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The proportion of local allergic rhinitis to *Dermatophagoides pteronyssinus* in children

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ABSTRACT

Background: Local allergic rhinitis (LAR) is diagnosed by the positive response to nasal allergen provocation test (NAPT) to aeroallergen and/or local synthesis of specific IgE (sIgE). This entity is found in half of the adults with nonallergic rhinitis (NAR). In children, very few data of the prevalence and characteristics of LAR were reported.

Methods: Children 8-18 years with NAR were recruited. A NAPT with *Dermatophagoides pteronyssinus* extract (NAPT-DP) at 200, 600 and 2000 AU/mL, respectively, at 15-minute interval was performed. The immediate response was assessed using the clinical symptoms score, peak nasal inspiratory flow (PNIF) and acoustic rhinometry (ARM). The nasal tryptase and sIgE-DP were measured at baseline, 15 min and 1 hr after a positive NAPT-DP. Two allergic rhinitis (AR) patients were used as positive controls.

Results: Fifty-four NAR children (61.1% boys) with the mean $\pm$ SD age of 11.1 $\pm$ 2.1 years were enrolled. The median duration of disease was 6.3 years. The most frequent comorbidity was asthma (38.9%). Eighty seven percent of patients had mild persistent severity. NAPT-DP was positive in 2/54 (3.7%) of NAR children who had increased symptoms score and decreased minimal cross-sectional area (MCA) on ARM as well as PNIF. However, there

was no change in the nasal tryptase and sIgE-DP. The control AR patients had positive NAPT-DP and increased nasal tryptase at 15 min without the change of sIgE-DP.

Conclusion: LAR is an uncommon condition in children. The further investigation in a large population of children with NAR is needed.

Key words: Acoustic rhinometry, allergic rhinitis, children, *Dermatophagoides pteronyssinus*, local allergic rhinitis, nasal allergen provocation test, peak nasal inspiratory flow, tryptase, sIgE

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Abbreviations

LAR:	Local allergic rhinitis
sIgE:	Specific IgE
NAPT:	Nasal allergen provocation test
NAR:	Nonallergic rhinitis
AR:	Allergic rhinitis
NAPT-DP:	Nasal allergen provocation test with <i>Dermatophagoides pteronyssinus</i> extract
PNIF:	Peak nasal inspiratory flow
ARM:	Acoustic rhinometry
MCA:	Minimal cross-sectional area
Dp:	<i>Dermatophagoides pteronyssinus</i>

ECP:	Eosinophilic cationic protein
VAS:	Visual analogue scale
SPT:	Skin prick test
PBS:	Phosphate buffer saline

INTRODUCTION

Chronic rhinitis is a global health problem that causes impairment of work productivity and school performance. It is frequently associated with asthma, conjunctivitis and rhinosinusitis (1, 2). Based on the clinical history and skin prick test (SPT) or specific IgE (sIgE) to aeroallergens, patients with chronic rhinitis can be classified as having allergic rhinitis (AR) and nonallergic rhinitis (NAR). AR is caused by an IgE-mediated reaction resulting in symptoms of sneezing, itching, rhinorrhea and nasal congestion. NAR is characterized by nasal symptoms similar to AR but without positive skin test or sIgE (3, 4). The proportion of NAR and AR in children with chronic rhinitis is approximately 1:3 that is similar to adult population (5, 6). Nasal pruritus, sneezing and eye symptoms are predominant findings in AR while snoring and sinusitis are predominant findings in NAR (5).

Rondon *et al.* revealed that 24% of adults with NAR had *de novo* sensitization to aeroallergens over time (7). In Thailand, children who had the diagnosis of NAR were reevaluated after 3-5 years and found that 41% of them developed sensitization to aeroallergens and were reclassified as having AR (8). The most sensitized aeroallergen was *Dermatophagoides pteronyssinus* (Dp). These results support the concept that NAR can progress to AR over time.

