

Long-Term Treatment with Beclomethasone Dipropionate Aerosol in Asthmatic Children, with Special Reference to Growth

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Thirty-one children, 19 boys and 12 girls, aged 3.4-10.8 years, with severe perennial bronchial asthma were treated with beclomethasone dipropionate aerosol (BDA) for 16-40 months. The dose was initially 400 µg a day and was gradually reduced to the lowest level giving control of symptoms. Earlier steroid or ACTH-treatment in six children was stopped during the BDA-treatment. At the start of the treatment the mean deviation of height compared with normal values for Swedish children was -0.10 s.d. for the boys and -0.51 s.d. for the girls. At the end of the observation period the deviation was -0.22 s.d. and -0.58 s.d., respectively. The increase in deviation was not significant. Bone age was also slightly retarded before beclomethasone treatment but this deviation was not accentuated during the observation period. It is concluded that treatment with BDA does not retard growth or skeletal maturation in children. The number of acute admissions to hospital was reduced by more than 50% during the first year of treatment.

Key words: beclomethasone dipropionate aerosol; bone age; bronchial asthma; childhood; growth; skeletal maturation; steroid therapy.

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Treatment of severe childhood asthma with beclomethasone dipropionate (Becotide) in aerosol form (BDA) is a well-established mode of therapy. This potent steroid has a good and dependable clinical effect on the bronchial asthma and no serious side effects have been reported (2, 4, 5, 6, 7) at the recommended dose level, 400 µg a day. However, some of the reports are short-term studies (1, 9, 14) and it is not possible to draw any conclusions about the long-term effect of beclomethasone dipropionate on growth and skeletal maturation in the children treated. This investigation has been undertaken mainly to study the long-term effects of treatment with this potent steroid on growth, skeletal maturation and the clinical condition in asthmatic children.

MATERIAL AND METHODS

Thirty-one children (19 boys and 12 girls) with severe perennial bronchial asthma, all of whom were treated as outpatients at the Allergy Department, Sachs' Children's Hospital or the Pediatric Department, Huddinge Hospital, were studied. All the children had been on BDA treatment for more than 1 year. In order to reduce the influence of the onset of puberty, all boys selected for the study were below 11 years of age and all girls were below 10 years of age at the beginning of the treatment period. The observation period ended for the boys at 12 and for the girls at 11 years of age. The mean age at the start of the study was 7.3 years, with a range of 3.4-10.8 years. The

average duration of BDA treatment was 25 months (range 16–40).

All patients had previously been treated with β_2 -receptor stimulants, theophyllamines and/or cromoglycate without satisfactory clinical results. Six children were on steroids or ACTH at the start of the BDA treatment.

All the children were initially given 100 μ g of BDA 4 times a day and the dosage was then gradually reduced to the lowest clinically acceptable level. At the end of the observation period the mean dose was 200 μ g a day. Steroid or corticotropine treatment was suspended during the first 2 months of BDA treatment in all six children who had been on these drugs. Treatment with cromoglycate was also suspended. Bronchodilator treatment was maintained. All patients were subjected to a clinical control examination every 4 to 8 weeks. Height and weight were measured every 2 months and were compared with normal values for healthy Swedish boys and girls (13). Deviations from the mean values in s.d. were calculated and Wilcoxon's test for paired observations was used for statistical analysis.

Skeletal maturation was determined according to the method of Greulich & Pyle (8) before the start of beclomethasone treatment and thereafter at 6-month intervals. All X-ray films of the wrist were evaluated by the same radiologist.

In order to elucidate whether BDA therapy reduces the frequency of severe asthma attacks, all acute admissions to the hospitals were registered for one year before the treatment period and during the first year of the treatment.

RESULTS

All children continued to grow as expected according to Swedish standard charts for growth during the observation period (Figs. 1 and 2).

The boys studied deviated from the expected mean value with respect to height

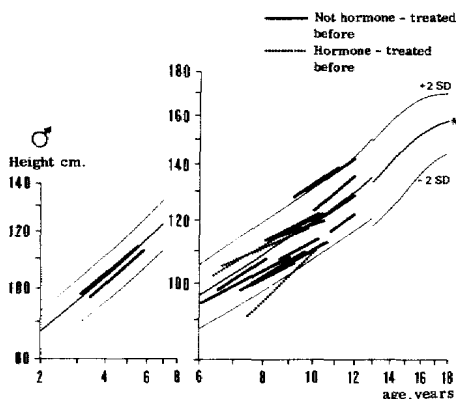


Fig. 1. Growth in 19 asthmatic boys treated with BDA.

by +0.06 s.d. 12 months before the trial started and by -0.10 s.d. at the beginning of the observation period (Fig. 3). After 1 year of treatment the deviation was -0.27 s.d. and at the end of the observation period it was -0.22 s.d. from the expected height. No deviation was significant. The girls tended to deviate from the normal population in a negative direction more than the boys: -0.55 s.d. ($P < 0.05$), -0.51 s.d. (n.s.), -0.68 s.d. ($P < 0.05$) and -0.58 s.d. ($P < 0.05$) and -0.58 s.d. ($P < 0.05$) at the above times, respectively.

