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NASAL PROVOCATIVE TEST IN PATIENTS ALLERGIC TO POLLEN

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Abstract: Nasal provocative test (NPT) can be defined as a method for recreating upper respiratory tract response to natural allergens or irritants. It can be used in solving nasal patophisiology problems: establishing whether and how the patient's nose is sensitive to antigens or irritants; quantitative evaluation of sensitivity; establishing factors influencing sensitivity. This method is employed to confirm clinical diagnosis in cases where difficulties arise in interpretation of diagnostic tests. The study based on nasal provocative tests establish an allergy to pollen in cases of pollinosis, and select appropriate components for the desensitising vaccine. Sample group included 53 patients, 29 were females and 24 were males, aged 15–42 years, selected from 1,021 patients diagnosed between 1999–2002 in the Allergology Department of the ENT Department of the MMI. The sample patients were diagnosed based on additional tests with allergic inflammation of the nasal mucosa caused by allergy to pollen of such plants as birch, grass, rye, mugwort and plantain. Research methods included: subjective physical examination, prick tests, total and specific IgE levels in serum, nasal provocative tests and rhinomanometric examination. Allergen solution was administered onto the mucosa with a calibrated atomiser. NPT solutions containing pollen of birch, grass, rye, mugwort and plantain were used. Provocative test was considered positive if, following allergen provocation, rhinomanometric examination revealed an increase in respiratory resistance by at least 40% in comparison with the control test. On the basis of the study, 2 conclusions were drawn: 1) Nasal provocative test is an essential element in diagnostics of allergic nasal obstruction. 2) Rhinomanometry, as an objective method of examining nasal patency, is crucial for evaluating the nasal provocative test.

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INTRODUCTION

In nasal diseases diagnostics, the provocative test is used to confirm the diagnosis of allergic disease, to develop and monitor the therapy, or to evaluate the course of the allergic reaction in scientific research [21]. The provocative test allows evaluation of the reactivity of the nose as the target organ of the allergy, as well as - in uncertain cases or in cases of coexistence of allergies - to establish the allergen which is the source of the symptoms [23]. The nasal provocative test (NPT) with an allergen consists in administering the allergen onto the surface of the nasal cavity mucosa and then evaluating the exacerbation of the symptoms, using objective as well as subjective methods. The allergen is preferably administered on the nasal mucosa by means of an atomiser calibrated in such a manner to which allow for the volume administered nasally to fluctuate by no more than ± 10%. Paper discs impregnated with the allergen (in the amount of 10 µl) are also used. The allergen concentration used in NPT varies depending upon the allergen strength of the extract and the expected level of

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the patient's hypersensitivity. The NPT is conducted using 5 different allergen dilutions. In order to ensure the repetitiveness and comparativeness of provocative tests conducted in the same patient and between patients, standardized allergens should to be used [1, 17, 19].

In NPT evaluation, the following symptoms are taken into consideration: sneezing, nasal catarrh and the level of nasal blockade. In the first minute the sneezing appears, followed in the 2nd-3rd minute by coughing and increase in serum discharge; next, within about 10 min following the provocation, oedema of the nasal mucosa appears. The symptoms begin to subside after about 20–30 min. The evaluation of symptom exacerbation may be too subjective, and therefore the utilization is recommended of a technique which allows an objective assessment of the results of the test: anterior active rhinomanometry, acoustic rhinometry, rhinostereometry and maximal nasal flow [3, 6, 9, 12, 24].

The diagnostics should not always be based solely on the interview, clinical examination, results of the skin prick tests and on the level of specific IgE. A recommendation for NPT is a discrepancy between the interview and the results of additional tests, or between the results of various other tests in case of doubt regarding the diagnosis. Positive skin test and the level of specific IgE result with the chose allergen is not an univocal argument, that symptoms allergic rhinitis are due to contact with this allergen. This proof is not a positive NPT result [7]. According to the experts from the European Rhinologic Society (ERS), NPT is advisable before starting a specific immunotherapy as it is essential to confirm the diagnosis before starting a long-lasting and costly treatment [5, 14].

The aim of the work was to establish a suitable composition of the desensitizating vaccine (created on the basis of the provocative nasal test) for the patients allergic to the pollen of birch, grass, rye, mugwort and plantain.

MATERIAL AND METHODS

The study sample consisted of 53 patients, including 29 females and 24 males, aged from 15–42 (mean age 27.6 years). The subject were selected basing on initial diagnostic tests conducted in 1,021 patients referred to the Allergology Department of the Otolaryngology Clinic of the MMI between 1999–2002, in which allergies of the upper respiratory tract were suspected. Based on allergological diagnostics (interview, clinical examination, results of the skin prick tests and on the level of specific IgE), allergy to pollen of such plants as birch, grass, rye, mugwort and plantain was found in these patients. In the research group, there were no patients who would be allergic solely to birch pollen. The division into 5 groups of patients was based on interviews, clinical examination and positive skin tests, confirmed by the presence of specific allergens IgE against the chosen groups of allergens: group I - subjects allergic to pollen of birch, grass, rye and mugwort; group II - subjects allergic to pollen of birch, grass, rye, mugwort and plantain; group III - subject allergic to pollen of grass, rye, mugwort and plantain; group IV - subjects allergic to pollen of grass, rye and plantain; group V - subjects allergic to pollen of grass, mugwort and plantain.

