Detection of Growth Suppression in Children During Treatment With Intranasal Beclomethasone Dipropionate

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ABSTRACT. Objective. Intranasal beclomethasone dipropionate (BDP) has generally been considered to have no systemic activity at recommended doses, but the potential for long-term effects on growth has not previously been evaluated. This study was undertaken to assess the effects of 1 year of treatment with intranasal BDP on growth in children.

Study Design. In this double-blind, randomized, parallel-group study, 100 prepubertal children 6 to 9 years old with perennial allergic rhinitis were treated with aqueous BDP 168 µg twice daily (n = 51) or placebo (n = 49) for 1 year. Subjects’ baseline heights were required to be between the 5th and 95th percentile, and skeletal age as determined by left wrist radiograph was required to be within 2 years of chronological age. Washout periods for medications known to affect growth, including other forms of corticosteroids, were established, and these medications were prohibited during the study. However, short courses of oral prednisolone lasting no more than 7 days, and short courses of dermatologic corticosteroids lasting no more than 10 days, were allowed. Height was measured with a stadiometer after 1, 2, 4, 6, 8, 10, and 12 months of treatment. The hypothalamic-pituitary-adrenocortical axis was assessed by measurements of 8 AM basal cortisol concentrations and response to .25 mg cosyntropin stimulation.

The primary safety parameter was the rate of change in standing height. Statistical analyses were based on all randomized subjects who received at least 1 dose of medication (intent-to-treat principle). The rate of change in standing height was analyzed for all subjects who entered the study and for those completing the full 12 months of treatment (n = 80). The rate of change in standing height over the 1-year study was calculated as the slope of a linear regression line fitted to each subject’s height measurements over time. Because there was a statistically significant between-group difference in standing height at baseline, an analysis of covariance was performed for all analyses of standing height data.

Results. Of the 100 subjects enrolled, 90 completed the study. The 2 treatment groups were generally comparable at baseline; however, at baseline, mean age and mean height were significantly greater in the BDP treatment group that the in placebo treatment group. In both analyses, overall growth rate was significantly slower in BDP-treated subjects than placebo-treated subjects. The mean change in standing height after 1 year was 5.0 cm in the BDP-treated subjects compared with 5.9 cm in the placebo-treated subjects. The difference in growth rates was evident as early as the 1-month treatment visit, suggesting that the effect on growth occurred initially.

The growth-suppressive effect of BDP remained consistent across all age and gender subgroups, and among subjects with and without a previous history of corticosteroid use. Use of additional exogenous corticosteroids during the study was similar in both groups and did not affect the results.

Because there was a baseline imbalance in height, a supplemental analysis of the differences in prestudy growth rates was performed. This analysis found no baseline imbalance in prestudy growth rates.

To determine whether the difference in growth rates during the study could be attributed to preexisting growth rates, a z score analysis was performed. The heights of both groups were normalized at baseline and at the end of the study using the US National Center for Health Statistics data for mean and standard deviations of height. This analysis confirmed that the difference in growth rates between the 2 groups was primarily attributable to the treatment rather than to any preexisting difference in growth. Additional analyses confirmed that the results were not influenced by outlier values.

No significant between-group difference were found in the hypothalamic-pituitary-adrenocortical axis assessments. No unusual adverse events were observed.

No evidence of other systemic effects of BDP was found, including analysis for fluid and electrolyte imbalances; alterations in protein, lipid, or carbohydrate metabolism; alterations in formed elements in blood; and alterations in differential white blood cell counts, including eosinophils.

Conclusions. Additional study is warranted to define the clinical relevance of these findings. This study suggests, however, that intranasal BDP may slow growth rate in children without suppressing basal 6 AM cortisol concentrations or the response to cosyntropin stimulation, which are commonly used clinically to test for adrenal suppression. The effect on final height is unknown.

