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# Role of Allergy in the Therapeutic Response of Nasal Polyps

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**SUMMARY** **The objective of this study was to determine whether the allergy factor affects therapeutic response of nasal polyps. A total of 68 patients were enrolled between 1 October 1999 and 1 January 2002 at the Allergy and Rhinology Clinic, Faculty of Medicine, Songklanagarind Hospital. Allergy skin prick test was performed in order to divide patients into a positive skin test group and a negative skin test group. Their medical history was recorded including age, sex, nasal symptoms, concomitant diseases and medications. Patients in both groups were treated over a 6 week period with Budesonide nasal spray. Nasal symptoms, polyp size, nasal and oral expiratory peak flow were evaluated at each visit. Overall assessment of treatment efficacy was evaluated by patients at 3 and 6 weeks after treatment. The mean value of these variables during treatment and a baseline period were compared within and between groups. After 3 and 6 weeks of treatment of nasal polyps with topical Budesonide nasal spray, nasal symptoms, polyp size, nasal and oral expiratory peak flow index and overall response to treatment were improved within both groups. Comparing the two groups, there were greater improvements in the negative skin test group compared to the positive skin test group in all variables. These differences in variable scores between groups showed a tendency to increase overtime after treatment was terminated. The results demonstrate that nasal polyps with positive allergen skin test had less improvement compared to nasal polyps with negative allergen skin test in all nasal signs and symptoms and these differences in improvement showed a tendency to increase over time after treatment.**

Nasal polyposis is a common disease in ear, nose and throat practice.[1] The management of nasal polyps may involve medical and surgical modalities. Most rhinologists treat small and medium-sized nasal polyps with a trial of topical corticosteroids for one month and assess the response. If the polyps do not respond then they should be removed surgically.[2] The major therapeutic problems are that about one half of patients do not respond to medical treatment and there is a high recurrence rate over 31% of patients after the treatment.[2-4] Factors not currently considered essential in the management of the individual patient may affect the outcome of the treatment.

Allergy is the main pathogenesis theory of nasal polyps.[5-8] The factors that point to an allergic cause include the presence of certain clinical symptoms such as sneezing and nasal itching, elevated histamine and IgE in extracellular polyp fluid, degranulated mast cells in polyps and marked tissue eosinophilia.[9] But the role of allergy for a prognosis of treatment success is still not clarified. There have been few directed studies of this relationship. Larsen and Tos[3] found a positive correlation between allergy and repeated polypectomy. But Drake-Lee *et al.*[10] did not find this correlation. However, these studies did not point to the direct effect of allergy on the response to therapy for nasal polyps. The aim of this study was to determine whether allergy affected the therapeutic outcome of nasal polyps

## MATERIALS AND METHODS

A prospective cohort study was conducted on 68 patients at the Allergy and Rhinology Clinic, Department of Otolaryngology, Faculty of Medicine, Songklanagarind Hospital, Prince of Songkhla University, Songkhla, Thailand, from 1 October 1999 to 1 January 2002. Thirty-seven patients were male and thirty-one patients were female. The protocol was approved by the Ethic Committee of the Faculty of Medicine, Prince of Songkla University. All patients gave informed consent for the study. The following

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inclusion and exclusion criteria of the patients were used in this study. The inclusion criteria were were: 1) clinical diagnosis of small and medium-sized nasal polyps (grade I, II) by nasal endoscope and confirmed by biopsy and 2) age above 15 years. The exclusion criteria were: 1) systemic steroid within 1 month, 2) topical nasal steroid within 2 months, 3) decongestant within 1 day, 4) antihistamine within 2 days, 5) contraindication for skin test and 6) patient with a severe underlying disease or an immuno-compromised host.

