Effect of Treating Allergic Rhinitis With Corticosteroids in Patients With Mild-to-Moderate Persistent Asthma*

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Study objectives: Rhinitis and asthma are considered to be synchronous or sequential forms of the same allergic syndrome. Treating the inflammation associated with allergic rhinitis influences the control of asthma. However, few studies have investigated the effect of treating perennial rhinitis on persistent asthma and vice versa. We determined the effects of inhaled or topical nasal beclomethasone dipropionate (BDP) administered separately or in combination on the control of asthma and bronchial hyperresponsiveness (BHR) in patients with the rhinitis/asthma association.

Design: A double-blind, parallel, three-group study.

Setting: Outpatient clinic of Pulmonary Division/Heart Institute (InCor) and the Division of General Internal Medicine, University of São Paulo Medical School, São Paulo, Brazil.

Patients: Seventy-four patients with mild-to-moderate asthma and allergic rhinitis (median age, 25 years).

Interventions: Patients received nasal or inhaled BDP separately or in combination for 16 weeks after a 2-week placebo run-in period.

Measurements and results: Nasal and pulmonary symptoms, as well as pulmonary function and BHR, were compared among the three groups after 4 weeks and 16 weeks of treatment. Patients in all three groups demonstrated a progressive and significant decrease in nasal and pulmonary symptoms, which started after 4 weeks (p < 0.05) and continued through the end of treatment (p < 0.001). Clinical improvement was similar and parallel in the three groups. Asthma-related morbidity, evaluated by quantifying absence from work, emergency department visits, and nighttime awakenings, also decreased in the three groups (p < 0.05).

Conclusions: Failure to consider treatment of rhinitis as essential to asthma management might impair clinical control of asthma. Furthermore, these data suggest that asthma and rhinitis in some patients can be controlled by the exclusive use of nasal medication.

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Key words: allergy; asthma; bronchial reactivity; inhaled corticosteroids; rhinitis

Abbreviations: BDP = beclomethasone dipropionate; BHR = bronchial hyperresponsiveness; ED = emergency department; MDI = metered-dose inhaler; PC_{20} = provocative concentration of histamine causing a 20% decrease in FEV1; PEF = peak expiratory flow

Asthma and allergic rhinitis probably are synchronous forms of the same inflammatory syndrome of allergic origin. Their association is not a cause-effect relationship, and both entities, although anatomically different, show pathophysiologic similarities. However, the physiologic mechanisms that link the upper and lower airways remain controversial, as does the best way to measure inflammation at both sites and their relationship.

Over the last few years, various attempts have been made to determine the influence of the presence of rhinitis on asthma-related morbidity. Rhinitis usually precedes the occurrence of asthma and may represent a risk factor for its development. Treating the inflammation associated with allergic rhinitis may have a true impact on the control of asthma, while the failure to treat rhinitis may impair asthma control. Thus, the optimal therapeutic approach should focus on the simultaneous treatment...
of both conditions. The Allergic Rhinitis and its Impact on Asthma workshop report states that the concomitant treatment of rhinitis is fundamental to asthma control, although it is not obligatory according to the Global Initiative for Asthma report.10

Until 1998, few studies had evaluated the effect of treatment of perennial rhinitis on persistent asthma.11 Furthermore, most studies that evaluated the impact of isolated treatment of allergic rhinitis on asthma and vice versa compared the effects of topical nasal steroids and placebo. To our knowledge, no prior study has compared the effects of topical nasal steroids and inhaled corticosteroids on the clinical control of rhinitis and, mainly, asthma.12–15 The objective of the present study was to evaluate the effects of inhaled or topical nasal beclomethasone dipropionate (BDP), administered separately or in combination, on clinical and functional measures of asthma and bronchial hyperresponsiveness (BHR) control in patients with the rhinitis/asthma association.

**Materials and Methods**

Patients were recruited from the asthma outpatient clinic for an 18-week/120-day study period. Patients with mild-to-moderate persistent asthma and allergic rhinitis who had been corticosteroid naïve for at least 3 months were included. Asthma was diagnosed and classified according to the criteria of the Global Initiative for Asthma.16 Patients selected had the following: (1) a clinical history of asthma and/or rhinitis during the previous 12 months; no use of oral, injected, or inhaled corticosteroids, and no current use of theophylline or leukotriene antagonists; and the absence of a history of antiinflammatory drug-induced asthma.

