Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children

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In a controlled prospective study we have measured growth and pulmonary function in children with asthma during long-term treatment with inhaled budesonide and compared these findings with those obtained from children not treated with corticosteroids. Two hundred and sixteen children were followed at 6 monthly intervals for 1–2 years without inhaled budesonide and then for 3–6 years on inhaled budesonide. Sixty-two children treated with theophylline, β2-agonists and sodiumcromoglycate but not with inhaled steroids were also followed for 3–7 years (controls).

During the period of budesonide therapy the mean daily dose decreased from 710 to 430 µg (P<0.01) and no signs of tachyphylaxis to the treatment were seen. Budesonide treatment was associated with a significant reduction in the number of annual hospital admissions due to acute severe asthma (from 0.03 to 0.004 per child, P<0.001). In patients not treated with budesonide an annual decrease in % predicted FEV1 of 1–3% was seen. In contrast FEV1 improved significantly with time during budesonide treatment, both compared with the run-in period and with the control group (P<0.01). Furthermore, there was a significant (P=0.01) relationship between the duration of asthma at the start of budesonide and the annual increase in FEV1 during budesonide therapy. After 3 years of treatment with budesonide, children who started this therapy later than 5 years after the onset of asthma had significantly lower FEV1 (96%) than the children who received budesonide within the first 2 years after the onset of asthma (101%) (P<0.05). No statistically significant changes in growth velocity (run-in=5·6 cm year⁻¹, controls=5·6 cm year⁻¹, budesonide=5·5 cm year⁻¹) or weight gain (run-in=3·5 kg year⁻¹, controls=3·6 kg year⁻¹, budesonide=3·5 kg year⁻¹) were seen during budesonide treatment.

We conclude that inhaled budesonide in doses up to 400 µg per day does not stunt growth in children with asthma and that early intervention with this treatment may prevent the development of irreversible airway obstruction and reduce the risk of under-treatment. Finally, continuous long-term treatment is not associated with the development of tachyphylaxis.

Introduction

Because of their clinical efficacy and anti-inflammatory properties, inhaled corticosteroids are now accepted as first line treatment of asthma in adults, even in patients with mild symptoms (1,2). Inhaled corticosteroids are not yet as widely accepted in the treatment of children with asthma (3), and a fear of systemic side effects, such as stunting of growth, is one major reason.

For many years, inhaled corticosteroids were reserved for patients with severe asthma in our clinic. Remaining children were treated with inhaled or systemic β2-agonists, theophylline, or sodiumcromoglycate (SCG) as recommended for children with mild and moderate asthma (3). In 1986 this strategy changed and inhaled glucocorticosteroids were to be introduced earlier in the course of treatment. When the change occurred, we designed the present study to assess statural growth, weight, pulmonary function, number of hospital admissions due to acute severe asthma, and dose of inhaled corticosteroid required in children with asthma during long-term inhaled corticosteroid treatment and to compare the measurements with those obtained in children in whom inhaled corticosteroids were not given.

Patients and Methods

Children with mild and moderate asthma and no other chronic disease were studied. To be included, the children had to have visited the clinic at 6 months intervals for at least 1 year (three visits). During this...
period, the children were to have been treated according to the normally recommended guidelines (3) and not to have used inhaled or oral corticosteroids for more than 2 weeks per year. This corticosteroid-free period is referred to as the ’run-in’ period.

After the run-in, the children started treatment with inhaled budesonide 800 µg day⁻¹ for 6–8 weeks to establish optimal or acceptable asthma control. If optimal control was achieved the budesonide dose was gradually reduced by 25% at monthly intervals until acceptable control had been established and the dose remained at that level until the next clinic visit. If the initial budesonide treatment did not result in optimal or acceptable control and compliance was assessed to be good, the budesonide dose was increased and/or other treatment (theophylline or oral β₂-agonists) added. Inhaled β₂-agonists were always taken morning and evening and p.r.n. The effect of changing the budesonide dose was monitored by diary recordings and PEF measurements at home before and 3–6 weeks after each change. Often these measurements were supplemented with lung function measurement at the hospital. Furthermore, throughout the study a standardized exercise test was used at the discretion of the clinician to assess the bronchial hyperreactivity of the child. Treatment with (SCG) was always stopped when budesonide treatment was started.

