



Asthma control and steroid doses 5 years after early or delayed introduction of inhaled corticosteroids in asthma: a real-life study

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Summary We evaluated asthma control and medication use 5 years after introduction of an inhaled corticosteroid (budesonide via Turbohaler[®]) in 462 patients with persistent asthma and symptoms of different duration. An early treatment group with symptoms for <2 years (group A) was compared with a delayed treatment group (group B) (median duration 5 years and 3 months). Most patients received budesonide 400 µg twice daily as initial dose. We report 5-year follow-up data on 404 patients (group A $n = 253$; group B $n = 151$) and on a few more patients after treatment for 6 months, 1 year and 3 years. At 5 years the mean maintenance doses of budesonide were 412 µg (A) and 825 µg (B), respectively ($P < 0.001$). Nevertheless, treatment goals (normal lung function, normal exercise tolerance, minimal use of reliever medication, no asthma exacerbations) were all statistically significantly more frequently achieved in group A. At 5 years group B patients also used significantly more additional asthma medications, e.g. inhaled long-acting β_2 -agonists by 64% compared with 6% in group A. In group A 43 patients (17%) had been able to stop budesonide treatment compared to five patients (3%) in group B. A subgroup of group B patients with higher mean baseline FEV₁ values than group A showed nevertheless significantly poorer response. No treatment-related serious adverse events were reported. Budesonide was well tolerated in both groups.

Conclusion: Duration of asthma symptoms when starting treatment with an inhaled corticosteroid is an important determinant for the response. Early treatment gives significantly better airway function and asthma control than delayed treatment and at lower maintenance doses.

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Introduction

Asthma management and treatment guidelines recommend inhaled corticosteroids as first-line treatment for patients with mild, moderate or

severe persistent asthma.^{1,2} For a long time we have been interested in early use of inhaled corticosteroids. The first 2-year, double-blind, parallel-group study in Finland showed that the inhaled corticosteroid, budesonide, was more effective than the inhaled β_2 -agonist, terbutaline, when given regularly as first-line treatment to patients with newly detected asthma.³ The follow-up study, when terbutaline-treated patients received budesonide during a third treatment year,

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showed improvements in lung function and reductions in bronchial hyperresponsiveness (BHR), use of reliever medication and asthma symptoms, but the patients did not reach the same level of asthma control as those patients treated with budesonide from the beginning.⁴ Our retrospective analysis evaluating the relationship between duration of asthma symptoms and response to treatment with budesonide supported these results.⁵ A statistically significant negative correlation was found between duration of asthma symptoms and improvements in lung function (forced expiratory volume in 1 s, FEV₁; peak expiratory flow, PEF). Patients with symptoms for more than 2 years responded less well than patients with a shorter duration of symptoms. The best improvements in lung function were seen in patients who had had asthma symptoms for less than 6 months when starting treatment with budesonide.⁵ Similar observations have been reported in children with asthma.⁶

In the present observational study we started treatment with budesonide (Pulmicort[®] Turbuhaler[®], Astra Pharmaceuticals, Sdertlje, Sweden) in a large series of patients not previously treated with inhaled corticosteroids. Some 3¹/₂-year results have previously been briefly reported.⁷ The aim of this paper is to report 6-month, 1-, 3-, and 5-year follow-up data in patients with asthma starting treatment with budesonide early, when they had had asthma symptoms for less than 2 years, compared to patients who had had symptoms for a longer period of time.

Material and methods

Study design

Asthma patients seen at the Mjlbolsta hospital in Finland and not previously treated with an inhaled corticosteroid were prescribed budesonide as regular maintenance treatment. They were then followed at regular intervals, approximately 3, 6 or 12 months apart, when lung function was measured (FEV₁; forced vital capacity, FVC; FEV₁% predicted normal), symptoms, use of reliever medication and adverse effects recorded, and the dose of budesonide adjusted up or down depending on the clinical situation. Before a clinic visit patients were asked to record morning and evening PEF for 1–2 weeks. Patients did not themselves change prescribed doses between visits, but were allowed to contact the hospital at any time, if necessary, and then the dose could be adjusted.