Alterative explanations for the finding of drug-induced growth suppression, including the possibility that the results were affected by either differences in height and age at baseline between the 2 groups or by outlier values, were discounted upon additional analysis. The results of this study were considered by the Food and Drug Administration in the development of recently proposed new class labeling for all inhaled and intranasal corticosteroids, which states that these agents may cause a reduction in growth velocity in pediatric patients (see reference 21). However, both the Food and Drug

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Administration and several professional bodies in the United States concur that, depending on disease severity, the benefits of intranasal corticosteroid therapy may outweigh the risks (see reference 22). Because the effect, if any, on final height in not known, the height of children receiving long-term therapy should be monitored periodically during treatment, and should be plotted on a growth or growth-velocity chart to monitor for growth suppression. To minimize the risks of systemic corticosteroid exposure, including growth suppression, dose-reduction strategies should be considered. For patients who concomitantly receive exogenous corticosteroids via other routes for other conditions, such as inhaled corticosteroids for asthma, clinicians should consider the total corticosteroid exposure and titrate each patient to the lowest effective dose. Clinicians should also consider each medication’s potential for systemic effects when selecting among the various available corticosteroids. ABBREVIATIONS. BDP, beclomethasone dipropionate; ACTH, adrenocorticotropic hormone; HPA, hypothalamic pituitary adrenal; BID, twice daily; BUD, budesonide; FDA, Food and Drug Administration.

Intranasally administered corticosteroids have repeatedly been shown to be effective in controlling the symptoms of allergic rhinitis in children. Although long-term systemic use of oral or parenteral corticosteroids in children has been associated with growth suppression and other significant adverse effects, intranasal corticosteroids have been considered to be relatively free of systemic effects and to be an effective treatment option for children with allergic rhinitis. Beclomethasone dipropionate (BDP) aqueous nasal spray has been demonstrated to be well tolerated and effective in the treatment of rhinitis in adults and in children 6 years of age and older. The corticosteroid activity of BDP has been thought to be primarily confined to the application site, and only minimal systemic effects have been reported at recommended intranasal dosages. One study in healthy adult volunteers found that intranasal BDP 336 µg/day for 4 days had only insignificant effects on overnight urinary cortisol excretion and on serum cortisol after adrenocorticotropic hormone (ACTH) stimulation. In contrast, 24-hour urinary cortisol was significantly suppressed in another study of adult volunteers after 1 year of treatment with intranasal aqueous BDP 168 µg administered twice daily (BID). The study protocol and statement of informed consent were reviewed and approved by an institutional review board before study initiation, and written informed consent was obtained from the parent or guardian of each patient.

Inclusion criteria for this study were a diagnosis of allergic rhinitis with the duration of at least 1 year, stadiometric height measurements within the 5th and 95th percentile on standard growth charts, a cosyntropin stimulation test that was within normal limits at screening, and at least 6 years of age. Boys could be no older than 9 years and 6 months of age at baseline, and girls could be no older than 9 years at baseline. Patients were required to have no evidence of sexual maturation (Tanner stage 1). Skeletal age, as determined by left wrist radiographs, was required to be within 2 years of the patient’s chronological age at screening. Patients were also required to have a stadiometer height measurement between the 5th and 95th percentiles on standard height charts taken between 3 and 24 months before screening. This height measurement could not have deviated by >10 percentiles from the screening height measurement. If no stadiometer height measurement was available, patients were required to have 2 nonstadiometer height measurements between the 5th and 95th percentiles within the 3- to 24-month period before screening. These height measurements could not deviate by >15 percentiles from the screening height measurement. Patients were excluded from the study if there was a history or evidence of abnormal growth or the presence of a disease or condition that might substantially affect growth or require concomitant corticosteroid therapy. However, mild to moderate asthma that was well controlled without the use of corticosteroids was allowed. Patients were excluded if they had received >2 courses of systemic corticosteroids within the 12 months before enrollment, or if they had received inhaled corticosteroids for asthma for >2 months within the 12 months before enrollment. In addition, patients must not have used any form of corticosteroid (systemic, intranasal, ocular, inhaled, or topical) during the 4 weeks before the screening visit. Medications that were thought to possibly affect growth (eg, methylphenidate) were excluded during the course of the study.

Fifty-one patients were assigned to treatment with BDP 168 µg BID and 49 to placebo; randomization was stratified by gender and history of previous corticosteroid use (defined as the use of oral, inhaled, nasal, or topical corticosteroids during the previous 12 months). After washout periods of varying duration for agents that might influence the study results (ie, corticosteroids, cromolyn compounds, antihistamines, decongestants, spironolactone, or other investigational drugs), the first dose of study medication was administered to 50% of the study population. The total duration of topical hydrocortisone treatment throughout the study was not to exceed 4 weeks, and no individual treatment episode could exceed 10 days.

