Efficacy of Pollen Blocker Cream in the Treatment of Allergic Rhinitis

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Objective: To assess the efficacy and safety of a pollen blocker cream for prophylaxis of symptoms in patients with seasonal or perennial allergic rhinitis.

Design: Double-blind, randomized, placebo-controlled, crossover study conducted from November 2001 through September 2002 in 2 outpatient centers in Germany and 1 in Russia. Ninety-one patients aged 18 to 55 years with at least a 2-year history of seasonal or perennial allergic rhinitis confirmed by history and positive skin test results were randomly assigned to receive pollen blocker cream (n=43) or carboxymethylcellulose in gel (placebo) (n=48) applied sparingly to the lower internal nose region 4 times daily for a total of 9 days. The efficacy of treatment was assessed by means of nasal provocation testing. The investigators assessed the nasal symptom severity scores (range, 0-6), and the changes in nasal airflow after allergen application were measured by anterior rhinomanometry.

Results: The median score fell from 4 to 1 after application of the pollen blocker cream (P<.001) and from 4 to 3 in the placebo group (P<.05). The difference between the 2 groups after the second provocation was highly significant (P<.001). The increase in airflow in response to treatment was roughly 20% in the blocker group compared with only about 10% in the placebo group, relative to an airflow rate (299 mL/s) measured after provocation on day 1.

Conclusions: The blocker was significantly more effective than placebo and reduced the typical symptoms of allergic rhinitis in response to nasal challenge with allergen by nearly 60% (placebo reduced symptoms by 25%). The pollen blocker cream did not produce any adverse effects. Therefore, the efficacy of the investigational product can be rated as good.

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Allergies are common and are most frequently caused by inhalation and/or oral ingestion of the causative allergens. A classic example of an inhalation allergy is hay fever, which is generally caused by airborne pollen and typically causes acute seasonal allergic rhinitis. House dust, mites, and animal dander are common triggers of perennial allergic rhinitis. The methods for treatment of inhalation allergies vary and may include mechanical measures for pollen reduction1,2 and/or different pharmacologic agents.3-5 Medications can lead to various adverse effects, and therefore physicians and patients alike are always seeking safer alternative remedies.

Dr. Theiss Alergol pollen blocker cream (Phyt-Immun GmbH, Homburg, Germany) could be a suitable alternative for symptomatic treatment for allergic rhinitis.2,6 Alergol has already been investigated by nasal provocation testing in an open-label study.7 Intranasal ointments have only few known adverse effects, most of which are attributable to improper use (eg, when applied to open wounds or inhaled into the bronchi).9-11

Study Design and Schedule

The present study was designed as a multicenter trial performed at 3 centers: the Ear, Nose and Throat Clinic Frankfurt/Main, Frankfurt, Germany; the Department of Ear, Nose and Throat Diseases, Charité University Hospital, Berlin, Germany; and the Institute of Immunology, Federal Scientific Research Center, Moscow, Russia. The study protocol called for 110 participants to be tested a total of 6 times during the
9-day crossover study. The patients were provided the necessary information on the nature and scope of the clinical study. All participants were required to submit a signed informed consent form at least 24 hours before the start of treatment. Each patient was assessed at each visit regarding challenge to his or her allergy and symptoms. The ethics commission of Charité Hospital approved the study on August 9, 2001. Before starting the baseline examination or a phase of treatment, the investigator evaluated each patient for eligibility to participate in the study using a predefined list of inclusion and exclusion criteria (Table 1).

Drug efficacy in patients with allergic rhinitis was assessed by means of nasal provocation testing. As specified in the position paper of the German Society of Allergology and Clinical Immunology,12 the nasal provocation test was designed to “reproduce the response of the nasal mucosa to a substance inhaled from the environment under controlled conditions.” The investigators documented the typical responses of the nasal mucosa to these challenges (eg, hypersecretion, itching, and sneezing). The changes in nasal airflow after allergen application were measured by anterior rhinomanometry12 at a transnasal pressure difference of 150 Pa, starting with the initially more patent nostril. The nasal provocation testing was performed before or after the pollen season in patients with seasonal allergic rhinitis. During this study, all patients with perennial allergic rhinitis tried to avoid any contact with their causative allergens. Exposure to allergens during the test phase did not occur in a single patient. Nevertheless, all patients used their ointment 4 times daily to prevent unexpected exposure to allergens during the test phase.

**NASAL PROVOCATION TESTING**

Each patient was tested according to a fixed protocol (Figure 1). In accordance with the position paper of the German Society for Allergology and Clinical Immunology,12 the nasal provocation test was performed with the allergen that showed the highest reaction in the skin prick test by delivering allergen extracts—pollen, house dust, and/or animal dander—through a face mask. The extract concentration was increased (1:1000, 1:100, and 1:10) until a positive result was observed. A positive response was defined as a nasal airflow decrease of 40% or greater or a symptom score of 3 or higher (Table 2).

