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The relationship between allergy and rhinosinusitis*

Virat Kirtsreesakul and Suwalee Ruttanaphol

Department of Otolaryngology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, 90110, Thailand

SUMMARY

Background: *IgE-mediated hypersensitivity is considered by some to be a predisposing factor for developing rhinosinusitis, although the theory is still controversial. The purpose of this study was to evaluate the relationship between allergy and rhinosinusitis.*

Design: *A cross-sectional study.*

Methods: *198 rhinitis patients were enrolled. An allergy skin prick test was done and the subjects categorized as allergic or nonallergic. Nasal endoscopy and sinus radiography were performed. The criteria for diagnosis of rhinosinusitis were rhinitis symptoms and positive nasal endoscopy (discharge from middle and/or superior meatus) and/or abnormal sinus radiography.*

Results: *Allergic patients were significantly more likely to have abnormal findings on sinus radiography than non-allergic patients ($p < 0.001$) and would therefore fulfill the criteria on which rhinosinusitis may be diagnosed, but the two groups were not significantly different in positive nasal endoscopy results ($p = 0.553$). Among the patients with abnormal sinus radiography, the allergic patients were significantly less likely to have a positive nasal endoscopy compared to the nonallergic patients ($p = 0.006$).*

Conclusions: *Allergic rhinitis subjects were significantly more likely to have abnormal findings on sinus radiography compared with nonallergic subjects potentially leading to a diagnosis of rhinosinusitis. However, they were also significantly more likely to have abnormal sinus radiography with negative nasal endoscopy than the nonallergic subject. These findings could suggest an association between allergic rhinitis and rhinosinusitis via IgE mediated hypersensitivity.*

Key words: allergic rhinitis, nonallergic rhinitis, sinusitis, nasal endoscopy, sinus radiography

INTRODUCTION

Rhinosinusitis is one of the 10 most common diagnoses made in ambulatory practice and is the fifth most common diagnosis for which antibiotics are prescribed [(1)].

Rhinosinusitis occurs in both children and adults and is accompanied by decreased productivity and impaired quality of life. The normal sinus physiology might be altered by allergic inflammation in several ways. The most commonly proposed mechanism is ostial obstruction.

Allergic mucosal edema causes ostial obstruction that interferes with drainage and ventilation from the sinuses, promoting mucus accumulation, serum transudation, and decreased oxygenation within the sinuses. These changes result in impaired ciliary movement, retained secretions, and bacterial growth. It follows then that IgE-mediated hypersensitivity may be a significant player in the development of rhinosinusitis; however, this has never been proven conclusively [(2-14)]. As well as triggering infectious processes, IgE-mediated hypersensitivity is also believed to directly affect the sinus mucosa. Several studies have examined the association between allergy and rhinosinusitis [(2-11)]. Some of these studies showed that patients with rhinosinusitis have a higher prevalence of positive allergy skin tests than the normal population [(2-4)]. Other studies showed a higher prevalence of rhinosinusitis in allergic patients [(5-9)]. In these studies, the results may be criticized because the control groups were made up of normal subjects. A higher prevalence of rhinosinusitis in allergic patients, who were suffering from chronic nasal inflammation, which can easily extend to the contiguous sinus mucosa, compared to normal subjects would not be unexpected. To determine the role of IgE-mediated allergic reactions in rhinosinusitis, the differences in the nasal endoscopic and sinus radiographic findings and prevalence of rhinosinusitis between patients with allergic rhinitis and control subjects with nonallergic rhinitis were examined.

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MATERIALS AND METHODS

Patients

A cross-sectional study was conducted on 198 patients at the Allergy and Rhinology Clinic, Department of Otolaryngology, Faculty of Medicine, Songklanagarind Hospital, Prince of Songkla University, Songkhla, Thailand, between October 1st, 2000 and September 30th, 2006. Seventy patients were men and 128 patients were women. The protocol was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University.

The following inclusion and exclusion criteria were used in this study.

Inclusion criteria were:

1. A history of ≥ 2 nasal symptoms (nasal blockage, rhinorrhea, postnasal drip, sneezing/itching, facial pain/pressure or loss of smell) for at least 3 months.
2. Age above 15 years.

