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Nasal carriage of *Staphylococcus aureus* in children with allergic rhinitis and the effect of intranasal fluticasone propionate treatment on carriage status

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Summary

Objective: The aim of this study is to determine the rate of nasal carriage of *Staphylococcus aureus* (NCSA) in children with allergic rhinitis (AR) and to determine the effect of intranasal fluticasone propionate spray on the NCSA.
Patients and methods: Nasal swabs were taken from the children admitted to general pediatrics and pediatric pulmonology clinics. Patients were divided into two groups according to the presence or absence of AR. Diagnosis of AR was based on the patient's symptoms. Nasal swabs were taken from AR patients before and after the treatment with intranasal fluticasone propionate, and from the control group at the beginning and after 2 months.
Results: Whole NCSA rate was 17.9%; it was 21.4% for AR patients and 15.9% for control group, respectively ($p > 0.05$). Treatment with intranasal fluticasone propionate spray did not influence NCSA in AR patients.
Conclusion: It seemed that NCSA was not increased in children with AR and treatment with intranasal fluticasone propionate spray did not change NCSA in AR patients. It is obvious that better understanding of the factors affecting the acquisition and loss of NCSA might increase our knowledge about the relationship between NCSA, allergic airway diseases and their treatments.

Allergic rhinitis (AR) is a common disease which is associated with functional and physical impairments. Chronic allergic rhinitis was also linked to the development and exacerbation of other airway

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disorders, such as asthma, otitis media, chronic sinusitis, and nasal polyposis [1].

Carriage of *Staphylococcus aureus* (*S. aureus*) in the nose appears to play a key role in the epidemiology and pathogenesis of infection associated with bacteria. Nasal carriage of *Staphylococcus aureus* (NCSA) has been shown to be an important risk factor for nosocomial and community-acquired infections [2].

The relationship of NCSA to AR is obscure. It was proposed that *S. aureus* enterotoxins might be involved in the symptomatology of AR [3,4]. In adults, it was demonstrated that NCSA was more common in patients with perennial allergic rhinitis and NCSA was found to aggravate symptoms of rhinitis [4]. Intranasal corticosteroids were being used with high efficacy in the treatment of AR to decrease the symptoms and inflammation within the nasal cavity [5]. It would be interesting to investigate the effects of intranasal corticosteroids on the NCSA. However, the effect of nasal corticosteroid use on the NCSA was not widely studied in children.

In this study, we examined the rate of NCSA in children with AR. We also examined the relationship of NCSA to nasal symptoms in patients with AR. Lastly; the effect of treatment with intranasal corticosteroid (fluticasone propionate) spray on the NCSA was investigated.

1. Materials and methods

This study was composed of two parts; first part consists of the prevalence data of NCSA, and relationship of NCSA to nasal symptoms. In the second part of the study, effect of treatment with fluticasone propionate on the NCSA was investigated. Participants were selected from the general pediatrics and pediatric pulmonology clinics of our university hospital. Children with diabetes mellitus, chronic renal failure, cerebral palsy, immunodeficiency and current infection were not included in this study. Children, who have used antibiotics and nasal corticosteroids one month before joining the study, were also excluded. This study was approved by the ethical committee of Abant Izzet Baysal University. Informed consent was obtained from both parent and children.

Patients were divided into AR and control (non-allergic rhinitis patients) groups. Control group mostly consisted of patients with enuresis voiding dysfunction, constipation, short stature and healthy children.

Allergic rhinitis was diagnosed clinically. Patients were evaluated with clinical history and physical examination and laboratory tests (serum IgE) when necessary. In the history, the presence of at least two nasal symptoms of nasal discharge, itching, nasal congestion and rhinorrhea were required for the diagnosis of AR. These symptoms must be present at least one hour on most days and not associated with upper respiratory tract infections [6]. A study form was filled for every subject enrolled in the study. Recorded parameters were age, gender, presence of health care worker in the family, hospitalization within one year, presence of eczema, asthma, recurrent upper viral respiratory tract infections ($>$5/year), recurrent sinusitis and recurrent acute otitis media/otitis media with effusion, and nasal symptoms. Definitions of these infections were made according to international guidelines [7,8].