Patients were evaluated at the investigator’s office initially after 1 week of treatment and subsequently at the end of 1, 2, 4, 6, 8, 10, and 12 months. A review of concomitant medications, vital signs, and adverse events/intercurrent illnesses was conducted at each visit. Compliance was assessed by asking patients whether they had taken their medication as instructed, by reviewing diary cards, and by examining the medication bottles. Height, measured with a Harpenden Stadiometer (Holtain, Ltd, Crosswell, Wales),
and weight were recorded after 1 month and at each subsequent visit. Routine clinical laboratory tests and urinalysis were performed at screening and after 6 and 12 months, and an assessment of sexual maturity by Tanner staging was repeated at the 12-month visit.

**Cosyntropin Testing**

Cosyntropin stimulation testing was performed to assess HPA-axis function at screening and at the 6- and 12-month visits. At 8 AM (±1 hour), a plasma sample was taken to determine the prestimulation plasma cortisol concentration. This was followed by the intravenous or intramuscular injection of 25 mg of cosyntropin. A second plasma sample was taken to measure cortisol concentrations 60 minutes after the injection to determine adrenocortical response. At screening, the prestimulation (8 AM) plasma cortisol concentration was required to be ≥7 μg/dL and the 60-minute postcosyntropin concentration was to have increased at least 7 μg/dL above the baseline value for the patient to be eligible for enrollment.

**Statistics**

Analyses were based on all randomized patients who received at least 1 dose of medication (intent-to-treat principle). For the primary parameter (the rate of change in standing height) additional analyses were based on the standing height data of patients who had data for each of the visits throughout the 12 months of study.

The rate of change in standing height over the 1-year study period was calculated as the slope of a linear regression line fitted to each patient’s height measurements over time. The slopes were calculated using the actual patient data, including baseline. Similar rates of change over the available pretreatment data were also calculated for each patient. Because there was a statistically significant between-group difference in standing height at baseline, an analysis of covariance, including effects attributable to treatment and center, was performed for all analyses of standing height data, including the primary variable, with baseline height as the covariate.

Additional confirmatory analyses were performed. To perform a score analysis, the heights of both groups were normalized at baseline and at the end of the study, using the US National Center for Health Statistics data for mean and standard deviations of height to determine whether differences in growth rates during the study could be attributed to preexisting growth rates. In addition, height-adjusted age and outlier values were assessed.

Plasma cortisol concentrations and body weight were analyzed by analysis of variance, including effects attributable to treatment and center. Summaries of clinical adverse events, laboratory test values, and vital signs were based on all treated patients.

**RESULTS**

A total of 100 patients was randomized and treated in this study. An average of 12 to 13 patients (range: 3–21) was enrolled at each of the 8 centers. In general, the 2 treatment groups were comparable with respect to baseline demographic and disease characteristics (Table 1). However, the children in the BDP-treatment group were significantly older and taller than were those in the placebo-treatment group (P ≤ .04). Forty-five of the BDP-treated patients and 35 of the placebo-treated patients completed the entire 12-month course of treatment; 6 patients randomized to BDP and 14 randomized to placebo discontinued the study before completion. Reasons for treatment discontinuation are given in Table 2. At the end of treatment, 1 patient treated with BDP and 3 patients treated with placebo were no longer in stage 1 of the Tanner classification of sexual maturity. The rate of change in standing height was evaluated for all patients who participated in the study and for those who completed 12 months of treatment. Approximately 50% of the patients in each treatment group had a history of corticosteroid use (oral, inhaled, intranasal, or dermatological) within the 12 months before enrollment. Six patients in the BDP group and 7 in the placebo group reported short courses (average of 5 days each) of oral corticosteroids during the study.

**Change in Rate of Growth**

For all patients who entered the study, the rate of growth in the BDP-treated patients was significantly slower than in placebo-treated patients. The mean overall rate of growth was .013 cm/day in BDP-treated patients and .017 cm/day in placebo-treated patients (P < .01). Differences between treatment groups in changes from baseline height were observed after the first month of treatment (P = .04) and also at months 6, 8, 10 and 12 (Fig 1). An analysis that excluded patients who received courses of oral corticosteroids during the course of the study found these patients to not have any significant impact on the study results.

Similar results were found in the analysis of patients who completed all 12 months of treatment. In this group of patients, the differences between treatment groups in mean changes from baseline were statistically significant at all visits from 1 month to the end of the study (P ≤ .05; Fig 2). The overall rate of growth was .014 cm/day in the BDP-treated patients and .016 cm/day in the placebo-treated patients (P < .01). At month 12, the mean change in
Standing height from baseline was 5.0 cm for the BDP-treated patients and 5.9 cm for the placebo-treated patients (\( P < .01 \)).