At the first visit, patients answered a clinical questionnaire designed to quantify symptoms. A maximum score of 18 points corresponding to the presence/frequency of rhinitis (nasal obstruction, rhinorrhea, sneezing, itchy nose, facial congestion) and a maximum score of 90 points corresponding to the presence/frequency/intensity of asthma (dyspnea, coughing, and wheezing) were recorded. The number of nighttime awakenings, missed work days, and emergency department (ED) visits due to asthma before entering the study also were recorded. In addition, the patients underwent morning spirometry and bronchoprovocation testing with histamine, according to the modified technique of Cockerot et al.13 PC_{20} was recorded in milligrams per milliliter.

Patients underwent a 2-week run-in period and received a diary card to score symptoms of asthma (dyspnea, cough, presence of wheezing attacks, and nighttime awakening) and rhinitis (nasal obstruction, pruritus, sneezing, and rhinorrhea) during home self-assessment. The scores ranged from 0 to 4 (0 = no symptoms, to 4 = many symptoms/more than six times a day). The diary card was also used to record the best of three morning and evening peak expiratory flow (PEF) measurements. Patients were instructed to use nasal spray and metered-dose inhaler (MDI) placebos (two puffs to each nostril and two inhaled puffs, respectively) every 12 h. Only salbutamol and short courses of type-1 antihistamines were allowed as rescue medication during this period. Patients with asthma and rhinitis exacerbations that could not be controlled with rescue medication were excluded during this placebo run-in period.

In the run-in period, the patients were randomized to one of the following three double-blind, parallel groups: (1) a nasal group: BDP nasal spray, two puffs q12h (400 µg/d) and placebo MDI; (2) a pulmonary group: placebo nasal spray and BDP MDI bid (1,000 µg/d); and (3) a nasal-plus-pulmonary group: BDP nasal spray and MDI at the doses described above. Based on previous studies12–15 in similar patients, we planned to enroll 21 patients in each group (power = 0.8, α = 0.05). We chose BDP because it is an inexpensive inhaled steroid that is available worldwide. In addition, BDP has well-defined and adjusted doses for asthma and rhinitis severity in most international guidelines.

Clinical reassessments were performed every 2 weeks, for a total of 10 medical visits over a period of 18 weeks (a 2-week placebo run-in period and 16 study weeks). At each visit, the physician evaluated pulmonary function, repeated the initial asthma and rhinitis questionnaire, and supplied patients with blank symptom diary cards and study drugs. The returned nasal spray and MDI canisters were weighed, and a 20% reduction in initial weight was considered a measure of treatment compliance. Bronchoprovocation was repeated only after 4 weeks and 16 weeks of treatment.

Severe exacerbations of asthma and rhinitis during the study were treated with prednisone, 40 mg po for 5 days, postponing bronchoprovocation. The persistence of symptoms after this period was a criterion for patient withdrawal. The same rescue medication used during the run-in period was allowed. The Research Ethics Committee of the University of Sao Paulo Medical School approved the study, and all patients signed an informed consent form.

**Statistical Analysis**

Multivariate analysis of repeated measures was used to compare self-assessed asthma and rhinitis scores, the sum of both scores (total score), and PEF between week periods (placebo, 4, and 16 2-week periods). Rhinitis and asthma clinical symptoms, FEV_{1}, and PC_{20} obtained at the initial visit, at randomization (after placebo), and after 4 weeks and 16 weeks of treatment were also analyzed by multivariate analysis of repeated measures.20 The means and SDs (95% confidence interval) were then compared between treatment groups (nasal, pulmonary, and nasal-plus-pulmonary groups).

