The determining factors of peak nasal inspiratory flow and perception of nasal airflow in asthmatics*

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Abstract

Background: The effect of pulmonary pathology on peak nasal inspiratory flow (PNIF) remains largely unknown. We investigated an association between a diagnosis of asthma and of lung function on PNIF when adjusted for possible confounders. Further, we investigated the perception of nasal obstruction in asthmatics compared to healthy controls when adjusted for PNIF.

Methodology: Eighty-seven asthmatics and 92 non-asthmatic controls underwent PNIF (categorized into groups of high, medium and low), acoustic rhinometry (AR) and spirometry, and we assessed symptoms of nasal obstruction on visual analogue scales (VAS) in three categories.

Results: PNIF was significantly associated with asthma and forced expiratory volume in the first second (FEV1) (% predicted). Other factors associated with PNIF were the degree of nasal obstruction measured both subjectively on a VAS and objectively with AR, age and disease status. Asthma patients were 19 times more likely to be in a higher VAS category compared to non-asthmatic controls independent of PNIF group.

Conclusion: Special care has to be taken when interpreting PNIF values in patients with asthma or reduced FEV1 (% predicted). The sensation of nasal obstruction in asthmatics is different from controls despite being in the same PNIF group.

Key words: asthma, rhinitis, Peak Nasal Inspiratory Flow, acoustic rhinometry, spirometry

Introduction

A large body of evidence supports the concept of a unified airway in which signs of disease in one part of the respiratory tract should be considered as a disease of the whole. This concept is sometimes expressed as “one airway, one disease”15-18. Clinical studies show that bronchial provocation with grass pollen extract can induce nasal inflammation19 and nasal allergen challenge in patients with allergic rhinitis can lead to increased airway responsiveness15.

The incidence of asthma is increasing, and the concomitant presence of rhinitis and chronic rhinosinusitis with asthma is frequently seen15. Assessment of the degree of sino-nasal dysfunction in asthmatic patients has significant clinical impact since it is important to diagnose and treat pathology in the upper airways to relieve symptoms from the lower airways17,18. It is also known that rhinitis can be the first sign of a lower respiratory tract disorder and the degree of upper airway disease can to some extent determine the severity of lower airway disease15.
A patient’s sensation of nasal patency may be a challenge for the clinician because it can be difficult to relate the subjective feeling to anatomical and physiological variables, such as the internal nasal valve with minimal cross sectional area (10) and airflow. Further, nasal patency assessment with objective measures, such as Peak Nasal Inspiratory Flow (PNIF), has been evaluated in a large number of studies on healthy individuals (11-13), patients complaining of nasal obstruction (14), medical treatment of the nose (15), nasal surgery procedures (16,17) and repeatability (18). However, despite the well-known association between diseases in the upper and lower airways, very few have studied the use of PNIF on patients with pulmonary disorders (19,20).

The aim of the present study was to investigate the effect of a diagnosis of asthma and of lung function on PNIF when adjusted for possible confounders. Further, we investigated the perception of nasal obstruction in asthmatics compared to healthy controls when adjusted for PNIF.

Materials and methods

Study population

A cross-sectional study was conducted on 179 adult subjects consisting of 87 physician-diagnosed asthma patients and 92 non asthmatic controls. The sample, nasal recordings, questionnaires, and additional recordings were extracted from a database described previously (21).

Asthma was defined as the presence of typical asthma symptoms, variable airflow obstruction and in accordance with the British Thoracic Society criteria (22). Variable airflow obstruction was defined by at least one of the two following criteria: an increase of ≥12% and ≥200 ml in the forced expiratory volume in the first second (FEV1) from baseline and after administration of salbutamol, or a positive bronchial provocation test, defined as the provocative dose of methacholine of ≤ 1600µg that causes a fall in FEV1 of at least 20% from baseline. Exclusion criteria were pregnancy, a history of cancer, previous nasal surgery, systemic disease with potential affection of the nose such as granulomatosis with polyangiitis (Wegener’s granulomatosis), cystic fibrosis, primary ciliary dyskinesia, Kartagener’s syndrome and sarcoidosis, and the presence of acute and chronic rhinosinusitis and nasal polyposis on oto-rhino-laryngological examination as defined by the EPOS2012 criteria (23). Control subjects with allergy were not investigated in the pollen season (May-August) and asthmatic subjects were investigated from September 2009 to February 2010.