A medical history was recorded for each patient at the first clinic visit, including age, sex, nasal symptoms, concomitant diseases and medications. 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.). A wheal size at least 3 mm more than the negative control was considered a positive skin reaction.[11-13] Histamine phosphate 2.75 mg/ml was used as positive control, glycerin saline as negative control. The test was read in 20 minutes.[14] 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. Patients in both groups were treated over a 6-week period with

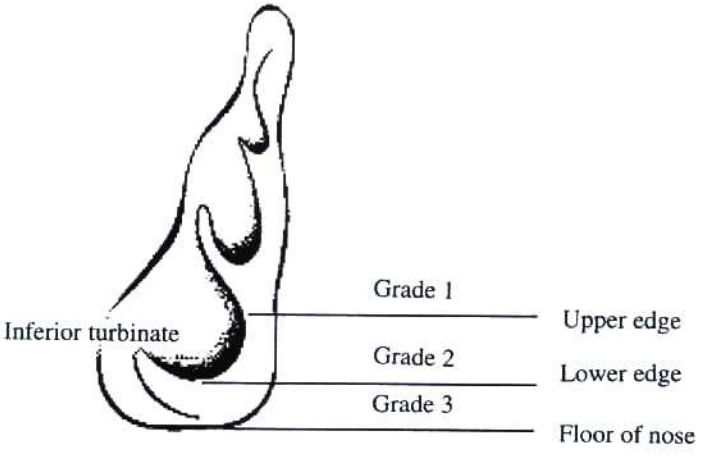


Fig. 1 Right nasal cavity. The numbers indicate the classification of the sizes of the nasal polyps with reference to inferior turbinate. Score 0 = grade 0, no polyps; score 1 = grade 1, mild polyposis (small polyps, extend downward from upper nasal cavity but not below the upper edge of the inferior turbinate, cause only slight obstruction); score 2 = grade 2, moderate polyposis (medium sized polyps, extend downward from upper nasal cavity and reach between the upper and lower edge of the inferior turbinate, cause troublesome obstruction); score 3 = grade 3, severe polyposis (large sized polyps, extend downward from upper nasal cavity and reach below the lower edge of the inferior turbinate, cause total or almost total obstruction).

Budesonide nasal spray 100 μg twice daily (400 μg/day) in each nostril.

## Clinical assessment

At each visit a symptom evaluation was performed by the patient giving scores for blocked nose, runny nose and sneezing as follows:[15,16] Score 0 = no symptom; score 1 = mild symptoms - present but not troublesome; score 2 = moderate symptoms - frequently troublesome but not sufficient to interfere with normal daily activities or night-time sleep and score 3 = severe symptoms - sufficiently troublesome to interfere with normal daily activities or night–time sleep. The total symptom score was calculated as the sum of the scores for each symptom. The size of nasal polyps was also assessed by nasal endoscopy technique and scored on a 0-3 scale as described in Fig. 1.[1,15,16] The total polyp score was calculated as the sum of the polyp scores for each nostril. Additionally, the nasal and oral expiratory peak flows (PEF) were measured and the highest value out of three efforts was recorded. The PEF index was calculated as nasal PEF divided by oral PEF, in order to compensate for changes in lung function.[1,16]

At 3 and 6 weeks after treatment, the patient was evaluated for the overall treatment efficacy. The evaluation was based on a 5-step scale.[15,16] Score 0 = symptoms were aggravated, score 1 = no control over symptoms, score 2 = minor control over symptoms, score 3 = substantial control over symptoms and score 4 = total control over symptoms.

### Statistical analysis

Mean value of the nasal symptom score, polyp score, PEF index and overall assessment of treatment efficacy during the treatment and a baseline period were compared within each positive and negative skin test group using the Wilcoxon signed-rank test. The comparisons between groups at each visit were made with the Wilcoxon rank sum test. In all tests of significance, two-tailed alternatives were used. A value of $p < 0.05$ was considered statistically significant.