Subgroup analyses for age, gender, and history of corticosteroid use were also performed. Age and height imbalances at baseline likely had an effect on the magnitude of the treatment difference. However, consistent with the overall results, placebo-treated patients in each of the subgroups generally grew faster than BDP-treated patients (Table 3). Among the placebo patients, no difference was noted in the growth rates of boys and girls, whereas only a slightly higher growth rate was observed for 6- to 7-year-old children, compared with 8- to 9-year-old children. A history of previous corticosteroid use (oral, inhaled, intranasal, or dermatological use in the 12 months preceding the study) in these patients was associated with a slightly lower growth rate than no history of corticosteroid use. Similar observations were noted for BDP-treated patients: there was no difference in growth rates between boys and girls, a slightly higher growth rate was observed for 6- to 7-year-old children, compared with 8- to 9-year-old children, and a history of corticosteroid use was associated with a slightly lower growth rate than no history of corticosteroid use.

Because there was a baseline imbalance in age and height, a supplemental analysis of the differences in prestudy growth rates was performed. This analysis found no baseline imbalance in prestudy growth rates (\( \sim .017–.018 \) cm/day or 6.2–6.6 cm/year for both treatment groups), although the rate of growth was higher than average for a population of this age (6.0 cm/year).10

Analysis of normalized heights (z score analysis) confirmed that the difference in growth rates between the placebo- and BDP-treated patients was primarily attributable to the treatment rather than to any preexisting difference in growth. Also, ages were adjusted by baseline height and compared with 12-month height median ages. Significant differences in height-adjusted age were evident. Additional analyses confirmed that the results were not influenced by outlier values.

**HPA-Axis Function**

No significant differences between treatment groups were found for either the prestimulation plasma cortisol concentrations or the response to cosyntropin stimulation at any time point. Normal prestimulation plasma cortisol concentrations and normal increases in cortisol concentrations after cosyntropin stimulation (\( \geq 7 \mu g/dL \)) were reported for all patients (Fig 3).

**Adverse Events**

Adverse events reported during the study were similar to those that have been observed with other intranasal corticosteroids, and most adverse events were considered by the investigators to be unrelated to treatment. Adverse events that were judged by the investigator to be related, or probably or possibly related to treatment, were reported by 33% of patients treated with BDP and 49% of patients treated with placebo (Table 4). Treatment-related adverse events were mild to moderate in severity. Only 2 patients, both of whom were treated with placebo, discontinued treatment because of adverse events, both of which were judged by the investigator to be unrelated to treatment.

Laboratory test values were typical of those found in children with allergic rhinitis but were otherwise unremarkable. There was no evidence of any systemic effects of glucocorticoids, such as fluid and electrolyte imbalances, alterations in protein, lipid or carbohydrate metabolism, alterations in formed ele-
ments in blood, or alterations in differential white blood cell counts, including eosinophils, in either treatment group. No clinically relevant laboratory abnormalities were found.

**DISCUSSION**

The present study found that treatment with intranasal aqueous BDP 168 μg BID for 12 months significantly slowed growth rate in prepubescent children. This difference in growth was evident as early as 1 month after treatment initiation and remained statistically significant over months 6 through 12 of the study. Because height was not monitored after the completion of therapy, the possibility that normal growth rates resumed after discontinuation of treatment or that catch-up growth occurred could not be assessed. BDP was well tolerated and no other systemic effects of corticosteroid therapy or clinically relevant changes in laboratory values were detected.

The finding of a significant reduction in the rate of growth in children who had received intranasal BDP for 1 year was not anticipated. However, the consistency of the reduction in growth rate observed in the various subgroup analyses could represent a subtle systemic corticosteroid effect, sufficient to slightly blunt growth, but insufficient to depress basal 8 AM cortisol concentrations or responsiveness to stimulation with .25 mg cosyntropin. Thus, growth in children may be a more sensitive index of systemic glucocorticoid effects than commonly used assessments of the HPA axis. However, it should be noted that the HPA-axis assessments used in this study may be less sensitive at detecting the systemic effects of corticosteroids than other tests such as the low-dose (.5 μg) cosyntropin stimulation test or measurement of 24-hour area under the plasma cortisol concentration–time curve.11,12

Several alternative explanations for the finding of drug-induced growth suppression were discounted on additional analyses. For example, there was a difference in height between the 2 groups at baseline—BDP-treated patients were older and taller. (The results of the height measurements were analyzed by an analysis of covariance to control for this imbalance.) The difference in baseline height suggests the possibility that there may have been some differences in expected growth rates because the older children (8–9 years of age) in this study grew at a slower rate than the younger children (6–7 years of age). However, even when analyzed by age subgroups, the BDP-treated patients grew at a slower rate than the placebo-treated patients. Thus, the possibility that the results were skewed by the baseline imbalance in age and height is remote. However, it is possible that the magnitude of the difference between the 2 treatment groups was affected by the baseline differences.

