

Clinical aspects of allergic disease

The effectiveness of once-daily dosing of inhaled flunisolide in maintaining asthma control

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Objective: The purpose of this study was to evaluate the feasibility of switching to once-daily (qd) administration of flunisolide in patients with asthma that was controlled by twice-daily (bid) dosing of this inhaled steroid.

Methods: Three hundred sixty-six adults and children with bronchial asthma that was controlled with inhaled steroids were recruited for this prospective, double-blind, parallel-group study. After a 4-week, stable baseline period of flunisolide administration, 2 inhalations (500 µg) twice daily, each patient was randomized into one of four 12-week flunisolide treatment groups: group 1, 2 inhalations (500 µg) bid; group 2, 4 inhalations (1000 µg) qd in the morning; group 3, 4 inhalations (1000 µg) qd in the evening; or group 4, 2 inhalations (500 µg) qd in the morning. Outcome measures included morning and evening asthma symptoms (scale of 0 to 3), daytime and nighttime albuterol use, morning and evening peak expiratory flow rate (PEFR), FEV₁, and methacholine PC₂₀. In addition, a subset of patients in each group had 24-hour urinary cortisol levels measured before and after randomization.

Results: Outcome measures in the four groups were not significantly different at baseline before randomization. The three groups that received maintenance therapy with flunisolide, 1000 µg daily, did not show significant changes from baseline values and remained comparable in all outcome areas. Asthma control in the group randomized to flunisolide 500 µg qd, however, deteriorated significantly: morning symptoms increased by 0.21 units (48%), evening symptoms increased by 0.15 units (31%),

daytime albuterol use increased by 0.42 inhalations per day (37%), nighttime albuterol use increased by 0.48 inhalations per night (91%), morning PEFR decreased by 17.1 L/min (4%), and evening PEFR decreased by 12.6 L/min (3%). There were no significant changes in PC₂₀ or 24-hour urinary cortisol levels in any group.

Conclusions: For patients with asthma that was stabilized by 2 inhalations of flunisolide (500 µg) bid, switching to 4 inhalations (1000 µg) qd in either the morning or evening is effective in maintaining asthma control. Reducing the dose to 2 inhalations (500 µg) qd in the morning, however, leads to a deterioration in asthma control. (*J Allergy Clin Immunol* 1997;99:278-85.)

Key words: Asthma, inhaled steroids, outcome measures, daily dosing

Twice-daily (bid) use of inhaled steroids is now recommended for the treatment of moderate asthma in children and adults.^{1, 2} Although oral steroids are frequently given as a single daily dose for treatment of asthma, the effectiveness of once-daily (qd) dosing of the inhaled form of these medications has received relatively little attention. The use of qd inhaled steroids would be more convenient and would possibly lead to better compliance. Although previous studies evaluating the effect of qd dosing on compliance have involved oral medications in nonasthmatic individuals,^{3, 4} it has been demonstrated that simplifying the frequency of inhaled steroid use from four to two times daily considerably improved compliance.⁵

Recently, three studies have focused on the qd use of inhaled steroids in asthma. In a study of 340 patients with asthma of mild to moderate severity, Jones et al.⁶ found that 400 µg of inhaled budesonide taken qd in either the morning or evening was as effective as 200 µg bid. In a second study, Gagnon et al.⁷ demonstrated that 1000 µg of inhaled beclomethasone used qd in either the late afternoon or evening was as effective as 500 µg bid. In a third study, Pincus et al.⁸ showed that 800 µg of triamcinolone taken at 3:00 PM was equal to 200 µg taken four times daily.

In this investigation, we tested the feasibility of qd dosing of flunisolide in maintaining control of asthma in

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Abbreviations used

bid:	Twice daily
qd:	Once daily
PEFR:	Peak expiratory flow rate

patients with their disease already stabilized and well-controlled by use of inhaled steroids. Our primary intent was to compare qd use with bid use of this inhaled steroid. Additionally, we sought to compare the efficacy of morning versus evening use in patients taking the drug qd. Twenty-four-hour urinary cortisol levels were used as a measure of adrenal function. Four dosing schedules were evaluated: 2 puffs (500 μ g) bid, 4 puffs (1000 μ g) qd in the morning, 4 puffs (1000 μ g) qd in the evening, and 2 puffs (500 μ g) qd in the morning.

