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Nasal fluid secretory immunoglobulin A levels in children with allergic rhinitis☆

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ABSTRACT

Objectives: There is growing knowledge about the immunoregulatory and possibly preventative roles of immunoglobulin A (IgA) in allergic diseases. This study aimed to investigate secretory immunoglobulin A (SIgA) levels in the nasal fluid of children who were either being treated for their allergic rhinitis (AR) with intranasal mometasone furoate or were not receiving treatment.

Methods: The study population contained 55 children with persistent AR. Group I included 27 newly diagnosed AR patients not taking any medication and group II included 28 patients treated with intranasal steroids for at least 6 months. 27 healthy control subjects were also enrolled in the study. Total symptom scores (TSS) were calculated for each patient. Nasal secretions were obtained using a new modified polyurethane sponge absorption method, and samples were analysed by ELISA.

Results: The median value for nasal fluid SIgA level in each group was 127.2 μg/ml (interquartile range; 67.3–149.6) in group I, 133.9 μg/ml (102.1–177.8) in group II and 299.8 μg/ml (144.5–414.0) in the control group. Groups I and II both had statistically significant reductions in nasal fluid SIgA levels compared to the control group ($p < 0.001$). However, there was no statistically significant difference between groups I and II ($p = 0.35$). A statistically significant and negative correlation also existed between TSS and nasal fluid SIgA levels in both groups I and II ($p = 0.006$, $rho = -0.512$ and $p = 0.01$, $rho = -0.481$, respectively).

Conclusions: SIgA levels in the nasal fluid are significantly reduced in children with AR independent of treatment and are negatively correlated with the TSS.

1. Introduction

Allergic rhinitis (AR) is characterised by sneezing, rhinorrhea, nasal congestion, itching and eye symptoms [1]. According to a large multicentre study, the overall prevalence of AR in children aged 6–7 and 13–14 was 8.5% and 14.6%, respectively [2]. Mucosal surfaces are the main gateway for antigens. The local production of secretory immunoglobulin A (SIgA) composes the primary component of mucosal immunity [3]. SIgA is the major immunoglobulin present on mucosal surfaces and it has pronounced antimicrobial effects. SIgA performs bacterial agglutination, endotoxin and virus neutralisation, and it can impede epithelial adherence and invasion by pathogens [4].

Alongside, there is an increased body of literature about the immunoregulatory roles of SIgA. Allergic disorders appear to be common in patients with IgA deficiency [5]. The bronchoalveolar lavage fluid SIgA contents of asthmatic patients are decreased compared to healthy controls, and there was a correlation between spirometric values and asthma symptoms [6,7]. High salivary SIgA levels were associated with a lesser development of allergic symptoms in sensitised children [8]. In animal models, a lack of secretory antibodies may cause immune dysfunction and intolerance against foods [9]. The administration of cholera toxin B, which is a mucosal adjuvant, to the lungs induces the production of IgA, thereby suppressing the clinical and laboratory features of asthma [10].

Intranasal corticosteroids (INSs) are a mainstay of AR treatment, and their effects on nasal symptoms are well described [11]. But, some studies showed that even short-term systemic corticosteroid treatment can cause prolonged reductions in serum immunoglobulin G and A levels [12,13]. However, there is not enough data about the effects of INSs on nasal SIgA levels in

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children. Our literature search reveals there are insufficient and conflicting results about nasal fluid SIgA levels in AR patients and no studies about whether INSs affect nasal fluid total SIgA concentrations in children. Therefore, we aimed to measure SIgA levels in the nasal fluids of paediatric AR patients, both newly diagnosed and those taking regular INS treatment, to investigate the possible role of SIgA in the pathogenesis of AR, as well as the effects of steroid treatment on nasal fluid SIgA levels.

2. Materials and methods

2.1. Patients

This study was designed with a case-control study format and performed in the Bezmialem Vakif University Paediatric Allergy and Immunology Department between July 2014 and January 2015. In total, 216 consecutive patients with persistent AR were evaluated for their eligibility to enrol in the study. Inclusion criteria were (1) age between 6 and 18 years; (2) AR diagnosis established according to criteria defined in the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [14]. Exclusion criteria were (1) acute or chronic infectious or inflammatory diseases (including asthma and atopic dermatitis); (2) history of maternal or paternal smoking; (3) use of any medications except for mometasone furoate (Nasonex®, Merck, NJ, USA) including other INSs, oral or inhaled corticosteroids, antihistamines, montelukast, poly-vitamins or minerals; (4) treatment period of less than 6 months, or dosage different than 100 mcg/day if patients taking mometasone; (5) non-compliance with mometasone therapy.

