

The effect of fluticasone propionate on functional status and sleep in children with asthma and on the quality of life of their parents

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Background: Although in the past drug interventions were measured primarily on the basis of their efficacy and safety, today we are increasingly interested in what impact treatments have on the patient's day-to-day activities and quality of life. **Objectives:** We sought to assess the effect of treatment with fluticasone propionate (FP) on functional status and sleep disturbances in children with asthma and to evaluate possible changes in the quality of life of the parents of these children after treatment.

Methods: As part of a randomized, double-blind, parallel-group, placebo-controlled, multicenter study on the effects of FP powder (50 or 100 µg twice daily) on growth in children aged 4 to 11 years with mild-to-moderate asthma ($n = 325$), parents/caregivers completed the following questionnaires at baseline and at weeks 24 and 52 of treatment: Functional Status IIR (FSII), Sleep Scale-Children (SLP-C), and Quality of Life of Parents of Asthmatic Children (QOL-PAC). Change from baseline to weeks 24 and 52 within each treatment group was analyzed by using paired t tests, and differences between treatment groups were analyzed by using analysis of covariance.

Results: Mean FSII and SLP-C scores improved significantly over baseline values with either 50 or 100 µg FP at weeks 24 and 52 ($p < 0.05$) and were significantly better than scores in the placebo group ($p < 0.05$). In contrast, FSII scores at week 52 and SLP-C scores at weeks 24 and 52 decreased significantly in the placebo group ($p < 0.05$). QOL-PAC results revealed that scores on the Burden scale were significantly improved in both FP groups at weeks 24 and 52. Subjective Norms and Social scales improved significantly only in the 100 µg FP group at week 52.

Conclusions: The results of this study show that FP (either 50 or 100 µg twice a day) was associated with significant improvements in functional status and decreased sleep disturbances in children with asthma. In addition, treatment of children with FP was associated with a decreased burden on the parents of these children with asthma. (*J Allergy Clin Immunol* 1998;102:19-23.)

Key words: Fluticasone propionate, quality of life, children, asthma

Abbreviations used

ANCOVA: Analysis of covariance

FP: Fluticasone propionate

FSII: Functional Status IIR

QOL-PAC: Quality of Life of Parents of Asthmatic Children

SLP-C: Sleep Scale-Children

Asthma is the most common chronic childhood disease,¹ affecting an estimated 2.7 million children under the age of 18 years.² Results from the National Health Interview Survey, based on data from 17,110 households, revealed that children with asthma experienced approximately 10 million more missed school days, 13 million more contacts with medical doctors, and 200,000 more hospitalizations than did children without asthma.² Additionally, 30% of children with asthma had some limitation in activity compared with only 5% of children without asthma. Besides the negative impact on the children's lives, there are additional consequences for the parents of these children. These are not only obvious consequences, such as increased health care utilization and costs, which are considerable, but also more subtle ones, such as the burden of their children's illness on their own quality of life.³

Although in the past drug interventions were measured primarily on the basis of their efficacy and safety, today we are increasingly interested in what impact treatments have on the patient's day-to-day activities and quality of life. As part of a 1-year clinical trial evaluating the effects of the inhaled corticosteroid fluticasone propionate (FP) on growth in children with asthma,⁴ we also assessed the effects of treatment on functional status and sleep disturbances of these children through questionnaires completed by their parents or caregivers. Because we now recognize the association between family well-being and childhood asthma,^{5,6} and studies have identified factors that may affect the quality of life of parents of a child with asthma,^{3,7} we also administered a questionnaire that measured changes in the quality of life of the parents of the children participating in the study.