METHODS

Patients

This study evaluated qd versus bid dosing of inhaled flunisolide in patients with asthma that was already well-controlled with inhaled steroids. Three hundred sixty-six patients from 10 centers were recruited. Inclusion and exclusion criteria were as follows: (1) a clinical diagnosis of moderate bronchial asthma, which was well-controlled according to National Heart, Lung, and Blood Institute guidelines⁹; (2) age range from 6 to 70 years; (3) regular use of inhaled steroids for asthma control; (4) clinical stability of asthma during the 2 months before randomization into the study; (5) no use of systemic steroids during the 2 months preceding the study; (6) FEV₁ at initial screening equal to or greater than 80% of predicted value; (7) current nonsmoking status for at least 1 year (less than 10 pack-years of total cigarette consumption); (8) no significant cardiopulmonary or other disease that might interfere with the likelihood of completing the study.

Study design

The primary aim of this double-blind, randomized, parallel-group study was to compare the effectiveness and side effects of qd dosing of inhaled flunisolide with conventional, bid dosing of this drug. A secondary aim was to compare morning versus evening qd dosing for efficacy and effect on cortisol production. The study lasted 16 weeks with a 4-week stabilization period and a 12-week treatment period.

The study was approved by each center's institutional review board. After informed consent was obtained and a clinical assessment was made at the initial visit, all study patients were treated for a 4-week, open-label period with flunisolide, 2 puffs (500 μ g) bid, administered through a commercial spacer device (Aerochamber, Monaghan Medical Corp.). In addition, patients were instructed to use an albuterol inhaler, 2 puffs (180 μ g) as needed (prn) for treatment of asthma symptoms. Other inhaled steroids and antiinflammatory drugs, such as cromolyn sodium or nedocromil, and oral β -agonists were stopped at this time. Oral theophylline, if taken at study entry, was continued with its dose unchanged during the remainder of the study.

If clinical stability was maintained during the initial 4-week, open-label baseline period with administration of 500 μ g of flunisolide bid, each patient was then randomized at the second visit to one of four flunisolide treatment groups: group 1, 2 puffs (500 μ g) taken twice daily in the morning on arising and in the

evening before retiring (total daily dose = 1000 μ g); group 2, 4 puffs (1000 μ g) taken daily in the morning on arising; group 3, 4 puffs (1000 μ g) taken daily in the evening before retiring; and group 4, 2 puffs (500 μ g) taken in the morning on arising.

To assure proper blinding, a double-dummy method was used. Patients were instructed to take 2 inhalations from each of two canisters in the morning and 2 inhalations from each of two other canisters in the evening. The test drug canisters contained either active drug or placebo, depending on the treatment group. A spacer device (Aerochamber) was used with the test drugs.

The treatment period lasted 12 weeks with follow-up visits at 4, 8, and 12 weeks. One course of oral corticosteroids, lasting up to 10 days, was allowed during the treatment period. If the study patient required two courses of oral steroids or a single course with a duration longer than 10 days, participation in the study was discontinued at that point.

Outcome variables

Asthma symptoms. Asthma symptoms were rated by the patient in the morning on arising (morning symptoms) and in the evening before retiring (evening symptoms). For this scoring, a 4-point scale was used; zero indicated no symptoms; 1, mild symptoms; 2, moderate symptoms; and 3, severe symptoms. This information was recorded twice a day in a diary format.

Peak expiratory flow rate (PEFR). PEFR was also measured twice daily, in the morning on arising (morning PEFR) and in the evening before retiring (evening PEFR). A MiniWright peak flow meter (Clement Clarke International, Ltd.) was used, with the best of three efforts recorded in the patient's diary. Patients were instructed to measure PEFR before using albuterol as needed.

As-needed albuterol requirement. The number of nighttime albuterol inhalations for the preceding night was recorded in diary format in the morning on arising, and the number of daytime inhalations was recorded in the evening before retiring.

FEV₁. Spirometry was performed at baseline and at each monthly follow-up visit. Inhaled medications were withheld for at least 4 hours before testing. FEV₁ was expressed as a percent of predicted value.

Methacholine PC₂₀. Methacholine bronchoprovocation testing was performed at the end of the baseline period (after administration of flunisolide, 500 μ g bid, for 4 weeks) and at the end of the treatment period. For this test, a dosimeter was used to deliver 5 breaths of doubling concentrations of methacholine, beginning at 0.06 mg/ml, at 5-minute intervals until the FEV₁ decreased by 20% or more from baseline or until a concentration of 25 mg/ml was reached. Results were expressed as the provocative concentration required to decrease the FEV₁ by 20% (PC₂₀). If the 25 mg/ml concentration of methacholine was reached without a 20% decrease in FEV₁, a PC₂₀ value of 25 mg/ml was arbitrarily assigned.