A linear model was adopted to estimate the intercept and slope of the mean line obtained for the self-assessed total score for each group.21 This approach permitted analysis of the entire study period (18 weeks/120 days). The chi-square test was used to determine the proportion of patients in each group whose PC_{20} doubled between the initial visit, after 4 weeks, and after 16 weeks. The proportion of patients in each group who experienced nighttime awakenings, absence from work, and ED visits between the initial visit and after 16 weeks was analyzed using the marginal homogeneity test.22 A descriptive level of p < 0.05 was adopted for all tests.
RESULTS

Although 74 patients were recruited, 15 patients were excluded because they attended < 4 weeks of treatment, 7 of them after randomization (nasal group [n = 1], pulmonary group [n = 3], nasal-plus pulmonary group [n = 3]). Of the remaining 59 patients, 21 patients received nasal BDP (nasal group), 18 patients received inhaled BDP (pulmonary group), and 20 patients received both drugs (nasal-plus pulmonary group). During the study, two patients were excluded due to severe asthma exacerbations (nasal group [n = 1], nasal-plus-pulmonary group [n = 1]); another patient (pulmonary group) was excluded due to a severe airway infection. In addition, two patients asked to discontinue treatment (nasal group [n = 1], nasal-plus-pulmonary group [n = 1]). Therefore, the results reflect data through the fourth week of treatment from 59 patients and data corresponding to the whole study period from 54 patients. Table 1 summarizes demographic data and baseline FEV1, PC20, and symptom scores.

The whole study group consisted of young adults, with a discrete predominance of women. The onset of asthma preceded the symptoms of rhinitis. Most patients had moderate persistent asthma. Although some of them presented with an initial FEV1 > 80% of predicted, BHR was severe in all subjects. The groups were similar, but the pulmonary group had a lower rhinitis diary score at baseline.

Patients in all groups showed significant improvement in rhinitis and asthma symptoms, as determined by a reduction in the diary self-assessment scores (Table 2). A wide variability in symptom scores was noted, as demonstrated by the variation in their SDs. During the run-in period, a placebo effect was observed in symptoms after 2 weeks compared to baseline scores in the pulmonary and nasal-plus-pulmonary groups. The rhinitis and asthma symptom scores of patients in the nasal and pulmonary groups only significantly changed at the end of treatment (Table 2). In contrast, symptom scores tended to improve in the nasal-plus-pulmonary group from the fourth week on, and markedly decreased by the end of the 16 weeks of treatment.

The slope of the mean line of the self-assessed total rhinitis and asthma scores obtained for the 120 days of the study demonstrates the parallel decline in symptoms (Fig 1). Consistent with the self-assessment scores, asthma scores on the questionnaire administered at clinical visits showed improved disease control in all groups at the medical visits (Table 3). However, no significant difference was observed between the 4th and 16th weeks, ie, the asthma symptoms decreased during the first 4 weeks and then remained stable, irrespective of the treatment group. The rhinitis scores on the clinical questionnaire did not significantly decrease, although the nasal and nasal-plus-pulmonary groups tended to experience fewer symptoms (p = 0.09). The pulmonary group maintained lower rhinitis scores on the questionnaire during the study, which was in accordance with their lower rhinitis diary score at baseline.

Morning and evening PEF measurements did not change during the study period. The mean absolute FEV1 showed a significant increase compared to baseline in all groups (Table 4), but an increase in FEV1 of 200 mL was observed only after 4 weeks of treatment in the nasal-plus-pulmonary group.

No significant variations in the mean absolute PC20 were observed between groups or treatment times (Table 4). However, a twofold higher PC20 between baseline and after 4 weeks of treatment and at the end of the study was observed in eight patients.

