Nasal Airway Resistance and Latent Lower Airway Involvement in Allergic Rhinitis

Aparna Iyer¹, Amita Athavale²

Abstract

Introduction: Allergic rhinitis (AR) and asthma are closely linked atopic conditions, often termed as one airway one disease. Nasal airflow obstruction is a cardinal symptom of AR and objective assessment of resistance to nasal airflow in rhinitis can be measured by active anterior rhinomanometry. This study was aimed at correlating the degree of resistance to nasal airflow (NAR) with the clinical severity of allergic rhinitis. In addition, it aimed at determining the proportion of patients with latent lower airflow involvement in AR and studying the impact of ARIA severity grade and NAR on this value.

Materials and Methods: A prospective prevalence study was conducted wherein 32 patients diagnosed with allergic rhinitis underwent determination of nasal airway resistance by active anterior rhinomanometry and lung function evaluation by spirometry. If spirometry was normal; histamine challenge test was performed to check for bronchial hyper-reactivity.

Results: 94% of patients with moderate-severe allergic rhinitis had significantly elevated nasal airway resistance compared to 56% of patients with mild rhinitis. (p=0.014).

71.9% of patients with allergic rhinitis but no symptoms of asthma had bronchial hyper-reactivity with a positive histamine challenge or airflow obstruction on lung functions.

87.5% patients with significantly elevated nasal airway resistance compared to 25% with lower values had lower airflow involvement. (p=0.001).

94% of patients with moderate-severe rhinitis and 83% of patients with persistent rhinitis compared to 50% patients with mild and 44% with intermittent symptoms had lower airways involved. (p<0.05)

Conclusions: Significantly greater proportion of patients with moderate-severe and persistent allergic rhinitis had elevated nasal airway resistance values.

72% patients with allergic rhinitis had lower airflow involvement despite having no symptoms of asthma, prevalence being greater in patients with severe and persistent disease.

Proportion of patients with lower airway hyper-responsiveness is significantly higher among patients with raised nasal airway resistance as determined by rhinomanometry.

This study thus concludes that measurement of nasal airway resistance determined by active anterior rhinomanometry is a good objective tool to measure severity of nasal obstruction in allergic rhinitis with good correlation with the ARIA clinical severity grade. It may also be a promising tool to identify allergic rhinitis patients who are at a higher risk of having latent lower airflow involvement.

Introduction

Allergic rhinitis (AR) is a symptomatic disorder of the nose induced by an IgE mediated inflammation after exposure of the membranes of the nose to allergens.1 AR has been classified into four categories as per duration of symptoms (intermittent/persistent) and grade of the disease (mild/moderate-severe).1 Further; both intermittent and persistent disease can have mild or moderate-severe symptoms. Prevalence of allergic rhinitis in adults is estimated at 17-28% in Europe and incidence has been on the rise in parts of the world where it was low earlier especially in Asia.2

Cardinal symptoms of AR are sneezing, mucus discharge and nasal obstruction. Rhinitis is often associated with a sensation of obstruction to airflow through the nose which is termed “nasal dyspnoea.”3 Active anterior rhinomanometry (AAR) is the measurement of resistance encountered by air passing through the nasal cavity and is an objective method of assessing the nasal airway resistance.4

The relationship between AR and asthma is of paramount importance as AR is known to precede the development of symptomatic asthma- also called ‘the allergic march’. Prevalence of asthma in AR has been estimated at 15-38%.5

A longitudinal study from asthma surveys conducted in 1968, 1974 and 2004 revealed that childhood allergic rhinitis was associated with a significant 2- to 7-fold increased risk of incident asthma in preadolescence, adolescence, or adult life.6 This risk is likely to be higher in moderate-severe rhinitis.7

Studies in patients with AR who did not have symptoms of asthma have shown evidence of inflammation in lower airways, in BAL fluid, bronchial biopsy and induced sputum.1,8
Asthma is characterized by reversible airflow obstruction and FEV1 and its ratio with FVC are considered the main parameters to evaluate the same. There is an increasing interest to consider the involvement of small airways in the pathogenesis and forced expired flow at 25% and 75% of the pulmonary volumes might be considered as a measure of the caliber of the distal airways, particularly in subjects with normal FEV1.