## RESULTS

Sixty-eight patients were enrolled, and all patients completed this study. Based on the history taking, all patients gave a positive history of rhinitis. Forty-four patients were in the group with at least one positive skin test and twenty-four patients were in the group with negative skin tests. The characteristics of patients in both groups are presented in Table 1. There were no statistically significant differences in either demographic data and baseline nasal signs or symptoms between the two groups.

Patients in both groups were treated over a 6-week period with Budesonide nasal spray, 100 μg twice daily (400 μg/day) in each nostril. The results of each variable scores are shown in Table 2.

During the treatment period, the scores for blocked nose, runny nose, sneezing and total symptoms improved within both groups (Table 2). In comparison between groups at 3 and 6 week after treatment, the negative skin test group showed greater improvement than the positive skin test group. However, the different nasal symptom scores between groups were not significant statistically but showed a tendency to increase over time after the treatment.

### Size of polyps

During the treatment period, the polyp score was improved within both groups (Table 2). Comparing between groups, the negative skin test group showed greater improvement than the positive skin test group. The differences increased over time after treatment although they were not significant different statistically (Table 2).

### PEF index

During the treatment period,

**Table 1** Characteristics of patients (N = 68)

| Characteristics | Positive skin prick test group (N = 44) | Negative skin prick test group (N = 24) |
|---|---|---|
| **Age** (years) | | |
| -Mean | 43.02 | 49.38 |
| -Range | 17-71 | 16-71 |
| **Sex ratio** (M/F) | 23:21 | 14:10 |
| **Duration of symptoms** (years) | | |
| -Mean | 3.29 | 3.35 |
| -Range | 0.17-20 | 0.09-17 |
| **History** (N) | | |
| - Rhinitis | 44 | 24 |
| - Asthma | 4 | 2 |
| **Baseline** (Mean ± SD) | | |
| - Blocked nose score | 1.95 ± 0.11 | 1.96 ± 0.19 |
| - Runny nose score | 1.57 ± 0.94 | 1.45 ± 0.19 |
| - Sneezing score | 1.05 ± 0.12 | 1.08 ± 0.17 |
| -Total symptom score | 4.57 ± 0.19 | 4.50 ± 0.43 |
| -Total polyp score | 2.98 ± 1.19 | 2.96 ± 0.81 |
| **PEF index** | 0.47 ± 0.03 | 0.41 ± 0.03 |
| **Overall assessment of treatment efficacy** | 1 ± 0 | 1 ± 0 |

**Table 2** Comparison of blocked nose score, runny nose score, sneezing score, total symptom score, PEF index and overall assessment of treatment efficacy at each visit between groups

| | Blocked nose score | | Runny nose score | | Sneezing score | | Total symptom score | | Total polyps score | | PEF index | | Overall assessment of treatment efficacy | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Positive skin test group | Negative skin test group | Positive skin test group | Negative skin test group | Positive skin test group | Negative skin test group | Positive skin test group | Negative skin test group | Positive skin test group | Negative skin test group | Positive skin test group | Negative skin test group | Positive skin test group | Negative skin test group |
| **Baseline** (Mean ± SD) | 1.95 ± 0.75 | 1.96 ± 0.91 | 1.57 ± 0.62 | 1.45 ± 0.93 | 1.05 ± 0.77 | 1.08 ± 0.83 | 4.57 ± 1.25 | 4.50 ± 2.09 | 2.98 ± 1.19 | 2.96 ± 0.81 | 0.47 ± 0.18 | 0.41 ± 0.16 | 1 ± 0 | 1 ± 0 |
| **At 3rd wk after treatment** (Mean ± SD) | 1.02 ± 0.9 | 0.63 ± 0.65 | 0.66 ± 0.65 | 0.45 ± 0.59 | 0.41 ± 0.59 | 0.33 ± 0.48 | 2.09 ± 1.51 | 1.42 ± 1.21 | 2.68 ± 1.36 | 2.17 ± 0.87 | 0.52 ± 0.19 | 0.62 ± 0.74 | 2.34 ± 10.3 | 3 ± 0.83 |
| **At 6th wk after treatment** (Mean ± SD) | 0.88 ± 0.99 | 0.42 ± 0.50 | 0.59 ± 0.76 | 0.29 ± 0.62 | 0.29 ± 0.51 | 0.17 ± 0.38 | 1.77 ± 1.89 | 0.88 ± 0.89 | 2.5 ± 1.53 | 1.88 ± 0.85 | 0.54 ± 0.18 | 0.71 ± 0.17 | 2.61 ± 1.42 | 3.71 ± 0.55 |
| **Difference in score between groups at baseline** (*p*-value) | 0.985 | | 0.564 | | 0.85 | | 0.866 | | 0.945 | | 0.154 | | - | |
| **Difference in score between groups at 3rd wk after treatment** (*p*-value) | 0.085 | | 0.209 | | 0.712 | | 0.084 | | 0.125 | | 0.045 | | 0.009 | |
| **Difference in score between groups at 6th wk after treatment** (*p*-value) | 0.078 | | 0.077 | | 0.312 | | 0.079 | | 0.078 | | 0.001 | | 0.001 | |