At the second part of the study, post-treatment nasal swabs were obtained from AR patients who have received intranasal fluticasone propionate 100 μg/day (for children below 12 years) and 200 μg/day (for those above 12 years) for at least two months. Nasal swabs of control group were also obtained two months after the first sampling. Both groups were compared in terms of changes in NCSA prevalence.

Nasal specimens were collected from patients using two sterile dry cotton—wool swabs for each patient from 1/3 anterior nares. Cultures of the anterior nares were obtained by three clockwise and three counter-clockwise rotation of a sterile swab in each nasal passage [9]. The swabs were immediately placed in the transport medium before being inoculated onto 5% sheep blood agar and Chapman agar plates. The plates were incubated at 37 $^{\circ}$C for 48 h. *S. aureus* isolates were identified by routine laboratory procedures. Gram-positive, catalase-positive cocci were tested for mannitol fermentation on salt mannitol agar and results were confirmed by tube coagulase test. API Staph (BioMerieux, Marcy l'Etoile, France) strips were used for identification of *Staphylococcus* species.

Chi-square test was used to compare NCSA rate between two groups, NCSA prevalence according to the nasal symptoms in AR and change in the NCSA prevalence before and after the treatment.

2. Results

One hundred ninety six children [94 girls, and 102 boys, mean age of 7.6 $\pm$ 3.7 years] were included in the study. There were 70 patients (35.7%) in AR group and 126 patients (64.3%) in the control group. The prevalence of NCSA was not different between these groups. Comparison of two groups was shown in Table 1.

The prevalence of NCSA was 17.9% in the whole study population. NCSA showed no difference with respect to gender (19.1% of girls and 19.6% of boys

Table 1 The prevalence of airway diseases and sociodemographic factors in allergic rhinitis patients and control group

	Allergic rhinitis positive $n = 70$ (%)	Allergic rhinitis negative $n = 126$ (%)	P (OR, 95% CI)
Age (mean ± S.D.)	7.0 ± 3.6	8.0 ± 3.7	0.07
Gender F/M	31/39 (44/56)	63/63 (50/50)	0.4
Nasal carriage of *Staphylococcus aureus*	15 (21.4)	20 (15.9)	0.3
Recurrent URTI (+)	23 (32.9)	20 (15.9)	0.006 (2.5, 1.3–5.1)
Recurrent sinusitis (+)	10 (14.3)	10 (7.9)	0.1
Recurrent AOM/OME (+)	13 (18.6)	12 (9.5)	0.06 (2.1, 0.9–5.0)
Asthma (+)	18 (25.7)	6 (4.8)	0.000 (6.9, 2.5–18.4)
Health care worker in family	4 (5.7)	9 (7.1)	0.7
Hospitalization within one year	17 (24.3)	31 (24.6)	0.9

NCSA: nasal carriage of *S. aureus*, URTI: upper respiratory tract infection, AOM: acute otitis media, OME: otitis media with effusion.

were carriers). There was no relationship of the nasal symptoms to NCSA in both AR and control groups (Table 2). The prevalence of NCSA was not significantly different between the nasal symptoms of AR patients and between AR patients and control group. The prevalence of NCSA was not different in subgroups of patients (20.8%, 16.0%, 10.0%, 16.3% for asthma, AOM/OME, recurrent sinusitis and recurrent URTI, respectively).

At the second part of the study, we investigated the effect of fluticasone propionate on NCSA status. After the dropouts, either due to the lack of follow up or use of antibiotics due to the interfering illnesses, 88 children remained (38 with allergic rhinitis and 50 controls). There were no difference between the dropouts and the remaining children in terms of demographic features. Although NCSA has decreased after treatment with intranasal fluticasone propionate, this decrease was not statistically significant (Table 3).