Bronchial hyper-reactivity is another important feature of asthma. Patients with AR frequently have increased airway reactivity to methacholine even though they may not have symptoms of asthma or abnormal spirometry. Although AR does not appear to be a serious disease as it does not have significant mortality or morbidity, it causes significant disturbance to quality of life and economic burden due to frequent loss of work productivity. Poor quality of sleep, resultant irritability, impairment of cognitive function and impact on scholastic performance are known. Also its propensity to be a harbinger of asthma mandates its early detection and treatment.

Lacunae in knowledge: The severity of AR has traditionally been evaluated by clinical parameters and visual analogue scales. There is a need to identify an objective parameter akin to spirometry in asthma that can grade nasal airflow obstruction in AR as subjective perceptions can be quite variable and inconsistent. The correlation of NAR values with clinical severity of rhinitis is an area that still needs to be researched upon. Also, in children many studies including the ISAAC studies have estimated the prevalence of AR and asthma in AR but data in adults is still understudied. We attempted to prospectively estimate the proportion of latent lower airway involvement in adult AR patients with no symptoms of asthma attending our tertiary care hospital in India.

Aims and objectives of this study:
1. Determine correlation of clinical ARIA severity grade of allergic rhinitis with nasal airway resistance values obtained by active anterior rhinomanometry.
2. Determine prevalence of airflow limitation and bronchial hyper reactivity in adult patients with allergic rhinitis but no symptoms or signs of asthma.
3. Compare the proportion of patients with airflow limitation or bronchial hyper reactivity amongst allergic rhinitis patients with and without significantly elevated nasal airway resistance as determined by rhinomanometry.

**Materials and Methods**

This prospective cross-sectional study recruited 32 adult patients who were diagnosed with allergic rhinitis and referred to the pulmonary medicine department from the department of otolaryngology at our tertiary care hospital.

**Inclusion criteria**

Adult patients diagnosed as having allergic rhinitis and allergic rhino-sinusitis by the department of otolaryngology and referred to the pulmonary medicine clinic

**Exclusion criteria**

1. Patients with diagnosed asthma or symptoms of asthma
2. Patients with confounding respiratory illness such as COPD, Tuberculosis or ILD
3. Patients with absolute contraindications for performing spirometry or bronchial challenge tests
4. Unwilling or unable to provide written informed consent

Patients were diagnosed as allergic rhinitis by the department of otolaryngology on basis of the presence of cardinal symptoms and clinical examination and referred to the department of pulmonology at our tertiary care hospital in urban India. A physician administered the questionnaire for rhinitis and asthma and if asymptomatic for asthma the patient was included in the study. The severity of allergic rhinitis was classified as per ARIA guidelines into mild or moderate-severe and intermittent or persistent rhinitis. The study was conducted after a written and informed consent. Permission to conduct the study was obtained from the hospital institutional ethics committee.

**Rhinomanometry**

Active anterior rhinomanometry was performed wherein a leak free mask with a pressure tube that was inserted to seal one nostril, was used. The patient breathes normally through the patent nostril and the air is passed out through a pneumotachograph which measures flow (Figure 1). The Medisoft Spiroair machine was used to perform the rhinomanometry.

Graphs obtained display the flow in accordance with the pressures and slopes of the curves represent the value of the resistance. The plot displays the curves obtained from both right and the left nostril and the inspiratory and expiratory phase (Figure 1). As per standard guidelines the results were obtained at a pressure of 150 Pa and corrected laminar resistance R (mixte) for each nostril was obtained by Rohrer equation. Total nasal airway resistance
Spirometry and histamine challenge

FVC maneuver was performed to obtain flow-volume loops and values were interpreted as % predicted using S.R. Kamat standards applicable to the Indian population. Post bronchodilator testing was done after 20 minutes of administration of 1 cc salbutamol nebulisation (2.5 mg).