Additional asthma medication could be added or changed as required.

Based on our earlier experiences^{4,5} we divided the clinical series into patients with early asthma, i.e., with asthma symptoms for less than 2 years when starting treatment with budesonide, and the rest, i.e., those with delayed treatment with symptoms for more than 2 years when starting treatment with budesonide.

The aim was to investigate to what degree the goals given in asthma treatment guidelines could be achieved with early vs. delayed treatment with an inhaled corticosteroid, and how much additional medication was required, if necessary, to achieve the best possible result. We also wanted to investigate to what extent there would be a difference in response to treatment in terms of improved airway function between patients with a short and a long duration of symptoms when starting treatment with budesonide.

Study population

A total of 462 patients with persistent asthma started treatment with budesonide Turbuhaler. The series consists of consecutive patients visiting the hospital for the first time between 1988 and 1995 and not previously treated with inhaled corticosteroids. However, based on hospital statistics we estimate that approximately 17% of all patients with persistent asthma and not previously treated with inhaled corticosteroids did not start or accept treatment with budesonide at the time of the study. In patients starting treatment the duration of asthma symptoms was less than 2 years in 301 (group A; median duration of symptoms 13 months) and longer in 161 patients (group B; median duration of symptoms 5 years and 3 months). Demography and baseline lung function data are shown in Table 1. The differences between groups A and B in FEV₁ per cent predicted and baseline reversibility were statistically significant, $P < 0.01$ and $P < 0.001$, respectively. The difference in PD₂₀ histamine mean values was not statistically significant.

We have been able to follow 455 patients for 6 months, 433 for 1 year, 418 for 3 years and 404 (87%) patients for 5 years. Five-year data could be obtained in 253 group A (84%) and 151 group B patients (94%). The proportion of patients with mild persistent asthma (FEV₁ ≥ 80% predicted normal) and moderate-to-severe persistent asthma (FEV₁ < 80% predicted normal) did not differ statistically significantly between groups A and B, indicating that as groups they were similar in terms

Table 1 Demographic data when starting treatment with inhaled budesonide.

	Early treatment (Group A)	Delayed treatment (Group B)	Total series of patients
Number of patients (%)	301 (65)	161 (35)	462 (100)
Female/Male (%)	172/129 (57/43)	74/87 (46/54)	246/216 (53/47)
Mean age (range), years	34 (16–69)	39 (18–78)	37 (16–78)
Median duration (range) of asthma symptoms	13 months (3–23 months)	5 years 3 months (2.5–18 years)	
FEV ₁ , L (mean ± SD)	3.06 ± 0.98	2.41 ± 0.81	2.85 ± 0.92
FEV ₁ , % pred norm, mean ± SD	78.6 ± 18.1	74.3 ± 20.5	77.2 ± 18.6
Percentage of patients with FEV ₁ ≥ 80% pred normal	42	39	41
Reversibility %, mean ± SD	18.4 ± 4.3	15.9 ± 5.8	17.8 ± 5.6
PD ₂₀ FEV ₁ histamine, mg, mean ± SD	0.24 ± 0.70*	0.11 ± 0.39 [†]	0.22 ± 0.56 [‡]
Smoker/nonsmoker (%)	25/276 (9/91)	17/144 (12/88)	42/420 (10/90)

**n* = 152.[†]*n* = 118.[‡]*n* = 270.

of asthma severity, and thus only differed in terms of duration of disease. In group A 42% of the patients had mild persistent asthma (FEV₁ > 80% predicted normal) and in group B 39%. As, however, the mean level of FEV₁ differed statistically significantly between groups A and B we further analysed a subgroup of group B patients with individual FEV₁ values ≥ 80% predicted normal. Thus, this subgroup of patients (*n* = 63) with a median duration of symptoms of 6 years and 7 months did not have a more severe disease than group A, but only a longer duration of asthma symptoms.