Written informed consent was obtained from all subjects. The study was approved by the Regional Committees for Medical and Health Research Ethics of Norway and investigations were performed in accordance with the principles of the Declaration of Helsinki.

Peak Nasal Inspiratory Flow (PNIF)

Nasal patency was assessed with a portable PNIF meter (Incheck DIAL, Clement Clarke International, Harlow, Essex, UK). A forced maximum inhalation through the nose from residual volume was performed with the subject sitting in an upright position. Three satisfactory maximal nasal inspirations were obtained, and the mean value was calculated. The scale on the PNIF meter was from 15 to 120 liters/minute (L/min). A flow in excess of 120 L/min was recorded as 120+ L/min, and for the purpose of statistical analysis set to 120 L/min.

Spirometry

Lung function was assessed by flow-volume spirometry measurements (Spirostar USB spirometer, Medikro Oy, Kuopio, Finland) at room temperature. The best FEV1 in liters and percentage of predicted (% predicted) of three acceptable attempts was recorded, in accordance with international guidelines (24). Predicted normal values were based on reference values of Crapo et al. (25). The aim of the present study was to investigate the effect of a diagnosis of asthma and of lung function on PNIF when adjusted for possible confounders. Further, we investigated the perception of nasal obstruction in asthmatics compared to healthy controls when adjusted for PNIF.

Nasal minimal cross sectional area

The cross sectional areas from the nasal orifice to a depth of 5.2 cm into the nasal cavity were assessed with acoustic rhinometry (RhinoMetrics SRE2100, Rhinoscan version 2.5, built 3.2.5.0; Interacoustics, Minneapolis, MN, USA) by two trained operators throughout the study. Recordings were performed according to published protocols (26). Three recordings were made from each nasal cavity. The mean value for each side was calculated from contiguous cross sectional areas from 0 to 3 cm and from 3 to 5.2 cm. To account for variations between nostrils due to the nasal cycle, the average of the two mean values for each partition was calculated. The lower of the two averages was defined as the nasal minimal cross sectional area (MCA cm²).

Allergy

Sensitization to pollen (birch, grass and mugwort), cladosporium, house dust mite (Dermatophagoides pteronyssinus), and animal epithelia (horse, dog, and cat) was determined by skin prick testing (Soluprick SQ, ALK-Abello, Horsholm, Denmark) or measurement of specific IgE (AlaTOP, Diagnostics Products Corp., Los Angeles, CA, USA). Antihistamines were discontinued 4 days prior to the skin prick test. Allergy was defined as a positive test (reaction with a ≥3-mm-diameter wheal or specific IgE concentration of 0.7 IU/ml or greater) and typical symptoms of hypersensitivity on exposure to the allergen(s).

Nasal obstruction

The subjective degree of nasal obstruction during the previous week was assessed on a 100 mm Visual Analog Scale (NO-VAS) and the endpoints were 0 mm (never) and 100 mm (always).
Table 1. Demographic data on asthmatics and controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total, n = 179</th>
<th>Asthma, n = 87</th>
<th>Control, n = 92</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years median, (range)</td>
<td>44 (19-65)</td>
<td>44 (19-64)</td>
<td>44 (20-65)</td>
<td>0.91</td>
</tr>
<tr>
<td>BMI, kg/m² median, (range)</td>
<td>25.4 (18.0-44.3)</td>
<td>25.7 (18.5-44.3)</td>
<td>25.0 (18.0-35.4)</td>
<td>0.08</td>
</tr>
<tr>
<td>Sex, Male/female</td>
<td>76/103</td>
<td>36/51</td>
<td>40/52</td>
<td>0.78</td>
</tr>
<tr>
<td>Allergy n (%)</td>
<td>72 (40)</td>
<td>52 (60)</td>
<td>20 (22)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking status: Ever/Never</td>
<td>32/147</td>
<td>11/76</td>
<td>21/71</td>
<td>0.08</td>
</tr>
<tr>
<td>Level of education in year</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≤ 9 years n (%)</td>
<td>36 (20)</td>
<td>15 (42)</td>
<td>21 (58)</td>
<td></td>
</tr>
<tr>
<td>10 to 12 years n (%)</td>
<td>75 (42)</td>
<td>47 (63)</td>
<td>28 (37)</td>
<td></td>
</tr>
<tr>
<td>≥ 13 years n (%)</td>
<td>68 (38)</td>
<td>25 (37)</td>
<td>43 (63)</td>
<td></td>
</tr>
</tbody>
</table>

