

Optical rhinometry: Application on children and adolescents for nasal provocation tests

Mittenzwey H, Wüstenberg EG, Leupold W. Optical rhinometry: Application on children and adolescents for nasal provocation tests. *Pediatr Allergy Immunol* 2007; 18: 372–377.

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Optical rhinometry is a new method that allows the direct, real time measurement of changes in swelling of the nasal mucosa by external measurement. The measurement is carried out with monochromatic near-infrared light. The change of intensity of the swelling is displayed and recorded. Different preceding studies on adults already showed the reliability and absence of side effects of the measuring method. With the help of a prototype of an optical rhinometer specially developed for children, 65 measurements were performed on a total of 13 children and adolescents having one-sided nasal provocation tests with histamine and allergens, negative provocation tests with control solution and decongestion with xylometazoline. The nasal provocation tests were implemented by optical rhinometry while simultaneously using the established method of active anterior rhinomanometry. We found significant differences between positive and negative provocation tests in both methods ($p < 0.01$). Decongestion was different from all other groups in both methods ($p < 0.01$). No clear connection could be made between the percentage increase of rhinometric extinction and the percentage increase of obstruction measured by anterior rhinomanometry. The evaluation of the nasal provocation test via continuous direct measurement of swelling of the nasal mucosa membrane seems feasible in children. Data which so far could not be measured, such as the beginning of swelling and the time of the maximum state of swelling, might increase the diagnostic validity of provocation tests.

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Key words: optical rhinometry; nasal provocation test; allergens; rhinomanometry; children

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Accepted 14 August 2006

Objective measurement of changes in swelling of the nasal mucosa is particularly important for diagnosing allergies (1, 2, 4, 7, 9, 13, 14, 15). Nasal provocation tests serve to prove the clinical relevance of an allergen and thus the connection between sensitization and symptoms. Changes in swelling of the nasal mucosa, such as those which occur during nasal provocation tests, can be measured using a variety of methods. The standard method for this is active anterior rhinomanometry (2, 3, 8, 9, 11, 12, 14, 15), which measures changes in nasal swelling indirectly by a change in the resistance of the nasal airway. Anterior rhinomanometry of children in particular can be problematic due to the relatively unpleasant measurement procedure (7). Septum perforation, choanal atresia and lack of pressure due to nasal polyposis can make the

measurement impossible. Nasal swelling can also be measured directly using relatively elaborate procedures such as acoustical rhinometry, ultrasound, computerized and magnetic resonance tomography (11, 12).

Optical rhinometry is a new method that allows the direct, real time measurement of changes in mucosal oedema of the nose via external measurement with a measuring head consisting of a light emitter and an optical receiver (5, 6, 16). In this procedure, the nose is radiographed with monochromatic light in the near-infrared wavelength range and the change of the light absorption by the nasal tissue is documented over time. In case of a nasal congestion caused by an inflow of blood, more light is being absorbed which leads to an increase of light extinction by the nasal tissue. Therefore,

statements can be made on the extent of the swelling in the nose based on the light absorption compared with the initial intensity. Measurement is based on a proportional absorption of the light transmission or increase of the extinction for mucous membrane swelling, which corresponds to an inflow of blood and water into the swelling tissue. Because of the continuous measurement, nasal provocation tests can be monitored in real time using this procedure.

A study has proven the reliability and absence of side effects of this measuring method on adult patients (16). The aim of the present study was to test the applicability of this procedure on children for nasal provocation tests.

Methods

The required nasal provocation tests were implemented via optical rhinometry while simultaneously using the established procedure of anterior rhinomanometry so no additional risk resulted. Experience of measurements in adults led the authors to believe that problems were to be expected when applying the procedure to children. Previous measurements showed that the endonasal swelling during nasal provocation is largely caused by an inflow of blood (6, 16). For this reason, the number of light sources was reduced and a wavelength of 800 nm was selected as this is at the isobestic point of haemoglobin, i.e. a point at which reduced and oxidized haemoglobin have the same absorption properties. Therefore, the change in blood volume in the radiographed tissue is measured via the absorption of haemoglobin, and oxygenization artefacts can be ruled out (Fig. 1).

As children's noses are smaller than adults', the light extinction caused by the nose was

measured before the actual measurement after the sensor is attached. The light intensity at the emitter was then regulated automatically based on the strength of the detector signal, so that the light intensity was in the optimal measurement range of the detector. The light intensity set was not changed after this process.