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TABLE I. Background characteristics of patients

Characteristic	Placebo (n = 106)	50 µg FP (n = 111)	100 µg FP (n = 108)
Sex (%)			
M	25	26	24
F	75	74	76
Age (yrs)			
Mean	8.5	8.5	8.2
Range	4.2-12.0	4.5-11.9	4.0-11.9
Ethnic origin (%)			
White	84	88	90
Black	11	8	4
Hispanic	2	2	4
Other	3	2	2
FEV ₁ % predicted (SEM)	89 (1)	86 (1)	88 (2)

METHODS

Patients

Boys between 4 and 11 years of age and girls between 4 and 9 years of age (i.e., premenarchal) with mild-to-moderate asthma (meeting the diagnostic criteria of the American Thoracic Society⁸) were eligible for enrollment. At study entry, each child had an FEV₁ of at least 60% of the predicted normal value for the child's age, height, and sex. Patients had been treated with inhaled corticosteroids, β_2 -agonists, or both for the previous month.

Study design

Health outcomes assessments were conducted as part of a randomized, double-blind, parallel-group, placebo-controlled, multicenter study to assess the long-term effects of FP on growth in children with asthma.⁹ Patients received 50 or 100 µg FP or placebo twice daily through a breath-actuated multidose powder inhaler (Diskhaler) for 52 weeks. All patients were allowed to take inhaled albuterol as needed for acute symptoms. Parents/guardians provided written informed consent, and the study protocol was approved by institutional review boards.

Questionnaires

Three questionnaires were completed by parents/caregivers at baseline and at weeks 24 and 52: the Functional Status IIR (FSII), the Sleep Scale-Children (SLP-C), and the Quality of Life of Parents of Asthmatic Children (QOL-PAC). If a patient withdrew from the study before its completion, the week 52 questionnaire was completed at study discontinuation.

The FSII instrument is particularly strong in measuring the health status of children who have chronic physical disorders but are not disabled,¹⁰ and at the time of the study it was one of the few validated instruments for use in children with chronic illnesses. There is both a long version (43 items) and a short version (14 items) of the FSII, and the short version, which has been shown to have strong psychometric properties and provides concise measures of health status in children,¹¹ was used in this study. The FSII has two probes. The first assesses a child's eating and sleeping patterns, mood, attention, energy, and behavior during the previous 4 weeks, and the second assesses whether impairment is related to the disease. For the purpose of this study, the second probe was modified slightly to assess whether any impairment was due to the child's asthma rather than some other condition. The first probe is scored on a 5-point scale (with higher scores reflecting better functional status), and the second probe is scored on a 3-point scale (0 = no, not due to asthma; 1 = yes,

TABLE II. Mean ($\pm$ SD) scores on the FSII questionnaire

Visit	Placebo		50 µg FP		100 µg FP	
	n	Score	n	Score	n	Score
Baseline	104	94.3 (8.8)	110	93.5 (10.4)	107	92.3 (10.7)
Week 24	93	92.0 (12.2)	103	96.9 (7.3)*†	97	95.7 (8.5)*†
Week 52	96	91.5 (11.5)*	104	95.7 (7.7)*†	101	95.3 (12.0)*†

* $p < 0.05$ change from baseline (paired t tests).

† $p < 0.01$ versus placebo (ANCOVA).

due to asthma; and 2 = sometimes due to asthma). If the second probe indicated that the behavior under consideration was not related to the child's asthma, then the response in the first probe was recoded to indicate no impairment. FSII scores in this article are presented as a percentage of the total possible points. The minimum change in FSII score that can be considered important or clinically meaningful to the patient has yet to be determined.

Because nocturnal asthma symptoms are characteristic of the disease,¹² we wanted to assess separately the effect of the child's asthma on nighttime awakenings and the consequent impact on normal daily activities. The SLP-C, derived from the 3-item Sleep Scale¹³ by modifying the questionnaire to reflect the parent's opinion of the child's sleep patterns, was administered for this purpose. The SLP-C asked the following three questions: (during the past 4 weeks) how much sleep did the child lose due to asthma; how much did feeling tired or lack of sleep interfere with the child's normal daily activities; and how many nights did the child awaken at least once because of asthma? These three items were scored to produce a single SLP-C score ranging from 0 to 100, with 100 representing the best possible score. As with the FSII, the minimum change in SLP-C score that can be considered important or clinically meaningful to the patient has yet to be determined.