In 1975, Huggins and Brostoff reported patients who had clinical of AR with negative SPT. The nasal allergen provocation test (NAPT) was positive and sIgE in nasal secretion was detected (9). Later on, a number of studies confirmed that local production of sIgE occurred in some NAR patients who had nasal symptoms after the NAPT with common

aeroallergens (10-12). As a result, the term local allergic rhinitis (LAR) was proposed. LAR is characterized by the local production of sIgE, a nasal Th2 response during the natural exposure to aeroallergen and a positive response to NAPT without evidence of systemic entropy (13). In the nasal lavage fluid, patients with LAR and those with AR had increasing eosinophils, basophils, mast cells, CD3⁺T cell and CD4⁺T cell while exposed to aeroallergens (10). The immediate or dual response to nasal challenge in LAR patients is accompanied by the releasing of tryptase, eosinophilic cationic protein (ECP) and sIgE in nasal secretion.

LAR was reported in 25.7% of adults with rhinitis and 36% of these patients had the onset of rhinitis during the childhood (14). Recent studies showed that the prevalence of LAR in patients previously diagnosed with NAR was 47% (10, 11). Most of these reports were done in adults. In children, Fuiano *et al*, studied both symptomatic and asymptomatic rhinitis children who had SPT positive. They showed that higher proportion of nasal sIgE was found in symptomatic (77.5%) than asymptomatic children (13.6%) (15). They also investigated the rhinitis children suffering from *Alternaria* spores. Using NAPT to *Alternaria* as a reference, positive nasal sIgE and NAPT was found in 69.6% while positive SPT and NAPT was found in 26.8% of children, indicating an important role of nasal sIgE (16).

The objective of this study was to determine the proportion of LAR in children with NAR. The immediate response after NAPT to *Dp* extract was evaluated as well as the level of tryptase and sIgE to *Dp*.

METHODS

Subjects

The study was approved by the Ethical committee of the Siriraj Institutional Review Board (759/2556[EC3]), (ClinicalTrials.gov number, NCT02271620). Informed consent was obtained from the parents.

The study recruited NAR children from the Pediatric Allergy Clinic, Siriraj Hospital Mahidol University, Thailand from May 2014 to April 2015 when the patients had stable symptoms. The patients were excluded if they had chronic rhinosinusitis and/or nasal polyposis, immunological diseases, chronic renal diseases, liver diseases, cardiovascular diseases, cancer, uncontrolled asthma or a respiratory infection in the previous 4 weeks. The patients were instructed to avoid any treatment with systemic corticosteroid for 4 weeks, intranasal corticosteroid for 2 weeks, and systemic antihistamine for 1 week prior to the study. In addition, two patients with AR were recruited as positive controls. .

Data collection

The demographic and clinical data were obtained. NAR was defined by the presence of two or more nasal symptoms (sneezing, itching, rhinorrhea and/or nasal blockage) which occurred ≥ 2 consecutive days for >1 hour on most day for at least 1 year plus a negative SPT to aeroallergens (17-19).

The persistence rhinitis symptoms were classified according to the Allergic Rhinitis and its Impact on Asthma guideline (4). The rhinitis was classified as ‘intermittent’ (symptoms present <4 days/week or for <4 consecutive weeks) or ‘persistent’ (symptoms present >4 days/week or for >4 consecutive weeks) (4). For the rhinitis severity, the number of impaired items (sleep, daily activities/sport/leisure, work/school performance, and troublesome symptoms) was used to grade the rhinitis as ‘mild’ (no affected item) or ‘moderate to severe’ (at least one of affected items) (4).

Clinical symptom score

Following the Lebel symptom score scale, the score was mainly based on the symptoms of nasal obstruction (breathing difficulty [1 point], 1 nasal cavity [2 points], 2 nasal cavities [3 points]), rhinorrhea (anterior [1 points], posterior [1 point]), itchiness (nose [1 point], ear or palate [1 point]), sneezing (0-2 times [0 point], 3-4 times [1 point], ≥ 5 times [3 points]) and ocular symptoms (1 point). The maximum possible score was 11 points (20).