Table 1—Demographic Data, Pretreatment Functional Values, and Baseline Symptom Scores Obtained for the Three Groups*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nasal Group</th>
<th>Pulmonary Group</th>
<th>Nasal-Plus-Pulmonary Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>21</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Female gender</td>
<td>13</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Age, yr</td>
<td>25 ± 7</td>
<td>24 ± 8</td>
<td>27 ± 11</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>2.6 ± 0.52</td>
<td>2.86 ± 0.73</td>
<td>2.74 ± 0.69</td>
</tr>
<tr>
<td>FEV1, %</td>
<td>76.4 ± 18</td>
<td>84.6 ± 16.3</td>
<td>82.8 ± 19.9</td>
</tr>
<tr>
<td>PC20, mg/mL</td>
<td>0.29 ± 0.4</td>
<td>0.21 ± 0.19</td>
<td>0.26 ± 0.26</td>
</tr>
<tr>
<td>Duration of asthma, yr</td>
<td>15 ± 6</td>
<td>12 ± 9</td>
<td>17 ± 12</td>
</tr>
<tr>
<td>Duration of rhinitis, yr</td>
<td>13 ± 7</td>
<td>10 ± 5</td>
<td>11 ± 8</td>
</tr>
<tr>
<td>Rhinitis diary score</td>
<td>4.35 ± 3.05</td>
<td>3.07 ± 2.19†</td>
<td>4.03 ± 3.03</td>
</tr>
<tr>
<td>Asthma diary score</td>
<td>2.64 ± 1.85</td>
<td>2.85 ± 2.69</td>
<td>3.04 ± 2.48</td>
</tr>
<tr>
<td>Rhinitis clinical questionnaire (initial visit)</td>
<td>6.9 ± 4.4</td>
<td>7.7 ± 3.6</td>
<td>7.5 ± 4.3</td>
</tr>
<tr>
<td>Asthma clinical questionnaire (initial visit)</td>
<td>15.0 ± 11.0</td>
<td>18.9 ± 8.9</td>
<td>18.5 ± 12.1</td>
</tr>
</tbody>
</table>

*Data are presented as No. or mean ± SD. There was no significant difference between groups, except where indicated. †p = 0.02.

Clinical Investigations
(38.1%) in the nasal group, four patients (22.2%) in the pulmonary group, and in seven patients (35%) in the nasal-plus-pulmonary group.

There was a significant reduction in the number of ED visits after 16 weeks of treatment in all groups (Fig 2). In the nasal group, nine patients (45%) reported ED visits before treatment vs only one patient (5%) after treatment. In the pulmonary and nasal-plus-pulmonary groups, seven patients (43.8%) and nine patients (50%), respectively, reported ED visits before treatment, but no patient in either group visited the ED after treatment.

Table 2—Self-Assessed Diary Symptom Scores Obtained During Run-in Period (First 2 Weeks), and After 4 Weeks and 16 Weeks of Steroid Treatment*

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Nasal Group</th>
<th>Pulmonary Group</th>
<th>Nasal-Plus-Pulmonary Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rhinitis symptom score</td>
<td>Pulmonary symptom score</td>
<td>Total score (asthma plus rhinitis)</td>
</tr>
<tr>
<td>2 (run-in)</td>
<td>4.42 ± 3.32</td>
<td>2.35 ± 1.28</td>
<td>7.19 ± 5.14</td>
</tr>
<tr>
<td>4</td>
<td>4.4 ± 3.11</td>
<td>2.33 ± 2.43</td>
<td>6.44 ± 4.45</td>
</tr>
<tr>
<td>16</td>
<td>3.13 ± 2.63 †</td>
<td>2.22 ± 1.91 †</td>
<td>4.93 ± 3.88 §</td>
</tr>
<tr>
<td>2 (run-in)</td>
<td>2.77 ± 2.55</td>
<td>1.91 ± 1.11</td>
<td>4.25 ± 1.89</td>
</tr>
<tr>
<td>4</td>
<td>1.97 ± 2.48</td>
<td>1.93 ± 1.67</td>
<td>4.26 ± 3.68</td>
</tr>
<tr>
<td>16</td>
<td>1.8 ± 1.89 †</td>
<td>1.21 ± 1.53 †</td>
<td>3.44 ± 3.12 §</td>
</tr>
</tbody>
</table>

*Values are reported as the mean ± SD.
†p = 0.002, 2 weeks vs 16 weeks; p = 0.014, 4 weeks vs 16 weeks.
‡p = 0.0001, 2 weeks 16 weeks; p = 0.04, 4 weeks vs 16 weeks.
§p = 0.0002, 2 weeks vs 16 weeks; p = 0.014, 4 weeks vs 16 weeks.