Asthma control was defined as optimal when four of the following criteria were fulfilled:

(a) The child leads a normal life, including normal physical activity.
(b) Use of rescue terbutaline ≤1 per week.
(c) Diurnal variation in PEF <10% on ≥5 days per week.
(d) Asthma symptoms ≤once a week.
(e) PEF and/or FEV₁ ≥100% of predicted normal.
(f) ≤10% fall in FEV₁ after a standardization exercise test (if performed).

When control was optimal a reduction in budesonide dose was attempted.

Asthma control was defined as acceptable when four of the following criteria were fulfilled:

(a) The child leads a normal life, including normal physical activity.
(b) Use of rescue terbutaline ≤3 per week.
(c) Diurnal variation in PEF <10% on ≥5 days per week.
(d) Asthma symptoms ≤3 days per week.
(e) PEF and/or FEV₁ ≥90% of the patient’s best.
(f) <20% fall in FEV₁ after a standardized exercise test (if performed).

When control was acceptable no changes in budesonide dose were made.

Asthma control was considered unacceptable when the criteria for acceptable control were not fulfilled. In that case the budesonide dose was increased or other treatment added.

If any of the following criteria:

(a) A fall in morning PEF >20%.
(b) Use of >5 inhalations of rescue terbutaline.
(c) ≥one-step worsening in symptom score (i.e. from 0 to 2 or from 1 to 3).

were fulfilled on each of each of three consecutive days the dose of budesonide was doubled until optimal or acceptable control had been achieved for 2 weeks. Then the dose was gradually reduced according to the guidelines mentioned above.

During both run-in and the subsequent treatment with inhaled budesonide, the children visited the clinic every 6 months. At each visit, the number of hospital admissions due to acute severe asthma during the previous 6 months, age, height (Harpenden stadiometer, mean of three measurements), weight, pulmonary function (vitalograph, best of three measurements), use of concurrent medicine, dose of inhaled budesonide, and inhalation device used were recorded. Furthermore, it was evaluated whether a dose reduction in budesonide should be attempted.

Between hospital visits, changes in the budesonide dose or other asthma medication were always made under the supervision of the clinic so that transient changes in treatment during periods of worsening of asthma symptoms were recorded. In such periods, the budesonide dose was normally doubled until asthma had been controlled for 1–2 weeks. These recordings made it possible to calculate the average dose of inhaled corticosteroid during the previous 6 months.

The same two nurses performed all of the measurements at the clinic between 09.00 h and 15.00 h. At each clinic visit the child was seen by the same paediatrician. On the day of the clinic visit, the children took their normal morning medication with the exception of any inhaled β₂-agonists. Both during run-in and during treatment with inhaled budesonide, all other asthma medication (except oral steroids for more than 2 weeks per year) was allowed.

Children, who required oral steroids for more than 2 weeks per year, were excluded from the study.

Some parents did not want their child on inhaled corticosteroids because they were afraid of side effects. These children continued in the study on their normal regular medication and were not put on inhaled corticosteroids. They will be referred to as ’controls’. If the parents of a control child later
Table 1  Demographic data (mean and range) of the two groups of children at the start of the run-in period

<table>
<thead>
<tr>
<th></th>
<th>Budesonide</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>216</td>
<td>62</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>148/68</td>
<td>46/16</td>
</tr>
<tr>
<td>Age (years)</td>
<td>6.2 (3-11)</td>
<td>6.1 (3-11)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>116 (95-158)</td>
<td>115 (93-152)</td>
</tr>
<tr>
<td>Height SDS</td>
<td>-0.093 (-3.2-3.5)</td>
<td>-0.184 (-2.3-2.3)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>22.1 (13.4-58.3)</td>
<td>20.7 (14.3-48.7)</td>
</tr>
<tr>
<td>Weight SDS</td>
<td>-0.18 (-2.7-3.3)</td>
<td>-0.29 (-2.3-4.1)</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>81.3 (34-115)</td>
<td>79.2 (37-110)</td>
</tr>
<tr>
<td>FMEF (% predicted)</td>
<td>56.2 (25-85)</td>
<td>56.3 (21-89)</td>
</tr>
<tr>
<td>Asthma duration (y)</td>
<td>3.7 (0.5-10)</td>
<td>3.5 (0.5-10)</td>
</tr>
</tbody>
</table>