Visual analogue scale

The severity of ocular and nasal symptoms, including obstruction, rhinorrhea (watery, mucous, or purulent), itching, sneezing and ocular symptoms, was recorded by visual analogue scale (VAS) of 10 cm. Each symptom was categorized as 'mild' (VAS 0–3 cm), 'moderate' (VAS >3–7 cm), or 'severe' (VAS >7 cm) (14).

Skin prick testing

SPT was performed with a panel of the most prevalent local aeroallergens, including house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), American and German cockroaches, cat and dog dander, grass pollens (Bermuda and Johnson), Acacia, Careless weeds, and molds (*Alternaria* spp., *Cladosporium* spp., *Penicillium* spp., *Aspergillus* spp., and *Fusarium* spp.). Commercial allergens from ALK-Abello, Port Washington, NY, were used. Histamine (10 mg/mL) and saline were used as positive and negative controls, respectively. A positive SPT was defined as a wheal diameter of ≥ 3 mm compared with the negative control, to ≥ 1 aeroallergen. The participants were requested to stop taking antihistamine for ≥ 7 days before SPT.

Nasal lavage and sample processing

Nasal lavage was performed using the following procedures. The subjects extended their necks approximately 30° from the horizontal while in a sitting position. Three milliliters of normal saline were instilled into each nostril while the subjects did not breathe or swallow. After 10 seconds, the subjects flexed their necks, expelling the mixture of mucus and saline into a bowl, which was stored on ice until the end of the study (21). The samples were kept at 4°C until they were centrifuged at 2000 rpm (1069 g) for 7 minutes at 4°C. The supernatant was stored at -20°C until further analysis (10, 12).

Nasal allergen provocation test

A standard anterior rhinoscopy was done to exclude patients with pre-existing condition within the nose. A challenge test to phosphate buffer saline (PBS) was performed to exclude a nonspecific nasal hyperreactivity. If patients had no reaction to PBS, a NAPT with *Dp* (NAPT-DP) was performed using *DP* extract solutions at 200, 600 and 2000 AU/mL at 15-min interval, respectively. Two puffs (0.125 mL each) of the solution were applied to each nasal passage with the use of nasal metered pump spray. The immediate response to NAPT-DP was assessed using clinical symptoms score, VAS, peak nasal inspiratory flow (PNIF) and acoustic rhinometry (ARM). NAPT was considered positive when the nasal obstruction was observed as the following: (1) the ARM showed the reduction of >25% of the minimal cross-sectional area (MCA) of the nasal cavity or (2) the nasal airflow decreased >40% of the baseline value, regardless of the clinical symptom score. If the nasal airflow decreases >20% of the baseline value, it must be combined with a symptom score greater than 5 (22, 23). The nasal tryptase and sIgE-DP were measured at baseline, 15 min and 1 hr after positive NAPT-DP.

Peak nasal inspiratory flow

The nasal airflow was assessed by PNIF (in-check inspiratory flow meter with facemask; Clement Clarke, Harlow, UK.). The highest value of PNIF from 3 measurements was used for calculation (22, 23).

Acoustic rhinometry

The nasal patency was assessed by ARM (ECCOVISION; AR-I 1003, Hood Laboratories, Pembroke, MA) following the guidelines of the committee on ARM (24). The MCA was measured for each nasal cavity separately and the mean of the MCA of both cavities was calculated (25).

Nasal tryptase and sIgE-DP analysis

In nasal lavage fluid, total tryptase and sIgE-DP levels were measured by UniCAP Tryptase immunoassay according to the manufacturer's instructions (Pharmacia, Uppsala, Sweden).