the PEF index improved within both groups (Table 2). Comparing the two groups at 3 and 6 weeks after the treatment, the negative skin test group showed a significantly greater improvement than the positive skin test group with differences in the scores of 0.10 and 0.16 ($p = 0.046$ and $p = 0.001$), respectively.

### Overall assessment of treatment efficacy

During the treatment period, the overall assessment of treatment efficacy score improved within both groups (Table 2). Comparing between groups at 3 and 6 weeks after treatment, the negative skin test group showed a significantly greater improvement than the positive skin test group with differences in the scores of 0.66 and 1.09 ($p = 0.009$ and $p = 0.002$), respectively.

## DISCUSSION

The mainstay treatment of small and medium-sized nasal polyps is intranasal corticosteroids.[2,17] But there are individual variations in the therapeutic response. Up to one half of the patients do not respond to medical treatment and need surgical intervention.[2] Allergic factors not currently considered essential in the management of the individual patient may affect the treatment outcome.

The pathogenesis of nasal polyps is still undefined. Numerous hypotheses have been formulated but allergy is the most plausible, widely discussed theory.[5-8,18-21] Many researchers have found an association between nasal polyps and allergy.[5-8] In particular, perennial allergic rhinitis, that causes long lasting inflammation of the nasal mucosa, may be a relevant factor in the pathogenesis of nasal polyps.[5,8] Therefore, allergy may be a main factor that affects the therapeutic response. There have been few direct studies of this relationship. Larsen and Tos[3] found a positive correlation between allergy and repeated polypectomy. But Drake-Lee *et al.*[10] did not find this correlation.

Budesonide (Rhinocort) nasal spray, with a high ratio of local to systemic effects, has proven to be a safe and effective treatment for nasal polyps.[15,20,22,23] Therefore, Budesonide was considered an appropriate intranasal steroid for this study.

In this study nasal polyp patients in the positive skin test group had less improvement than those in the negative skin test group in all variables. These differences in improvement between the groups showed a tendency to increase over time after treatment. This result suggests a relationship between allergic disposition (allergy skin test) and failure of medical therapy. However, further study is needed for the clarification.

In conclusion, nasal polyp patients with a positive allergen skin test had less improvement than those with negative allergen skin tests in all nasal signs and symptoms (blocked nose score, runny nose score, sneezing score, total symptom score, total polyp score, PEF index and overall assessment of treatment efficacy). The difference in improvement between groups showed a tendency to increase over time after treatment was terminated.