Figure 1. Lines represent the 2-week diary total score (rhinitis and asthma) for the 18 weeks (120 days) of the study. The first 15 days correspond to placebo followed by treatment with steroids (mean line, p<0.001; 0 days vs 120 days). Group N = nasal BDP; group P = inhaled BDP; group NP = nasal and inhaled BDP.
Four patients (20%) in the nasal group, one patient (6.3%) in the pulmonary group, and six patients (33.3%) in the nasal-plus-pulmonary group experienced nighttime awakenings before entering the study (Fig 2). There was a significant reduction in nighttime awakenings due to asthma, but one patient from the pulmonary group still reported this complaint after treatment. Finally, a vast improvement in asthma-related absence from work was observed in the pulmonary and nasal-plus-pulmonary groups: four patients (25%) and eight (44.4%) reported this complaint before treatment vs none after treatment, respectively.

**DISCUSSION**

The initial hypothesis in the present study was that failure to treat rhinitis would impair the optimal management of asthma and that the asthma-rhinitis relationship could be evaluated based on improvements in pulmonary function and BHR after treatment. The results show that nasal BDP alone has a similar effect on the control of asthma symptoms as inhaled and combined applications of the drug, without a significant variation in either pulmonary function or BHR. Our findings also demonstrate that the combined administration of BDP results in a greater reduction in asthma-related morbidity, as measured by ED visits, missed workdays, and nighttime awakenings.

Other investigators have evaluated the beneficial effects of topical steroids in patients with rhinitis associated with asthma. Only Aubier et al compared the use of nasal vs inhaled steroids, but their objective was to determine BHR in nonasthmatic subjects. Our study demonstrates the importance of each treatment strategy in the clinical control of airway disease. Although having a placebo group would have clarified the response to steroids, it would be unethical to postpone the treatment of asthma in this population of asthmatic patients.

The reassessment after 4 weeks and 16 weeks of BDP treatment allowed determination of the cumulative antiinflammatory benefits. One month of treatment with inhaled corticosteroids reportedly reduces the pathologic signs of inflammation associated with asthma. However, Woolcock and Jenkins proposed that reductions in BHR might occur up to 6 months after introduction of inhaled steroids. Studies on the effects of nasal steroids on asthma have ranged from 14 days to 6 weeks, and only Armitage et al extended the treatment phase to 3 months. In

![Figure 2. Number of patients with asthma-related ED visits, nighttime awakenings, and missed days of work before and after treatment.](Image 310x587 to 538x737)

**Table 3—Questionnaire Scores Obtained During the Clinical Visit at Randomization (After Placebo) and After 4 Weeks and 16 Weeks of Steroid Treatment**

<table>
<thead>
<tr>
<th>Visits</th>
<th>Nasal Group</th>
<th>Pulmonary Group</th>
<th>Nasal-Plus-Pulmonary Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhinitis questionaire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>6.8 ± 4.2</td>
<td>5.4 ± 2.9</td>
<td>5.1 ± 3.6</td>
</tr>
<tr>
<td>Week 4</td>
<td>7.0 ± 2.9</td>
<td>5.2 ± 2.7</td>
<td>4.1 ± 4.3</td>
</tr>
<tr>
<td>Week 16</td>
<td>4.9 ± 3.3</td>
<td>5.5 ± 3.6</td>
<td>4.2 ± 2.9</td>
</tr>
<tr>
<td>Asthma questionaire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>15.5 ± 12.6</td>
<td>14.2 ± 11.1</td>
<td>17.2 ± 11.1</td>
</tr>
<tr>
<td>Week 4</td>
<td>8.0 ± 6.6</td>
<td>12.9 ± 11.6</td>
<td>9.0 ± 9.3</td>
</tr>
<tr>
<td>Week 16</td>
<td>11.3 ± 12.6</td>
<td>10.6 ± 13.2</td>
<td>9.6 ± 9.5</td>
</tr>
</tbody>
</table>

Values are reported as the mean ± SD.

*p = 0.001, 2 weeks vs 4 weeks.

*p = 0.009, 2 weeks vs 16 weeks.