Treatment

When inhaled corticosteroid treatment was initiated the starting dose of budesonide was mostly 400 µg twice daily, but varied from 100 to 800 µg twice daily. The initial dose was maintained until a normal airway function (or best possible) and good exercise tolerance had been achieved, the night-

time sleep was undisturbed and the need of reliever medication (rapid-acting inhaled β₂-agonists) reduced to 2–3 doses per week indicating infrequent symptoms. The daily dose was then reduced by 200–400 µg per day, which could be given once daily. When a daily dose of 100–200 µg had been achieved treatment could be discontinued and the patient followed in the same way as before. If necessary, treatment with budesonide was re-instituted. The degree of BHR (histamine challenge test) was not used on a routine basis for adjustment of budesonide doses. If an acceptable response was not seen the dose was increased step-wise to a maximum of 2400 µg per day and then adjusted downward, if possible, as earlier described. Additional asthma medications could be prescribed as considered necessary.

During the later part of the study period doses above 1200 µg per day of budesonide were rarely used. Instead combination treatment, especially with long-acting inhaled β₂-agonists, was the preferred treatment.^{8,9}

As a general recommendation patients should rinse their mouth after inhalation with a gulp of water.

Efficacy assessments and use of asthma medication

Lung function. Spirometry (FEV₁, FVC, and FEV₁ % predicted normal) was performed on a routine basis at the outpatient department during the 5 years of the follow-up using a Vitalograph compact spirometer (Vitalograph Ltd., Buckingham, UK).

Asthma symptoms. Asthma symptoms were registered during 2-week periods prior to clinic visits and by asking the patients for cough, shortness of breath at rest and during/after exercise, chest tightness, and night-time awakenings due to asthma.

Exercise tolerance. Exercise tolerance was estimated by asking the patient and classified as normal, acceptable or poor.

Exacerbations. The definition of an exacerbation was hospitalization or emergency room visit because of asthma, use of a course of oral corticosteroids or doubling or more of the dose of the inhaled corticosteroid.

Drug usage. Patients were asked about their use of budesonide during the last month and whether it was in accordance with the actual prescription. The use of any additional asthma medication was recorded. At the follow-up examination some patients were not treated with budesonide Turbuhaler but were using another inhaled corticosteroid (beclomethasone dipropionate, BDP, or fluticasone propionate, FP). The doses were then calculated as follows: 200 µg budesonide Turbuhaler = 200 µg FP Diskhaler/Diskus = 400 µg BDP pressurised metered-dose inhaler (pMDI)/Diskhaler/Easyhaler.¹⁰⁻¹³

Treatment goals. The goals for asthma management and treatment are given in international¹ and national guidelines.² Treatment should aim at a normal lung function (or best possible), normal exercise tolerance, normal night-time sleep, no or minimal use of reliever medication, no exacerbations, and no side effects of drugs.

Safety assessments

Patients were asked about adverse experiences including local side effects at regular clinic visits. Routine laboratory tests such as erythrocyte sedimentation rate, peripheral blood counts, blood glucose, serum creatinine, sodium and potassium, liver enzyme tests and urinalysis were performed at regular intervals at least once a year. Tests of the

hypothalamic-pituitary-adrenal axis (serum and 24-h urinary cortisol, ACTH tests) were performed only in specific cases on high-dose treatment or in cases of electrolyte disturbances.

At clinic visits inspection of throat was routinely done for detection of clinically important oropharyngeal candidiasis.

Statistical analysis

Group mean values of budesonide doses, baseline lung function and PC₂₀ values and percentages of achieved treatment goals were compared with *t*-tests. Differences in changes in lung function values were analysed using an analysis of variance (ANOVA) with baseline FEV₁ as a covariate. *P* values <0.05 were considered statistically significant. Calculations on changes in FEV₁ over time included all patients with data at each time point. Separate calculations were performed from time 0 to 1 year, and from time 0 to the 5-year endpoint. The slopes were estimated with a mixed effect model: SAS Proc Mixed procedure—SAS Institute.¹⁴ Regression estimates were adjusted for patient differences in number of observations contributing to the model and for within-patient variations. Fixed effects were time, with baseline FEV₁, age and sex as covariates.

