FIRST PAGE OF THE MANUSCRIPT

Title

Accuracy of peak nasal flow to determine nasal obstruction in patients with allergic rhinitis

Running title:

Peak nasal flow in allergic rhinitis

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Abstract

Objective: The aim of this study was to further investigate the ability of Peak Nasal Inspiratory Flow (PNIF) and Nasal Expiratory Flow Peak (PNEF) measures to predict symptoms of nasal obstruction. **Methods:** This is a cross-sectional study, carried out in 131 individuals (64 with symptomatic allergic rhinitis and 67 asymptomatic) aged between 16 and 50 years. **Results**: PNIF and PNEF were higher among non-rhinitis. In the curve analysis (receiver operating characteristic), the value of 115 for the PNIF with a sensitivity of 98.4% and specifcity of 87.5% (AUC = 0.99, $p < 0.001$) and 165 in PNEF with a sensitivity of 65.7% and specifcity of 85.1% (AUC = 0.92, $p < 0.001$) was found. **Conclusions:** PNIF and PNEF values were lower in patients with AR when compared to asymptomatic. Our findings present reference values of PNIF and PNEF measures in the evaluation of nasal obstruction symptoms and reinforce the importance to complement the more refined assessment of patients' symptoms. PNEF can be a valuable tool in screening patients and to complement the PNIF measurement.

Key words

Diagnostic techniques, Nasal Obstruction , Respiratory system, Rhinitis.

MAIN BODY OF MANUSCRIPT FOR ORIGINAL ARTICLES

Introduction

Nasal obstruction is a frequent complaint in patients with allergic rhinitis(AR)[1–4]. Studies have shown that this symptom has a significant impact on patients' quality of life, work productivity and sleep quality[1–4]. Patients with persistent and more intense forms of AR even in asymptomatic phases may experience constant mucosal inflammation and chronic nasal obstruction resulting from mucosal inflammation and mucus secretion[1].

In clinical practice nasal obstruction is difficult to quantify[2]. Initial investigations are usually performed based on patients' subjective perception[3]. However, subjective perception of obstruction involves complex mechanisms and some authors[2–5] argue that in addition to patient impression, the association of objective measures may be recommended to complement the assessment.

Peak nasal inspiratory flow(PNIF) and peak nasal expiratory flow(PNEF) are techniques that have been proposed as an objective method to help in understanding nasal obstruction. The PNIF was shown to have a good accuracy[6–8], however we did not find precise diagnostic parameters for the PNEF[4,9]. The main advantage of this objective technique is the fact that it is a low-cost, non-invasive, easy-to-perform method that can be performed in multiple settings, such as clinics, hospitals, and the individual's own home[6,7].

The increasing use of objective methods in research has raised questions about the value that these measures add to clinical evaluation[6–10]. This study was conducted to: (i) further investigate the contribution of objective methods to clinical practice in the evaluation of nasal patency, notably on PNIF and PNEF measurements in patients with rhinitis and without allergic rhinitis and (ii) assess the ability of these measures to predict the symptoms of obstruction, including in patients having difficulty in perceiving their symptoms, to help as a complementary measure in the diagnosis.

Materials and methods

Study design, population and ethical procedures.

This is a cross-sectional clinical study, conducted at the Allergology and Immunology Service of the Clinical Hospital of the Federal University of Pernambuco, Recife, Pernambuco, Brazil. Volunteers were the groups of patients with allergic rhinitis, screened by the regular flow of care in allergy and immunology clinics, otorhinology and allergy of the institution and the control group was individuals without diagnosis of AR and no respiratory complaints.

The comparison group was recruited from a university environment and consisted of people with no clinical diagnosis of allergic rhinitis, no complaints of nasal symptoms, and especially no history of nasal obstruction, confirmed by a clinical symptom score adapted by Gomes et al[13]. Inclusion criteria for the control group were: a final score value of zero and the visual analog scale for nasal obstruction(VAS), with its final value also being zero. The study was approved by the institution's Ethics Committee(nº 063/11). All parents or guardians and the adolescents signed terms of informed consent as requested by the Brazilian regulatory agency.