If any evidence of airflow limitation in as determined by FEV1/FVC ratio of <70 % with an improvement of 200 ml and 12 % in FEV1 it was considered significant.

Small airway obstruction as determined by MEF 25-75 <65 % predicted with an improvement of 30 % in post bronchodilator study was considered significant.

In such instances, bronchoprovocation test was deferred. If spirometry was normal, histamine challenge test was performed.

After noting baseline values, serial dilutions of histamine ranging from 0.03mg/ml to 5mg/ml were administered by nebulisation and FEV1 values noted after each dose.

The test was interpreted as positive if the FEV1 dropped by 20% or more from baseline values and negative if no significant drop was noted after administration of 5mg/ml of histamine.

Data thus obtained was analyzed using statistical software to obtain the results.

Pearson chi square was used to determine statistical significance for discrete data and students unpaired ‘t’ test was used for continuous data.

Results and Analysis

Data obtained consisted of nasal airway resistance determined by active anterior rhinomanometry, spirometry and results of the histamine challenge test, conducted on 32 patients with allergic rhinitis.

20 males and 12 females participated in the study. Nasal airway resistance did not vary significantly with gender or age in this study.

50 % (16) patients had mild and 50 % had moderate-severe rhinitis as per ARIA grading.

28 % had intermittent and 72 % had persistent AR.

6/32 patients also had occupational history of exposure to irritants.

Mean NAR in the study population was 1.039 pa /cc/s

Nasal airway resistance (>0.3 Pa/cc/s) was elevated in 24 (81 %) of patients.

Further the results of this study are presented in 4 parts:

1. Nasal airway resistance in allergic rhinitis: Correlation between severity of allergic rhinitis and NAR values:

   a. Mean NAR in patients with clinically mild allergic rhinitis was 0.684Pa/cc/sec and 1.751 pa/cc/sec in patients with moderate to severe allergic rhinitis.

   b. Considering NAR values above 0.3 Pa/cc/sec as significant, 56% of patients with mild allergic rhinitis and 94% of patients with moderate-severe rhinitis had NAR >0.03 Pa/cc/sec. This difference was statistically significant (p=0.014) when analyzed using Chi square test.

   c. 55% of patients with intermittent and 82% of patients with persistent AR had significantly raised NAR values. This difference however was not statistically significant.

2. Allergic rhinitis and lower airway involvement:

   a. 23/32 (71.9%) patients with allergic rhinitis alone had evidence of lower airway involvement when judged by pre and post bronchodilator spirometry or a positive response to histamine, although they had no symptoms of asthma. Of these 1 had an abnormal FEV1/FVC ratio, 20 (66 %) had reduced flow rates in small airways and 2 (6 %) had a positive bronchial challenge test (Graph 1)

   b. Among patients with normal spirometric values and MEF25-75 values greater than or equal to 65%, only two patients reacted to histamine. However, it was noted that both the patients had borderline MEF25-75 values- 65% and 68% predicted respectively, as compared to a much higher average of 93.88% predicted for patients who failed to respond to histamine. None of the patients with MEF25 above 80% reacted to histamine.

3. Relation between the severity of allergic rhinitis and prevalence of lower airway involvement:

   a. 50% of patients with mild and 94% of patients with moderate-severe AR showed evidence of airway pathology in the tests conducted. This difference was highly significant (p= 0.006)

   b. 83% of patients with persistent disease had airway involvement as compared to 44% of patients with intermittent disease. This value was also statistically significant. (p= 0.031)

4. Correlation of objective parameters: Relation between significant nasal airflow resistance and the proportion of patients with airway involvement (Graph 2):

   The relationship was indeed significant (p=0.001), confirming that greater proportion of patients with elevated resistance to airflow in allergic rhinitis had presence of lower airway involvement as determined by spirometry or histamine challenge.