The reason we chose to conduct this study in patients more than 6 years of age was to be able to perform lung function studies and to facilitate the tolerance of the nasal sample collection procedure. To attempt to eliminate possible confounding factors related to the pharmacological properties of drugs and dosage regimens, we created a homogeneous study group that took the same dosage of the same drug. We chose mometasone furoate for the INS because it is the most commonly prescribed INS in our country. Some reports have suggested that asthma, smoking and vitamin supplementation may affect SIgA levels and its expression in some biological fluids; therefore, all these factors are considered exclusion criteria [7,15–17]. All AR patients were evaluated using a standard questionnaire in terms of the exclusion criteria and drug usage mentioned above. Patients who had asthma that was diagnosed by a doctor or signs or symptoms consistent with asthma or abnormal lung function studies were also excluded from study. The clinical diagnosis of asthma was determined using the criteria defined in the Global Initiative for Asthma guidelines [18]. The reasons for exclusion from the study were presence of asthma (59 patients), use of other medications (48 patients), maternal or paternal smoking (11 patients), presence of atopic dermatitis (9 patients), non-compliance with mometasone treatment (13 patients), different dosing regimens or shorter treatment duration (5 patients). Seventy-one patients in total met the criteria and enrolled in the study. Seven patients whose parents refused permission for their participation in the study, 5 patients who could not tolerate the nasal secretion sampling procedure, and 4 patients whose nasal secretions could not to be obtained even with proper application of the procedure were excluded from the study despite initially meeting the exclusion criteria. After this exclusion, the total number of the study participant was determined as 55.

Group I consisted of 27 patients newly diagnosed with persistent AR who had never before received therapy, and group II consisted of 28 patients with persistent AR who had been regularly taking intranasal mometasone furoate at a dose of one puff per nostril once a day (total: 100 μgr/day) as monotherapy for at least 6 months. These patients had been attending the same outpatient clinic regularly every 2 months. Compliance with the dosing regimen was assessed every 2 months through observation of the nasal spray devices and dose calculations as well as through each patient's mother signing a diary card indicating that the drug had been administered. If the drug was not taken for more than 10% of the scheduled doses, the patient was considered non-compliant with therapy and excluded from the study.

The control group consisted of 27 healthy children who periodically attended paediatric clinics at the same hospital for regular developmental check-ups. Children were included in the control group if they had no history of any allergic disease or paternal or maternal smoking and were not taking any other medications, including vitamins, minerals and analgesics. Children enrolled in the study also had no signs or symptoms of acute or chronic infectious or inflammatory disorders. The study was performed in accordance with the Declaration of Helsinki Good Clinical Practice guidelines and was approved by the Bezmialem Vakif University Ethical Committee (71306642/050-01-04/169). Informed consent was obtained from the parents of all children.

2.2. Collection of nasal secretions

Nasal secretions were obtained using a polyurethane sponge nasal secretion collector (NSC) according to the method described by Lü et al. but with minor modifications [19]. A sixty pores per inch reticulated polyurethane sponge was cut into rectangular prism shapes (base of 5 × 10 mm and height 20 mm) using a homemade cutting device, and the pieces were sterilised by autoclaving for 20 min at 121 °C prior to use. A single-use metal rod with a tip clamp was used to hold the sponge during sample collection (Fig. 1). The sponge was inserted and placed on the floor of the nasal cavity between the septum and the inferior turbinate for at least 5 min. The sponge containing nasal secretions was pulled out from the nostril and inserted into an inner tube that was in the outer centrifuge tube (Fig. 1). We pierced the bottom of a 2 ml Eppendorf tube (Eppendorf AG, Hamburg, Germany) using a 21-gauge needle and created 15 standard holes to allow nasal secretions to pass into the outer tube during centrifugation. The outer tube was a standard 10 ml vacuum blood collection tube. Next, this device was centrifuged at 3000 × *g* for 10 min to recover the nasal fluid. We obtained a median volume of 300 microlitres (μl) of nasal fluid from patients and control subjects (interquartile range [IQR]; 200–450 μl) using this method. The extracted fluid was stored at −80 °C until assayed.

2.3. Measurement of SIgA levels

SIgA levels in nasal fluid samples were measured using a secretory IgA ELISA kit (Salimetrics, Suffolk, UK). Samples were thawed at room temperature and then centrifuged at 3000 rpm

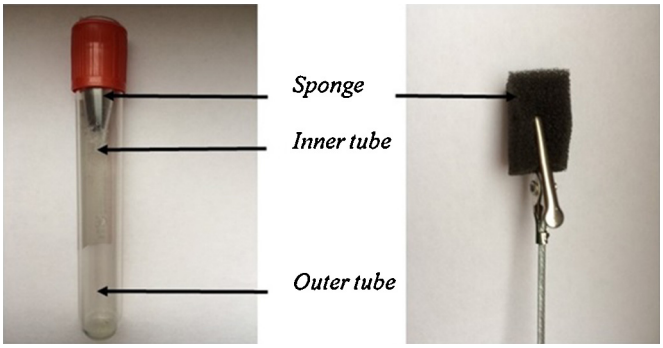

Fig. 1. Picture of nasal sample collector.