Exclusion criteria were:

1. Systemic steroid use within 1 month or topical nasal steroid used within 2 months previously.
2. Decongestant used within 1 day previously.
3. Antihistamine used within 2-7 days previously.
4. Antibiotic used within 7 days previously.
5. Immunotherapy previously.
6. Severe underlying systemic disease or immuno-compromised host
7. Patient with nasal polyps or abnormal anatomy that may cause osteomeatal complex obstruction, e.g. severe deviated nasal septum, concha bullosa and paradoxical middle turbinate
8. Prior sinus surgery.
9. Contraindication for skin test.

Data collection procedures

The medical history, including age, sex, nasal symptoms, concomitant diseases and medications, was recorded. An allergy skin prick test was performed with 19 common aeroallergens (Bermuda 1:20 w/v, Johnson 1:20 w/v, Acasia 1:20 w/v, Careless weed 1:50 w/v, Alternaria 1:10 w/v, Aspergillus mix 1:10 w/v, Candida albicans 4:10 w/v, Penicillium mix 1:10 w/v, Fusarium 1:10 w/v, Cat pelt 10,000 BAU/ml, Dog epithelium 1:20 w/v, Mixed feathers 1:20 w/v, Kapok 1:20 w/v, House dust 10,000 PNU/ml, Dermatophagoides pteronyssinus 10,000 AU/ml, Dermatophagoides farinae 10,000 AU/ml, American cockroach 1:20 w/v, Pyretrum 1:20 w/v, Cladosporium sphaerosperium 1:10 w/v) from Allertech CO., Ltd. Histamine phosphate 2.75 mg/ml was used as a positive control, glycerin saline as a negative control. The test was read in 20 minutes. The criterion for diagnosis of positive allergy skin test was reaction to at least 1 aeroallergen with a wheal size ≥ 3 mm greater than the negative control skin reaction.

These results were used to divide the patients into 2 groups: 1) the positive skin test group: patients who had a positive skin reaction to at least 1 aeroallergen, and 2) the negative skin test group: patients whose skin reactions were all negative. Nasal endoscopy and sinus radiography (Caldwell and Waters' view) were performed to assess the presence/absence of any sinonasal inflammation. A positive finding on nasal endoscopy was defined as nasal mucosal inflammation with mucoid or mucopurulent discharge from the middle and/or superior meatus. Positive sinus radiography was defined as ≥ 1 abnormal finding of plain film paranasal sinus (haziness, opacity, air-fluid level and mucosal thickening ≥ 5 mm). The criteria for diagnosis of rhinosinusitis were a history of ≥ 2 nasal symptoms and either positive nasal endoscopy and/or positive sinus radiography.

Statistical analysis

Demographic data between groups were summarized as mean and range. The numbers and percentages of positive nasal endoscopy, positive sinus radiography and rhinosinusitis were determined. The possible associations between allergy and sinonasal findings were estimated by odds ratios (ORs). Chi-square test was used to test statistical significance of the difference between the two groups. A value for $p < 0.05$ was considered statistically significant.

RESULTS

One hundred and ninety-eight rhinitis patients were enrolled. The characteristics of the patients are presented in Table 1. There were no statistically significant differences in demographic data and duration of symptoms between the two groups. All patients had had nasal symptoms for at least 6 months. Allergic patients had significantly more sneezing and nasal itching than nonallergic patients ($p < 0.0001$ and $p = 0.036$, respectively), but not nasal blockage, rhinorrhea, postnasal drip, facial pain/pressure and loss of smell.

Table 1. Characteristics of patients (n = 198).

Characteristics	**Allergic patients (n = 103)**	**Nonallergic patients (n = 95)**
Age (Yrs): Mean (Range)	33.4 (16-63)	37.3 (16-64)
Sex ratio (M/F)	35:68	35:60
Duration of symptoms (Yrs):		
Mean (Range)	1.3 (0.5-18)	1.5 (0.5-20)
History of asthma	17	15
Nasal symptoms (%)		
- Nasal blockage	80.6	89.5
- Rhinorrhea	88.3	80.0
- Postnasal drip	61.2	60.0
- Sneezing	94.2	66.3
- Nasal itching	61.2	46.3
- Facial pain/pressure	26.2	24.2
- Loss of smell	14.6	13.7

Sinus radiography

Fifty-eight of 103 (56.3%) allergic patients and 30 of 95 (31.6%) nonallergic patients had abnormal plain film paranasal sinus. Among these abnormal findings, mucosal thickening was the

Table 2. Comparisons of nasal endoscopic and sinus radiographic findings between allergic and nonallergic patients.

