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Correlation Between Peak Nasal Inspiratory Flow Measurements and Subject Allergy Symptom Assessments in the Environmental Exposure Unit

EEU The Environmental Exposure Unit

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Abstract

Rationale: Besides using symptom assessment to evaluate disease severity in allergic rhinitis patients, a simple, inexpensive, robust method – peak nasal inspiratory flow (PNIF) can be used to provide an objective measure of nasal patency. The purpose of this work is to evaluate the correlation between PNIF measurements and subject assessment in participants with induced seasonal allergic rhinitis symptoms.

Methods: Pre-dose data from a randomized, double-blind, four-way crossover study (NCT03443843) for allergic rhinitis was analyzed. Participants scored their allergy symptoms and performed PNIF measurements at pre-defined time points during a two-hour ragweed pollen exposure in an Environmental Exposure Unit (EEU). The relationships between PNIF and several symptom composite scores were determined through calculation of the Spearman rank correlation coefficients.

Results: Statistically significant, moderate correlations were found between PNIF and various nasal symptom endpoints following allergen exposure (TNSS, T3NSS, and the nasal congestion score). In contrast, there were no consistent correlations found between PNIF (a nasal airflow measurement) with ocular symptoms (TOSS) or a symptom composite that included ocular symptoms (TSS).

Conclusions: A significant correlation exists between nasal airflow PNIF measurements and subject nasal symptom scores, showing as PNIF values increase, nasal symptom composite scores decrease. Nasal airflow measurements can provide another perspective of allergic rhinitis disease severity.

Introduction

In clinical studies of allergic rhinitis, changes in symptom severity is commonly assessed by subjects. In addition to self-assessment, other aspects of nasal obstruction have been evaluated by measuring airflow through the nose via peak nasal inspiratory flow (PNIF) – a simple, inexpensive, and sensitive tool. Some research has found PNIF correlate with subject assessment of nasal symptoms.[1-9]

The Environmental Exposure Unit (EEU) is a controlled environment in which a uniform amount of allergen is released over a specified time frame. This unique testing methodology allows for the conduct of multiple allergic rhinitis studies at different times using comparable settings.[10,11]

Objective

The objective of this work was to investigate the relationship between peak nasal airflow intake and subject symptom assessments in allergic rhinitis study participants following exposure to ragweed pollen in the EEU.

Methods

The EEU study (NCT03443843) consisted of a screening visit, a priming period, and additional four periods separated by 14-day washouts. Participants were healthy volunteers between the ages of 18 and 64, with a history of seasonal allergic rhinitis confirmed by a positive skin prick test for the ragweed pollen. On four separate days, participants were exposed to two hours of ragweed pollen in the EEU to induce allergy symptoms. On each testing day, participants scored their allergy symptoms and measured their PNIF prior to exposure and at pre-defined time points: 30, 60, 90, 120 minutes after the start of pollen exposure. Participants rated a series of nasal and ocular symptoms on a 4-point scale, identifying the severity of each one as either "none"(0), "mild"(1), "moderate"(2), or "severe"(3). The six allergy symptoms evaluated were nasal congestion, sneezing, itchy nose, runny nose, itchy eyes, and watery eyes, yielding a possible maximum total symptom score (TSS) of 18. Other symptom score composites summarized in Table 1 are: Total Nasal Symptom Score (TNSS), Total 3 Nasal Symptom Score (T3NSS), Total Ocular Symptom Score ((TOSS). Immediately following symptom assessment by the participants, nasal airflow measurements were obtained using a Peak Nasal Inspiratory Flow Meter (In-check™, UK). Participants were trained prior to the beginning of each exposure visits, on how to correctly use the PNIF meter to collect nasal airflow measurements. The standard method of collecting PNIF measurement is to record the highest one of three PNIF measurements at each time point. The relationships between PNIF and various symptom composite scores were determined through calculation of the Spearman rank correlation coefficients.

Table 1. Description of the Symptom Composite Scores

Name of Symptom Composite	Symptoms Included	
Total Nasal Symptom Score (TNSS)	• Nasal congestion • Sneezing	• Itchy nose • Runny nose
Sum of 3 Nasal Symptom Scores (T3NSS)	• Sneezing • Itchy nose	• Runny nose
Total Ocular Symptom Score (TOSS)	• Watery eyes	• Itchy eyes
Total Symptom Score (TSS)	• Nasal congestion • Sneezing • Itchy nose	• Runny nose • Itchy eyes • Watery eyes

Results & Discussion

Seventy-seven participants completed the four-period crossover study and their data included in this per-protocol analysis. Mean PNIF values declined progressively over the course of two-hour pollen exposure sessions, with higher PNIF values at pre-exposure baseline upon entering the EEU and lower values after 120 minutes of pollen exposure. (See Figure 1) In comparison and as expected, mean symptom scores increased progressively for each of the composites: TNSS, T3NSS, TOSS, and TSS, following allergen exposure.