When the deviations in height were compared between the different measure-

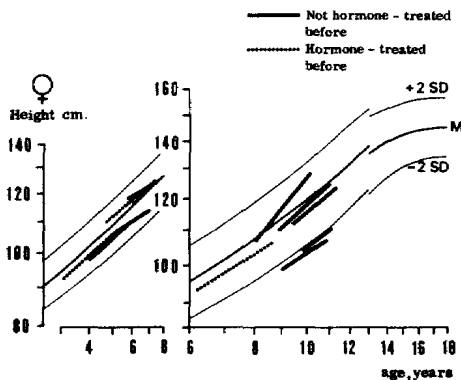


Fig. 2. Growth in 12 asthmatic girls treated with BDA.

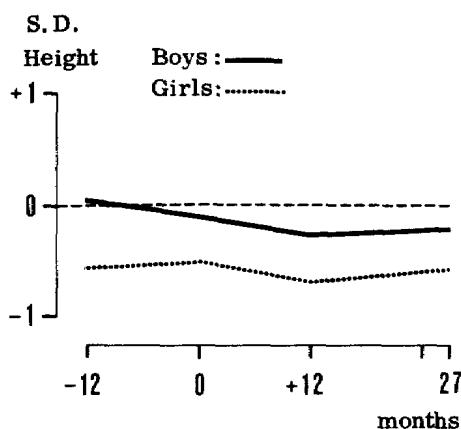


Fig. 3. Mean deviation in height in 31 asthmatic children before and during BDA treatment for 16-40 months.

ments, the boys showed a significant deviation ($P < 0.01$) at the end of the observation period compared with 12 months before BDA treatment was started. Other changes were less pronounced ($P < 0.05$) or not significant.

For skeletal maturation, there was a slight retardation in the whole group before BDA treatment was started. During the treatment

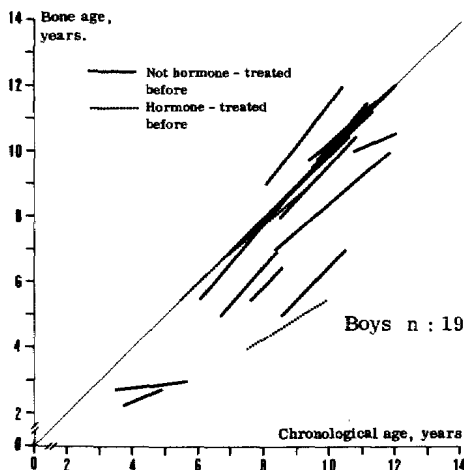


Fig. 4. Bone age in relation to chronological age in 19 asthmatic boys treated with BDA.

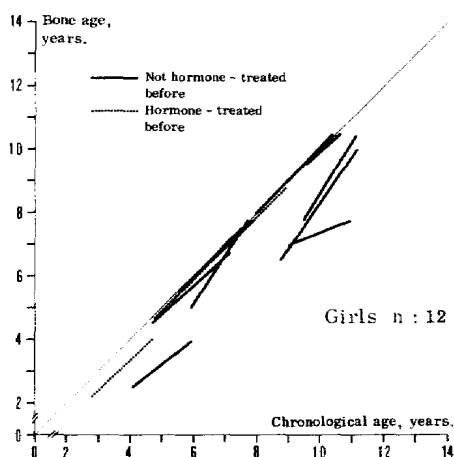


Fig. 5. Bone age in relation to chronological age in 12 asthmatic girls treated with BDA.

period there was no deviation from the expected bone age compared with the chronological age for either girls or boys (Figs. 4 and 5) with the exception of three boys and one girl. These children showed a marked deviation in bone age but their height development was quite normal. There was also good agreement between bone age and heights as shown in Figs. 6 and 7, in which, for practical reasons a metric scale is used.

The clinical effect of the BDA therapy was very good. The frequency of acute visits to the outpatient clinics decreased by 53% and the number of acute admissions to hospital decreased by 63% during the first year of steroid aerosol treatment compared to the preceding year (Table 1).