Inclusion and exclusion criteria

Patients of both sexes, aged 16 to 50 years, whose diagnosis of persistent allergic rhinitis were included[11]. Those with diagnosed asthma or history suggestive of asthma who had a positive response to any of the following data in the clinical history were excluded: previous wheezing crisis, tiredness, recurrent wheezing after physical activity without investigation, dry night cough for no apparent reason or other respiratory diseases that compromise pulmonary or nasal function. Those who were on regular medication for nasal symptoms including: topical corticosteroids and systemic vasoconstrictors, antihistamines at the time of the study, or who had used them for four weeks prior to the study. Those who used nasal decongestants in the last 48 hours, patients with endoscopic findings of marked septum deviation and signs suggestive of concomitant acute infectious sinusitis. Smokers, asthmatics, or individuals with upper respiratory tract infection at the time or 15 days before data collection were also excluded. Cognitive level alteration that compromised the technique was also a reason for exclusion.

Instruments and data collection

Definition of clinical diagnosis

The clinical diagnosis of AR was established by a specialist physician based on patient history, physical examination and allergic skin test for aeroallergens. Persistent rhinitis was classified by the same specialist according to modified ARIA[12](Allergic Rhinitis and its Impact on Asthma) criteria based on the presence of one or more of the six nasal signs or symptoms that included: nasal congestion, sneezing, rhinorrhea, pruritus, oropharynx, nasal and ocular pruritus for more than four days a week or more than four weeks before admission. All patients had positive aeroallergen pick-tests.

Clinical evaluations

Patients from both rhinitis and non-rhinitis groups underwent subjective evaluation (visual analog scale and clinical score) and objective evaluations of the PNIF and PNEF by independent examiners.

Patients with AR were referred to one of the researchers after consultation with a specialist, prior to any prescribed drug intervention. Initially they were asked about the perception of nasal obstruction using the VAS presented in a color grading, taking as reference the light blue color, at the far right of the scale that corresponded to the absence of nasal obstruction and at the far left, represented by the red color that corresponded to the nose completely blocked. Subsequently, they marked a point on the scale that seemed to them more corresponding to their nasal obstruction state. The color grading presented to the patients was visualized by the researcher on a scale numbered from 0 to 10, graduated in mm and after the patient registration the corresponding point was recorded by the researcher. To perform the appointment it was necessary that the patients had no doubts about the appointment.

The clinical score of nasal symptoms, adapted by Gomes et al[8]., was used to evaluate the intensity of rhinitis through nasal symptoms that included: nasal congestion, sneezing, rhinorrhea, oropharyngeal pruritus, nasal and ocular pruritus. We used a scale from zero to 3 points, where zero indicated absence of symptoms, 1 mild symptom point, well tolerated, does not interfere with sleep or daily activities, 2 well defined symptom points, uncomfortable, interfering only with activities that require greater concentration, but does not interfere with the patient's routine, 3 points- Intense symptom, very uncomfortable, poorly tolerated, making it difficult to

sleep and activities daily activities. The total score ranged from 0 to 18 points allowing AR to be classified as mild (1-6 points), moderate (7-12 points), or severe (13-18 points) [8,11]. The comparison group performed the same subjective measures as the criterion for inclusion in the study with the final VAS result and the nasal symptom score equal to zero.

Evaluation of Objective Measures

Patients with allergic rhinitis were asked to perform nasal hygiene to eliminate secretion prior to verification of the PNIF and PNEF. The PNIF was measured by the nasal inspiratory peak flow meter (In-Check Nasal Clement Clarke, England), with the patient sitting comfortably wearing a face mask that was held by one of the researchers' hands on the patient's face, with a necessary pressure to prevent air leakage. Patients were instructed to perform maximal inspiratory effort through the nose with the lips closed. The maneuver was repeated three times, and the largest of the three measurements was recorded, with a variation up to 10%.

PNEF measurements were obtained using the peak expiratory flow meter (Assess peak flow meter respironics, New Jersey) where a face mask was fitted through a universal connector. The patient was seated in a comfortable position, with the mask fixed by the hand of one of the researchers on the face, with a pressure necessary to prevent leakage or air leakage. The patients were instructed to perform maximal expiration through the nose with their lips closed after maximum inspiration from the residual volume. Three measurements were taken in a row, the largest one being considered, considering a variation between them of up to 10%.

Statistical analysis

Data were processed and analyzed using the Statistical Package for the Social Sciences(SPSS, version 20.0). The Kolmogorov-Smirnov test was applied to test the normality assumption. Mean and SD were used to present continuous variables, while categorical data were presented using absolute and relative frequencies. Bilateral values of p were calculated, and the significance level adopted was 5%. T test was used to evaluate the comparison between the means in the different groups

To assess the cutoff point of PNIF and PNEF, a ROC curve was plotted and the area under the curve was calculated. From the value found in PNIF and PNEF we calculated the positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio.