In addition to the above outcome variables, urinary cortisol excretion was measured in a randomly chosen subset of the patients. For this, 24-hour urine collections were obtained at the baseline visit (after 4 weeks of flunisolide administration, 500 μ g bid) and at the end of the treatment period. Results were expressed as total amount of cortisol (in micrograms) per 24 hours.

Data analysis

Outcome variables measured daily in diaries (morning and evening symptoms, daytime and nighttime albuterol use, morn-

TABLE I. Patient characteristics

	Group 1 (500 µg bid)	Group 2 (1000 µg AM)	Group 3 (1000 µg PM)	Group 4 (500 µg AM)
Male/female	50/51	33/59	35/56	38/54
Age (yr)	29.8 ± 16.4	30.3 ± 14.4	29.8 ± 13.1	31.1 ± 14.8
FEV ₁ (% pred)	93 ± 13	94 ± 14	93 ± 12	91 ± 12
PC ₂₀ (mg/ml)	4.5 ± 7.6	4.5 ± 7.1	4.3 ± 7.3	3.0 ± 6.2

TABLE II. Outcome variables: Baseline values and changes from baseline

	Group 1 (500 µg bid)	Group 2 (1000 µg AM)	Group 3 (1000 µg PM)	Group 4 (500 µg qd)	Intergroup comparison <i>p</i> values		
Daytime symptoms (0-3)							
Baseline	0.46 ± 0.53	0.42 ± 0.51	0.52 ± 0.54	0.44 ± 0.52	G1-G2: 0.54	G1-G3: 0.68	G1-G4: 0.0002
Change from baseline	0.00 ± 0.44	0.06 ± 0.40	-0.04 ± 0.44	0.21 ± 0.46	G2-G3: 0.30	G2-G4: 0.002	G3-G4: 0.0001
Nighttime symptoms (0-3)							
Baseline	0.51 ± 0.57	0.42 ± 0.45	0.50 ± 0.55	0.49 ± 0.55	G1-G2: 0.46	G1-G3: 0.91	G1-G4: 0.003
Change from baseline	0.00 ± 0.49	0.06 ± 0.42	-0.03 ± 0.51	0.15 ± 0.42	G2-G3: 0.39	G2-G4: 0.02	G3-G4: 0.002
Day albuterol (INH)							
Baseline	0.93 ± 1.17	1.08 ± 1.49	1.10 ± 1.38	1.15 ± 1.70	G1-G2: 0.69	G1-G3: 0.62	G1-G4: 0.03
Change from baseline	0.13 ± 1.15	0.25 ± 1.21	0.00 ± 0.93	0.42 ± 1.54	G2-G3: 0.37	G2-G4: 0.07	G3-G4: 0.008
Night albuterol (INH)							
Baseline	0.45 ± 0.70	0.44 ± 0.60	0.54 ± 0.72	0.53 ± 0.92	G1-G2: 0.51	G1-G3: 0.96	G1-G4: 0.001
Change from baseline	0.05 ± 0.65	0.21 ± 0.85	0.02 ± 0.52	0.48 ± 1.20	G2-G3: 0.47	G2-G4: 0.007	G3-G4: 0.0007
Morning PEFR (L/min)							
Baseline	427 ± 106	430 ± 101	430 ± 103	426 ± 115	G1-G2: 0.06	G1-G3: 0.53	G1-G4: 0.0001
Change from baseline	8.4 ± 36.0	-5.5 ± 34.5	4.0 ± 24.8	-17.1 ± 40.9	G2-G3: 0.22	G2-G4: 0.009	G3-G4: 0.0001
Evening PEFR (L/min)							
Baseline	429 ± 109	435 ± 101	435 ± 102	431 ± 116	G1-G2: 0.23	G1-G3: 0.08	G1-G4: 0.0007
Change from baseline	7.9 ± 35.8	-2.2 ± 33.0	-1.5 ± 44.0	-12.6 ± 32.8	G2-G3: 0.55	G2-G4: 0.03	G3-G4: 0.09
FEV ₁ (% pred)							
Baseline	93.3 ± 12.9	94.5 ± 14.3	93.1 ± 11.6	91.5 ± 12.1	G1-G2: 0.63	G1-G3: 0.74	G1-G4: 0.03
Change from baseline	-2.1 ± 10.1	-3.5 ± 14.8	-0.7 ± 10.7	-4.5 ± 10.3	G2-G3: 0.41	G2-G4: 0.08	G3-G4: 0.01
PC ₂₀ (mg/ml)							
Baseline	4.47 ± 7.58	4.48 ± 7.12	4.29 ± 7.26	3.01 ± 6.15	The overall F statistic was not significant; pairwise comparisons were not performed.		
Change from baseline	0.23 ± 7.07	-0.92 ± 4.52	0.51 ± 4.61	-0.89 ± 4.36			