Table 2 The prevalence of NCSA for each nasal symptom according to the groups

Symptoms	Allergic rhinitis group NCSA, n (%)	Control group NCSA, n (%)
Itching	10/38 (26.3)	1/11 (9.1)
Nasal congestion	11/57 (19.3)	5/38 (13.2)
Rhinorrhea	4/32 (12.5)	1/13 (7.7)
Sneezing	9/45 (20.0)	2/15 (13.3)

Table 3 The effect of intranasal fluticasone propionate on the nasal *S. aureus* carriage

Group	Pre-treatment nasal *S. aureus* carriage (n, %)	Post-treatment nasal *S. aureus* carriage (n, %)
Treatment group ($n = 38$)	7 (18.4)	6 (15.7)
Control group ($n = 50$)	10 (20.0)	10 (20.0)

3. Discussion

The evidence for the role of NCSA in the etiology of allergic diseases was growing [3,4]. However, predisposing risk factors for NCSA are still to be identified. In adults, it was proposed that there might be a relationship between AR and NCSA. As far as we know, there is not much study investigating the prevalence of NCSA in childhood AR. Moreover, this is the first study that explores the effect of intranasal corticosteroid on the NCSA in children with AR. In this study, the prevalence of NCSA in children with AR was found to be 21.4% and was not different from that of control group. Treatment with fluticasone propionate nasal spray (100 μg/day (for children below 12 years) and 200 μg/day (for those above 12 years) for two months) did not influence the NCSA rate in AR patients.

In contrast to our findings, the rate of NCSA in adult AR patients was shown to be significantly higher than that of control subjects [4]. Authors have suggested that allergic nasal mucosa might provide better nutrition and less host defense. They also proposed that the increased prevalence in rhinitis might be due to increased hand-to-nose contact caused by nasal symptoms. In two studies performed on children with AR and nasal polyposis, NCSA was also found to be increased [10,11]. Contamination of nasal steroid inhalers and recurrent antibiotic usage were also said to predispose AR patients to the increased NCSA prevalence [12,13]. We could not find an increased

prevalence of NCSA in pediatric AR patients. Whether the subtype or definition of AR might be important in this regard is not known. In fact, NCSA might differ between AR subtypes mainly due to the duration of mucosal pathology. Although perennial AR was demonstrated to lead to a higher NCSA compared to healthy controls in adults, there is no study comparing the NCSA prevalence between perennial and seasonal AR.

Local mucosal administration of Staphylococcal enterotoxins was shown to trigger an inflammatory response [14]. It has also been shown that NCSA might result in higher nasal symptom scores in adults [4,15]. Even though we did not measure the severity of AR symptoms, we could not demonstrate a relationship between NCSA and the presence of nasal symptoms both in AR and control groups.

Although glucocorticoid use in nasal polyposis has been proposed to increase nasal carriage of MRSA, the actual relation of nasal corticosteroid use and NCSA was largely unknown [11]. Intranasal corticosteroids have broad anti-inflammatory effects and some of these might favor against the NCSA [16,17]. Corticosteroids show an inhibitory effect on fibronectin production, which is one of the proposed binding sites of *S. aureus* [17]. Corticosteroids also decrease the inducing cytokines of adhesion molecules (mainly ICAM-1 and VCAM-1) [18]. These molecules were proposed to be important in the cellular adhesion of *S. aureus* [18,19]. However, in a small, placebo-controlled, double-blind study by Parikh et al, it was shown that fluticasone propionate did not increase intranasal infection rate compared to placebo in adults with chronic rhinosinusitis [20]. Similarly, in a recent study in adult AR patients, it was demonstrated that two months treatment with triamcinolone acetonide aqueous nasal spray had no effect on NCSA [21]. Alike, we also could not demonstrate any effect of nasal CS use on NCSA in children with AR. Although corticosteroids presumably have the potential to decrease NCSA there might be other factors that are dominant in favor of the NCSA.

Although we did not find an increased NCSA prevalence in children with AR, it might be better if AR would have been categorized into subtypes. It's obvious that better understanding of the factors affecting the acquisition and loss of NCSA might increase our knowledge about the relationship between NCSA, allergic airway diseases and their treatments.

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