Table 2  Use of asthma medication, number of hospital admission due to acute severe asthma, changes in weight and height, weight and height standard deviation scores and changes in pulmonary functions in 62 asthmatic children followed for 3-7 years without treatment with inhaled corticosteroids, and in 216 children followed for 1-3 years without treatment with inhaled corticosteroids (run-in) and thereafter 2-6 years on continuous treatment with inhaled budesonide. SCG=sodiumcromoglycate. Mean values and 95% confidence limits are given

<table>
<thead>
<tr>
<th></th>
<th>Controls (A)</th>
<th>Budesonide run-in (B)</th>
<th>Budesonide treatment (C)</th>
<th>A vs. B</th>
<th>C vs. A and C vs. B</th>
</tr>
</thead>
<tbody>
<tr>
<td>% on SCG</td>
<td>58</td>
<td>40</td>
<td>0</td>
<td>NS</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>% on theophylline</td>
<td>64</td>
<td>56</td>
<td>12</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>% on oral β₂-agonist</td>
<td>42</td>
<td>46</td>
<td>8</td>
<td>NS</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Hospitalizations (no/child/year)</td>
<td>0.030</td>
<td>0.026</td>
<td>0.0041</td>
<td>NS</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Δ Weight (kg year⁻¹)</td>
<td>2.96; 4.16</td>
<td>3.13; 3.83</td>
<td>3.20; 4.04</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Prepubertal Δ weight (kg year⁻¹)</td>
<td>2.58; 3.48</td>
<td>2.62; 3.14</td>
<td>2.37; 2.85</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Δ Weight SDS (change year⁻¹)</td>
<td>-0.006; 0.116</td>
<td>-0.002; 0.104</td>
<td>-0.001; 0.061</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Δ Height (cm year⁻¹)</td>
<td>5.62</td>
<td>5.59</td>
<td>5.48</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Prepubertal Δ height (cm year⁻¹)</td>
<td>5.07; 6.17</td>
<td>5.41; 5.77</td>
<td>5.31; 5.65</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Δ Height SDS (change year⁻¹)</td>
<td>-0.003</td>
<td>-0.004</td>
<td>-0.012</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Δ FEV₁ % predicted (change year⁻¹)</td>
<td>-1.17</td>
<td>-3.09</td>
<td>3.88</td>
<td>NS</td>
<td>P=0.019</td>
</tr>
<tr>
<td>Δ FMEF % predicted (change year⁻¹)</td>
<td>-8.1; 5.8</td>
<td>-15.7; 9.6</td>
<td>2.5; 5.2</td>
<td>NS</td>
<td>P=0.006</td>
</tr>
</tbody>
</table>

changed their opinion the child was then put on inhaled budesonide as previously described. The child continued in the trial and the period without inhaled budesonide was used as run-in. The control children used diary recordings and PEF monitoring in the same manner as the budesonide group.

At present, more than 200 patients have received inhaled budesonide for ≥2 years in this study. The results from these patients and from the control patients are presented. The study is presently ongoing to follow the patients and others, who at present have been on inhaled budesonide for less than 3 years. The study will follow the children into adulthood to measure their final height, weight, lung function, and required dose of budesonide.

STATISTICS

In addition to measured values the height and weight measurements are presented as height and weight standard deviation scores (SDS):
Results

A total of 278 children have completed the run-in period; 62 of these are control patients who have not taken inhaled corticosteroids for an average of 5.2 years (range 3-7 years). The remaining 216 children have received inhaled budesonide for 2-6 years (mean 3.7 years) after a run-in period of 1-3 years (mean=1.6 years). A total of 3006 hospital visits at which the various variables were recorded have now been made (729 in the control group and 2275 in the budesonide group, of these 678 were during run-in).

Demographic data for the two groups are given in Table 1. There were no statistically significant differences in age, height, weight, height SDS, weight SDS, pulmonary function, asthma duration or asthma treatment between the two groups at the entry to the study (Table 2). Throughout the study all 278 children received $\beta_2$-agonists morning and evening and as needed. After starting on budesonide, no children required SCG and the use of slow release theophylline and oral $\beta_2$-agonists was also significantly reduced (Table 2).

HOSPITALIZATIONS

The number of annual hospitalizations due to acute severe asthma was the same in the two groups during run-in, before budesonide was started. During the subsequent budesonide treatment period, this number was markedly reduced whereas no significant changes were seen in the control children (Table 2).