INH, Inhalations.

ing and evening PEFR) were averaged during the baseline period and between each monthly visit during the treatment period. Means and standard deviations for the baseline outcome and the change from baseline to end point are reported. Outcome variables were compared among the four treatment groups by using a one-way analysis of covariance model with intention to treat. The change from baseline to end point was used as the dependent variable, and the baseline was used as the covariate. All reported *p* values were two-tailed with no adjustment for the multiple pairwise comparisons. Pairwise comparison *p* values were not reported if the overall test result for equality of treatment groups was not statistically significant. A *p* value of 0.05 or less was considered to be statistically significant. Statistical analyses were performed by using the Statistical Analysis System (SAS) version 6.09 (SAS Institute).

Sample size determination

Of the 366 patients enrolled, three did not provide efficacy data from the 12-week double-blind portion of the study, leaving 363 patients for efficacy analysis. This number, which

was across four treatment groups, was adequately powered to show differences between groups 1 to 3 (4 puffs per day) and group 4 (half dose, 2 puffs every morning) and to show therapeutic equivalence between groups 1 to 3 (4 puffs per day). A sample size of 75 patients per treatment group was originally planned for this study to provide adequate power of 80% to detect a standardized treatment group difference (treatment group difference/standard deviation) between 0.4 and 0.5. Approximately 90 patients per treatment group were actually enrolled in this study, providing 80% power to detect standardized treatment group differences of 0.42.

RESULTS

Patients

Of the 366 patients recruited, 56 were dropped from the study, leaving 310 (85%) who completed the study. Because of the unanticipated length of patient accrual into the study, 35 of the 56 dropout patients had test medication that expired, and further participation in the study was terminated. Of the 21 remaining discontinua-

