Effect of Orciprenaline on School Absenteeism in Asthma

ANDREW BOGDAN

From Scarborough Hospital, Scarborough, Yorkshire

The prevalence of school absenteeism in asthmatic children has had little systematic attention from paediatricians, who are mainly concerned with the causation and treatment of this disease. This aspect clearly seems to be deserving of attention from a clinical viewpoint, and this paper summarizes some initial results which reveal that asthma is indeed a frequent cause of recurrent absence from school, and that this situation can be much improved.

There is a surprising lack of available data on school absenteeism in asthmatic children, but some idea of the scope of the problem may be obtained from known facts about the incidence of asthma in children of school age. Eilertsen (1954) reported an incidence of 1·8% amongst 7-year-old school-children in Bergen, while Kraepelien (1954) drew attention to a figure of 1·4% in the 7 to 14 age-group in Stockholm. Smith (1961) writing about Birmingham schoolchildren found an incidence of 1·8%. A more recent survey from Aberdeen (Dawson *et al.*, 1969) reveals a prevalence of 4·8% (i.e. 121 asthmatics) in a 1 in 5 sample of 2500 children aged 5 to 11.

Clinical Material

Assessments were made of 46 children (29 male and 17 female) attending the Scarborough Group of Hospitals during the period from December 1963 to August 1965. Their ages ranged from 8 weeks to 14 years on enrolment for follow-up. At the initial assessment, the length of history of asthmatic episodes was as shown in Table I. In addition there were 6 patients in their first attack of asthma.

In the youngest child the first attack had occurred at 8 weeks, and in the case of the 14-year-old, at the age of 10. In most, however, the length of history was 2 to 3 years less than the chronological age. In all cases except those in their first attack,

previous treatment had obviously not been entirely satisfactory.

Theoretical Considerations

The particular asthmatic symptom responsible for school absenteeism is disabling shortness of breath due to reversible airways obstruction. If this could be prevented, school absenteeism would decrease dramatically. In planning how to achieve this it was necessary to find an effective and safe bronchodilator which would be acceptable to children and which would not only lessen liability to bronchoconstriction but which could also be used to relieve this symptom, when necessary, by extra doses.

Methods

It was decided to use orciprenaline in the form of Alupent Syrup* in morning and evening dosage, the primary aim being to keep the children 'wheeze-free' (i.e. even on auscultation), and hence able to attend school. At the same time if wheezing should occur, extra doses could safely be introduced to treat their asthma. This paper is not concerned with the purely clinical evaluation of orciprenaline, though some data were naturally acquired during the study and justify mention.

Breathing exercises. All children unless too young to learn, were taught breathing exercises, and had these been sufficient to keep them symptom-free, no other form of therapy would have been used. Because of the severity of asthma in this group, however, breathing exercises alone proved inadequate.

Breathing exercises plus expectorant. In 16 of the 46 children both breathing exercises and a proprietary expectorant† were used. The standard

*Boehringer Ingelheim Limited.

†Benylin Expectorant containing diphenhydramine 14 mg., ammonium chloride 135 mg., sodium citrate 57 mg., chloroform 22·5 mg., menthol 1·1 mg. in 5 ml. (Parke-Davis & Company.)

TABLE I
Duration of Asthma

No. of Patients	Duration (yr.)
11	5-6
10	4-5
7	3-4
3	2-3
4	1-2
5	0-1
Total 40 patients	

dose was 5 ml. morning and evening, up to 8 years of age, when the dose was doubled. In these children episodes of bronchoconstriction were reported to be less severe, less frequent, and of shorter duration. 24 of the 46 were too young to learn breathing exercises and were given the expectorant alone. In all 24, some improvement was observed, indicating the value of assisting the elimination of mucoid secretion in the presence of bronchoconstriction. However, the ideal of continuous freedom from bronchoconstriction had yet to be achieved if school absenteeism was to be prevented.

Breathing exercises, expectorant *plus* orciprenaline.