**Table 4—FEV1 and PC20 Values in the Three Study Groups at Baseline, After Run-in, and After 4 Weeks and 16 Weeks of Treatment**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nasal Group</th>
<th>Pulmonary Group</th>
<th>Nasal-Plus-Pulmonary Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1, mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2.60 ± 0.52</td>
<td>2.86 ± 0.72</td>
<td>2.74 ± 0.69</td>
</tr>
<tr>
<td>After run-in</td>
<td>2.69 ± 0.67</td>
<td>2.93 ± 0.67</td>
<td>2.71 ± 0.77</td>
</tr>
<tr>
<td>Week 4</td>
<td>2.68 ± 0.58</td>
<td>2.91 ± 0.72</td>
<td>2.94 ± 0.63†</td>
</tr>
<tr>
<td>Week 16</td>
<td>2.78 ± 0.52‡</td>
<td>2.99 ± 0.76‡</td>
<td>2.78 ± 0.75</td>
</tr>
<tr>
<td>PC20, mg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.27 ± 0.39</td>
<td>0.20 ± 0.19</td>
<td>0.26 ± 0.25</td>
</tr>
<tr>
<td>After run-in</td>
<td>0.19 ± 0.17</td>
<td>0.19 ± 0.22</td>
<td>0.22 ± 0.30</td>
</tr>
<tr>
<td>Week 4</td>
<td>0.33 ± 0.77</td>
<td>0.17 ± 0.13</td>
<td>0.47 ± 0.77</td>
</tr>
<tr>
<td>Week 16</td>
<td>0.53 ± 1.01</td>
<td>0.22 ± 0.21</td>
<td>0.61 ± 1.01</td>
</tr>
</tbody>
</table>

*p = 0.006.

†p = 0.017.

*p = 0.05. ERbefore = nighttime awakenings before treatment; ERafter = nighttime awakenings after treatment; NAbefore = nighttime awakenings after treatment; NAafter = nighttime awakenings after treatment; MWDbefore = missed days of work before treatment; MWDafter = missed days of work after treatment; see Figure 1 legend for expansion of abbreviations.
that asthma symptom scores tended to improve findings in the present study, Watson et al13 showed its protective effect on the lung. Similar to the first weeks of the study, their spirometric data and BHR remained almost unchanged. Some investigators27 have observed a placebo effect during drug therapy trials, especially in those involving patients with asthma.

The symptom scores were reduced after the first month of treatment, regardless of whether the rhinitis and asthma symptoms were evaluated separately or in combination. The nasal application of BDP produced a more intense reduction in asthma symptoms than the reduction of rhinitis symptoms achieved with inhaled administration. These results are supported by clinical improvement reported by patients during the visits and measured by a clinical questionnaire. Agreement between the two scoring systems was observed. However, the clinical importance of this result must be interpreted in the context of the present study: the small number of patients evaluated in each group.

A reduction in asthma symptoms with nasal BDP has been demonstrated in previous studies. Reed et al12 reported a 10-fold increase in asthma symptom scores in a placebo group compared with a treatment group that received 336 μg/d of nasal BDP, indicating its protective effect on the lung. Similar to findings in the present study, Watson et al13 showed that asthma symptom scores tended to improve during the second to third weeks of treatment with 400 μg/d of nasal BDP. Pedersen et al14 observed the same result with the application of 1,292 μg/d of nasal budesonide. However, it should be emphasized that, in contrast to our study, these other studies only compared the intensity of symptoms after treatment with nasal steroids vs a placebo. Furthermore, Pedersen et al14 used elevated doses of a nasal steroid administered through a nasal inhalation system equipped with a spacer device. This permitted both nasal and bronchial deposition of budesonide and, thus, support the findings obtained in this study with 400 μg/d of nasal BDP and 1,000 μg/d of inhaled BDP.

The reduction in asthma symptoms observed after the exclusive use of nasal BDP, comparable to improvement seen in the other two groups, demonstrates the importance of treating rhinitis in the clinical management of asthma. Although not extensive, we also observed a reduction in symptoms such as itchy nose, sneezing, and rhinorrhea with the exclusive use of inhaled BDP. Greiff et al29 reported similar results with inhaled budesonide. This improvement supports the hypothesis of Bucca et al,29 that extrathoracic receptors stimulated by upper-airway inflammatory processes trigger both asthma and rhinitis attacks. The coexistence of extrathoracic hyperresponsiveness and BHR in patients with rhinitis and asthma, and particularly their improvement after treatment, suggests an allergic-based impairment involving all airways.30