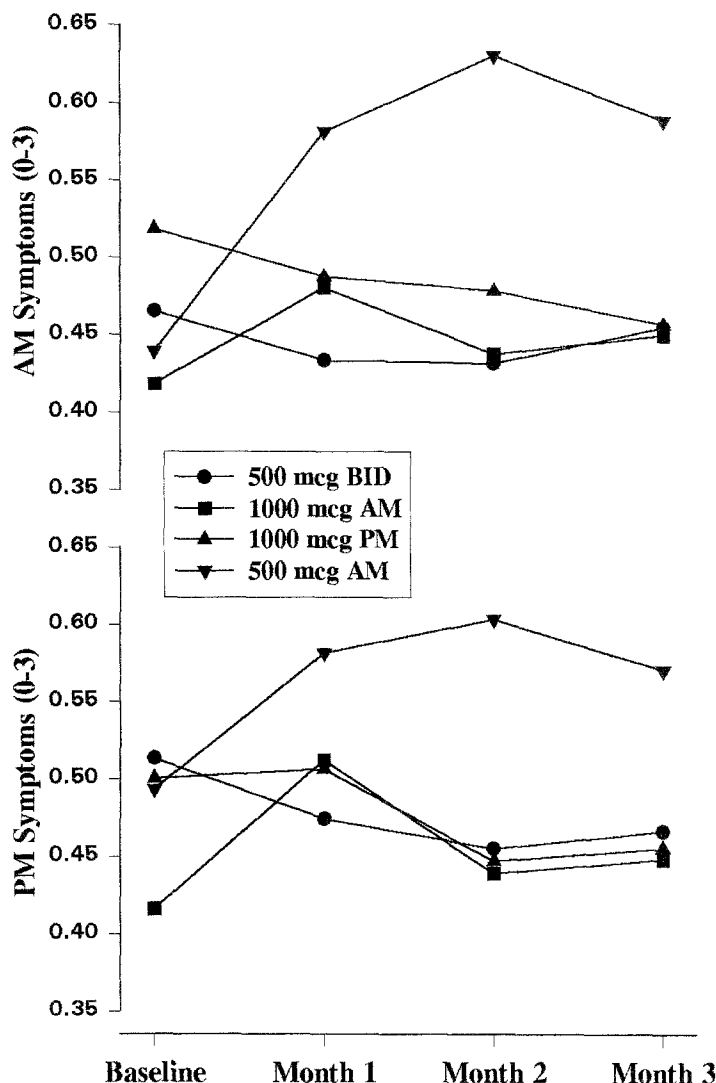


FIG. 1. Mean morning (top graph) and evening (bottom graph) symptoms for the study patients for the baseline period and the 3 study months. Asthma symptoms were rated on a scale of 0 to 3: 0 indicated no symptoms; 1, mild symptoms; 2, moderate symptoms; and 3, severe symptoms. Probability (*p*) values for end-point data are given in Table II.

tions, three were due to adverse events (one because of paroxysmal atrial tachycardia, one because of an asthma exacerbation, and one because of intermittent headache), seven were due to insufficient therapeutic effect, and 11 were due to noncompliance or withdrawal of informed consent. The four groups did not significantly differ in dropout rate or cause. Because the percent of dropouts for reasons other than study drug expiration was only 6%, an intent-to-treat analysis of outcome variables was performed.

Table I gives patient characteristics at the initial visit. As Table I indicates, the patients studied had a normal to near-normal FEV₁ before bronchodilator administration and mild hyperresponsiveness to methacholine. During the baseline period, the patients had minimal

symptoms, averaging from mild to absent. Their mean albuterol use was approximately 1 inhalation during the daytime period and about one-half inhalation over the nighttime period. The mean daily dose of inhaled steroids on study entry (849 μ g in group 1, 820 μ g in group 2, 892 μ g in group 3, and 850 mg in group 4) was not significantly different among groups. Theophylline was used by 9% of patients in group 1, 12% of patients in group 2, 10% of patients in group 3, and 7% of patients in group 4 (*p* = NS).

The percent of patients requiring one or more courses of oral corticosteroids during the 12-week treatment period was not significantly different in the four groups: group 1, 14.4%; group 2, 14.4%; group 3, 17.6%; and group 4, 19.6% (*p* = 0.76).

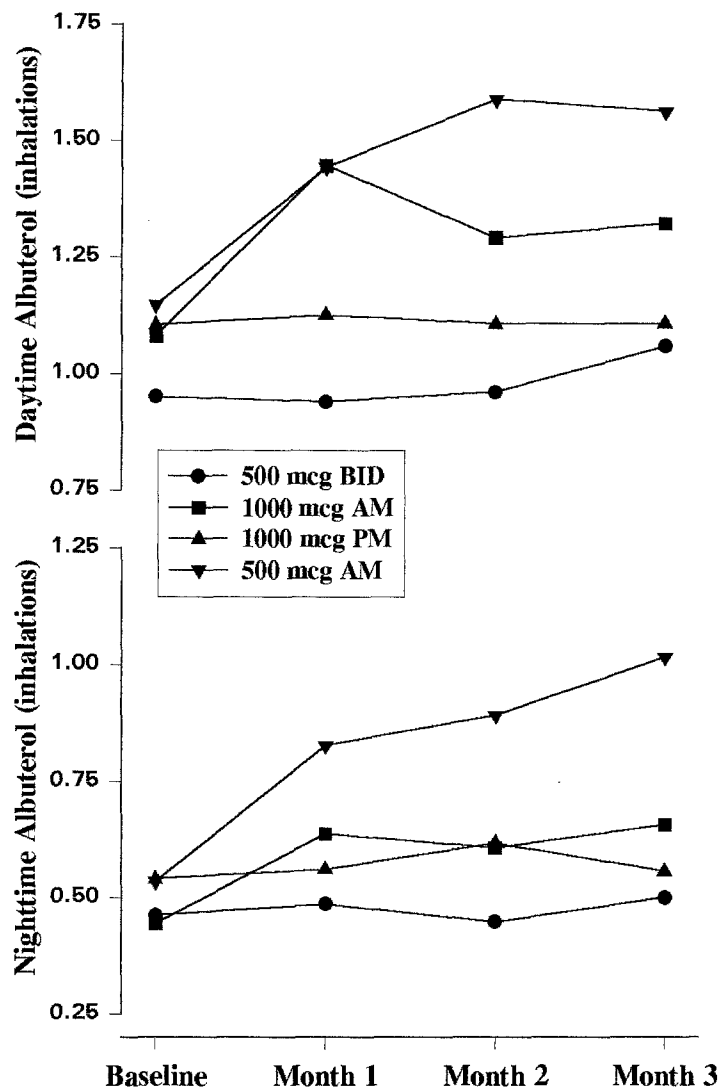


FIG. 2. Mean daytime (top graph) and nighttime (bottom graph) albuterol requirements. Albuterol use is indicated in inhalations per day for the baseline period and the 3 study months. Probability (*p*) values for end-point data are given in Table II.

