nor unique. Every acute children’s ward has its problems which are the outcome of its history and geography; all share the problem of being at the mercy of unpredictable factors and of emergency admissions. They suffer also from the problem of having to cope with 2 different sizes of bed or cot. I am certain that similar experiences are common in district general hospitals throughout the country.

The object of this short report is to point out to administrators, and to others who do bed-occupancy sums, that they should not always use the same criteria to indicate efficiency in hospital action. They should look at each separate case and discover whether a full or part-empty ward really represents efficient management of resources.

Reference


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Ketotifen in the prophylaxis of childhood asthma

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SUMMARY A double-blind crossover trial of ketotifen, a mast cell stabilising antihistamine, was performed in a group of 23 young asthmatic children. No useful prophylaxis against bronchoconstriction could be shown.

Ketotifen, an orally-active cycloheptathiophene antihistamine, stabilises mast cells in vitro. This resembles the action of sodium cromoglycate in the prophylaxis of atopic asthma in cases where mast cell stabilisation prevents the release of histamine and other mediators on antigen challenge. Ketotifen has been shown to be effective in blocking antigen-induced bronchoconstriction in adults, and long-term studies have shown useful prophylaxis can be achieved in a proportion of atopic asthmatics with increasing effects over a period of up to 3 months (J Pepys, E Carrasco, in preparation). However, little is known about its effect in children.

Ketotifen is administered twice daily by mouth and in this respect it may be better than sodium cromoglycate, especially for children who are too young or too uncooperative to use a spinhaler. Apart from slight drowsiness, generally settling during the first few weeks of treatment, no significant side effects have been reported. We studied the usefulness of this drug in a group of young asthmatic children who were unable to use sodium cromoglycate by spinhaler satisfactorily.

Patients and methods

Twenty-three children (14 boys and 9 girls) completed a double-blind crossover trial with 2 months each on active and placebo treatment. The children ranged in age from 1 year 11 months to 5 years 3 months (median 3 years). Nineteen were between the 3rd and 97th centiles for height, 2 were above the 97th, and 2 were below the 3rd. One child was below the 3rd centile for weight but the other children were between the 3rd and 97th centiles.

Each one had suffered from recurrent wheezing attacks for between 10 months and 5 years. The onset of symptoms had been in the first year in 14 children, and in the second year in a further 8. Eighteen had a family history of asthma or atopic disease. Questioning revealed that wheezing attacks were precipitated by upper respiratory infections in all 23, by obvious allergy in 9, and by exercise in 18. Twelve children suffered from eczema also. Fifteen had at some time been admitted to hospital for asthma, and 9 had received courses of oral steroids. Of the 11 children who had skin tests performed, 10 showed multiple positive reactions to common antigens.

At the start of the trial each child showed moderate or poor control of his asthma with routine treatment. Routine treatment was regular or intermittent oral salbutamol alone in 16, and accompanied by orciprenaline in 2, and theophylline in 2. One child had a nebuliser at home and was treated with regular nebulised cromoglycate (Intal) plus salbutamol. Two children were receiving steroids: alternate-day oral prednisolone on a regular basis in one and beclomethasone dipropionate (Becotide) rotacapsules in the other. Regular treatments were kept constant throughout the trial.

Reference

The dose of ketotifen used during the active phase of the trial was 0.5 mg twice daily in infants over 10 kg (this is half the adult dose), and 0.25 mg twice daily in the 2 children who each weighed less than 10 kg. Response to treatment was assessed using diary cards recording wheeze and cough during the day and night. Symptoms were scored, 0 = well, 1 = mild, 2 = moderate, and 3 = severe, in each category. Bronchodilator consumption was also recorded. In those children old enough to co-operate, the peak expiratory flow rate (PEFR) was measured once daily—at 0800 hours. Any significant event—such as admission to hospital or the need for a short course of oral steroids—was noted.

Results

Mean symptom scores, PEFRs, and additional treatment requirements for the active and placebo periods are shown in the Table. The last 4 weeks were analysed separately to avoid any carry-over effects and to detect increasing activity with time.

Symptom scores did not vary greatly between the two periods, either when the entire 8 weeks or only the final 4 were compared. This remained true when scores for cough and wheeze (either daytime or night time) were considered separately. Bronchodilator consumption was very similar during the two periods, but like symptom scores tended to be higher during the active period; mean daily PEFR was slightly lower during the active phase. Rather more children required admission to hospital and courses of oral steroids during the active phase. The parents of 12 of the children could detect no difference between the treatment periods, while 5 preferred the active phase and 4 the placebo.

Mean weight gains were 0.66 kg during the active phase and 0.33 kg during the placebo. This just reaches statistical significance at the 5% level (Student’s t test). No side effects were noted except that one child suffered slight drowsiness during the active period. Interestingly this child’s condition was apparently improved by the active drug.

Discussion

In most parameters there was a small trend towards benefit with placebo, and we were unable to detect any evidence of useful prophylaxis with ketotifen. Compared with studies in adults, there were very few side effects. This suggests that the dose may have been too small. Adult asthmatics are generally treated with 2–3 mg/day which is in line with the weight-adjusted dosage of 0.50 to 0.94 mg/kg a day used in our trial. However ketotifen undergoes hepatic metabolism and the liver is known to be more active at this age. There was no evidence of any age-related effects within our group of patients.

It is thought that ketotifen, like sodium cromoglycate, may be most beneficial in milder asthmatics and not useful in those who require steroids. The overall pattern of results did not change when children who had been treated with steroids, either before or during the trial, were excluded.

Ketotifen is closely related to pizotifen, which is marketed in West Germany as an appetite stimulant. We were interested to find a greater weight gain during the period of treatment.

Although no evidence of benefit has been shown, an orally active prophylactic agent would be most useful in this young age group and we feel that further work with higher doses of ketotifen is justified.

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References


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