Statistical analysis

Data analysis was performed using a computer base and SPSS statistical software (version 16.0). Continuous data were demonstrated as the mean and standard deviation (SD) or median and range. Categorical data were described as percentage.

RESULTS

Subjects

Fifty-four NAR children were recruited. The baseline characteristics are shown in Table 1. The mean age was 11.1 ± 2.0 years. The median onset and duration of disease was 4.5 and 5.8 years, respectively. There was a predominance of male with the male/female ratio of 1.5:1. Twenty-six patients (48%) had the family history of atopy. Eighty-seven percent had mild persistent severity of rhinitis. The most common triggering factor was temperature change (83.3%), followed by house dust (42.6%) and irritant exposure (7.4%). The most frequent comorbidity was asthma (38.9%).

NAPT and immediate response

None of the NAR patients had nonspecific nasal hyper-reactivity. Among all 54 NAR patients, 2 patients (3.7%) had a positive response to NAPT-DP at 2000 AU/mL of mite concentration (Fig 1, 2). The VAS of both patients at baseline, 15 min and 1 hr after NAPT were 0, 10, 5 and 2, 22, 13, respectively (Fig 1A). The symptom score of both patients at baseline, 15 min and 1 hr after NAPT were 0, 6, 5 and 2, 8, 6, respectively (Fig 1B). The reduction of MCA of both patients compared to baseline, were 23.2% and 56.7%, respectively (Fig 2A, 2B). The reduction of PNIF of both patients compared to baseline, were 31.6% and 61.5%, respectively (Fig 2A, 2B). Both patients were designated as having LAR based on the change of PNIF $\geq 20\%$ plus symptom score > 5 (22, 23). Patient no.1 and 2 were female who had mild persistent severity of rhinitis for 7 and 2.7 years, respectively. The temperature change was the major triggering factor for both patients. Only patient no.1 had comorbidity with adenotonsillar hypertrophy and a family history of AR.

During an immediate response, the most frequent and severe symptoms in patient no.1 were rhinorrhea and nasal obstruction, respectively while in patient no.2 were rhinorrhea and sneezing, respectively. The nasal levels of tryptase and specific IgE for *DP* were $<0.01 \mu\text{g/L}$ at baseline and remained unchanged after positive challenges.

NAPT-DP was positive in both AR patients. The VAS of both patients at baseline, 15 min and 1 hr after NAPT were 4, 19, 16 and 5, 32, 13, respectively (Fig 1C). The symptom score of both patients at baseline, 15 min and 1 hr after NAPT were 2, 7, 5 and 2, 8, 8, respectively (Fig 1D). The reduction of MCA of both patients at symptomatic mite concentration compared to baseline, were 65.7% and 47.7%, respectively (Fig 2C, 2D). The reduction of PNIF of both patients at symptomatic mite concentration compared to baseline, were 60.9% and 36.1%, respectively (Fig 2C, 2D). The nasal tryptase of both patients at baseline, 15 min and 1 hr after NAPT were 0.16, 0.75, 0.35 and 0.15, 1.87, 0.40 $\mu\text{g/L}$, respectively (Fig 3). The nasal sIgE for *Dp* of both patients at baseline, 15 min and 1 hr after NAPT were 0.12, 0.18, 0.13 and 0.15, 0.25, 0.14 kUA/L, respectively (Fig 3). The first AR patient had a positive response at 200 AU/mL of *Dp* extract while the second AR patient responded at 600 AU/mL.

DISCUSSION

A study by Rondon *et al.* in adult suggested that LAR is an entity well differentiated from AR (26). In this report, the percentages of SPT and/or sIgE positivity after 5-year follow-up were not different in LAR patients and healthy controls. The LAR associated with conjunctivitis and asthma (26). However, Sennekamp *et al.*, retrospectively followed 42 LAR patients (age 3-70 years old) for 1-27 years. Forty percent of these patients had the conversion of negative to positive SPT. The change rate was higher in younger (≤ 25 years

old) than older patients (27). A long-term study on the natural history of LAR may provide additional information on the link of LAR and AR.