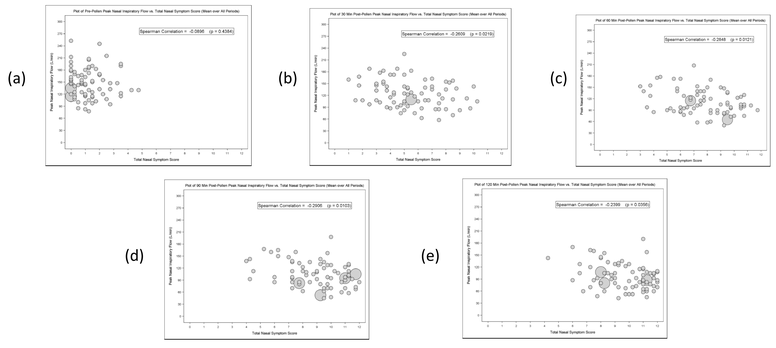
Spearman rank correlation analysis revealed significant inverse correlations between PNIF and subject-rated nasal symptom scores. It is a non-parametric statistical test that assesses the degree of association between two variables, in this study PNIF (a continuous variable) and the selected symptom composite score (an ordinal variable), and its use does not require the assumption of a specific distribution for the underlying data. The values of PNIF was found to vary inversely with subject assessments – as symptom scores increased due to more severe symptoms, nasal airflow decreased reflecting less airflow through restricted nasal passages.

Table 2 reports the measure of significance between PNIF and various symptom composite scores from 30 to 120 minutes after the start of pollen exposure. Prior to entering the EEU when there was no exposure, no significant correlation exist between PNIF and TNSS (p=0.4384), T3NSS (p=0.5774), and Nasal Congestion Score (p=0.6755). As exposure continued, the correlations between PNIF and TNSS or T3NSS became significant from 30 to 120 minutes. For nasal congestion, significant correlation started to occur at 60 minutes and remained significant until the end of exposure. Additionally, the change in PNIF from baseline (CFB PNIF) were shown a moderate strength of correlation with the nasal symptoms. With all time points included, CFB PNIF varied with TNSS, T3NSS, and Nasal Congestion and the Spearman correlation coefficients were -0.57, -0.53, and -0.53, respectively.

Table 2. Significance of Spearman Correlations between Peak Nasal Inspiratory Flow (L/min) and Allergy Symptom Composites and the Correlation Coefficients Assessed using Change from Baseline (CFB) PNIF at different time points after the start of pollen exposure.

Significance (p-values) of the Correlation	30-min	60-min	90-min	120-min
PNIF and TNSS	0.0219*	0.0121*	0.0103*	0.0356*
PNIF and T3NSS	0.0181*	0.0249*	0.0313*	0.0518
PNIF and Nasal Congestion Score	0.1089	0.0147*	0.0025*	0.0346*
PNIF and TOSS	0.6444	0.5486	0.3994	0.3925
Spearman Coefficients	**30-min**	**60-min**	**90-min**	**120-min**
CFB PNIF and TNSS	-0.61*	-0.57*	-0.51*	-0.38*
CFB PNIF and T3NSS	-0.60*	-0.53*	-0.48*	-0.37*
CFB PNIF and NC	-0.52*	-0.50*	-0.40*	-0.33*

Figure 1. Correlation plots of Peak Nasal Inspiratory Flow (L/min) vs Total Nasal Symptom Score (TNSS) at (a) prior to entering the EEU; and various time points after the start of pollen exposure (b) 30 minutes; (c) 60 minutes; (d) 90 minutes; (e) 120 minutes



Conclusion

This study revealed the presence of a significant inverse correlation between PNIF and subject-rated nasal symptom scores, suggesting that as participants report worsening nasal symptoms (evidenced by increasing TNSS, T3NSS, and nasal congestion), nasal airflow declined (evidenced by decreasing PNIF values and larger change in PNIF from baseline). Measuring peak nasal inspiratory flow is a simple, objective, noninvasive, and reliable way to assess inspiratory flow rates that can be used real-time in clinical studies, and the nasal airflow measurement can provide valuable perspective on the degree of nasal obstruction or restriction within the nasal air passages.

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