On day 1, a preliminary examination was performed to assess patient symptoms and eligibility to participate in the study (inclusion and exclusion criteria) and to establish a symptom score after provocation with no drug or placebo present (minimum score of 3 for inclusion in the study). If the patient was eligible to participate, he or she was randomly assigned to one of the treatment groups.

On day 2, the active nasal ointment (Alergol) or placebo (gel containing 5% carboxymethylcellulose, 83.5% water, 10% glycerol, 0.5% citric acid, and 1% potassium sorbate) was applied. This particular placebo was chosen because most of the pollen are destroyed in water, thereby leading to allergen release. The second nasal provocation test was performed using previously determined optimal allergen extract concentration. The rate of airflow in the nasal airway was measured by rhinomanometry, and the patient’s nasal symptoms were scored.

During days 2 through 5, the patients applied the investigational product or placebo sparingly to the lower internal nose region every 4 hours, 4 times daily. On day 5, another nasal provocation test was performed after the patient had applied the investigational product or placebo; nasal airflow was then measured, and the patient’s nasal symptoms were scored. Testing was followed by a 1-day washout period. The patients returned their test product to the investigator and did not use it after the provocation test on day 5.

Day 6 marked the beginning of the second phase of treatment. On that day, the patients checked in and were issued the test product that they had not used in the first phase (investigational product or placebo) in accordance with the crossover design schedule. All tests were then repeated under identical conditions. The patients used the issued product on days 6 through 9 in the same manner as they had applied the former product on days 2 through 5. On day 9, the patients presented for the final examination, and all tests were repeated.

**Equipment**

A manual inhalation system with a face mask was specifically designed for standardized nasal provocation testing. As is shown in Figure 2, the inhalation unit consisted of a breathing mask (Nebu Tec, Elsenfeld, Germany), an exhaled air filter (Nebu Tec), a holding chamber (Aerotrap, Elsenfeld), a nebulizer (Nebu Tec), and a compressor (PulmoCar AC, Elsenfeld). The protocol specified that all components had to be dry and cleaned before use.

The patients breathed in the allergens mixed with ambient air in the holding chamber. This was done by loading a defined

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**Table 1. Inclusion and Exclusion Criteria**

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>Male or female older than 18 y</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Signed informed consent form</td>
<td>Major cardiovascular disease</td>
</tr>
<tr>
<td>Confirmed diagnosis of allergic rhinitis (as determined by history and positive skin test results) induced by pollen (birch, grass, or mugwort pollen), house dust, or animal dander</td>
<td>Use of cortisone for treatment of bronchial asthma</td>
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<tr>
<td>Abstention from all substances prohibited in the general restriction period before nasal provocation testing</td>
<td>Severely obstructed nasal breathing</td>
</tr>
<tr>
<td>Symptom score ≥3</td>
<td>Use of ACE inhibitors or β-blockers</td>
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</tbody>
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Abbreviations: ACE, angiotensin-converting enzyme; HIV, human immunodeficiency virus.
allergen solution into the nebulizer, transforming it into a fine spray with the aid of the compressor, and redirecting the spray into the holding chamber. The patients then inhaled the allergen-saturated air through a tightly sealed facemask for 30 seconds.

Test Protocol and Symptom Score

Each patient was tested to a fixed protocol (Figure 1). The symptom score was calculated as the sum of the individual scores for amount of nasal discharge (determined semiquantitatively), number of bouts of sneezing, and assessment of distant symptoms. Each variable was assessed using a 3-point scale and assigned a value of 0, 1, or 2. The scoring system is detailed in Table 2. The maximum score was 6 points. A minimum score of 3 points after allergen provocation was a prerequisite for participation in the study.

Rhinomanometry

The procedure was performed with the test subject seated. The subject was instructed to breathe normally through the nasal olive of the rhinomanometer and continue breathing at rest long enough to ensure that the resting respiratory state had been achieved. The nasal olive was then switched to the other nostril, and the measurement procedure was repeated. Measurements were first made for both nostrils, first the right nostril, followed by the left.