Our study evaluated the proportion of LAR in children. We found that this entity is rare in children with only 3.7% of NAR children had a positive NAPT-DP. In contrast, LAR was found in 47-62.5% of NAR in adults (11, 28). Our study, could not demonstrate the increased of nasal tryptase or sIgE-DP after positive NAPT-DP in both LAR patients. However, 2 AR patients showed the immediate response with a peak of nasal tryptase at 15 min after challenge.

From previous studies, the increased of nasal tryptase or sIgE-DP after positive NAPT were not demonstrated in all LAR patients. Rondon *et al.* studied the NAPT-DP in patients with persistent NAR and found that 54% showed a positive challenge. However, only 22% of these patients had nasal sIgE-DP (10). Lopez *et al.* reported increases in nasal tryptase and sIgE to DP in 48% and 31% of LAR patients, respectively (12). Although the measuring of sIgE in nasal lavage is useful to detect local sensitization after exposure or challenge with common aeroallergens, the sensitivity of the test is 22-40% (10, 29). This may be due to the dilutional effect of the sample collecting technique which is insufficient to detect a very low amount of sIgE in the nasal secretion. For this reason, the diagnosis of LAR is based on the positive response to NAPT and/or local synthesis of sIgE (30).

The typical LAR is found in the young female, nonsmoker, family history of atopy, urban lifestyle, persistent perennial rhinitis and frequently associated with conjunctivitis and asthma. *Dp* is the main sensitizing aeroallergen and the most frequent symptoms are nasal itching and watery rhinorrhea (26, 30). Our result revealed that the NAPT-DP was positive in two female children who had persistent rhinitis similar to the clinical profile of LAR patient in adults. The family history of atopy was reported in only one patient. The different profiles were the temperature change as a trigger and adenotonsillar hypertrophy as comorbidity.

However, these data are not enough to conclude the clinical characteristics of LAR in children due to a small number of LAR children.

In conclusion, the result of our study indicated that LAR is an uncommon condition in children. The clinical characteristics are unclear due to a small number of positive cases. Further investigation in a large population of children with NAR is needed to identify the prevalence and natural history of LAR in children.

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REFERENCES

- 1 Roberts G, Hurley C, Lack G. Development of a quality-of-life assessment for the allergic child or teenager with multisystem allergic disease. *J Allergy Clin Immunol*. 2003; 111: 491-7.
- 2 Lack G. Pediatric allergic rhinitis and comorbid disorders. *J Allergy Clin Immunol*. 2001; 108: S9-15.
- 3 International Consensus Report on the diagnosis and management of rhinitis. International Rhinitis Management Working Group. *Allergy*. 1994; 49: 1-34.
- 4 Bousquet J, Khaltaev N, Cruz AA, *et al*. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008; 86: 8-160.

- 5 Vichyanond P, Suratannon C, Lertbunnaphong P, Jirapongsananuruk O, Visitsunthorn N. Clinical characteristics of children with non-allergic rhinitis vs with allergic rhinitis. *Asian Pac J Allergy Immunol*. 2010; 28: 270-4.
- 6 Molgaard E, Thomsen SF, Lund T, Pedersen L, Nolte H, Backer V. Differences between allergic and nonallergic rhinitis in a large sample of adolescents and adults. *Allergy*. 2007; 62: 1033-7.
- 7 Rondon C, Dona I, Torres MJ, Campo P, Blanca M. Evolution of patients with nonallergic rhinitis supports conversion to allergic rhinitis. *J Allergy Clin Immunol*. 2009; 123: 1098-102.
- 8 Veskitkul J, Vichyanond P, Visitsunthorn N, Jirapongsananuruk O. The development of allergic rhinitis in children previously diagnosed as nonallergic rhinitis. *Am J Rhinol Allergy*. 2013; 27: 43-7.
- 9 Huggins KG, Brostoff J. Local production of specific IgE antibodies in allergic-rhinitis patients with negative skin tests. *Lancet*. 1975; 2: 148-50.
- 10 Rondon C, Romero JJ, Lopez S, *et al*. Local IgE production and positive nasal provocation test in patients with persistent nonallergic rhinitis. *J Allergy Clin Immunol*. 2007; 119: 899-905.
- 11 Wedback A, Enbom H, Eriksson NE, Moverare R, Malcus I. Seasonal non-allergic rhinitis (SNAR)--a new disease entity? A clinical and immunological comparison between SNAR, seasonal allergic rhinitis and persistent non-allergic rhinitis. *Rhinology*. 2005; 43: 86-92.