## REFERENCES


1. Johansen LV, Illum P, Kristensen S, *et al.* The effect of Budesonide (Rhinocort) in the treatment of small and medium–sized nasal polyps. Clin Otolaryngol 1993; 18: 524-7.
2. Lee ABD. Nasal polyps. In: Kerr AG, eds. Scott Brown's Otolaryngology. Oxford: Butterworth Heinemann, 1997; 4(10):1-14.
3. Larsen K, Tos M. Clinical course of patients with primary nasal polyps. Acta Otolaryngol (Stockholm) 1994; 114: 556-9.
4. Mangi RJ. Allergy skin tests. Otolaryngol Clin North Am 1985; 18: 719-23.
5. Pumhiran P, Limitlaohapan C, Wasuwat P. Role of allergy in nasal polyps of Thai patients. Asian Pacific J Allergy Immunol 1999; 17: 13-5.
6. Bernstein JM, Gorfien J, Noble B. Role of allergy in nasal polyposis. Head Neck Surg 1995; 113: 724-30.
7. Settipane G, Chafee F. Nasal polyps in asthma and rhinitis. J Allergy Clin Immunol 1977; 59: 17-21.
8. Asero R, Bottazzi G. Nasal polyposis: a study of its association with airborne allergen hypersensitivity. Ann Allergy Asthma Immunol 2001; 86: 283-5.
9. Keith P, Dolovich J. Allergy and nasal polyposis. In: Mygind N, Lildholdt T, eds. Nasal polyposis: an inflammatory disease and its treatment. Copenhagen, Aarhus: Munksgaar, 1997; 68-77.
10. Drake-Lee AB, Lowe D, Swanston A, Grace A. Clinical profile and recurrent of nasal polyps. J Laryngol Otol 1984; 98: 783-93.
11. Smart BA. Allergy testing using *in vivo* and *in vitro* techniques. Immunol Allergy Clin North Am 1999; 19: 35-45.
12. Ownby DR. Allergy testing: *in vivo* versus *in vitro*. Pediatr Clin North Am 1988; 35: 995-1009.
13. International Rhinitis Management Working Group: international consensus report on the diagnosis and management of rhinitis. Allergy 1994; 49 (Suppl): 5-34.
14. Pumhirun P, Towiwat P, Mahakit P. Aeroallergen sensitivity of Thai patients with allergic rhinitis. Asian Pacific J Allergy Immunol 1997; 15: 183-5.
15. Tos M, Svendstrup F, Arndal H, *et al.* Efficacy of an aqueous and a powder formation of nasal budesonide compared in patients with nasal polyps. Am J Rhinol 1998; 12: 183-9.
16. Lildholt T, Rundcrantz H, Lindquist N. Efficacy of topical corticosteroid powder for nasal polyps: a double- blind, placebo-controlled study of Budesonide. Clin Otolaryngol 1995; 20: 26-30.
17. Kanai N, Denburg J, Jorfana M, Dolovich J. Nasal polyp inflammation: effect of topical nasal steroid. Am J Respir Crit Care Med 1994; 150: 1094-1100.
18. Keith PK, Couway M, Evans S, *et al.* Nasal polyps: effects of seasonal allergen exposure. J Allergy Clin Immunol 1994; 93: 567-74.
19. Shatkin JS, Delsupehe KG, Thisted RA, Corey JP. Mucosal allergy in the absence of systemic allergy in nasal polypsis and rhinitis: a meta-analysis.

20. Granstrom G, Jacobsson E, Jeppsson PH. Influence of allergy, asthma and hypertension on nasal polyposis. Acta Otolaryngol (Stockholm) 1992; 402 (Suppl): 22-7.
21. Voegel RL, Santoro P, Butugan O, Formigoni LG. Nasal polyposis and allergy: is there a correlation? Am J Rhinol 2001; 15: 9-14.
22. Ruhno J, Andersson B, Denberg J, *et al.* A double-blind comparison of intranasal Budesonide with placebo for nasal polyps. J Allergy Clin. Immunol 1990; 86: 946-53.
23. Allen D. Systemic effects of intranasal steroids: An endocrinologist's perspective. J Allergy Clin Immunol 2000; 106 (Suppl): 4179-90.