Outcome variables

Table II shows baseline values and changes from baseline to the end treatment for the outcome measures. Baseline values for morning and evening symptoms, daytime and nighttime albuterol use, and morning and evening PEFR represent the means for the last 3 weeks in the open-label period during administration of flunisolide, 500 μ g bid. Baseline values for FEV₁ and PC₂₀ were measured at the end of this period. The end-of-treatment value is the mean for the last month of the treatment period.

Baseline values of all four groups were similar with respect to morning and nighttime symptoms and albuterol use, morning and evening PEFR, and FEV₁.

With respect to changes in outcome variables from baseline to the end of the treatment period, the three groups receiving 1000 μ g of inhaled flunisolide per day

(group 1, 500 μ g bid; group 2, 1000 μ g qd in the morning; and group 3, 1000 μ g qd in the evening) did not show significant changes from baseline values, and treatments were comparable in effectiveness. However, daytime and nighttime symptoms, daytime and nighttime albuterol use, morning and evening PEFR, and FEV₁ in group 4 (500 μ g qd in the morning) deteriorated significantly during the treatment period, and with few exceptions, were significantly worse at the end of the treatment period than those of the other three groups. Morning and evening symptoms increased by 0.21 units (48%) and 0.15 units (31%), respectively; daytime albuterol use increased by 0.42 inhalations/day (37%); and nighttime use increased by 0.48 inhalations/night (91%) over baseline. In addition, morning PEFR decreased by 17.1 L/min (4%), evening PEFR decreased by 12.6 L/min (3%), and FEV₁ decreased by 4.4% in this group.

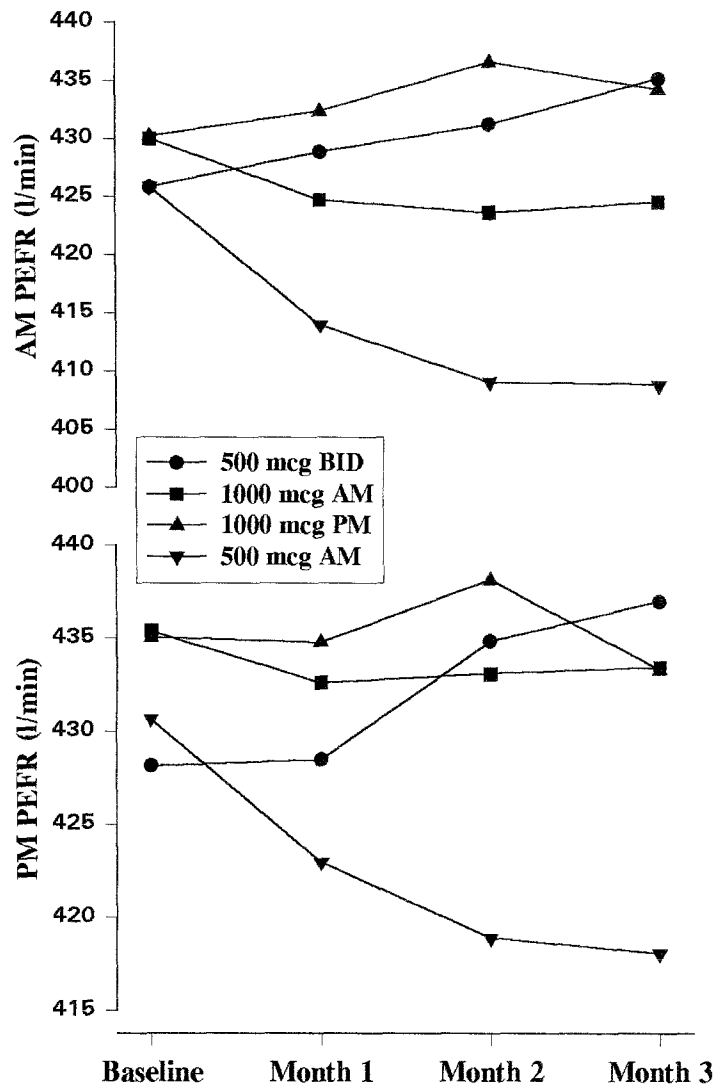


FIG. 3. Mean morning (top graph) and evening (bottom graph) PEFR, in liters per minute, for the baseline period and the 3 study months. Probability (*p*) values for end-point data are given in Table II.