Results

A total of 131 individuals (69.5% men) participated in the study, of which 75 (57.2%, Control group. Among the 64 subjects with rhinitis, most had moderate rhinitis(65.6%). (Table 1).

Peak inspiratory flow and Peak expiratory flow were higher among non-rhinitis, even when separated by gender (Table 2). In non-rhinitic patients, men had higher peak flows.

Figure 1 shows the analysis of the ROC curve for the PNIF (sensitivity of 98,4% and specificity of 87,5%) and PNEF (sensitivity of 65,7% and specificity of 85,1%), with area under the ROC curve of 0.99 and 0.92 (95% CI,0.97to1.00 and 0.92to0.97, respectively; both $p<0.005$).

The predictive values (positive and negative), accuracy, and likelihood ratio values (positive and negative) are in Table 3.

Discussion

This study examined the utility of PNIF and PNEF measurements as objective precision parameters for the diagnosis of obstruction in patients with allergic rhinitis. Our results show lower PNIF and PNEF values in patients with AR when compared to normal individuals and present reference values in the understanding of the evaluation of nasal obstruction symptoms in rhinitis.

Most patients with allergic rhinitis are affected by nasal obstruction[4–11]. This symptom is particularly important in patients with persistent allergic rhinitis because even during asymptomatic periods of the disease, mucosal inflammation and nasal congestion may persist to a lesser extent[4–11]. However, some patients may find it difficult to reliably identify the presence and the intensity of nasal obstruction due to chronic symptoms or lack of normal breathing. Standardized measures may be an interesting alternative to complement the assessment of these patients making them more aware of nasal obstruction These measures may also be used in epidemiological research[4–11].

Teixeira et al.,[11] studying PNIF as a tool for assessing nasal patency in 78 individuals aged 19 to 67 years without rhinitis and with allergic rhinitis also showed lower PNIF values(114l/min) in individuals with rhinitis compared to individuals

without allergic rhinitis(154.3l/min). Thus, reduced nasal flow in patients with allergic rhinitis may be a proxy for nasal obstruction, because the nasal flow of these patients is quantitatively limited in relation to the normal values described[6,13]. To date no reference values have been described for adult patients with nasal obstruction, therefore the interpretation of these reductions is limited in terms of their clinical impact. However, studies have shown that a 20l/min difference is a clinically significant difference due to the high intra and inter-individual variability of PNIF results[14].

The study by Klossek et al.,[15] evaluated the PNIF of normal individuals in the French population and presented normal values below those found in other countries[13,16] and in our comparison group. However, it is important to consider the difficulty in establishing standardized PNIF measurements, as ethnic factors as well as participants' individual characteristics such as height, age and gender may influence the measurement[15]. In a recent study[17], unilateral PNIF was evaluated and normal values for adults were presented with values similar to those already described in the literature[17], showing a positive correlation for gender, height and inverse correlation with age. However, when considering unilateral PNIF and PEF, only height was a significant variable[17].

Reference values of the PNEF for the adult population are not widely reported in the literature[18]. Values around 260l/min have been reported as possible normality, although there is no range of altered values expected for individuals with Allergic Rhinitis[19]. Therefore, this hinders the ability to predict PNEF results in patients with AR and without rhinitis.

Our group previously demonstrated a strong positive correlation between PNIF and PNEF(c.c=0.74). However, despite this correlation, PNEF had little explanatory capacity(R^2=0.551) over PNIF. And therefore, it would not be recommended to replace the PNIF measures with the PNEF measure only[19].

Some authors have suggested whenever possible the association of objective measures to better evaluate the obstruction symptom in allergic rhinitis[7,20]. PNIF has often been studied in association with PEF, as reduced PNIF values may express reduced ventilatory capacity rather than nasal obstruction[21].

Historically PNIF has been successfully used for drug evaluation in the treatment of allergic rhinitis in adults, young people and children[22]. Part of the studies show that PNIF increases with the improvement of nasal obstruction symptom[1,23].

However, due to the complexity of subjective perception, the correlation between PNIF and nasal symptoms has been questioned by several studies[7,20].