Discussion

Active anterior rhinomanometry has in the recent years, shown promise as an objective modality for assessment in allergic rhinitis.

Values above 0.3 pa/cc/sec have been shown to correlate with symptoms of nasal blockage.\textsuperscript{13,14} Mean NAR obtained in this study revealed a much higher
In patients with allergic rhinitis, there have been ambiguous results in past studies regarding correlation of objective values of NAR and severity of symptoms.\(^{15}\)

If the subjective sensation was altered using coolants like menthol, there was an improvement in subjective scores without a parallel drop in NAR.\(^{16}\)

Apart from functional changes, exercise, smoking and structural abnormalities like deviated septum, sinusitis, polyps can potentially alter nasal resistance. Few studies have shown that AAR can detect a fall in nasal patency in patients with allergic rhinitis after a nasal allergen challenge similar to that seen in the FEV1 after a methacholine or histamine challenge test.\(^{17}\)

In this study it was found that mean NAR value obtained in patients with clinically mild allergic rhinitis was 0.684 Pa/cc/sec whereas a value of 1.751 Pa/cc/sec, i.e more than double the value was obtained in patients with moderate -severe allergic rhinitis.

When comparison between the proportion of patients with significantly raised NAR values (i.e > 0.3 Pa/cc/sec) in the two groups was made, it was observed that a much higher and statistically significant number of patients in the moderate-severe group had elevated NAR values.

As regards the discrepancy obtained in some previous studies, this probably only confirms the multifactor nature of the parameters involved in influencing perception of nasal dyspnea, further reaffirming the need for objective assessments.

Allergic rhinitis and asthma: Allergic rhinitis is a forerunner of asthma and up to 10.5% of patients with allergic rhinitis eventually develop airway disease.\(^{18}\)

Early detection and treatment are essential to prevent loss of lung function and limit morbidity.

71.9% of patients with allergic rhinitis included in this study had evidence of lower airway affection although clinically they had no evidence of asthma.

Among subgroups, 50% of patients in this study with mild and 94% of patients with moderate-severe AR showed evidence of airway pathology. This was highly significant ($p<0.05$).

Previous studies have found that persistent disease is more commonly associated with bronchial hyper reactivity.\(^{5}\) In this study also 83% with persistent rhinitis as compared to 44% of patients with intermittent disease had lower airway involvement. This value was statistically significant.

Also, the overall incidence of latent lower airway involvement of >70% in our study is a figure to reckon with. Considering the propensity of AR to lead to overt asthma, screening patients with severe and persistent AR for lower airway involvement with appropriate treatment may prove beneficial in halting the progress of the ‘allergic march’.

When analyzing lower airway involvement, only 1 patient had a low FEV1/FVC ratio while reduced small airway flow rates (MEF 25-75) were noted in over 20 patients, signifying the importance of these parameters in detecting early airflow obstruction.

Only two patients with normal spirometry showed a positive response to histamine.

However, it was noted that both the patients had borderline MEF 25 values-65% and 68% respectively as compared to a much higher average of 93.88% predicted for patients who failed to respond to histamine.

Finally, the two parameters obtained objectively that represented the upper and lower airways respectively were compared.

A larger proportion of patients with elevated NAR (>0.3 Pa/cc/sec) values had lower airway involvement when compared with patients without elevated NAR, the difference being statistically significant.

Conclusions

Elevated Nasal airway resistance measured by active anterior rhinomanometry correlates with severity of symptoms in allergic rhinitis. Circa 72 % of patients with allergic rhinitis alone had evidence of latent lower airway involvement in this study. A significantly greater proportion of patients with elevated NAR values had lower airway involvement compared to those without raised NAR. Hence, we concluded that active anterior rhinomanometry can prove to be a reliable objective measure of nasal airflow resistance allergic rhinitis. Its potential role for selecting AR patients who are more likely to have lower airway involvement may be worth further evaluation, thus giving an opportunity to identify latent asthma and intervening early in the disease process.

References