Results

The results are presented in Tables 2 and 3 and in Figs. 1 and 2.

Patients withdrawn from the study

There were 58 patients that we could not follow for 5 years (group A 48, group B 10 patients). As a group the withdrawn patients were young (mean age 27 years), had a mild disease with 37 of them having a baseline FEV₁ >80% predicted normal. The patients had been withdrawn for various reasons; considered themselves healthy without need for medication (*n* = 16), did not accept an inhaled corticosteroid as further treatment (*n* = 5), did not return to scheduled visit (*n* = 22), and moved to other cities (*n* = 15). Nobody was withdrawn because of adverse events.

Doses of budesonide

The initial doses of budesonide were 785 ± 133 µg (mean ± SD) in group A and 1062 ± 287 µg in the B group. Based on clinical judgements (symptoms,

Table 2 Five-year follow-up data.

Number of patients (%) Female/male	Early treatment (Group A)		Delayed treatment (Group B)	
	253 (84%) 156/97		151 (94%) 72/79	
	At start	After 5 years	At start	After 5 years
Budesonide, mean dose \pm sd (dose range)	785 \pm 133 μ g (400–1600 μ g)	412 \pm 76 μ g (0–1600 μ g)	1062 \pm 287 μ g (400–1600 μ g)	825 \pm 165 μ g (0–2400 μ g)
No of patients (%) not using an inhaled corticosteroid	100	43 (17%)	100	5 (3%)
Mean FEV ₁ % predicted normal (range)	80.3% (52–97%)	93.9% (73–132%)	75.6% (36–102%)	84.5% (54–115%)
Mean PEF % predicted normal (range)	83.1% (48–114%)	95.0% (78–136%)	74.0% (38–117%)	87.2% (51–109%)
Use of asthma maintenance medications (% of patients):				
LABA*	0%	6%	0%	64%
Theophylline	13%	0%	62%	25%
LRA [†]	0%	4%	0%	21%
Other [‡]	7%	0%	36%	8%
Local side effects, no of patients (%)	0 (0%)	4 (1.6%)	1 (0.7%)	6 (4.2%)

*LABA = long-acting inhaled β_2 -agonists.[†]LRA = leukotriene receptor antagonist.[‡]Other = disodium cromoglycate, nedocromil sodium, oral β_2 -agonists, antihistamine.**Table 3** Per cent patients achieving treatment goals.

Treatment goals	Early treatment (Group A)	Delayed treatment (Group B)	Difference
Lung function \geq 90% predicted normal*	77%	41%	$P < 0.001$
Normal exercise Tolerance [†]	72%	20%	$P < 0.001$
Normal sleep [†]	92%	75%	NS
Use of reliever medication \leq 3 doses per week	68%	29%	$P < 0.001$
Exacerbations [‡] per patient per year	0.07	0.34	$P < 0.001$

NS = not statistically significant.

*FEV₁ or PEF.[†]Self-reported.[‡]Hospitalization, emergency room treatment, course of oral corticosteroids (group A 84 exacerbations, group B 243).

use of reliever medication, PEF, sleep, exercise tolerance) the dose of budesonide was then adjusted up or down. The mean doses and dose ranges after treatment for 5 years are shown in Table 2. After 5 years 43 patients (17%) in the early

treatment group had been advised to stop treatment with the inhaled corticosteroid. Twenty-two of these patients reported taking an inhaled corticosteroid intermittently during a pollen season, when otherwise exposed to allergens, or in