Method of basic maintenance therapy. With this ideal in view all 40 known asthmatic children were given orciprenaline in the form of Alupent syrup. The basic dose was 10 mg. b.d. up to 8 years of age and 20 mg. b.d. above that age, given at the same time as the expectorant. If, despite this, acute episodic bronchoconstriction occurred, the same basic dose of orciprenaline was given 8-hourly, 6-hourly, or even 4-hourly, as determined by the clinical condition. When obvious infection appeared to be the main trigger of the attack, 6 doses were given at 4-hourly intervals concurrently with antibiotic therapy and the expectorant.

Emergency therapy by hourly extra dose technique (HEDT). To deal with acute apyrexial episodes, an alternative extra dose technique—still amounting to 6 doses in 24 hours—was used. For example, if after the first routine morning dose the wheeze was no better, a second dose was given an hour later. This was repeated hourly (HEDT) to a total of 6 doses, or until the wheeze cleared or became minimal. When HEDT was used to treat severe bronchoconstriction present

on waking, it was often possible for the child to be at school by noon that day. HEDT was used on one or more occasions in 20 of the 40 cases before the patient became wheeze-free, indicating the ease and efficacy of this technique. In only 3 cases was there an adverse reaction after 5-hourly doses (see below). Conversely, in one case, 10-hourly doses were given by the mother before relieving the child of wheeze, and there was no adverse reaction. This suggests that the margin of safety is considerable. This experience was most encouraging, as it showed that it was possible to prescribe a large amount of orciprenaline to relieve the condition and so ensure that failure was not the result of inadequate dosage.

Treatment in the first attack. Of the total of 46 children, 6 were in their first attack, and in these HEDT was used initially and the patients were then stabilized 'wheeze-free' using morning and evening dosage alone. The response of these 'neo-asthmatics' was such that it was unnecessary to teach them breathing exercises or to administer the expectorant. It was also our experience that when no episodic bronchoconstriction had occurred for one or two months, daily routine therapy ceased to be necessary.

An alternative to HEDT. Of the 20 children treated by HEDT, 7 were not rendered completely symptom free after 6 doses in 5 hours, and in these children another method of direct orciprenaline therapy was used. Oral orciprenaline and expectorant were discontinued, and Alupent 5% inhalant solution* was administered as a mist from a Croupaire apparatus†. 2.27 l. distilled water were added to 7.5 ml. Alupent 5% inhalant solution, and the resulting very dilute solution was continuously administered (refilling every 12 hours) until the child had been completely 'wheeze-free' for not less than 8 hours. In these 7 cases bronchospasm was successfully and completely eliminated.

School attendance data. 12 of the 46 children satisfied the following conditions: (1) Living in the Scarborough urban and rural districts, where accurate information could be obtained from the schools. (2) Attending school before orciprenaline therapy started.

Table II shows the data which were obtained on school attendance of these 12 children. From

*Boehringer Ingelheim Limited.

† Air Shields Inc.

this will be seen that the attendance record of each child improved after starting this treatment and the likelihood of this having occurred by chance is in the region of 1 in 4000 ($p < 0.001$).

Side-effects

In the majority of children (41 out of 46) there were no side-effects and the drug was well tolerated. Of the 3 experiencing side-effects, one had mild diarrhoea, and another had vomiting and 'rambling'. Sleep disturbance and visual hallucination developed in a third, and in this case orciprenaline was discontinued for 3 days and then resumed without further side-effects. A tranquillizing drug was given during the 3-day period. In these 3 children, the side-effects occurred when HEDT was used on several successive days. A fourth patient had developed nausea, and in a fifth swelling of the limbs occurred, but this was during the concurrent administration of tetracycline.

Edwards (1964) noted that in adults with chronic bronchitis side-effects were no more prominent with 60 mg. orciprenaline daily by mouth than with a placebo. His findings have thus been supported by this study in children where the drug has been shown to be well tolerated over a wide dose range.

Observations

Though this was not a controlled trial in the accepted sense, relevant data concerning the patients were compiled from clinical notes and questionnaires, and certain general effects were noted (Table III).

The effect of orciprenaline was most striking when used during a child's first attack of asthma. These children went home taking a morning and evening dose, and when they had remained 'wheeze-free' for several weeks it was possible to discontinue oral therapy.

In no case in this series was it found necessary to resort to treatment with steroids.