BMI = body mass index

Statistical analysis

Data were described with median and range for continuous variables and with count and percentages for categorical variables. Crude associations between pairs of categorical variables were assessed with Chi-square tests.

The level of education was categorized as either basic (≤ 9 years), secondary (10 to 12 years), or tertiary (≥ 13 years), that has been shown to be a good surrogate for socioeconomic status in Norway [27,28]. Subject co-morbidity was defined as the regular use of medication during the last 6 months prior to recruitment for asthma and allergy, pain relief, ischemic heart disease and hypertension, musculoskeletal disease, thyroid disorders, diabetes mellitus, anxiety and depression. Disease status was categorized as cardiovascular disease, other disease and no disease. Smoking status was dichotomized as smoker (current or ever smoked) and nonsmoker, as we did not have precise information about cigarette consumption.

NO-VAS was categorized as mild (0-30 mm), moderate (31-70 mm) and severe (71-100 mm)[29]. PNIF was used as a continuous variable for linear regression analysis and as an ordinal variable for ordinal logistic regression analysis. For the latter analysis, PNIF was categorized into the following 3 groups: (1) high: ≥ 120 L/min, (2) medium: 90 - 119 L/min and (3) low: 15 - 89 L/min. Of the spirometry variables, FEV1 is the most robust, and FEV1 (% predicted) was chosen for linear regression as that is based on height, age, sex and ethnicity of the subject. As there was a strong association between asthma and FEV1 (% predicted) (t-test, p < 0.001), we fitted two separate models for PNIF as a continuous variable to avoid multicollinearity. The associations between PNIF and asthma and between PNIF and FEV1 (% predicted) were modeled with linear regression. Possible confounders such as allergy, other diseases, education, NO-VAS, MCA, weight, height, age, sex and smoking were tested. The model fit was good and assumption of normally distributed residuals was fulfilled.

Further, we fitted ordinal logistic regression to assess possible association between VAS (in three categories) and having asthma. PNIF was omitted from the final model as we found the same ratio between having asthma and VAS score when stratified by PNIF group so there was no interaction between PNIF and asthma. The assumption of parallel lines was fulfilled and the model fit was good. The results were expressed as odds ratios (OR) with 95% confidence intervals (CI).

All statistical analyses were performed using PASW Statistics, version 20 for Windows (SPSS Inc., Chicago, IL, USA). A p-value of < 0.01 was considered statistically significant to correct for multiple testing.

Results

Subject characteristics are presented in Table 1. Allergy was present in 60% (n = 52) of asthmatics and 22% (n = 20) of controls. The association between asthma and PNIF is shown in Model 1 (Table 2A). PNIF was significantly associated with asthma, MCA and age (p < 0.01). When all other confounders were kept equal, PNIF was 10 L/min lower in asthmatics than non-asthmatics. Further, PNIF was increased by 4.9 L/min for a 0.1 cm² increase in MCA, and was decreased by 0.4 L/min per one year increase in age.