Denburg et al31 demonstrated a systemic effect of the allergic response, irrespective of the initial target organ. The massive presence of eosinophils in the airways of asthmatics seems to be a final systemic response to the persistent recruitment of basophils, eosinophils, and progenitor cells from bone marrow. Braunstahl et al32 demonstrated a bidirectional relationship between nasal and bronchial inflammation. In an initial study,32 they observed an increase in the number of eosinophils in the nasal and bronchial mucosa 24 h after allergen bronchoprovocation. In a second study,33 they observed an increased number of eosinophils in the nasal and bronchial epithelium after nasal provocation, which was positively correlated with increases in intracellular adhesion molecule, vascular cell adhesion molecule, and E-selectins in vessels supplying the nasal and bronchial tissue. Given this bidirectional pathophysiology, we hypothesized that intranasal BDP (nasal group) may act in the lungs, and inhaled BDP (pulmonary group) may act in the nasal mucosa. Our finding that asthma and rhinitis could be controlled exclusively by nasal medication in some patients is consistent with such a systemic effect of BDP, despite its local application.

In regard to pulmonary function, we found a small improvement of marginal clinical importance. This finding can be explained by the high baseline FEV1 (Table 1) and small sample size. These results do not completely disagree with other reports12–15 in the literature. Most studies12–15 comparing the effects of nasal steroids and placebo have shown only modest gains in lung volume, which did not reach statistical significance.

In the present study, none of the therapeutic strategies employed significantly decreased the BHR. Patients had severe BHR, and steroid treatment improved it in only one third to one fourth of the patients. Watson et al13 described a nasobronchial interrelationship, based on increased provocative concentration of methacholine causing a 20% fall in FEV1 values obtained after 4 weeks of nasal BDP vs placebo treatment. In two other studies,34,35 nasal corticosteroids prevented worsening of BHR during the pollen season. Aubier et al36 observed an improvement in BHR only in nonasthmatic patients who received nasal BDP compared to a parallel group who received inhaled BDP. However, no change in BHR with the use of nasal steroids or
respectively). Adams et al. found that in patients was reduced by 50%.

The importance of BHR in the rhinitis/asthma relationship is controversial. A study conducted on asthmatic patients with perennial allergic rhinitis was unable to establish a direct association between BHR and sputum and BAL cytology, with or without a bronchial biopsy. In response to this last study, Haley and Drazen confirmed that BHR seems to be the final phenotypic expression of a series of pathologic processes associated with the cellular or neural inflammatory response or with bronchial remodeling, which varies from patient to patient. The clinical improvement observed in our patients was accompanied and supported by the finding of fewer ED visits, night awakenings, and asthma-related absence from work. Patients who received nasal and inhaled steroids (nasal-plus-pulmonary group) did not experience any of these events during the study period, suggesting a synergistic treatment effect. These results have a direct impact on the morbidity of the disease, as they alter the routine of a patient’s life. In patients with allergic rhinitis and asthma who were treated or untreated for allergic rhinitis, Crystal-Peters et al. showed significant differences in the rates of ED visits (5.7% vs 3.1%, respectively) and hospitalizations (<1% vs 2.3%, respectively). Adams et al. found that in patients with three or more applications of nasal steroids, the relative risk of needing to visit the ED due to asthma was reduced by 50%.

**Conclusions**

The present results suggest that the failure to consider treatment of coexisting rhinitis as essential to the management of asthma may impair clinical control of the latter. Despite the small number of patients in this study, they were followed up in a close manner for almost 4 months. When asthma is approached as an exclusively pulmonary disease, the patient may require higher doses of oral corticosteroids and might demonstrate higher morbidity. Conversely, the parallel and similar response to nasal BDP might indicate that mild asthma can be controlled by the exclusive use of nasal medication. Together, these findings suggest that management of allergic rhinitis should be considered an integral part of treatment for asthma. Citing Tokias, assessment of the asthmatic patient in an isolated manner implies interruption of the physiologic systemic cross-talk between the nose and lung. Further studies employing a similar design are needed to confirm or contest the results presented here.

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