Methacholine PC₂₀ did not change significantly from baseline for any group.

Comparative changes in outcome variables over the treatment period are given in Figs. 1 to 3. Mean morning and evening symptoms for the baseline period and the 3 treatment months are shown in Fig. 1. Groups 1 to 3 did not show significant changes from their respective baseline values and did not differ significantly from each other during the study. However, both morning and evening symptoms in group 4 increased significantly during the first month of treatment and remained elevated for the remainder of the study; these were significantly higher than those of groups 1, 2, and 3 in each of the treatment months.

Daytime and nighttime albuterol use are shown in Fig. 2. Daytime albuterol use in groups 1 and 3 did not change significantly during this period. However, daytime albuterol use in group 2 increased from 1.08 ± 1.49

inhalations per day at baseline to 1.45 ± 1.77 puffs during the first treatment period; this mean daily use during the first treatment month was significantly greater than that of groups 1 and 3 (both, $p < 0.05$). By months 2 and 3, this use decreased somewhat and was not significantly different than that of groups 1 and 3 during these periods. In group 4, daytime albuterol use also increased significantly during the first treatment month, from 1.15 ± 1.70 to 1.44 ± 1.93 inhalations per day. This consumption was greater than that of groups 1 and 3 (both, $p < 0.05$) but not significantly different from that of group 2. Daytime albuterol use in group 4 during months 2 and 3 was significantly greater than that of groups 1, 2, and 3.

Nighttime albuterol use remained relatively constant for groups 1, 2, and 3 from baseline through the 3 treatment months. However, nighttime albuterol use in group 4 increased throughout the study period, from

TABLE III. Baseline and posttreatment urinary cortisol levels

	Group 1 (500 µg bid)	Group 2 (1000 µg AM)	Group 3 (1000 µg PM)	Group 4 (500 µg AM)
Baseline cortisol (µg/24 hr)	18.1 ± 14.6	14.2 ± 10.7	17.9 ± 22.0	19.3 ± 17.2
Baseline-treatment difference (µg/24 hr)	1.7 ± 19.2	0.7 ± 12.3	-2.3 ± 17.9	-2.2 ± 18.2

There were no significant between-group differences in baseline urinary cortisol levels ($p = 0.16$) or changes in cortisol after treatment ($p = 0.45$).

0.53 ± 0.92 inhalations per night during the baseline period to 0.83 ± 1.10, 0.89 ± 1.24, and 1.02 ± 1.46 inhalations per day for the 3 treatment months, respectively. By month 1, nighttime albuterol consumption in group 4 was significantly greater than that of groups 1 and 2 ($p < 0.01$ and 0.05, respectively); by months 2 and 3, it was significantly greater than that of groups 1, 2, and 3.

Morning and evening PEFs in groups 1, 2, and 3 did not significantly change from baseline and were not significantly different from each other during the treatment period. In group 4 both morning and evening PEFs gradually decreased throughout the study period, and by the first month, were significantly lower than those of groups 1, 2, and 3.

Although the PC₂₀ of group 4 was lower than that of the other three groups, this difference was not significant. Changes in PC₂₀ from the end of baseline to the end of the treatment period were not significantly different in the four groups.

Twenty-four-hour urinary cortisol excretion was measured in a subset of 219 patients at the end of the baseline period (when patients were receiving flunisolide, 500 µg bid) and at the end of the 12-week treatment period. Oral steroid use during the double-blind phase was not significantly different in the subsets of the four groups that had cortisol determinations. Results are given in Table III. No significant intergroup differences were present at baseline, and no significant change from baseline was noted for any treatment group.

DISCUSSION

The results from this study indicate that, for patients with stabilized moderate asthma who are relatively free of symptoms while receiving 2 inhalations of flunisolide bid, switching to an equivalent dose (4 inhalations, 1000 µg qd) in either the morning or evening is just as effective in maintaining asthma control. Thus asthma symptoms, peak flow rates, albuterol use, FEV₁, and methacholine bronchial hyperresponsiveness did not significantly change with qd use. Additionally, 24-hour cortisol excretion was not significantly different for any of the groups.