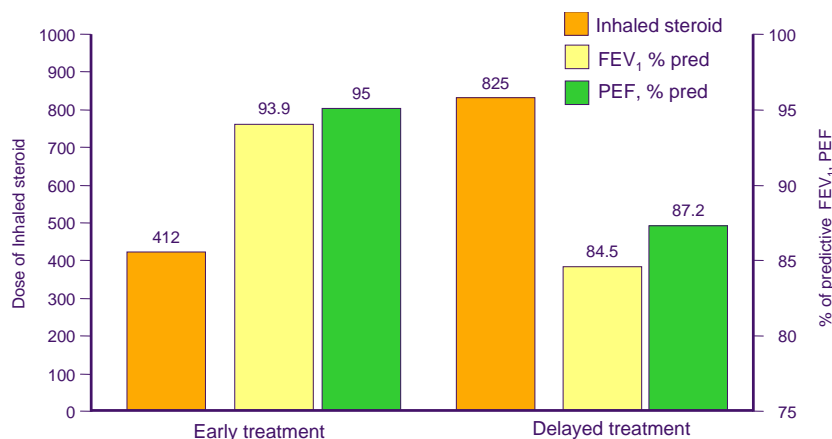


Figure 1 Mean inhaled corticosteroid dose and mean per cent predicted normal of FEV₁ and PEF after 5 years treatment in asthma patients with early or delayed introduction of treatment with budesonide Turbuhaler.

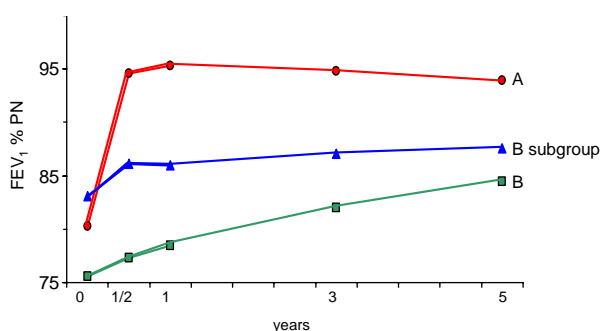


Figure 2 Mean FEV₁ values (% predicted normal) in patients with early (A) or delayed (B) intervention with budesonide. B_{subgroup} denotes the group B patients with individual baseline FEV₁ values > 80% predicted normal.

association with an upper respiratory tract infection. In the delayed treatment group five patients (3%) were treated without inhaled corticosteroids at the 5-year follow-up. Seventeen patients were using another inhaled corticosteroid. The mean doses at the 5-year follow-up between the early and delayed treatment groups are shown in Fig. 1. The difference in mean doses between the groups was statistically significant ($P < 0.001$).

Self-reported compliance, checked at clinic visits, was 92%.

Lung function

Lung function, measured both as FEV₁ and PEF, improved in both early and delayed treatment groups 5 years after starting treatment ($P < 0.001$ for early and $P < 0.01$ for delayed treatment). The difference between the groups in achieved lung function values was statistically significant

($P < 0.001$). As the difference in baseline FEV₁ and PEF between the early and delayed treatment groups was taken into account in the analysis the results reflect the difference in disease duration and not in disease severity. The mean values of FEV₁ and PEF after 5-year treatment are shown in Fig. 1. It can also be noted that the improvement in FEV₁, measured as per cent predicted normal values, improved much more rapidly in the early treatment group compared with the delayed treatment group (Fig. 2). The difference in change in FEV₁ between groups A and B from start and to 1 year was statistically highly significant ($P = 0.0002$) and also from start to the 5-year endpoint ($P < 0.001$).

Subgroup analysis. The development of lung function in the subgroup of patients in the delayed treatment group with baseline FEV₁ values above 80% predicted normal is also illustrated in Fig. 2. These subgroup patients had an initial mean FEV₁ of 83.1% predicted normal. These mean FEV₁ predicted normal values after treatment for 0.5, 1, 3 and 5 years were 86.1%, 86.0%, 87.1% and 87.6% predicted normal, respectively. The change in FEV₁ between this subgroup of group B and group A was very different with group A patients improving much more rapidly during the first treatment year (Fig. 2). The difference in change was statistically significant ($P = 0.0001$). The FEV₁ slopes over 5 years were not, however, statistically significantly different between the subgroup of group B patients and the rest of the group B population ($P = 0.39$).