- 12 Lopez S, Rondon C, Torres MJ, *et al.* Immediate and dual response to nasal challenge with *Dermatophagoides pteronyssinus* in local allergic rhinitis. *Clin Exp Allergy*. 2010; 40: 1007-14.
- 13 Rondon C, Campo P, Togias A, *et al.* Local allergic rhinitis: concept, pathophysiology, and management. *J Allergy Clin Immunol*. 2012; 129: 1460-7.
- 14 Rondon C, Campo P, Galindo L, *et al.* Prevalence and clinical relevance of local allergic rhinitis. *Allergy*. 2012; 67: 1282-8.
- 15 Fuiano N, Fusilli S, Passalacqua G, Incorvaia C. Allergen-specific immunoglobulin E in the skin and nasal mucosa of symptomatic and asymptomatic children sensitized to aeroallergens. *J Invest Allergol Clin Immunol*. 2010; 20: 425-30.
- 16 Fuiano N, Fusilli S, Incorvaia C. A role for measurement of nasal IgE antibodies in diagnosis of *Alternaria*-induced rhinitis in children. *Allergol Immunopathol (Madr)*. 2012; 40: 71-4.
- 17 Dykewicz MS. Clinical approach to diagnosis and treatment of nonallergic rhinitis. *Clin Allergy Immunol*. 2007; 19: 335-50.
- 18 Quillen DM, Feller DB. Diagnosing rhinitis: allergic vs. nonallergic. *Am Fam Physician*. 2006; 73: 1583-90.
- 19 Settipane RA, Lieberman P. Update on nonallergic rhinitis. *Ann Allergy Asthma Immunol*. 2001; 86: 494-507.
- 20 Lebel B, Bousquet J, Morel A, Chanal I, Godard P, Michel FB. Correlation between symptoms and the threshold for release of mediators in nasal secretions during nasal challenge with grass-pollen grains. *J Allergy Clin Immunol*. 1988; 82: 869-77.

- 21 Naclerio RM, Meier HL, Kagey-Sobotka A, *et al.* Mediator release after nasal airway challenge with allergen. *Am Rev Respir Dis.* 1983; 128: 597-602.
- 22 Dordal MT, Lluch-Bernal M, Sanchez MC, *et al.* Allergen-specific nasal provocation testing: review by the rhinoconjunctivitis committee of the Spanish Society of Allergy and Clinical Immunology. *J Investig Allergol Clin Immunol.* 2011; 21: 1-12.
- 23 Tantilipikorn P, Vichyanond P, Lacroix JS. Nasal provocation test: how to maximize its clinical use? *Asian Pac J Allergy Immunol.* 2010; 28: 225-31.
- 24 Hilberg O, Pedersen OF. Acoustic rhinometry: recommendations for technical specifications and standard operating procedures. *Rhinol Suppl.* 2000; 16: 3-17.
- 25 Keck T, Wiesmiller K, Lindemann J, Rozsasi A. Acoustic rhinometry in nasal provocation test in perennial allergic rhinitis. *Eur Arch Otorhinolaryngol.* 2006; 263: 910-6.
- 26 Rondon C, Campo P, Zambonino MA, *et al.* Follow-up study in local allergic rhinitis shows a consistent entity not evolving to systemic allergic rhinitis. *J Allergy Clin Immunol.* 2014; 133: 1026-31.
- 27 Sennekamp J, Joest I, Filipiak-Pittroff B, von Berg A, Berdel D. Local allergic nasal reactions convert to classic systemic allergic reactions: a long-term follow-up. *Int Arch Allergy Immunol.* 2015; 166: 154-60.
- 28 Powe DG, Huskisson RS, Carney AS, *et al.* Mucosal T-cell phenotypes in persistent atopic and nonatopic rhinitis show an association with mast cells. *Allergy.* 2004; 59: 204-12.
- 29 Rondon C, Dona I, Lopez S, *et al.* Seasonal idiopathic rhinitis with local inflammatory response and specific IgE in absence of systemic response. *Allergy.* 2008; 63: 1352-8.