Research methods included: the interview, clinical examination, skin tests, total and specific IgE levels in serum and nasal provocative tests, evaluated objectively by means of a rhinomanometric test, using the anterior active rhinomanometry method to measure nasal respiratory resistance.

The skin tests were performed with the use of the prick test. The skin of the palmar side of the forearm was covered with 1 drop of each allergen, placed at regular intervals of 5 cm. With the use of special knives, the skin was punctured within the limits of each drop. The same method was used to test the control solution and the 0.1% solution of histamine. The skin reaction was evaluated after 15 min by measuring the dimensions of the urtica and the erythema. A 5-grade scale, suggested by the producer, was used to assess the results. A lack of skin reaction or an erythema of the diameter smaller than 1 mm was described as a negative reaction (-). A small urtica and erythema not larger than 3 mm was defined as a weak positive reaction (+). The presence of a urtica measuring 3 mm was determined as a positive reaction (++), while the one measuring between 3–5 mm with a strong erythema was described as strongly positive reaction (+++). A very intensive reaction with the presence of pseudopodia was qualified as an extremely positive reaction (++++).

The NPT consisted in administration, using the Spray method, of the control solution or the test solution onto the nasal mucosa from a calibrated atomiser. When the

Table 1. Specification of positive NPTs in particular patients groups.

Patient groups	Positive NPT for birch pollen (N = 32)	Positive NPT for grass pollen (N = 53)	Positive NPT for rye pollen (N = 50)	Positive NPT for mugwort pollen (N = 47)	Positive NPT for plantain pollen (N = 28)
Group I (N = 25)	21 (84%)	22 (88%)	22 (88%)	24 (96%)	0
Group II (N = 7)	6 (86%)	6 (86%)	6 (86%)	6 (86%)	5 (71%)
Group III (N = 12)	0	11 (92%)	10 (83%)	11 (92%)	8 (67%)
Group IV (N = 6)	0	6 (100%)	5 (83%)	0	4 (67%)
Group V (N = 3)	0	3 (100%)	0	3 (100%)	2 (67%)
Patients with positive NPT	27 (84%)	48 (91%)	43 (86%)	44 (94%)	19 (68%)

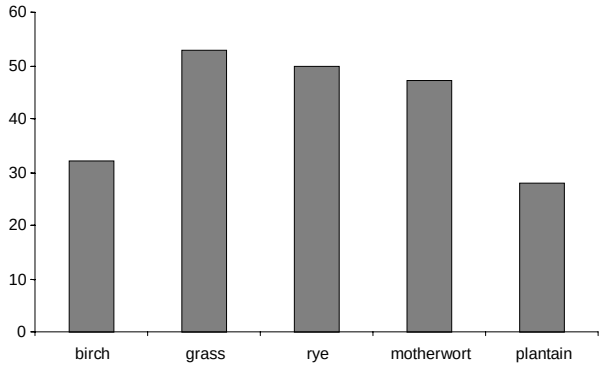

Figure 1. Specification of pollen allergies.

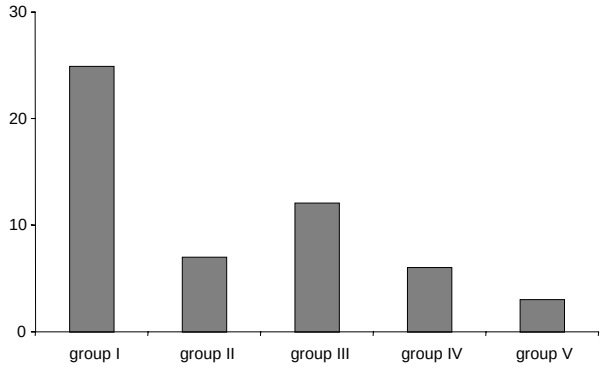

Figure 2. Specification of patients' groups.

solution was ready, the atomiser installed and the nasal tip fixed onto it, the patient was asked to blow his/her nose, lean back his/her head, and then to take and hold a deep breath. By pushing the nasal tip of the atomiser, the control solution or the test solution was sprayed onto the surface of the lower nasal concha. The patient then inhaled the air quickly through the nose to avoid the penetration of the lower respiratory tract by the allergen.

The solutions used in the study were standardised NPT solutions with pollen of birch, grass, rye, mugwort and plantain, produced by Allergopharma (Germany). The rhinomanometric tests was performed using a rhinomanometer produced by abcMed. The examined patients were qualified for specific immunotherapy. In order to develop the appropriate vaccine, in all patients nasal provocative tests were conducted using the allergens which had given a positive result in the skin test and an increased specific IgE level.