The association between FEV1 (% predicted) and PNIF was shown in Model 2 (Table 2B). PNIF was significantly associated with
Peak nasal inspiratory flow in asthmatics

Table 2. Multiple linear regression for PNIF as a dependent variable.
A) Model 1: Asthma as an independent variable adjusted for confounders. N=179

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate of β</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma [no=ref]</td>
<td>-10.2</td>
<td>-17.8 to -2.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Allergy [no=ref]</td>
<td>-0.1</td>
<td>-6.6 to 6.4</td>
<td>0.98</td>
</tr>
<tr>
<td>Disease status [no=ref]</td>
<td>-4.7</td>
<td>-8.6 to -0.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Education level [basic=ref]</td>
<td>2.5</td>
<td>-2.1 to 7.0</td>
<td>0.29</td>
</tr>
<tr>
<td>NO-VAS [mm]</td>
<td>-0.2</td>
<td>-0.3 to -0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>MCA [0.1 cm²]</td>
<td>4.9</td>
<td>2.2 to 7.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Weight [kg]</td>
<td>0.2</td>
<td>0.0 to 0.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Height [cm]</td>
<td>-0.1</td>
<td>-0.6 to 0.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Age [years]</td>
<td>-0.4</td>
<td>-0.6 to -0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sex [male=ref]</td>
<td>-3.1</td>
<td>-12.6 to 6.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Smoking [ever=ref]</td>
<td>0.5</td>
<td>-7.2 to 8.3</td>
<td>0.9</td>
</tr>
</tbody>
</table>

B) Model 2: FEV1 (% predicted) as an independent variable adjusted for confounders. N=179

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate of β</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (% predicted) [%]</td>
<td>0.3</td>
<td>0.1 to 0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Allergy [no=ref]</td>
<td>-0.3</td>
<td>-6.4 to 5.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Disease status [no=ref]</td>
<td>-6.1</td>
<td>-9.9 to -2.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Education [basic=ref]</td>
<td>4.5</td>
<td>0.4 to 8.6</td>
<td>0.03</td>
</tr>
<tr>
<td>NO-VAS [mm]</td>
<td>-0.2</td>
<td>-0.3 to -0.07</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>MCA [0.1 cm²]</td>
<td>5.1</td>
<td>2.5 to 7.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Weight [kg]</td>
<td>0.2</td>
<td>0.1 to 0.4</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking [ever=ref]</td>
<td>2.7</td>
<td>-4.9 to 10.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Estimate of beta = the amount of change in the response variable when the explanatory variable is increased by one unit. FEV1 = forced expiratory volume in the first second, MCA = minimal cross sectional area, NO-VAS = nasal obstruction visual analogue scale, PNIF = peak nasal inspiratory flow, ref = reference category for categorical variables.

FEV1 (% predicted), MCA, NO-VAS and other disease (p < 0.01). When all other confounders were kept equal, PNIF increased by 0.3 L/min per % increase in FEV1 (% predicted), and increased by 5.1 L/min for every 0.1 cm² increase in MCA. There was a decrease of 0.2 L/min in PNIF per mm increase in NO-VAS and a decrease of 6.1 L/min in PNIF in subjects categorized with a disease.

Allergy and smoking status were not significantly associated with PNIF in any of the adjusted analyses.

Asthma patients were 19 times more likely to be in a higher VAS category compared to non-asthmatic controls (OR = 19.4, 95% CI 7.2-52.5, p < 0.001). The odds ratio was independent of the PNIF group (Figure 1).
Discussion

This study demonstrates that PNIF is influenced by an asthma diagnosis and FEV1 (% predicted), and that asthmatics are more likely to be in a higher NO-VAS category which is independent of PNIF group. Other factors associated with PNIF are the degree of nasal obstruction measured both subjectively on a visual analogue scale and objectively with acoustic rhinometry, age and disease status. Thus in patients presenting with nasal obstruction PNIF recordings should be assessed in conjunction with an asthma diagnosis, spirometry and MCA.