Table 1 Baseline characteristics of the study population

Parameters	Patients with non-allergic rhinitis (n=54)
Age (mean±SD years)	11.1±2.0
Onset of disease (median, range years)	4.5 (1-10)
Duration of disease (median, range years)	6.3 (2.3-11.9)
Male, n (%)	33 (61.1)
Dwelling, n (%)	
Urban	33 (61.1)
Rural	21 (38.9)
Family history of atopic diseases, n (%)	26 (48.1)
Severity of rhinitis, n (%)	
Mild intermittent	3 (5.6)
Mild persistent	47 (87.0)
Moderate to severe intermittent	0 (0)
Moderate to severe persistent	4 (7.4)
Triggering factors, n (%)	
Temperature change	45 (83.3)
House dust	23 (42.6)
Irritant	4 (7.4)
Animal dander	2 (3.7)
Comorbidities, n (%)	
Asthma	21 (38.9)
Allergic conjunctivitis	12 (22.2)
Adenotonsillar hypertrophy	9 (16.7)
Food allergy	1 (1.9)
Others (chronic urticaria, vernal keratoconjunctivitis, etc.)	7 (13.0)

Figure legends

Fig 1 The changes in total visual analogue scale (VAS) symptoms in 2 local allergic rhinitis (LAR) (A) and 2 allergic rhinitis (AR) (C) patients, and symptoms scores after nasal allergen provocation test with *D. pteronyssinus* extract (NAPT-DP) in 2 LAR (B) and 2 AR (D) patients

Fig 2 The changes in minimal cross-sectional area (MCA) of acoustic rhinometry (ARM) and value of peak nasal inspiratory flow (PNIF) before and after nasal allergen provocation test with *D. pteronyssinus* extract (NAPT-DP) in 2 local allergic rhinitis (LAR) patients (A, B) and 2 allergic rhinitis (AR) (C, D) patients

Fig 3 The changes in nasal levels of tryptase (A) and specific IgE to *D. pteronyssinus* (Dp) extract (B) of 2 allergic rhinitis (AR) patients