In order to avoid having to make measurements in a darkened room or artefacts caused by ambient light, inconstant light irradiation with a frequency modulation was selected using modulation technology. Only signals with this frequency modulation are recorded by the detector. Moreover, the signal was demodulated phase synchronously on the detector side, allowing the phase of the light to be incorporated in identifying the correct signal.

Patients from the allergy department of the paediatric clinic at the University of Technology in Dresden took part in the study. The examinations required to diagnose their allergic illness, including the provocation tests, were carried out in the allergen test laboratory of the paediatric clinic.

The study was approved by the local ethics commission (EK81042004) and written consent was given by the children and their parents. Thirteen children and adolescents aged 5–17 yr were divided into five groups.

Histamine provocation

A one-sided nasal histamine provocation with a histamine concentration of 1 mg/ml was carried out on healthy voluntary non-allergic patients.

Positive allergen provocation

A one-sided nasal allergen provocation with an allergen concentration of 500 SBE/ml was carried out on allergic patients with a suspicious history of allergy and proven sensitization (positive result, increase in extinction).

Negative allergen provocation

A one-sided nasal allergen provocation with an allergen concentration of 500 SBE/ml was carried out on non-allergic patients with a negative history and no sensitization (negative result, decrease in extinction).

Negative provocation

A one-sided nasal provocation with a control solution (negative provocation) was carried out on allergic patients with a suspicious history and proven sensitization.

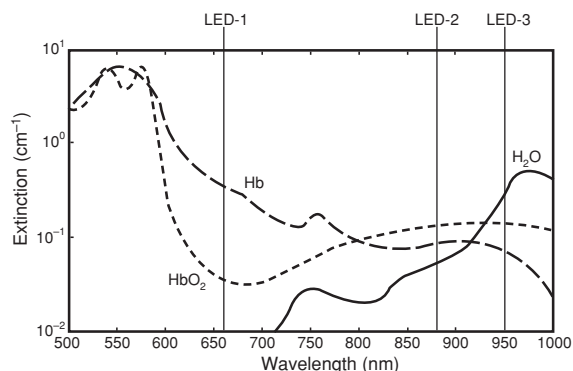


Fig. 1. Extinction spectrum of haemoglobin (Hb), oxidized haemoglobin (HbO₂) and water (H₂O). The position of the wavelength of the light emitter (800 nm) is shown (arrow).

Decongestion

Nasal decongestion with xylometazoline on healthy non-allergic test persons (test persons from group 1).

Inclusion and exclusion criteria

The inclusion criteria for all groups were age (5–17 yr), no history of airway infection within the last 4 wk; for allergic patients (groups 2 and 4) a positive prick test, radioallergosorbent test and corresponding history of sensitization against *Dermatophagoides pteronyssinus*, hazel, birch or *Alternaria alternata* as well as no intake of antiallergenic drugs in accordance with the German Association of Allergy and Clinical Immunology (DGAKI) guidelines (14). Acute infections, ages below 5 and over 17, pregnancy and intake of antiallergenic medicines led to exclusion from the study.

The mean age and gender distribution of the five groups are displayed in Table 1. The distribution of the allergens used in nasal provocation on allergic patients (group 2) and non-allergic patients (group 3) is shown in Table 2.

Active anterior rhinomanometry (Rhinotest 2000, Elektronik Vertriebs GmbH, Böhl-Iggelheim, Germany) was carried out on all test persons in accordance with the recommendations on carrying out provocation tests for the upper airway diseases (14). Optical rhinometry was then carried out according to the following measurement procedure.

Measurement procedure

After performing active anterior rhinomanometry the optical sensor was attached to the test person's nose (Fig. 2), the optimal light intensity was analysed during 2-min period, where the light absorption of the non-provoked nasal mucous membrane (initial measurement value)

Table 1. Gender distribution and mean age

	Group 1	Group 2	Group 3	Group 4	Group 5
Age (yr)	14.2 (±3.7)	13.2 (±4.5)	13.1 (±4.8)	13.2 (±4.2)	10.8 (±4.1)
Male	5	7	9	8	5
Female	8	6	4	5	8

Table 2. Allergen distribution of groups 2 and 3

	<i>Dermatophagoides pteronyssinus</i>	Hazel	Birch	<i>Alternaria alternata</i>
Group 2: positive test	9	1	2	1
Group 3: negative test	2	6	4	1

was determined. Afterwards 0.28 ml (two squirts) of the test substance (histamine-allergen-control solution-xylometazoline) was sprayed into one side of the nose while measurement was in progress and the change in swelling of the nasal mucosa membrane was continuously optically registered. The stock allergen solution was diluted 1/10 for provocation. The allergen concentration used in nasal provocation tests was 500 SBE/ml. The total duration of the procedure was about 15 min. Spectral extinction was then calculated (Fig. 3). In order to guarantee reproducible measurements and to gather objective parameters, a regression fit procedure was applied, in which the extinction data were approximated by a linear function.