Few previous studies have investigated the effects of intranasal corticosteroids on long-term growth in children; however, short-term knemometric studies have been conducted. Knemometry is very useful in determining relative systemic bioavailability of different glucocorticoids and in defining a no effect dose for a given corticosteroid but does not predict the extent of suppression in intermediate- or long-term studies. Two studies involving intranasal budesonide (BUD) in children with allergic rhinitis have yielded conflicting results. In the first study, a significant reduction in lower leg growth occurred with BUD 200 μg BID administered as a nasal aerosol spray, during which the growth rate was reduced from .59 mm/day during the run-in phase to .05 mm/day during treatment with BUD (n = 11).13 In the second study, no effect on growth was seen with BUD 200 μg (n = 14) or 400 μg (n = 13) administered once daily via nasal dry powder inhaler.14 These results suggest that different intranasal corticosteroids may have varying systemic effects when administered at recommended dosages. Whether these findings may reflect differences in bioavailability as well as those inherent in different formulations of intranasal glucocorticoids (ie, aqueous, dry powder, and aerosol) is unknown. To date, there are no published studies comparing the effects of different intranasal corticosteroid formulations on growth.

Findings of childhood growth suppression during treatment with exogenous corticosteroids have led to questions regarding whether the effect is initial or progressive. In the present study, the difference in growth rates between the 2 study groups was evident as early as 1 month after treatment initiation. These results suggest that the effect on growth occurred early in the study (within the first few months of treatment) and persists throughout the study. Findings that growth suppression by intranasal corticosteroids can occur during short-term growth studies also suggest that the effect on growth is an initial one. However, the interpretation of short-term findings in the context of long-term outcomes remains under debate.15 The suppression of intermediate-term growth in asthmatic children by inhaled corticosteroids has been documented.16,17 Although the results do not necessarily apply to children with allergic rhinitis, studies of asthmatic children treated with inhaled corticosteroids have yielded mixed results. One study of 67 children treated with inhaled BDP 200 μg BID for 1 year has found that the growth suppressive effect is progressive, resulting in an increasing deviation of growth rates from normal values over time.18 However, another study has found the opposite effect. In this study, 50 asthmatic children were treated with inhaled BDP 200 μg BID for

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>BDP (n = 49)</th>
<th>Placebo (n = 51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epistaxis</td>
<td>10 (20)</td>
<td>13 (27)</td>
</tr>
<tr>
<td>Nasal burning</td>
<td>4 (8)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Nasal irritation</td>
<td>3 (6)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Sneezing</td>
<td>0</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Lacrimation</td>
<td>0</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>0</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Coughing</td>
<td>0</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Total</td>
<td>17 (33)</td>
<td>24 (49)</td>
</tr>
</tbody>
</table>

* Considered by the investigator to be related or probably or possibly related to treatment.
been published as an abstract and have been pre-
mined.

Whether effects on childhood growth seen in inter-
mediate-term studies result in reduced final adult
height has also come into question. The long-term
effects of intranasal corticosteroids on linear growth
and final height in children with allergic rhinitis have
not been determined. Several studies have investi-
gated the long-term effects on height of inhaled cor-
ticosteroid therapy for the treatment of asthma; how-
ever, these results do not necessarily apply to children
with allergic rhinitis. Some studies suggest that
growth in these children may be delayed but
that they will eventually attain their expected adult
height. In 1 study, BDP-treated children with asthma
who were followed for a mean of 13.1 years achieved
predicted final adult height despite delayed pubertal
growth acceleration. This finding suggests that pa-
tients who experience a reduction in growth rate
attributable to corticosteroid therapy may still
achieve expected final height. However, another
study in which growth was significantly suppressed
by inhaled BDP found no significant catch-up
growth during a 4-month washout period. The rele-
ance of these findings to children with allergic
rhinitis treated with intranasal corticosteroids
requires additional investigation. Furthermore, whether these findings will predict outcomes in a
clinical practice in which dose-titration is used and
compliance and duration vary remains to be deter-