Figure 1

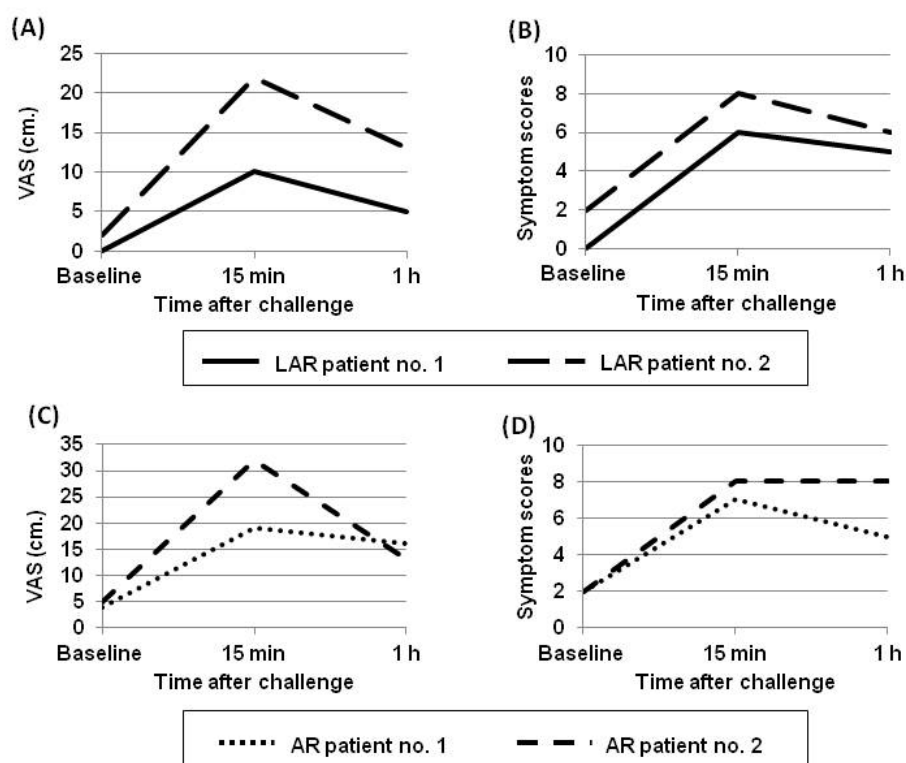


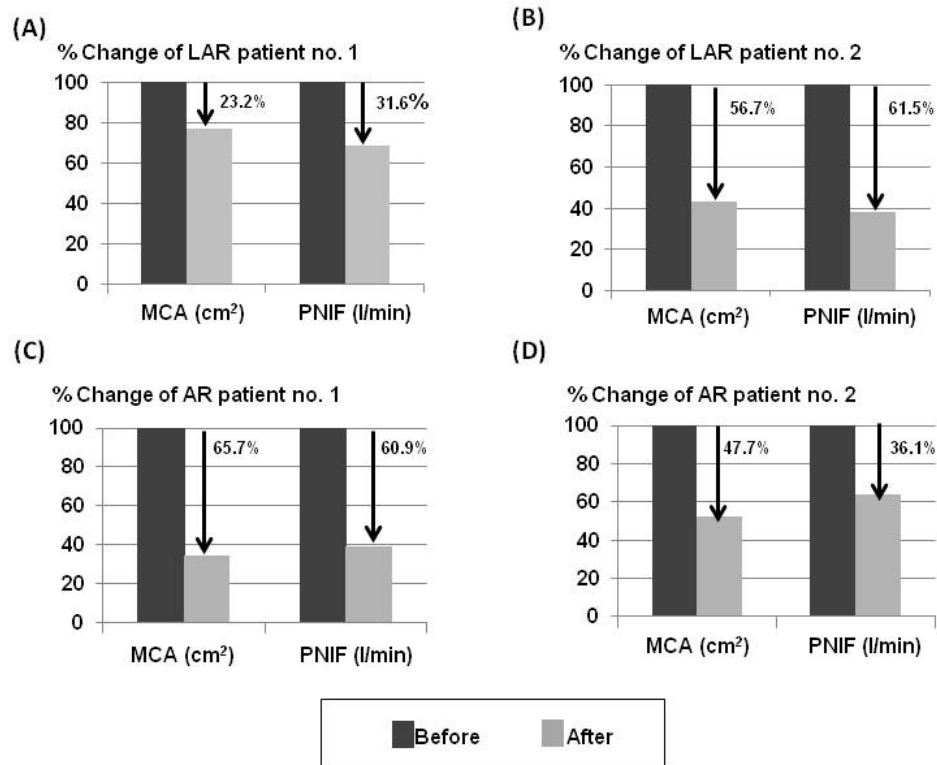
Figure 2

Figure 3