Recently, there has been an attempt to further investigate PNIF and PNEF as a diagnostic tool for clinical practice, however these procedures have usually been studied separately and there is no consensual way of correlating them[24]. In our study, we further tested the ability of PNIF and PNEF measurements to predict nasal obstruction symptoms through the performance of the ROC curve for PNIF and PNEF. Both evaluative methods performed well in identifying the presence of rhinitis, as indicated by the area under the curve (AUC) for PNIF (AUC=0.99) and for PNEF (AUC=0.92). The data also showed that PNIF is more sensitive in identifying the presence of rhinitis, while PNEF performs better in identifying negative conditions for allergic rhinitis. In the same manner, positive predictive values indicate that PNIF showed lower performance, since among patients with altered PNIF, the probability of rhinitis was 73%, compared to 84.8% for PNEF. However, the inverse occurs with the analysis of negative predictive values, since PNIF has a higher value (NPV=97.8) than PNEF (NPV=87.7). When analyzed globally, in terms of accuracy, which indicates the proportion of correct answers in relation to all possible outcomes, PNEF presents better overall performance (PNIF=81.7 and PNEF=86.3).

The same degree of specificity found in our study was also observed by Schwanz-Starling et al.,[9] when evaluating the reproducibility of the PNIF measurement in patients with rhinitis. The authors demonstrated that PNIF measurements may reflect the severity of nasal rhinitis symptoms in young adults. The use of PNIF has also been evaluated in patients undergoing tonsil removal surgery. Bathala and Eccles[25] demonstrated that 72% of patients had a 22% increase in PNIF values after tonsillectomy.

A recent study evaluated PNIF after patients underwent functional rhinoseptoplasty. In this study, Fuller et al.,[24] demonstrated that the nasal obstruction(Nose) scale score is lower in those patients with higher nasal PNIF values, which indicates a convergence between the two methods regarding the improvement of airway patency. Despite this, the data revealed a weak correlation between the two measures. Thus, these authors consider the use of PNIF as a diagnostic measure, although they emphasize the possibility of this tool as a follow-up measure in the prognosis of patients undergoing septum correction surgery.

A possible limitation of the study was not to carry out a follow up of these

patients according to the clinical response to treatment to evaluate the change of parameter settings. That way, all assessments could have been repeated after 15 days to make sure of reproducibility. Even so, this research has strengths as it is a pioneer in the analysis of symptom scores, visual analog scale, PNIF and PFEF.

Conclusions

Our findings reinforce the importance of PNIF and PNEF measures to complement the more refined assessment of patients' symptoms. The performance of the PNEF ROC curve gives us about this objective evaluation parameter, as this measure can be a valuable tool in screening patients who seek to exclude rhinitis symptoms and to complement the PNIF measurement.

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TABLES

Table 1- General characteristics of recruited individuals.

Variable	Total (n=131)
Age (years)	26,8 ± 8
SEX	
Male	91 (69.5)
Female	40 (30.5)
Education Level	
Undergraduate	75 (57.2)
Graduate	56 (42.8)
Symptom score system (Allergic rhinitis, n=64)	
Light	13 (20.3)
Moderate	42 (65.6)
Severe	09 (14.1)

Data were expressed as mean ± standard deviation or absolute numbers (%).

Table 2. Peak nasal inspiratory flow and Peak nasal expiratory flow by sex.Peak nasal inspiratory flow and Peak nasal expiratory flow by sex

Variable	SEX	Rhinitis	Without rhinitis
PNIF	**General**	65.94±18.32 [a]	130.73±26.64 [a]
	Male	70.0±15.95 [b]	145.0±29.75 [b g]
	Female	65.0±18.84 [c]	120.5±18.63 [c g]
PNEF	**General**	108.36±56.87 [d]	212.54±48.88 [d]
	Male	130.8±71.54 [e]	232.9±50.47 [e h]
	Female	103.2±52.39 [f]	198.0±42.62 [f h]

Data were expressed mean ± standard deviation. Same letters indicated statistically significant differences between pairs, considering $p \leq 0,01$ from test *t* onwards for independent samples.

Table 3. Sensitivity, specificity, predictive values and likelihood of PNIF and PNEF.

Sensitivity, specificity, predictive values and likelihood of PNIF and PNEF.

	PNIF (Cutoff point = 115)	**PNEF (Cutoff point = 165)**
Sensitivity	98,4	87,5
Specificity	65,7	85,1
positive predictive value (VPP)	73,3	84,8
negative predictive value (VPN)	97,8	87,7
Accuracy	81,7	86,3

Figure legends

Figure 1. Area under the curve from Peak nasal inspiratory flow (PNIF - A) and Peak nasal expiratory (PNEF-B). AUC = Area under the curve; CI = confidence interval