STATISTICAL ANALYSIS

The objective of the present study was to determine whether Alergol pollen blocker cream is an effective treatment for allergic rhinitis. The study was designed as a double-blind, randomized, placebo-controlled, crossover study. The investigator examined each test subject on 6 different occasions: at randomization, at the first and second treatments with Al-
PATIENT POPULATION

A total of 106 white patients with clinically proven allergic rhinitis were recruited. Fifteen of the patients did not fulfill all inclusion requirements and were therefore excluded, leaving a total of 91 study participants. Regarding their allergies, 16 patients were allergic to animal dander, 25 to house dust mites, and the remaining 50 were allergic to pollen. The minimum history of allergic rhinitis was 2 years, but in most cases, the disease had been present for much longer. The median age was 29 years. There was no significant difference between the treatment groups for skin test reactivity, symptom score, or air flow prior to treatment (Table 3).

The Russian and German centers had comparable patient populations (Table 3). The demographic data for the individual groups did not differ significantly. The participants were not allowed to use any antiallergy medications or drugs that could induce allergic rhinitis during the entire study period. Four patients used authorized medications: 1 used Latanoprost Ophthalmic Solution (Xalatan, Pfizer, New York, NY); 1, diclofenac sodium; 1, bisoprolol; and the last, amlopidine besylate. Bronchial asthma (not requiring cortisone therapy), chronic tonsillitis, chronic pharyngitis, and neurodermatitis were the most common accompanying diseases.

RESULTS

The median values and the lower and upper quartile values of the symptom scores for the 2 treatment groups are illustrated in Figure 3. Since the score decreases observed in the 2 phases for a given product (Alergol or placebo) were identical, we combined the data for the 2 identical phases (“first placebo, then investigational product” and “first investigational product, then placebo”) to yield 1 Alergol investigational product phase and 1 placebo phase.

The median score fell from 4 to 1 after application of the pollen blocker cream (P < .001). The median scores in the placebo group also decreased significantly (ie, from 4 to 3). All differences relative to the start value on day 1 were highly significant (P < .001) except for the initial value for the placebo phase (median score, 4), which had a level of significance of P < .05. The effect of the pollen blocker cream was also lowest at the first placebo test.

The symptom scores demonstrate that the pollen blocker cream had a significant effect. However, it became apparent that carboxymethylcellulose in gel was capable of capturing small quantities of pollen and therefore was not a true placebo. In addition, there appeared to be a learning curve with respect to cream application, so all scores measured after the use of Alergol or placebo were always lower than those observed in the beginning. This was true regardless of whether Alergol (43 patients) or placebo (48 patients) was the first product used. An additional explanation for this finding is the occurrence of priming effect following provocations.15-17 In fact, after 1 day, the symptom score was higher than that observed after 3 days (third provocation). This finding

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median</th>
<th>Lower</th>
<th>Upper</th>
<th>Drug/Placebo</th>
<th>P Values</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>29</td>
<td>23</td>
<td>36</td>
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<td>.96</td>
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<td>4+</td>
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<td>.25</td>
</tr>
<tr>
<td>Symptom score</td>
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<td>3</td>
<td>5</td>
<td>.65</td>
<td>.44</td>
</tr>
<tr>
<td>Air flow, mL/s</td>
<td>298</td>
<td>261</td>
<td>322</td>
<td>.89</td>
<td>.37</td>
</tr>
</tbody>
</table>

Table 3. Comparison Between the Active Treatment Group and the Placebo Group Prior to Treatment
is in agreement with the results of previous studies demonstrating that the priming effect was reversible when challenges stopped for 2 days.¹³

Twenty-three of the patients studied were classified as nonresponders (score decrease <1), 22 as responders (score decrease =1 or 2), and 46 as high responders (score decrease >2). Therefore, approximately 50% of patients were high responders, 25% were responders, and 25% were nonresponders. The patients allergic to house dust mites, animal dander, and pollen showed comparable responder and nonresponder distributions. Those allergic to grains, mugwort, hazel, cat dander, and Dermatophagoides pteronyssinus showed an excellent response rate.

The airflow rates measured for each product (Alergol or placebo) during the 2 test phases were averaged since it did not matter whether the product was used in the first or second phase. The increase in airflow in response to treatment was roughly 20% in the Alergol group compared with only about 10% in the placebo group, relative to the airflow rate measured after provocation on day 1 (Figure 4). The pollen blocker cream was therefore able to prevent two thirds of the airflow decrease observed after unprotected allergen provocation.

Both Alergol and the placebo led to a significant increase in the nasal airflow rate (P<.001). However, the investigational product was significantly more effective than the placebo. No adverse events were observed.

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In the present study, the nasal airflow through each nostril was measured to provide an objective assessment of treatment efficacy. Alergol reduced the airflow decrease after allergen exposure by 66%. The effect of the placebo ointment was only half as large. Therefore, this objective assessment clearly demonstrated that Alergol pollen blocker cream is a safe and effective alternative to the drugs normally prescribed for allergic rhinitis in conventional medicine.

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REFERENCES