The results of the present study have previously
been published as an abstract and have been pre-
ted to the Food and Drug Administration (FDA)
Pulmonary Allergy Drugs Advisory Committee and
Metabolic and Endocrinologic Drugs Advisory Com-
mittee. The results of this study were considered by
the FDA in the development of recently proposed
new class labeling for all inhaled and intranasal cor-
ticosteroids, which states that these agents may cause
a reduction in growth velocity in pediatric patients.
At the same time, noting the limited amount of in-
formation available, the FDA called for additional
study in this area. Both the FDA and relevant pro-
fessional bodies in the United States (American
Academy of Allergy, Asthma and Immunology; Ameri-
can College of Allergy, Asthma and Immunol-
y; American College of Chest Physicians; Ameri-
can Thoracic Society; and American Academy of Pe-
diatrics) concur that, depending on disease severity,
the benefits of intranasal corticosteroid therapy may
outweigh the risks. Because the effect on final
height is not known, the height of children on long-
term intranasal corticosteroid therapy should be
monitored periodically during treatment, using a sta-
diometer or similarly accurate device and should be
plotted on a growth or growth velocity chart to mon-
tor for growth suppression. Furthermore, clinicians
must be alert for the possibility of drug-induced
growth suppression so as not to misattribute it to
growth suppression related to other causes.

To minimize the risks of systemic corticosteroid
exposure, including growth suppression, dose-re-
duction strategies (eg, allergen-avoidance measures,
immunotherapy and concomitant treatment with antihistamines, or decongestants) should be consid-
ered. In addition, many allergic rhinitis patients
also receive corticosteroids via other routes for the
treatment of concomitant disorders, such as asthma
or atopic dermatitis. Therefore, physicians should take into account the patient’s total corticosteroid
exposure when prescribing an intranasal corticoste-
roid and should titrate each patient to the lowest
effective dose for each route to minimize systemic
exposure. Physicians also should consider each med-
ication’s potential for systemic effects when selecting
among the various available corticosteroids.

CONCLUSION

In summary, treatment with intranasal aqueous
BDP 168 μg BID for 1 year in children with allergic
rhinitis significantly slowed growth rate without
having any effect on the HPA axis as assessed by 8
AM cortisol concentrations or the response to stimu-
lation with .25 mg cosyntropin. However, the long-
term effects of intranasal BDP on final height remain
unknown.

ACKNOWLEDGMENTS

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port, has acted as a consultant, and spoken on speakers’ bureaus for Schering-Plough and Glaxo-Wellcome.

REFERENCES


3. Woithers OD, Jorgensen BA, Pedersen S. A double-blind, placebo-

4. Clossell SF, Heel RC. Budesonide. A preliminary review of its pharma-
codynamic properties and therapeutic efficacy in asthma and rhinitis. Drugs. 1984;28:485–518

5. Brogden RN, McTavish D. Budesonide. An updated review of its phar-
macological properties, and therapeutic efficacy in asthma and rhinitis. Drugs. 1992;44:375–407

6. Meltzer EO. Treatment options for the child with allergic rhinitis. Clin
Pediatr (Phil). 1996;35:1–10

7. Wilson AM, McFarlane LC, Lipworth BJ. Effects of repeated once daily
dosing of three intranasal corticosteroids on basal and dynamic mea-
sures of hypothalamic-pituitary-adrenal-axis activity. J Allergy Clin
Immunol. 1996;101:470–474

8. Wihl JA, Andersson KE, Johansson SA. Systemic effects of two nasally
administered glucocorticosteroids. Allergy. 1997;52:420–426

9. Brannan MD, Herron JM, Reidenberg P, Afrime MB. Lack of hypothal-
amic-pituitary-adrenal axis suppression with once-daily or twice-daily
beclomethasone dipropionate aqueous nasal spray administered to pa-

10. Tanner JM, Davies PS. Clinical longitudinal standards for height and

11. Lipworth BJ, Seckl JR. Measures for detecting systemic activity with

12. Chrousos GP, Harris AG. Hypothalamic-pituitary-adrenal axis suppress-
sion and inhaled corticosteroid therapy. 2. Review of the literature. Neuroimmunomodulation. 1998;5:288–308
22. 5 physician groups issue statement on corticosteroid safety. ACAAI Member Alert. November 16, 1998
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