Achievement of treatment goals

Achievements of asthma treatment goals are given in Table 3. Early treatment resulted in statistically

significantly higher percentages of achieved goals for lung function, exercise tolerance, exacerbations and use of as-needed reliever medication.

Adverse events

Three serious adverse events were recorded; one patient was hospitalized for pneumonia, one because of a renal stone, and one as a consequence of a traffic accident. None of them was considered related to the treatment with budesonide. No bone fractures or cataracts were reported.

A total of 14 ACTH tests had been performed in patients on higher doses of budesonide ($>1200\mu\text{g}$ per day) and all showed a normal response. Excretion of urinary cortisol during 24h was analysed in 36 patients with normal result in all but one. This 57-year-old woman had a borderline value which was normal on the same dose ($800\mu\text{g}$ per day) 3 month later.

Discussion

Inhaled corticosteroids reduce mortality, hospitalizations, emergency room visits, days missed from work or school, use of reliever medication, and overall costs for medication.^{15,16} Regular use of inhaled corticosteroids, even taken once daily,¹⁷ prevent asthma exacerbations and higher daily doses appear more effective than lower doses in patients with persistent asthma.^{9,18}

Clinical studies in Finland in the early 1990s showed that in patients with early mild-to-moderate asthma treatment with budesonide was more effective than regular treatment with the inhaled bronchodilator, terbutaline.³ A recent study in Finnish children showed an advantage of budesonide in comparison with disodium cromoglycate (DSCG). Also intermittent budesonide treatment, after initial treatment with a higher regular dose, was more effective in preventing asthma exacerbations than DSCG.¹⁹ A retrospective cohort study demonstrated a statistically significant negative correlation between duration of asthma symptoms when starting treatment with an inhaled corticosteroid and the response to treatment in terms of improved lung function.⁵ Similar results have been reported in studies from other countries, in children⁶ as well as in adults with asthma.²⁰

The results of the Finnish studies together with the gained clinical experience were utilized in the Finnish national asthma programme 1994–2004 issued by the Ministry of Social Affairs and Health.² Half-way through (1999) the results of this pro-

gramme indicated that the expected results in terms of reduced morbidity, mortality and cost-effectiveness could be fulfilled.²¹

At our hospital the strategy of early use of inhaled corticosteroids in patients with persistent asthma was early adopted. In the late 1980s one reason why patients refused to take inhaled corticosteroids was the high frequency of local side effects: approximately 25% of the patients using a pressurized metered dose inhalers (pMDIs) containing corticosteroids developed sore throat, voice problems or oropharyngeal candidiasis.²² We realized, however, that changing inhalation device from a pMDI to an inspiratory flow driven dry powder inhaler with an appropriate inbuilt resistance (Turbuhaler[®]) and containing pure drug substance (budesonide) without carrier powder (lactose) almost completely abolished the local side effects.²² We therefore decided to use budesonide Turbuhaler as our first-line inhaled corticosteroid, which in addition, was reported to have an improved systemic safety profile compared with the previously used inhaled corticosteroid, BDP.²³ We were also able to demonstrate that half the dose of budesonide Turbuhaler resulted in the same degree of clinical efficacy as twice as much BDP administered via pMDI.¹⁰ This finding has been confirmed in studies using a dose-reduction study design or a dose-response design with at least two doses of one of the inhaled corticosteroids.^{11,24}