BUDESONIDE DOSE AND DELIVERY SYSTEM

During the first part of the study period, the majority of children in the study group received budesonide via a large volume spacer (Nebuhaler). During the last part of the period, Turbuhaler replaced the Nebuhaler in a large number of children, who switched from Nebuhaler to Turbuhaler. The mean budesonide dose from the two devices required to achieve and maintain asthma control is shown in Fig. 1. A statistically significant decrease in the budesonide dose was found over time for both inhalers ($P<0.001$), and the mean dose from Turbuhaler (447; 95% confidence limits 420-466 $\mu$g day$^{-1}$) was significantly lower than the mean dose from Nebuhaler (612; 95% confidence limits 596-628 $\mu$g day$^{-1}$) ($P<0.001$). Yet mean pulmonary functions were significantly higher in children using Turbuhaler (mean FEV$_1$=98.3 ± 14.6% vs. 88.0 ± 13.6% in Nebuhaler group and mean FMEF=85.7 ± 22.1% vs. 76.8 ± 22.8% in Nebuhaler group) ($P<0.001$).

HEIGHT

There was a positive correlation between height SDS and % predicted FEV$_1$ in the controls and in the
budesonide children during run-in ($P=0.05; R=0.126$, 95% confidence limits 0.051), indicating that asthma severity influenced growth.

No statistically significant differences were seen between the two groups in measured height or height SDS at study entry (Table 1, Fig. 2) or at the end of the run-in period when mean measured height in the two groups was 124 cm (controls) and 125 cm (budesonide). Compared with run-in and with the control group treatment, inhaled budesonide did not cause any statistically significant changes in growth rate during the 3-5 years of treatment (Fig. 2). The annual increase in height was 5.62 cm (controls) and 5.48 cm (budesonide) and the measured height in the two groups at the end of the study was 142.5 cm (controls) and 143.7 cm (budesonide) (NS). A separate analysis of growth rate in prepubertal children gave similar results. No statistical significant differences were found between the two groups (Table 2).

Finally, linear regression was used to assess the mean annual change in height SDS for each individual child over the whole study period. This analysis showed that the mean annual change in height SDS was similar in the two groups and not significantly affected by the budesonide treatment (Table 2).

Because the dose of budesonide varied in each individual child during the treatment period the influence of budesonide dose upon growth could not be assessed. Therefore, the change in height SDS (A SDS) during each 6 months growth interval was calculated individually and used to compare budesonide growth rate in three different dose groups (≤400, 401-800, and >800 $\mu$g day$^{-1}$) with the growth rate in the control children. No statistically significant differences were found. The annual change in height SDS (mean and 95% confidence limits) being 0.011 (-0.010; 0.034) during run-in, 0.000 (-0.012; 0.012) during treatment with ≤400 (mean 322) $\mu$g day$^{-1}$, -0.033 (-0.056; 0.010) during treatment with 401-800 (mean 691) $\mu$g day$^{-1}$, -0.047 (-0.102; 0.007) during treatment with >800 (mean 1025) $\mu$g day$^{-1}$ and 0.000 (-0.024; 0.025) during control treatment. However, compared with run-in and low dose treatment (≤400 $\mu$g day$^{-1}$) high doses of budesonide (>400 $\mu$g day$^{-1}$) were associated with a significant reduction in (A) height SDS ($P<0.05$). Daily doses ≤400 $\mu$g did not adversely affect growth velocity. The number of treatment periods with Turbuhaler was too low to allow an accurate analysis of each inhaler separately.

**Weight**

A statistically significant correlation between weight SDS and % predicted FEV$_1$ was seen in the control children and budesonide children during run-in ($P=0.003; R=0.130$, 95% confidence limits 0.044; 0.214; weight SDS being lower in children with low FEV$_1$. There were no statistically significant differences between the two groups (A SDS) in these parameters (Tables 1 and 2). Measured weight in the two groups 3-5 years after the end of run-in was 36.8 kg (controls) and 38.5 kg (budesonide) (NS).
Separate analysis of weight gain in prepubertal children gave similar results. No statistical significant differences were found between the groups.