	Allergic patients	Nonallergic patients	OR	95% CI	p value
Sinus radiography					
- Positive sinus radiography	58	30	2.793	1.560-4.998	0.000
- Negative sinus radiography	45	65			
Nasal endoscopy					
- Positive nasal endoscopy	23	21	1.013	0.518-1.981	0.553
- Negative nasal endoscopy	80	74			
Nasal endoscopic finding in positive sinus radiography					
- Negative nasal endoscopy with positive sinus radiography	35	9	3.551	1.385-9.104	0.006
- Positive nasal endoscopy with positive sinus radiography	23	21			

most common sinus abnormality (48.3% and 46.7%), followed by haziness/opacity (44.8% and 43.3%) and air-fluid level (6.9 % and 10.0%) in allergic and nonallergic patients respectively.

Nasal endoscopy

Nasal endoscopy revealed some abnormality in 23 of 103 (22.3%) allergic patients and 21 of 95 (22.1%) nonallergic patients. Among these abnormalities, all cases had nasal mucosal inflammation with mucoid or mucopurulent discharge from the middle meatus and 9 of 103 (8.7%) allergic patients and 7 of 95 (7.4%) nonallergic patients also had discharge from the superior meatus. All patients who had positive nasal endoscopy also had abnormal sinus radiography.

Comparisons of sinus radiographic and nasal endoscopic findings between allergic and nonallergic patients

Allergic patients were 2.8 times more likely to have abnormal findings on sinus radiography than nonallergic patients (95% CI = 1.56 - 4.99, $p < 0.001$). The prevalence of positive nasal endoscopy in allergic patients was almost the same as nonallergic patients (22.3 versus 22.1, 95% CI = 0.52 - 1.98, $p = 0.553$) (Table 2). Assessing patients who had abnormal findings on sinus radiography, allergic patients were 3.6 times less likely to have mucoid or mucopurulent discharge from the meatus compared with the nonallergic patients (39.7% versus 70.0%, 95% CI = 1.39-9.10, $p = 0.006$) (Table 2).

Comparisons of clinical characteristics between rhinosinusitis and rhinitis patients

Those patients who fulfilled our diagnostic criteria for rhinosinusitis had significantly more rhinorrhea, facial pain/pressure, loss of smell and prevalence of positive skin test than rhinitis-only patients ($p = 0.030$, $p = 0.032$, $p = 0.013$ and $p = 0.001$, respectively) (Table 3).

DISCUSSION

Although there has been increasing evidence in recent years of an association between allergy and rhinosinusitis [2-11], the role of allergy in rhinosinusitis is questioned by other studies showing no increase in the incidence of infectious rhinosinusitis during the pollen season in pollen sensitized patients [12] and no difference in prevalence of purulent rhinosinusitis between patients with and without allergic rhinitis [13]. Rhinosinusitis is a heterogeneous group of diseases with different underlying etiologies and pathomechanisms and may indeed represent an umbrella covering different disease entities [15]; hence, the conflicting results may reflect differences in diagnostic criteria as well as the heterogeneity of rhinosinusitis per se.

To study the effect of IgE-mediated allergy on the sinus cavities, nonallergic rhinitis patients were used as a control group in this study. The findings showed that allergic rhinitis patients were 2.8 times significantly more likely to have abnormal sinus radiography than nonallergic rhinitis patients suggestive of rhinosinusitis. The pathophysiology of allergic rhinitis may explain the link between allergic rhinitis and rhinosinusitis. In patients with allergic rhinitis, specific allergens induce a Gell and Coombs type I immunologic reaction in the nasal cavities. Allergens are bound by IgE affixed to the mast cell membrane, which leads to degranulation and release of inflammatory mediators. These mediators cause increased vascular perme-

Table 3. Comparisons of clinical characteristics between rhinitis and rhinosinusitis patients.