In the present study, PNIF is 10 L/min lower in asthmatics than in non-asthmatics and increases by 0.3 L/min for every % increase in FEV1 (% predicted). Thus, when confronted with a patient with nasal obstruction without an obvious rhinological cause, the possibility of asthma should be considered. The clinician should enquire about lower respiratory tract symptoms suggestive of asthma and seek evidence of variable airway obstruction either with spirometry and reversibility testing or assessing the degree of bronchial hyperresponsiveness. Previous studies show a positive correlation between upper airway patency measured by PNIF and lower airway function measured by PEF in adults [12] and in children and adolescents [39]. Moreover, an increase in PNIF with a concomitant increase in FEV1 (% predicted) has been reported in allergic rhinitis after sauna treatment [31]. PNIF increased by 4.9-5.1 L/min per 0.1 cm² increase in MCA when modeled with respect to an asthma diagnosis (Model 1) or by FEV1 (% predicted) as in model 2. The MCA in our sample was located between 0-3 cm from the nasal orifice in almost all of our subjects (95% of asthmatics and 98% of controls) [21].

The internal nasal valve is generally accepted to be located at a distance of 2-3 cm from the nasal orifice [10,32], and surgical procedures performed at the internal nasal valve improve MCA [33-35]. Improvement in MCA should lead to a significant improvement in nasal airflow as Poiseuille’s law states that flow is directly proportional to the difference in pressure times the radius raised to the fourth power [36], even though modifications due to the complex flow patterns in the human nose must be taken into consideration [37]. Thus, in asthmatics with obstructed noses, surgical intervention with procedures aimed at the internal nasal valve, could lead to an improvement in nasal air flow which in turn might be beneficial for the lower airways.

We have also shown that asthmatics have a different sensation of nasal obstruction compared to non-asthmatics despite being in the same PNIF group. The likelihood of being in a higher NO-VAS category is 19-fold greater in asthmatics than in non-asthmatic subjects. However, the inter-individual variation is large, as confirmed by the wide confidence interval and it is thus difficult to quantify this association with better precision. Despite this, one can speculate whether an increased number of sensory sodium channels and sensory- and secretomotor nerve fibers in the nasal mucosa, that has been reported in allergic and non-allergic rhinitis [38,39], may account for the increased perception of nasal obstruction. The level of perceived breathing difficulty has been reported to be more important than the applied nasal load for the increased propensity of asthmatics to switch to oronasal breathing, compared with non-asthmatic subjects [40]. Premature switching to oronasal breathing results in inadequate conditioning and filtering of the inspired air, with drying and cooling of the lower airways, subsequent release of inflammatory cell mediators and development of an asthmatic response [41] and asthma chronicity.

The main strengths of our study are the large sample size, possibility to compare asthmatics with non-asthmatics, and the complete information of many possible confounders. However, the study has some limitations. Smoking is known to be under-reported, and we only have information about ever- and never smokers. The information about other diseases was self-reported and might be underestimated. The non-asthmatics were individuals recruited from businesses near the hospital or patients attending the hospital for other illnesses, which were thought not to affect the upper and lower airways. Those who chose to participate may have been more interested in their health than the general population, but still we regard measurements on these individuals to be representative for the general population.
There are different PNIF meters in clinical use, and our study is based on In-check DIAL which has a scale from 15 to 120 L/min. A normal value of greater than 120 L/min is commonly used. Regarding the individuals with PNIF > 120 L/min (5 asthmatics and 21 controls), we have performed sensitivity analysis where these individuals were omitted which confirms our original findings.

Mainly turbulent airflow prevails at tidal volumes reached during maximum inspiration and thus PNIF does not reflect the nasal resistance during resting respiration. Possible reasons for inaccuracy of the PNIF include random error and operation errors such as measurement with loose face masks or incompletely closed mouth, but these errors were minimalized by two trained operators throughout the study. The present study emphasizes that special care has to be taken when interpreting PNIF values in patients with asthma or reduced FEV1 (% predicted). The sensation of nasal obstruction in asthmatics is different from controls despite being in the same PNIF group.

Authorship contribution
WMT: Study design, data collection, statistical analysis, paper drafting; MSC: Data collection, paper drafting; VB: Data collection, paper drafting; MC: Statistical analysis; SKS: Study design, paper drafting.

Conflicts of Interest
None declared.

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