The QOL-PAC was used to assess the impact of the child's asthma on the quality of life of the person providing care and support for the child. This 48-item questionnaire, which was developed based on identified factors that affect the quality of life of parents of a child with asthma,⁷ measures six dimensions: Burden, Subjective Norms, Social, Financial, Physician, and Effect of Medication. As changes in the latter three dimensions were driven by protocol specifications (e.g., number and timing of study visits, cost of medication and physician visits [free], and choice and dosage of medication), these dimensions were excluded from our analyses, although the complete questionnaire was administered. For the dimensions analyzed in this study, the QOL-PAC is scored on a scale from 1 to 5, with 1 representing the best possible score. The minimum change in QOL-PAC score that can be considered important or clinically meaningful to the patient has yet to be determined.

Statistical analysis

Descriptive statistics were used to summarize mean scores at each visit by treatment group. Change from baseline to weeks 24 and 52 within each treatment group was evaluated with paired t tests. Differences between treatment groups were evaluated with analysis of covariance (ANCOVA), with baseline scores as the covariate. Additionally, a covariate was included to adjust for the potential confounding effect of the same or different caregiver responding at the three visits. For consistency in measuring quality of life in a particular caregiver, only responses from the same caregiver at all visits were included in the change score analysis of the QOL-PAC. For ANCOVA analyses, pair-wise comparisons were interpreted only when the overall comparison among the three treatment groups was statistically significant. None of the p values were adjusted for multiple comparisons. A p value of less than 0.05 was considered statistically significant.

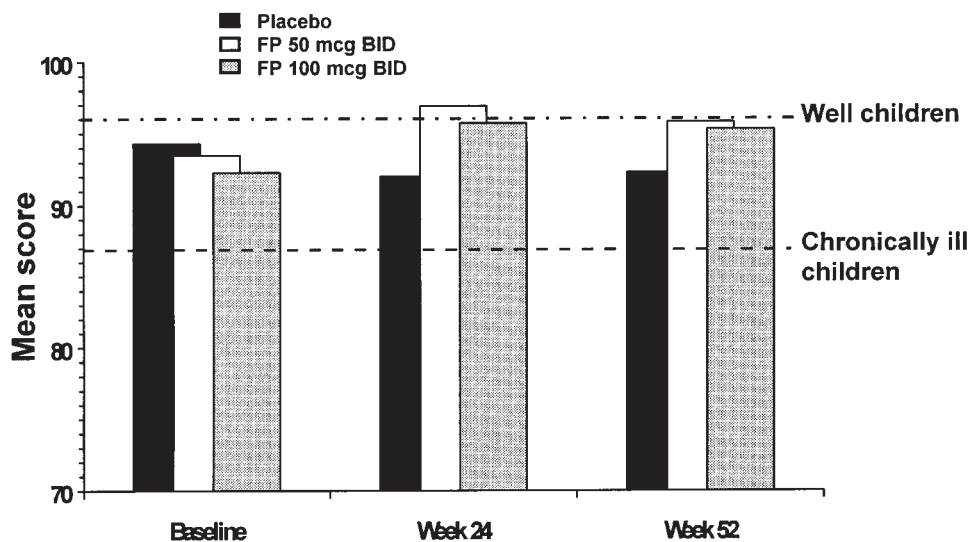


FIG. 1. Mean scores on FSII at baseline and after 24 and 52 weeks of treatment shown with scores from children with and without chronic physical, but not asthma-specific, conditions.