PULMONARY FUNCTIONS

Pulmonary functions were very similar in the two groups at study entry. At that time a negative correlation between % predicted FEV₁ and the duration of asthma was seen \( (P=0.07; \ R=-0.142; \ 95\% \ confidence \ limits \ -0.289; \ 0.012) \). Both FEV₁ and forced midexpiratory flow (FMEF) showed a statistically significant improvement over time during treatment with inhaled budesonide (Fig. 3), both when compared with run-in \( (P<0.001) \) and with the control group \( (P<0.001) \). The difference was significant after only 6 months and it was maintained throughout the treatment period.

Linear regression was used to assess the mean slope (annual change) in per cent predicted FEV₁ for each child. There were no statistically significant differences between the control children and the budesonide children during run-in when no corticosteroids were given (Table 2). The annual increase in pulmonary function was significantly higher during budesonide treatment than in the same children during run-in or than the control children (Table 2). Furthermore, the duration of asthma before budesonide treatment was started had a marked influence upon the rate of annual increase in % predicted FEV₁ and a statistically significant correlation between the duration of asthma at the start of budesonide treatment and the rate of annual increase in FEV₁ was seen \( (P=0.02; \ R=-0.171, \ 95\% \ confidence \ limits: 0.31; 0.03) \) (Fig. 4). As a consequence, FEV₁ after 3 years of budesonide treatment was lower in children who started budesonide treatment more than 5 years after the onset of asthma \( (mean=96.2 \pm 9.5\% \ predicted) \) than in children who started budesonide 1-2 years after onset \( (mean=101.0 \pm 13.6\% \ predicted) \) \( (P<0.05) \). At that time, mean FEV₁ in the control group \( (89.6 \pm 12.6\% \ of \ predicted) \) was significantly lower than FEV₁ in the children who started budesonide treatment more than 5 years after the onset of asthma. The
corresponding figures for FMFF (mean ± sn) were 90.3 ± 20% (>5 years delay), 96.3 ± 23% (<2 years delay) and 80.4 ± 17% (control group) (P<0.05). This effect of delay in budesonide treatment was not influenced by the previous asthma treatment given to the child.

The mean age at the start of budesonide treatment differed between the five groups in Fig. 4 (4.7, 6.1, 7.1, 8.2 and 9.3 years, respectively). Therefore, the influence of age upon the annual increase in FEV₁ was also evaluated. Similar results (slopes) were found in the various age groups, and the age adjusted mean annual changes in FEV₁ also varied significantly with delay in treatment: 8.7, 5.1, 2.3, 3.3 and 0.9% increase per year in the five delay groups, respectively (P=0.007). For comparison the corresponding values in children older than 10 years at the start of budesonide treatment were: 9.8, 6.2, 3.2, 3.4 and 2.0% per year.

**Discussion**

The present study evaluated the growth rate in children with asthma under controlled conditions in a clinical setting. Under these conditions there was no indication that long term treatment with inhaled budesonide adversely affected growth. This is in agreement with the findings in other often less controlled studies with shorter observation periods and lower numbers of patients (4–8) and a recent prospective controlled long study using a daily budesonide dose of 600 μg (9). Although the lack of a statistical significance on growth does not exclude the possibility of an adverse effect, the present study would have been sensitive enough to detect a 5% reduction in growth rate (3 mm year⁻¹) with a statistical power of >95% in children receiving budesonide doses ≤400 μg day⁻¹. So a clinically important growth suppression by budesonide in these doses is most unlikely. This conclusion is in good agreement with the findings in knemometry studies (11–13), which measure short term changes in lower leg length with a high accuracy and which are very sensitive in detecting growth reductions since the top of the growth suppressive dose–response curve is reached already at a daily dose of prednisolone of 2.5 mg (13).

Although no accurate dose related effects could be made the results suggested that high doses around 800 μg day⁻¹ may to some extent retard growth, though not to an extent that was detectable when the changes over the whole period were evaluated. In agreement with this 2 weeks treatment with 800 μg budesonide day⁻¹ was associated with a marked (50%) reduction in lower leg growth rate in knemometry studies on children with mild asthma (10,11). So further studies in asthmatic children requiring continuous long term high dose therapy are needed before firm conclusions about such treatment can be made.