Three parameters were recorded (optical rhinometry): t_1 , time swelling begins; t_2 , time



Fig. 2. Optical rhinometry sensor placed on a child.

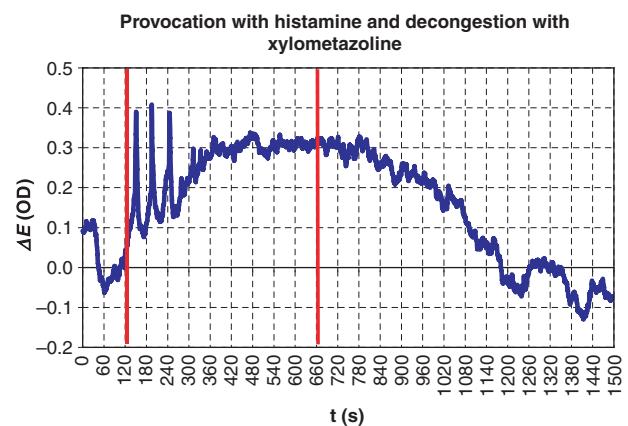


Fig. 3. Continuous measurement of a nasal provocation with histamine and following decongestion with xylometazoline: after set wait period of 2 min provocation with histamine, 9 min later application of xylometazoline. Shortly after provocation with histamine artefacts are depicted, presumably caused by sneezing.

swelling reaches maximum; ΔE , change of extinction of optical densities (OD).

Parameters t_1 and t_2 characterize the chronological development of the swelling. ΔE represents the degree of swelling or deswelling. If a provocation test is positive, the extinction, i.e. the light absorption, should increase due to the swelling of the tissue from t_1 ; by t_2 a stationary state has been reached beyond which the tissue does not swell. After reaching a stable plateau in optical rhinometry another active anterior rhinomanometric measurement was performed.

Statistics

After examination for a normal distribution, the data of both procedures were statistically evaluated with the program SPSS in multiple comparisons using Bonferroni and Mann–Whitney *U*-tests.

Results

Individual groups

Histamine provocation (group 1) Optical rhinometry. After provocation extinction increased in all test persons by an average of 0.32 ± 0.19 OD (Fig. 4). Light extinction increased 3.4 ± 1.7 times after calculating the change of light extinction divided by the noise-measurement. In the chronological evaluation, nasal swelling started on average of 18 ± 34 s after provocation with histamine and reached the maximum after 224 ± 122 s. This group was significantly different to groups 3, 4 and 5.

Rhinomanometry. The average flow decrease was $56.8 \pm 21.3\%$ (Fig. 5). This group was also significantly different to groups 3, 4 and 5.

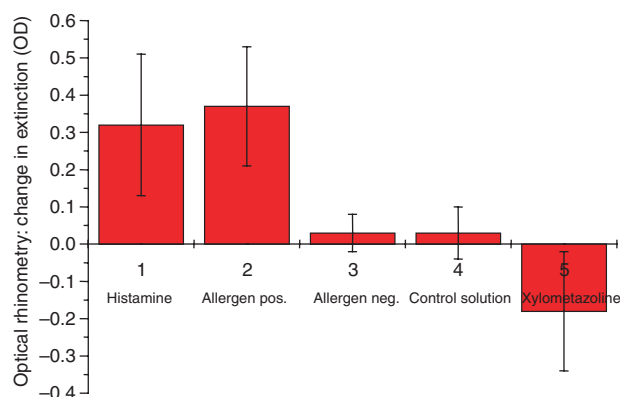


Fig. 4. Optical rhinometry: extinction (optical densities) after nasal provocation. Optical density values are expressed as geometric mean and 95% CI.