TABLE III. Mean ($\pm$ SD) scores on the SLP-C questionnaire

Visit	Placebo n	Placebo Score	50 μ g FP n	50 μ g FP Score	100 μ g FP n	100 μ g FP Score
Baseline	103	86.5 (16.1)	110	85.5 (16.6)	107	89.2 (16.5)
Week 24	91	78.9 (23.3)*	103	91.4 (13.4)*†	96	90.1 (15.0)*†
Week 52	95	79.2 (21.4)*	104	89.4 (15.1)*†	101	90.6 (15.1)*†

RESULTS

Of the 325 patients enrolled in the study, 263 completed the study. The majority of patients discontinued because of lack of efficacy (50 μ g FP group, 4; 100 μ g FP group, 4; placebo: 20) or protocol violations. A total of 321 respondents completed questionnaires at baseline (104, 110, and 107 in the placebo, 50 μ g FP, and 100 μ g FP groups, respectively). There were no significant differences among treatment groups with respect to baseline characteristics (Table I).

Functional status

At baseline, there were no significant differences between treatment groups in FSII scores (Table II). Despite relatively high scores at baseline, indicating only mild impairment, there were still statistically significant improvements over baseline values in both the 50 μ g FP and 100 μ g FP groups at weeks 24 and 52. In contrast, there was a significant decline in the placebo group by week 52. Pairwise comparisons of treatment groups indicate a statistically significant difference between either FP group and the placebo group at both weeks 24 and 52. There were no significant differences between the two FP groups.

To put the FSII scores in this population into perspective, Fig. 1 shows the scores from our study along with those

TABLE IV. Mean ($\pm$ SD) scores on the QOL-PAC questionnaire

Visit	Placebo n	Placebo Score	50 μ g FP n	50 μ g FP Score	100 μ g FP n	100 μ g FP Score
Burden dimension						
Baseline	104	1.75 (0.4)	110	1.75 (0.5)	107	1.79 (0.6)
Week 24	92	1.77 (0.6)	103	1.54 (0.5)*†	97	1.62 (0.4)*†
Week 52	96	1.82 (0.6)	104	1.59 (0.5)*†	101	1.61 (0.5)*†
Subjective Norms dimension						
Baseline	104	2.38 (0.7)	110	2.32 (0.7)	107	2.43 (0.7)
Week 24	92	2.39 (0.7)	103	2.37 (0.7)	97	2.29 (0.7)
Week 52	96	2.34 (0.7)	104	2.33 (0.7)	101	2.39 (0.6)*
Social dimension						
Baseline	104	1.71 (0.7)	110	1.72 (0.6)	107	1.77 (0.6)
Week 24	92	1.71 (0.5)	103	1.60 (0.5)	97	1.53 (0.5)‡
Week 52	96	1.73 (0.6)	104	1.67 (0.6)	101	1.57 (0.5)*†

* $p < 0.05$ change from baseline (paired t tests).

† $p < 0.05$ versus placebo (ANCOVA).

from another study of 732 children with and without chronic physical, but not asthma-specific, conditions.⁹ After 24 and 52 weeks of treatment with either 50 μ g or 100 μ g FP, FSII scores in this study most closely resembled those of children without a chronic physical condition.

Sleep scale

Treatment groups were similar at baseline with respect to SLP-C scores (Table III). Statistically significant improvements compared with baseline SLP-C scores occurred in both the 50 μ g and 100 μ g FP groups at weeks 24 and 52, whereas in the placebo group scores decreased significantly (i.e., worsened) at both weeks 24 and 52. Pairwise comparisons of treatment groups show a statistically significant difference between either FP group and the placebo group at weeks 24 and 52. Again, there were no significant differences between the two FP groups.

Quality of life of parents of asthmatic children

Mean QOL-PAC scores are shown in Table IV. No differences were observed among groups at baseline. For the Burden dimension, scores improved significantly over baseline values for parents of children in either the 50 μ g or 100 μ g FP groups at both weeks 24 and 52. Mean scores on the Subjective Norms and Social dimensions also improved significantly over baseline values, but only in the 100 μ g FP group. At both weeks 24 and 52, differences between groups were statistically significant for the 50 μ g or 100 μ g FP groups compared with placebo for the Burden dimension and for the 100 μ g FP group for the Social dimension. At week 24 only, the mean score on the Subjective Norms dimension was significantly better in the 100 μ g FP group than in the 50 μ g FP group.