Clinical characteristics	Rhinosinusiti (n = 98)	Rhinitis (n = 100)	p value
Duration of symptoms (Yrs):			
Mean (Range)	1.5 (0.5-18)	1.5 (0.5-20)	0.446
History of asthma	17	15	0.333
Nasal symptoms (%)			
- Nasal blockage	88.6	81.8	0.232
- Rhinorrhea	90.9	79.1	0.030
- Postnasal drip	65.9	56.4	0.190
- Sneezing	84.1	77.3	0.282
- Nasal itching	61.4	48.2	0.085
- Facial pain/pressure	32.9	19.1	0.032
- Loss of smell	21.6	8.2	0.013
Positive skin test (%)	65.9	40.9	0.001

ability and hypersecretion from the serous and mucous glands. Cytokines, formed from lymphocytes and mast cells, attract eosinophils, macrophages, lymphocytes as well as mast cells, which cause the late phase allergic response. Prolonged inflammation of the nasal mucosa in the region of the ostial meatal complex can cause obstruction of the paranasal sinus outflow tracts.

When the sinus ostia are obstructed, there is decreased oxygen tension in the sinus cavities. The stagnant secretions in the sinus become more viscous and acidic, further damaging the respiratory epithelium. This is an ideal environment for bacteria to proliferate and perpetuate tissue insult, causing a cycle of chronic inflammation. In addition to mechanical obstruction, the functioning of the cilia may be impaired in acute allergy attacks or in perennial allergic rhinitis [16,17]. The delay in mucociliary clearance adds to mucus stagnation and consequent bacterial overgrowth [3]. Interestingly, in this study the allergic rhinitis patients had significantly more abnormal sinus radiography without discharge from the sinuses than the nonallergic rhinitis patients. This may represent a form of rhinosinusitis caused by an allergic pathway, allergic rhinosinusitis. The pathomechanism is more likely a direct involvement of the sinus mucosa in the allergic reaction or a neurogenic inflammation, which follows the sensitisation of sensory afferent nerves than a blockage of the ostiomeatal complex and a bacterial superinfection of the sinuses. Pelikan and Pelikan-Filipek reported that 75% of their allergic patients showed an increase in maxillary mucosal thickening on sinus radiographs after a nasal allergen challenge [18]. Slavin *et al.* found that patients with ragweed sensitivity had increased hyperemia in the sinuses during the ragweed season, as well as increased metabolic activity in the bones around the sinuses using single photon emission computerized tomography [19]. Allergens may enter the sinus cavities and directly cause allergic inflammation in these cavities. Immunologic factors may play an important role as suggested by studies that have demonstrated the accumulation in the sinus mucosa of activated eosinophils and cytokines (such as interleukin-3 and granulocytemacrophage colony-stimulating factor), which promote eosinophil accumulation and activation [20,21]. Eosinophils may cause chronic mucosal inflammation even in the absence of microorganisms through the release of granules, which contain toxic proteins such as eosinophil cationic protein and major basic protein [9]. Finally, sinus mucosal inflammation may cause neurogenic inflammation through sensitization of sensory afferent nerves with allergic inflammation [22].

The limitations of this study merit careful consideration. Firstly, although conventional sinus radiography can be used as a screening method for rhinosinusitis, the numbers of false positive and false negative results are high [15]. Abnormal sinus radiography should be interpreted in the context of clinical examination, nasal endoscopy or both. CT scanning is the imaging modality of choice confirming the extent of pathology and the anatomy. An advantage of CT over plain films is improved visualization of the ethmoid complex, frontal recess and soft tissue. However, the limitations of CT imaging include increased cost and radiation dosage [23]. Another aspect to consider is the fact that radiological studies may not be specific enough to explore pathomechanism of rhinosinusitis, direct comparisons of signs and symptoms with cellular and cytokine profiles in sinuses between allergic and nonallergic rhinitis may assess more reliably the correlation between allergy and rhinosinusitis.

In conclusion, allergic rhinitis subjects had significantly more abnormal sinus radiography and abnormal sinus radiography with negative nasal endoscopy and diagnosed rhinosinusitis compared with nonallergic rhinitis subjects. These findings suggest a possible association between allergic rhinitis and rhinosinusitis via IgE mediated hypersensitivity. Patients with persistent rhinitis and suspected rhinosinusitis, especially those with rhinorrhea, facial pain/pressure and loss of smell, should be evaluated by allergy skin test and nasal endoscopy.

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Virat Kirtsreesakul, MD
Division of Allergy and Rhinology
Department of Otolaryngology
Faculty of Medicine
Prince of Songkla University
Hat Yai, Songkhla, 90110
Thailand

Tel: +66-74-429-620
Fax: +66-74-429-620
E-mail: kvirat2002@yahoo.com