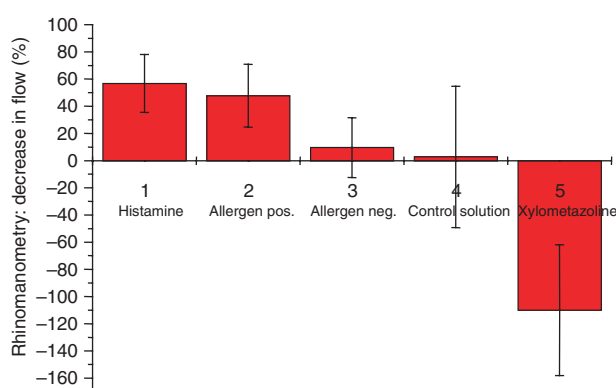


Fig. 5. Anterior rhinomanometry: change in flow after nasal provocation. Flow values are expressed as geometric mean and 95% CI.

Positive allergen provocation (group 2) Optical rhinometry. After provocation extinction increased in all test persons after provocation by an average of 0.37 ± 0.16 OD (Fig. 4). Light extinction increased 3.9 ± 1.6 times after calculating the change of light extinction divided by the noise-measurement. After positive allergen provocation, nasal swelling began after 120 ± 132 s on average and reached the maximum after 330 ± 170 s. This group was significantly different to groups 3, 4 and 5 ($p < 0.01$, multiple comparisons using Bonferroni).

Rhinomanometry. The average flow decrease in this group was $49.3 \pm 17.4\%$ (Fig. 5). This group was also significantly different to groups 3, 4 and 5 ($p < 0.01$).

Negative allergen provocation (group 3) Optical rhinometry. Extinction increased by an average of 0.03 ± 0.05 OD (Fig. 4). Light extinction increased 0.23 ± 0.44 times after calculating the change of light extinction divided by the noise-measurement. This group was significantly different to groups 1, 2 and 5 ($p < 0.01$, multiple comparisons using Bonferroni).

Rhinomanometry. The average flow decrease in this group was $9.6 \pm 22\%$ (Fig. 5). This group was also significantly different to groups 1, 2 and 5 ($p < 0.01$).

Negative provocation (group 4) Optical rhinometry. Provocation with the solvent did not bring about a significant difference in light absorption. Six of the test persons demonstrated an increase in extinction. Light extinction increased 0.03 ± 0.07 times after calculating the change of light extinction divided by the noise-measurement. On average, the increase in extinction was minimal (0.03 ± 0.07 OD; Fig. 4). There was a significant difference between this

group and groups 1, 2 and 5. There was, however, no significant difference to group 3.

Rhinomanometry. The average decrease in flow was $2.75 \pm 52\%$ (Fig. 5). A significant difference to groups 1, 2 and 5 was found ($p < 0.01$). There was no significant difference between groups 3 and 4.

Decongestion (group 5) Optical rhinometry. The extinction decreased in all test persons after xylometazoline was administered. The decrease in extinction was -0.18 ± 0.16 OD (Fig. 4). Light extinction increased 3 ± 2.5 times after calculating the change of light extinction divided by the noise-measurement. On average, decongestion began after 97 ± 100 s. Decongestion reached its maximum state after 183 ± 160 s. This group differed significantly from groups 1 and 2 ($p < 0.01$), but not from groups 3 and 4.

Rhinomanometry. On average, the flow increased by $110 \pm 48.1\%$ (Fig. 5). Group 5 differed significantly from all other groups in the decrease in flow ($p < 0.01$).

A correlation coefficient of $r = -0.57$ is calculated for all five groups by comparing the change of extinction of optical rhinometry and the flow decrease in active anterior rhinomanometry. By enlisting the relative change of extinction (change of light extinction divided by the noise-measurement before provocation), the correlation coefficient was $r = -0.6$.

Discussion

Nasal swelling can be measured indirectly in diagnosing allergies in children in conjunction with a nasal provocation test using standard procedures which includes active anterior rhinomanometry (11, 12). As it is an indirect form of measurement, active rhinomanometry carried out before and after provocation measures the nasal flow and the resistance in the airway via the pressure difference between the external air and that in the choanae. Especially in children active rhinomanometry is often problematic as oral breathing is not possible and active assistance is required (7). Moreover, the attached mask and a blocked nostril might lead to reactions of fear. The test is unpleasant for children if the nose is completely swollen. Insufficient nasal flow, perforation of the nasal septum or a lack of pressure can often make rhinomanometric measurement impossible (7). In contrast, optical rhinometry allows the direct, continuous measurement of nasal swelling without irritating endonasal structures. Nasal conchae and intumescencia septi nasi anterior are

sufficiently incorporated due to the spherical spread of the near-infrared light (5, 6).