An initial rhinomanometric test was performed in order to determine the nostril with the better patency, into which the negative control solution was administered. The patient received 0.1 ml of the control fluid solution which acted as a carrier for the allergens used in the following part of the study; the control fluid consisted of 0.4% phenol, dissolved in 0.9% NaCl solution. After 15 min time, control measurement of respiratory resistance was performed. If there were no significant changes in the nasal resistance after the application of a control solution into the nose, a provocation of the allergen was carried out. With the use of an atomizer, 2 doses of the allergen of each of the concentrations mentioned (0.5 BU/ml; 5 BU/ml; 50 BU/ml; 500 BU/ml and 5000 BU/ml) were administered into 1 nostril, each dose comprised 0.05 ml. After 15 min, the result is recorded by measuring the respiratory resistance in the nasal cavity. In the case of a negative result, the measurement was repeated after 30 min. The test was conducted by gradually increasing of the concentration until provocation proved positive. The provocative test is positive when after the provocation with the allergen the air flow diminishes by at least 40% in comparison to the control test. In the case of a positive reaction to the provocation, other responses occurred, such as itching of the nose, sneezing, rhinitis and nose blockade. However, in our test, only the measurements of the respiratory resistance in the nasal cavity in the rhinomanometry are mentioned as they are considered an objective method.

RESULTS

The sample group, 53 patients, amounted to 5.2% of all patients in which the initial test was conducted. In this group, allergy to grass pollen was found in all subjects, allergy to birch pollen in 32 subjects, allergy to rye pollen in 50 subjects, allergy to mugwort pollen in 47 subjects, and allergy to plantain pollen in 28 subjects. The results of positive skin tests were confirmed by the presence of specific allergens IgE.

Group I consisted of 25 patients, group II - 7 patients, group III - 12 patients, group IV - 6 patients, and group V - 3 patients.

Positive NPT results for birch pollen were found in 27 patients (84%), for grass pollen in 48 patients (91%), for rye pollen in 43 patients (86%), for mothewort pollen in 44 patients (94%), and for plantain pollen in 19 patients (68%).

Negative NPT results were least often found in the case of mugwort pollen - 3, as well as birch and grass pollen - 5 each. Rye pollen gave negative NPT results in 7 cases, and plantain pollen in 9 cases. Altogether, NPT results were negative in 30 cases, which amounted to 14.3% of all 210 NPTs performed in the course of the study.

DISCUSSION

The sample group (5.2%) was selected from among all patients referred to the Clinic with suspected seasonal or sporadic allergic rhinitis and qualified for specific immunotherapy. In most subjects (90.6%) an allergy to 4–5 allergens was found. It was therefore necessary to perform a specific nasal provocation in order to determine the appropriate components of the antiallergenic vaccine.

The test performed in the course of the study proved a high consistency of diagnostic tests with NPT for potential allergens; the consistency rate was 85.7%. Results obtained from our study are far better than those of similar studies. Bellussi *et al.* obtained 50% of positive NPT results in a sample consisting of 20 subjects [4],

while Śpiewak and Brewczyński - who performed NPT in 24 patients with documented seasonal allergic rhinitis – obtained negative results in 5 cases (21%) [22].

Following an analysis of each allergen, the consistency of NPT with other tests was undoubtedly very high in the case of mugwort pollen (94%) and grass pollen (91%), which in Poland are the allergens most commonly causing seasonal allergic rhinitis symptoms. For plantain pollen, the consistency rate was 68% [8]. A comparable result was obtained by Granel *et al.*, who performed NPT for plantain in 35 study subjects and obtained positive results in 22 cases (83%) [11].

In our study, 210 specific allergen nasal provocations were performed. The method used was one which is the most convenient from the point of view of cooperation with the patient, and at the same time simple and time-efficient. In most patients it proved necessary to perform 4–5 NPTs, but only 1 such test may be performed per day. In the choice of the method, the key factors are the way the allergen is administered and the way the test results are evaluated. There are many ways of allergen administration. In our study, we decided to spray the allergen by means of an atomiser. The spray method allows for the most even distribution of the allergen, while the size of the particles obtained (over 4 µm) was optimal for keeping them within the nasal cavities [7, 15, 16, 20].

The most commonly used objective method of evaluating nasal patency during NPT is the anterior active rhinomanometry [10, 24]. Most researchers favour the unilateral provocation [2,14]. The choice between uni- or bilateral provocation seems to be affected, amongst other factors, by the study method used. Is it impossible to conduct anterior active rhinomanometry when one of the nasal cavities is obstructed [13, 24]. Performing the NPT according to the principle put forward by the German researchers, namely on the less obstructed side, is justified by the fact that while administering the allergen, complete blockage occurs later on the less obstructed side. It has been found that in most cases during bilateral provocation the oedema which occurs is stronger on one side only. This is why some researchers, while conducting bilateral provocations, use the so-called more reactive side method [16, 18].

In our study, the NPT was performed by spraying the allergen onto the nasal mucosa by means of an atomiser, the allergen was administered unilaterally, and the reaction evaluated through frontal active rhinomanometry.

CONCLUSIONS

On the basis of the above study, the following conclusions were drawn:

1. The nasal provocative test helps to diagnose the exact allergens eliciting the allergic rhinitis.

2. Thanks to the nasal provocative test, a precise composition of the desensitizating vaccine may be established.

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