Table 1

Mean values of the number of acute visits to the outpatient clinics and admissions to hospital during 1 year before and during the first year of BDA treatment in 31 asthmatic children

	- 12 months	0	+ 12 months
	I	I	I
	Mean values		
As outpatients	4.9		2.3
As inpatients	2.7		1.0

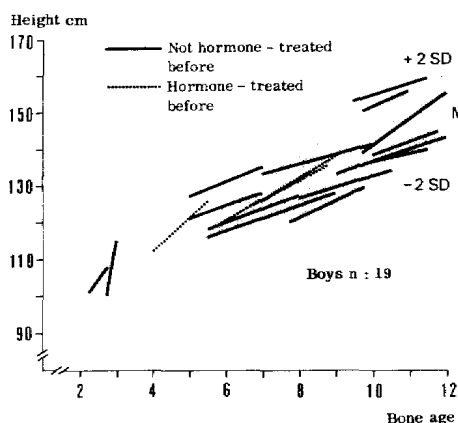


Fig. 6. Bone age in relation to height in 19 asthmatic boys treated with BDA.

DISCUSSION

Since the first reports on treatment of severe bronchial asthma with BDA, several reports documenting the safety and clinical efficacy of this drug have been published. In doses of up to 400 μ g a day no adverse systemic effects or increased frequency of respiratory tract infections have been reported. Temporary oral and pharyngeal colonization of *Candida albicans* is common but is seldom of any clinical importance. The influence of BDA therapy on growth and skeletal maturation in asthmatic children has not yet been satisfactorily investigated.

In this material, and in accordance with previous reports (3, 11, 12, 16), asthmatic children tended to deviate in a negative direction in height compared with healthy children of the same age. This is in accordance with what is to be expected in asthmatic children not treated with hormones and must be regarded as an effect of the disease itself. The girls deviated more from the normal population than the boys, but the differences were very small and cannot be regarded as significant. No differences were found between the sexes with respect to previous oral steroid treatment. Deviation between the sexes in this respect has previously been observed and

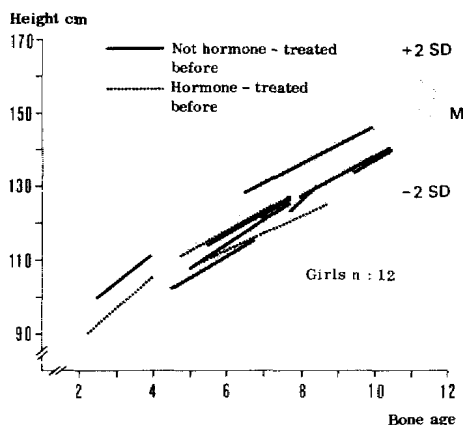


Fig. 7. Bone age in relation to height in 12 asthmatic girls treated with BDA.

might be explained by differences in physiological maturation (3, 15).

In earlier studies no retardation of growth during BDA treatment has been reported but the numbers of patients are small and the observation times are short (1, 9, 14). The present study, which comprises the greatest number of asthmatic children studied in this respect up to now, shows that growth continues as expected during BDA treatment. The boys deviated significantly ($P < 0.01$) in a negative direction at the end of the observation period compared with 12 months before BDA treatment was started. Most of this stunting in growth must be ascribed to the 12-month period preceding the study (Fig. 3). There was no significant difference in height deviation between the start of BDA treatment and the end of the observation period. No growth spurt was seen in the BDA-treated children.

There is no information available concerning the influence of long-term treatment with BDA in asthmatic children on skeletal maturation. In this study bone age has been investigated at the beginning and the end of the BDA treatment period. When compared with chronological age, it showed a slight retardation, particularly in the boys. Five out of six patients who had previously been treated with hormones showed normal

development: only one deviated markedly. It is concluded that earlier steroid treatment did not influence skeletal maturation in these children. The slight retardation is in accordance with what is to be expected in asthmatic children not treated with hormones (3, 12). On the other hand, bone age seems to be better correlated to height (Figs. 6 and 7). Thus, the retardation of bone age corresponds well with the retardation of height (3).

A very important aspect of BDA treatment is to what extent this therapy makes it possible to reduce the frequency of acute asthma attacks. In an earlier report (5) the number of hospital admissions was similar to that during the period before BDA treatment and in another study (10) it is suggested that failure to respond to BDA treatment might be due to psychosocial factors. In the present study there was a decrease by 53% in the number of acute visit to the outpatient clinics and by 63% in the number of acute admissions to hospital. This is very important because it shows that with proper medical treatment it is possible to reduce the costs to the community and the expense and inconvenience to patients with severe asthma.

BDA treatment, with a dose of 400 µg a day, does not seem to reduce the growth or retard skeletal maturation in asthmatic children. It greatly reduces the number of acute admissions to hospital and gives very good clinical results. BDA must be regarded as "the drug of choice" for treatment of severe childhood asthma.

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