DISCUSSION

The health status of children with asthma in this study was assessed with two valid and reliable instruments, the FSII, which measures functional status, and the SLP-C, which measures the occurrence of sleep disturbances and the subsequent effect on normal daily activities. On the basis of previous studies of the effectiveness of fluticasone propionate in adults,^{14,15} we hypothesized that asthma would be better controlled in children who received FP than in those who received placebo (plus inhaled albuterol as needed), with resultant improvements in daily functioning and behavioral activities such as eating, sleeping, and energy. The results of this study confirmed this. Functional status scores improved in both the group receiving 50 μ g FP twice a day and the group receiving 100 μ g FP twice a day over the 52 weeks of the study, whereas they declined in the placebo group over the same time period. Sleep disturbances, as measured by the SLP-C, also improved significantly in both FP groups, whereas they worsened in the placebo group.

It should be noted that for both the FSII and the SLP-C questionnaires, minimum measures for what constitutes a clinically meaningful improvement have not yet been established, but research is ongoing in this area. To put the scores into some clinical perspective, however, we compared the results from this study in children with primarily mild asthma, whose mean functional status score at baseline ranged from 93 to 94 (out of 100), with those from a large study of children with and without chronic physical, but not asthma-specific, conditions ($n = 732$).¹⁰ The healthy children had a mean FSII score of 96 (SD, 8.2), and the ill children had a mean score of 87 (SD, 15.7). Despite the fact that the sample of children in the present study resembled healthy children more than they did chronically ill children in terms of FSII scores, those who received fluticasone propionate still experienced statistically significant improvements in functional status compared with their baseline values (and with those who received placebo). Although no comparison has yet been done comparing FSII scores in children with

severe asthma with scores of children with mild asthma, it seems likely that the scores would be lower in those with severe asthma, and consequently, there would be even greater room for improvement in functional status after appropriate treatment.

In addition to the positive impact on the functional status of the children who received FP in this study, we also found that aspects of their parents' quality of life improved as well. Although burden of illness³ and quality of life¹⁶ research has been conducted previously in parents of children with asthma, to our knowledge this is the first asthma drug intervention study to assess quality of life in parents/caregivers of children with asthma. Previous research has shown these parents may feel burdened and frustrated, and often they may have to give up social or other activities because of the care needed by the child.⁷ In this study we were able to document positive changes in those domains that reflect these parental concerns over their child's asthma. There were statistically significant improvements in the dimensions of Burden in both the 50 μ g and 100 μ g FP groups and Social and Subjective Norms in the 100 μ g group after a year of FP treatment in their children.

Previous studies have demonstrated improvements in health-related quality of life in adult patients after treatment with FP.^{17,18} The present findings in children complement those earlier results by providing evidence that some aspects of quality of life, a difficult outcome to assess in children, improved during treatment with FP over a year-long period. It is still controversial whether a caregiver proxy can be used to assess the quality of life of a young patient. In a recent publication, Guyatt et al.¹⁹ concluded that in children with asthma under age 11 years, clinicians can gain complementary information from questioning both the children and the parents, whereas for children over 11 years, parents can provide little information beyond that obtained through questioning the child. That study, however, did not study children under the age of 7, whereas in this study the study sample included patients as young as 4 years. To date, however, no patient-completed asthma-specific quality of life questionnaire has been validated in children under the age of 7. Therefore we used a caregiver-completed functional status questionnaire that has been shown to be a valid measure for assessing health status of children as young as 4 years with chronic illnesses, and we modified the questionnaire to assess whether an impairment was due to the child's asthma rather than to some other condition.

In summary, the results of this study show that 50 μ g or 100 μ g FP given twice daily over a period of 24 or 52 weeks improved the functional status and decreased the sleep disturbances of children with mild-to-moderate asthma and decreased the burden of illness experienced by the parents of these children. Treatment with FP appeared to improve the well-being of these children with asthma, as well as improve the quality of life of the caregivers of these children.

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