV_1 and PEFR. Clinically side-effects didnot occur. For at least 5 hours after the last dose bronchodilatation was seen as shown by hourly PEFR-measurements. Since a good bronchodilator effect was shown with the use of a nebuhaler we conclude it to be a good device for inhalationtherapy in children, clinically comparable to the rotahaler; in our group, however, better bronchodilator effect was achieved with the rotahaler.

146 DURATION OF ACTION OF OXITROPIUM BROMIDE.

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Vagal reflexes may be a factor in nocturnal asthma and therefore treatment with a long acting anticholinergic would be appropriate. This study was designed to assess the duration and degree of protection afforded by the inhaled anticholinergic agent Oxitropium bromide (OB) against methacholine-induced bronchoconstriction. Ten subjects (6 children, 4 adults), with a wide spectrum of clinical asthma, were studied. After a control methacholine inhalation challenge, OB 200 mcg or placebo were given double-blind and methacholine challenges were repeated 1, 3 and 6 hours later. There was a statistically significant ($p<0.01$) increase in methacholine PC_{20} at 6 hours after OB 200 mcg. This however only represented >1 dilution increase in PC_{20} in 4 subjects and in 1 subject the PC_{20} had returned to within 1 dilution by 3 hours. The degree and duration of protection was only weakly related to sensitivity to methacholine, baseline lung function and the degree of bronchodilation induced. The seven subjects not fully protected were retested using OB 100 and 400 mcg on two further days, but no clear dose dependent response could be demonstrated. The prolonged anticholinergic action which was seen in some subjects suggests that inhaled Oxitropium bromide may be useful in treating nocturnal asthma.

147 ACUTE PROPHYLACTIC EFFECT OF DSCG, REPROTEROL AND THEIR COMBINATION ON ACETYLCHOLINE INDUCED BRONCHOCONSTRICTION

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The inhibition of asthmatic responses after antigenic challenges and of exercise-induced asthma by inhalation of sodium cromoglycate (DSCG) has been clearly demonstrated. Its short-term effect on acetylcholine inhalation challenge remains controversial. Twelve adolescent asthmatics in a clinical steady state (7 female, 5 male; aged 15-19 years; both extrinsic and intrinsic type) with proven bronchial hyperreactivity underwent acetylcholine inhalation tests (AIT) on five consecutive days: On day 1, after baseline assessment of spirometry (FEV 1) they inhaled increasing doses of acetylcholine (1 mg/0.5 ml, 1 mg/ml, 10 mg/ml) to measure the provocative dose causing a fall in FEV 1 of 20% (PD20). On days 2,3,4, and 5 - after baseline spirometry had confirmed that FEV 1 was within 10% of day 1 initial assessment - in a double blind intraindividual randomized study AIT was repeated 15 minutes after inhalation of DSCG 2 mg plus reproterol 1 mg, DSCG 2 mg, reproterol 1 mg, and placebo, respectively (two puffs of pressurizd aerosol). The combination of reproterol and DSCG proved to have the best acute protective effect on acetylcholine induced bronchoconstriction in adolescent asthmatics, giving the best or second best protection in 11 out of 12 individuals, followed by reproterol alone. Therefore it is possible to reduce bronchial hyperreactivity with the combination medication after single use in adolescent asthmatics.

148 NEBULISED SODIUM CROMOGLYCATE IN RECURRENTLY WHEEZY PRE-SCHOOL CHILDREN

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A double-blind cross-over study of nebulised sodium cromoglycate (SCG) was carried out on 27 asthmatic pre-school children over a one year period. All subjects had sufficiently severe asthma to have had at least one hospital admission. The active treatment was SCG 20 mg in 2 ml administered by nebuliser 4 times daily. Assessment was made by diary card and clinical examination.

Results were analysed in 24 subjects who completed the study. Statistical analysis allowed for treatment order and seasonal effects. Significant results in favour of SCG were obtained for night cough, day activity, percentage of symptom free days and overall asthma severity. During active treatment there was no reduction in hospital admission rate or intravenous drugs used. The wheeze score in the week after an upper respiratory infection was not reduced during SCG treatment.

Nebulised SCG is tedious prophylactic treatment for the very young asthmatic child, but worth a trial when other therapies have failed.

149 THE EFFECT OF M&B 22,948 (AN ORALLY ABSORBED MAST CELL STABILISER) ON EXERCISE INDUCED ASTHMA IN CHILDREN

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Since the introduction of sodium cromoglycate, attempts have been made to develop a drug with similar activity when taken orally. M&B 22,948 is an orally absorbed mast cell stabiliser which has previously been shown to block exercise induced asthma in adults. We conducted a trial in which 15 children with asthma each undertook three exercise challenges. They were pretreated with either M&B 22,948 or placebo, given double-blind, in randomly allocated order, prior to the second and third challenges. Our results failed to show a protective effect of M&B 22,948 against exercise induced asthma but the possible reasons for the discrepancy with the previous trial will be discussed.