One potential concern is that the 1000 µg total daily dose of inhaled flunisolide might have been so high as to mask subtle differences between bid and qd dosing. Thus asthma control might have been maintained with simpler dosing but only by using the drug in amounts higher than

needed. However, the significant decrease in asthma control, beginning in the first month of treatment with 500 µg qd, suggests that this was not the case.

Our results are comparable to those of the three previously cited studies demonstrating the effectiveness of qd inhaled steroids. However, the difference in patient populations between these studies and ours deserves comment. The overall asthma control in our patients was probably significantly better at study entry than that in the other studies. This was undoubtedly due to our strict inclusion criteria, which required an FEV₁ of 80% of the predicted value or greater. In contrast, the other investigators allowed lower cutoffs for airway obstruction, in the 50% to 60% range. These different inclusion criteria are reflected in the 24-hour as-needed albuterol consumption at baseline, which was between 3 and 4 inhalations per day in the three previous studies, but only about 1 and one-half inhalations per day in ours. Our reason for selecting patients with stable asthma in good control is that this group would most likely be considered for qd dosing. Realistically, the effectiveness of qd inhaled steroids in maintaining rather than establishing asthma control is more relevant for the clinician.

A secondary aim of this study was to compare morning and evening dosing of inhaled flunisolide. There is some evidence to suggest that giving oral steroids at 3:00 PM may produce optimal therapeutic effects.⁹ However, we chose to give the medication in the evening before patients retired because this would be much more convenient for the patients. Overall, morning and evening qd dosing were comparable in their ability to maintain asthma control. Thus these two groups were not significantly different at study termination in any of the outcome variables. There was a trend, however, for morning PEFs to be somewhat lower and daytime albuterol use to be somewhat higher with morning than with evening or bid dosing. These effects were minor and not statistically significant even with a large study such as ours. Of considerable importance, the two regimens did not differ from each other or from the standard bid dosing in their effect on urinary cortisol excretion. Therefore it appears that once the decision has been made to switch from bid to qd dosing, patient factors such as convenience should dictate the time of day at which the drug is to be taken.

In summary, for patients with asthma that is well-controlled by flunisolide, 2 inhalations bid, switching to

4 inhalations qd in either the morning or evening is just as effective in maintaining asthma stability. There does not appear to be a significant difference in therapeutic efficacy or adrenal function between morning and evening dosing.

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The following abstract was presented at the 1997 AAAAI/AAI/CIS Joint Meeting in San Francisco; however, it was omitted from the January 1997 supplement of this Journal.

CETIRIZIN EFFECTS ON CHILDREN WITH ATOPIC DERMATITIS. CORRELATION AMONG THE EOSINOPHIL CATIONIC PROTEIN (ECP), IL2R SOLUBLE (CD25), CD23 (B CELLS) AND CLINICAL SCORE.

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It has been published that the atopic dermatitis severity is correlated with interleukin 2 receptor soluble plasma levels. Some authors have probed that patients with high levels of ECP also have high levels of CD23. The purpose of the present study is to evaluate the Cetirizin effectivity in children with atopic dermatitis' treatment. We have tested 30 children between 5-15 years old ($x=7.2$) with atopic dermatitis (under Hanifin and Rajka criteria). We evaluated their clinical behaviour with score standard and we measured the ECP, IL2R and CD23 plasma levels before and after the Cetirizin treatment during 6 weeks. Group A: Cetirizin; group B: Placebo. The pathology severity was determined by the SCORAD INDEX and we measured ECP (RIA, PHARMACIA); IL2R soluble (EIA, IMMUNOTECH) and CD23 soluble (IMMUNOTECH). We got the following results:

	ECP (mgr/l)		IL2R (UI/ml)		CD23 (UI/ml)	
	Before	After	Before	After	Before	After
Group A (n=15)	42.77 ±4.99	9.66** ±2.33	962.67 ±117.93	395.33** ±72.48	110.13 ±14.07	92.13 ±12.02
Group B (n=15)	28.88 ±4.10	42.50 ±4.51	854.33 ±86.00	803.02 ±52.00	98.80 ±15.07	99.80 ±20.42

**p < 0.005 (Student paired T-Test)

We could see clinical improvements in patients treated with Cetirizin compared with placebo groups and a significant decrease of ECP and IL2R soluble levels (group A vs group B), while the CD23 remained unchanged. We conclude: 1. The Cetirizin is effective in the atopic dermatitis treatment. 2. The determination of ECP and IL2R soluble in plasma is important to evaluate the severity of the diseases.