It is sometimes suggested that once a child is on continuous treatment with inhaled corticosteroids there is a possible risk of tachyphylaxis and that over the years higher doses (with potential systemic side effects) would eventually be needed. The present study does not support this. All children were monitored closely 2–4 times a year throughout the study and the dose of inhaled budesonide was constantly tailored to suit the severity of asthma. Under these conditions there were no indications of an increase in budesonide dose during 3–6 years of continuous treatment. In contrast, the dose required to control the asthma tended to decrease throughout the study period without any loss of asthma control. The initial reduction in dose could be due to the treatment strategy of starting with a high initial dose and then subsequently reducing the dose. However, even after the first 6 months a continuous decline in the required dose was seen, indicating that once the asthma was well controlled, less inhaled corticosteroid was required for maintenance therapy or that the severity of asthma tended to decline with age, though this did not appear to be the case among the controls.

At present the influence of treatment upon the chance of growing out of the asthma cannot be assessed. However, the study is still ongoing and may provide such information in the future.

It was interesting that the children who were switched from the Nebuhaler to the Turbuhaler device were able to reduce their doses of budesonide by 50% and yet experience an improvement in asthma control, suggesting that Turbuhaler is more
effective than Nebuhaler. This observation agrees well with the findings in recent pharmacokinetic and pulmonary deposition studies and clinical trials (14–17).

All children suffered from mild and moderate asthma according to the generally accepted definition of asthma severity, and during run-in they were treated according to the normally recommended guidelines for these groups of children and the controls continued this treatment throughout the study (3). It was the clinical impression that the majority of the children benefited from this treatment. Yet most of them showed marked improvements in clinical symptoms and pulmonary functions and a substantial reduction in hospitalization rate due to acute severe asthma when they started treatment with budesonide. Such marked improvements were unexpected but in good agreement with the findings in adults (18,19). This suggests that the degree of asthma control achieved by a treatment is often overestimated probably because the child's personal best (optimal) control is not assessed as recommended in the guidelines for adult asthmatics (1,2).

Paediatric guidelines do not normally emphasize the importance of establishing the child's personal best asthma control by an initial period of aggressive treatment (3). As a consequence there is a risk that the patient is undertreated and symptoms underestimated because the clinical condition is compared with the situation when no treatment is given instead of being compared with optimal control.

It was surprising that treatment induced increases in \( \text{FEV}_1 \) and \( \text{FMEF} \) was related to the interval between the onset of asthma symptoms at the start of inhaled corticosteroid therapy. This effect of delayed treatment did not appear to be influenced by the previous treatment of the child. This finding in combination with the negative slope of annual change in % predicted \( \text{FEV}_1 \) during run-in and control treatment suggest that suboptimally treated asthma may result in irreversible airway obstruction in children. Furthermore, it seems that treatment with inhaled glucocorticosteroids can reduce this effect or maybe even prevent it if the treatment is started early after the debut of symptoms. This suggestion agrees well with the findings in a recent study: adults with mild asthma who were initially treated with inhaled terbutaline for 2 years and then with inhaled budesonide, could not achieve as high pulmonary function or as good asthma control as a comparable group of patients who were treated with inhaled budesonide as soon as they were diagnosed (20). Since the effect of inhaled glucocorticosteroids seemed to depend upon the duration of asthma symptoms before the start of treatment these findings suggest that inhaled corticosteroids should be first line treatment not only in adults but also in children assessed to suffer from mild and moderate asthma.

Inhaled corticosteroids are the only drugs which have been shown in controlled studies to reduce the chronic inflammation seen in the airways of asthmatic patients (21). Presumably the preserving effect on lung function is a result of this effect. Recently, however, excessive use of inhaled \( \beta_2 \)-agonist has also been suspected to adversely affect lung function in adults (22–24). Since the use of \( \beta_2 \)-agonists was markedly reduced by the introduction of budesonide treatment this mechanism may also have been important.

An accurate cost-benefit analysis was not performed. However, drug expenses were not higher during budesonide treatment and if the effect upon asthma control and number of acute admissions was considered this analysis also seemed to be in favour of the budesonide treatment.

Conclusion

Inhaled budesonide in doses up to 400 \( \mu \text{g} \ \text{day}^{-1} \) does not stunt long-term growth in children with asthma when the dose is regularly tailored to the severity of the disease. Early intervention with inhaled corticosteroids seems to be able to prevent the development of irreversible airway obstruction that occurs over the time if the asthma is under-treated. Furthermore, compared with other treatments early intervention with inhaled steroids reduces the risk of undertreatment. Finally, Turbuhaler is more effective than Nebuhaler in the treatment of asthma in school children.

References

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