Discussion and Summary

Orciprenaline is a sympathomimetic β -adrenergic receptor stimulating drug, the bronchodilator effect of which is considerably more prolonged than that of isoprenaline, whether used by dry aerosol inhalation, as shown by Hoffbrand *et al.* (1966), or by aqueous aerosol or oral administration (Edwards, 1964).

In this series of 46 asthmatic children, studied over a period of 20 months, it has been shown that a highly significant improvement in the severity, duration, and frequency of acute episodes may be

TABLE II
School Absenteeism Data

Case No.	No. of Absences in Consecutive School Terms (days)	
	Before Taking Alupent Syrup	While Taking Alupent Syrup
1	6	1
	4½	1½
	5	0
	12	6½
2	7	3
	12	2
	6	5
3	23	7
	15	—
4	10	9
	3	—
	10	—
5	37	14
	27	22
	30	8
	33	10
6	7½	4
	8	—
	1	5
	13½	—
	60	—
7	15½	17
	40	16
8	7	11
	22	13
	19	—
9	3	3
	10	6
	—	1
10	3	1
	7	1
	6	2
11	14	5
	17½	3
	—	7
	—	6
12	9	3
	4	8
	11	9

— No data available.

TABLE III
General Effects of Treatment

Effect Noted	No. of Patients
Lessening of duration of attacks ..	39 (87%)
Reduction in incidence of nocturnal attacks ..	37 (83%)
Reduction in severity of attacks ..	33 (72%)
Reduction in frequency of attacks ..	27 (59%)

achieved by treatment with orciprenaline syrup. This improvement has been reflected in a considerably improved school attendance in all 12 patients to whom this criterion could be applied.

In only 7 patients was control not achieved by the use of orciprenaline orally in association with breathing exercises and an expectorant. In these 7 patients the inhalation of a mist of dilute aqueous orciprenaline solution from a Croupaire apparatus provided an easy method of controlling the patient's asthma.

There is therefore no doubt that Alupent has a significant role in the treatment of childhood asthma, especially in maintaining the best possible attendance at school.

It is a pleasure to record my gratitude to the many people who have contributed to this study.

My grateful thanks go to Mrs. Patricia Bouault as a research secretary who co-ordinated the questionnaire inquiry and the school absenteeism data which she then tabulated with such impressive clarity. The Medical Staff and Nursing Staff of the Children's Ward and Out-patient Department at the Scarborough Hospital were responsible for the high standard of routine clinical records which enabled the easy extraction of data.

I am indebted to Dr. W. G. Evans, Senior School Medical Officer for Scarborough, and his department,

and especially Miss E. R. Clarke who provided the school absenteeism data.

Statistical advice was given by Michael Gent, Esq., M.Sc., of the University of Bradford, and I would like to record also my grateful thanks for his assistance.

Boehringer Ingelheim Limited made this study possible by their generous gift of orciprenaline syrup which was not available in this country at the time the project began. I am especially grateful to the Medical Director for this and to Dr. P. A. Knowlson of the Medical Staff, without whose help, advice, and encouragement, this paper would not have been completed.

REFERENCES

- Dawson, B., Horobin, G., Illsley, R., and Mitchell, R. (1969). Survey of childhood asthma in Aberdeen. *Arch. Dis. Childh.*, **44**, 135.
- Edwards, G. (1964). Orciprenaline in treatment of airways obstruction in chronic bronchitis. *Brit. med. J.*, **1**, 1015.
- Eilertsen, E. (1954). Astmahyppighet. *T. norske Laegeforen*, **74**, 322.
- Hoffbrand, B. I., Hoffbrand, M. I., Hill, I. D., and Heaf, P. J. D. (1966). Trial of bronchodilator drugs given by metered aerosol with a comparison of two bedside methods of estimating airway resistance. *Brit. med. J.*, **1**, 1014.
- Kraepelien, S. (1954). The frequency of bronchial asthma in Swedish school-children. *Acta paediat. (Uppsala)*, **43**, Suppl. 100, 149.
- Smith, J. M. (1961). Prevalence and natural history of asthma in schoolchildren. *Brit. med. J.*, **1**, 711.

Correspondence to Dr. A. Bogdan, Scarborough Hospital, Scarborough, Yorkshire.