We mostly used a starting dose of $400\mu\text{g}$ twice daily and then applied a step down and step up strategy depending on necessity. A high or low starting dose has been widely discussed,²⁵ especially as the dose response curve for inhaled corticosteroids is fairly flat.²⁶ A Dutch study showed no difference in efficacy between a 200 and $800\mu\text{g}$ per day of budesonide.²⁷ These patients, however, had a normal airway function at entry into the study. Similarly, a Finnish study showed no statistically significant difference in airway function (FEV₁, PEF) between $800\mu\text{g}/\text{day}$ budesonide compared to $200\mu\text{g}/\text{day}$ as an initial treatment dose.²⁸ The higher dose, however, gave a more marked decrease in BHR and reduction in serum markers of asthmatic inflammation; serum ECP $P = 0.008$ and serum EPX $P = 0.005$ for high vs. low dose budesonide.²⁸ We also reported the results of a double-blind, placebo-controlled study in patients with a duration of asthma symptoms <1 years compared with a group with symptom duration >2 years.²⁹ In patients with early asthma no difference in efficacy was seen between $100\mu\text{g}$ twice daily and $400\mu\text{g}$ twice daily, but in the patients with a longer duration of asthma symptoms (median 5 years) the

higher dose resulted in statistically significantly better airway function and asthma control.

It is obvious that asthma severity differs among individuals whatever group of patients is included in clinical studies. Disease severity may also easily be underestimated. We therefore consider the best strategy to be to initiate treatment on a reasonably high dose level but thereafter adjust the dose to the lowest possible maintenance dose, which usually, when budesonide is used, can be given once daily. It should be remembered, however, that patients with mild early asthma respond equally well to low doses. This was clearly seen in one part of the OPTIMA study in patients with mild persistent asthma not previously treated with inhaled corticosteroids and now receiving budesonide Turbuhaler 100 or 200 µg twice daily¹⁸ and in the START study with budesonide Turbuhaler 200 or 400 µg once daily.¹⁷

The results of this follow-up study show the advantages of early treatment. This was true not only of airway function and asthma symptoms but also of doses of budesonide used and requirement of additional asthma medications. In fact, for all studied variables early treatment resulted in significantly higher degree of achieved treatment goals except for night-time awakenings. This exception could be due to the large use of inhaled long acting β_2 -agonists in the delayed treatment group. It should be noted that inhaled long-acting β_2 -agonists had been considered necessary in 62% of the patients in group B (vs. only 6% in group A) and this had probably influenced the night-time sleep in a positive way in this group of patients. It is therefore obvious that early treatment is not only more effective resulting in better airway function and asthma control but also associated with lower treatment costs because of less maintenance medication and fewer exacerbations.

In the present study patients with early asthma (group A) had higher FEV₁ and PEF values when starting treatment with budesonide than patients in group B. However, the proportion of patients in each group having mild or moderate asthma, respectively, did not differ between the groups. The difference in baseline airway function was included as a covariate in the statistical analyses. We therefore conclude that the difference in treatment response between the early and delayed treatment groups was due to a difference in duration of asthma and not in disease severity. In addition, we did a subgroup analysis on group B patients with an FEV₁ value \geq 80% predicted normal at baseline, i.e. a subgroup having a mean FEV₁ above that of group A patients. Nevertheless, group A patients with a shorter duration of asthma

symptoms responded significantly better to treatment, indicating that the duration of asthma symptoms when starting treatment was a more important factor for the response than the baseline airway function. It can also be added that the proportion of smokers did not differ between groups A and B and smoking habits can therefore not explain the difference in response between the groups. The majority of patients withdrawn from the study belonged to group A and represented the short-duration type of asthma patients included in the study. We have consequently excluded the possibility that the results would have been influenced by more severe patients leaving the study.

The tolerability of budesonide was good in both treatment groups but obviously any risk of adverse events should be lowest in a group of patients with the lowest maintenance doses of the drug. In this study a 50% lower maintenance dose could be achieved with early introduction of budesonide, which also resulted in almost one-fifth of the patients (17%) being able to discontinue their budesonide treatment. Early introduction of inhaled corticosteroids is therefore the safest way of using these drugs for treatment of asthma.

This study shows the importance of early introduction of inhaled corticosteroids in patients with persistent asthma. Early treatment results in significantly better improvements in airway function, exercise tolerance, lower risk of exacerbations and less use of additional asthma medications as well as of as needed reliever medication. These obvious benefits can be achieved with significantly lower maintenance doses of budesonide thereby further reducing the risks of long-term side effects.

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