Pre-tests and a study with adult patients showed that optical rhinometry allowed the evaluation of nasal provocation tests (6, 16).

Variations of the curves during individual measurements correspond to local vasoregulatory processes, fluctuations in blood pressure, movements of the head and changes in heart rate, which occur to a considerably greater degree in the nose due to the spongy bodies.

When the wavelength of 800 nm is incorporated, there are no major differences compared to the measurements of adults after provocation with histamine (16). In children the extinction was lower than in adults. The differences in the chronological progression of the swelling are not statistically significant. Nasal provocation with histamine is tolerated well and is considered particularly valid with regard to nasal reactivity (2).

After provocation with the allergen, the average increase of extinction in children was 0.37 OD. The higher extinction in adults as shown by Wüstenberg et al. (16) can be explained by the overall smaller noses of children and the resulting lower swelling capacity. However, light extinction caused by the tissue depends on a range of factors, including light distribution and internal anatomic structures, which makes interpretation more difficult (5, 6, 16). In children, allergen-induced swelling begins after 120 s and reaches its maximum after 330 s, compared with 159 and 466 s in adults (16). These differences are not statistically significant. It is physiologically plausible that swelling begins faster after provocation with histamine than with allergens, as the reactive cascade after the application of an allergen does not lead to a discharge of histamine before an immunological reaction is started (14).

The minimal increase of extinction or the decrease in flow after the application of the control solution is most likely a reaction of the mucosa to the mechanical irritation of the squirt, or hypersensitivity to the solvent. The great variability of the rhinomanometric measurements can be explained by the difficulty of working with some children.

After provocation with xylometazoline, the decrease of light extinction is also less prominent in children. The starting point of deswelling in children after 97 s is very similar to that of adults after 128 s. However, a maximum is reached far earlier (183 vs. 454 s). This can be explained by the overall smaller internal nasal structures in children and the smaller mucous membrane surface. One

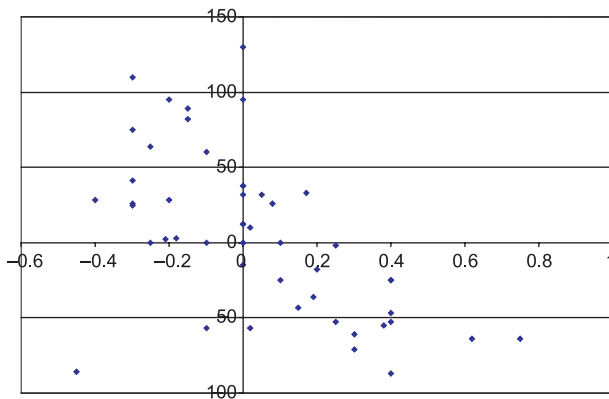


Fig. 6. Correlation between extinction (optical densities) and flow percentage: in comparison of both procedures, there was no clear association between the percentage increase of the rhinometric extinction and the degree of nasal obstruction (decrease in flow).

could also argue that the penetration route to the nasal spongy bodies is shorter. A study by Ohm et al. (10) in 2001 revealed lower nasal reactivity in non-allergic patients provoked with histamine than in non-allergic patients with nasal hyper-reactivity. The real time illustration of the curve progression allows the measurement of early beginnings of a change in extinction, as in the deswelling after administering xylometazoline and briefly effective irritations, which is not the case in procedures which do not measure in real time.

In comparing both procedures, no clear connection could be made between the percentage increase of rhinometric extinction and the percentage increase of obstruction which corresponds to the decrease in flow, as was the case for the study with adults (16; Fig. 6). That could be explained by the fact that the measuring methods are based on different procedures which makes direct comparison more difficult.

The disadvantages of optical rhinometry are the duration of measurement, which requires children to sit still for several minutes and the resulting measurement artefacts caused by movement. Moreover, absolute values cannot be measured, which allows measurements of relative changes, but does not permit comparison between individuals.

Overall, the results of the studies show that the evaluation of the nasal provocation test via continuous direct measurement of swelling of the nasal mucosa membrane is feasible in children and adolescents. Data which until now could not be measured, such as the beginning of swelling and the time of the maximum state of swelling, could increase the diagnostic validity of provocation tests.

Acknowledgment

This study did not receive any external support.

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