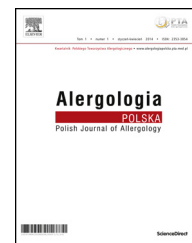


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Original research article/Artykuł oryginalny

The presence of atopy and its effect on bacterial colonization of the upper airways in children with adenoid vegetation

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ABSTRACT

Background: The aim of this study was to determine the frequency of atopy and the influence of atopy on bacterial colonization of upper airway in children with adenoid hypertrophy. **Material and methods:** Forty children were enrolled in the prospective study. Presence of atopy was diagnosed by skin-prick test. Differences in bacterial colonization of middle nasal meatus and nasopharynx according to the presence of atopy were analyzed. **Results:** Atopy was diagnosed in 75% children with adenoid hypertrophy. Presence of atopy was associated with significantly more often colonization of pathogenic bacteria (*Streptococcus pneumoniae*, *Hemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*) in the middle nasal meatus but not in nasopharynx ($P = 0.045$, $P = 0.483$, respectively). Identification of pathogenic bacteria in middle nasal meatus did not correlate with isolation of pathogenic bacteria in nasopharynx in both groups of children. **Conclusion:** There is a high incidence of atopy in children with adenoid hypertrophy. Atopy is related to increased colonization by pathogenic bacteria in middle nasal meatus but not in nasopharynx.

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Introduction

The pharyngeal tonsil is part of the lymphoid tissue that surrounds the pharynx: collectively defined as the Waldeyer's ring. Tonsils physiologically serve as a defence against inhaled antigens (microbes, allergens, etc.). Therefore, tonsils

are deeply involved in the innate and adaptive immune response because of their peculiar position at the entry of the upper aerodigestive tract. As consequence of chronic stimulation (result of prolonged antigenic exposure associated with chronic inflammation), pharyngeal tonsil may enlarge so it may almost fill the space in nasopharynx,

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limiting the airflow passage. Pharyngeal tonsil hypertrophy, also called adenoid hypertrophy or adenoid vegetation (AV) is detected in approximately one-third of the general paediatric population with maximum of appearance in pre-school children (60%) and constitutes the most frequent otorhinolaryngological indication for surgical intervention. AV has been associated with recurrent respiratory infections, respiratory dysfunction, recurrent otitis media and sleep disorders [1-3].

Allergic rhinitis (AR) is the most common immune-mediated disorder because it may affect up to 40% of the general population. AR is characterized by an inflammatory reaction after allergen exposure. AR is also frequently associated with relevant comorbidities, including other allergies, rhinosinusitis, recurrent respiratory infections, otitis media and adenoid hypertrophy. In this regard, there is firm belief that children with AR may have lymphoid hypertrophy of the upper airways, mainly concerning the adenoids [1, 4]. Moreover, it was clearly shown, that children with atopy suffer from higher frequency of respiratory infections compared to healthy children without atopic environment in the airways [5, 6].

Material and methods

Design of the study

The prospective study was conducted with 40 children divided into 2 groups according to the presence of atopy. All children enrolled in the study were scheduled to endoscopic adenotomy for adenoid vegetation at the Department of Otorhinolaryngology, Head and Neck Surgery, Comenius University, Jessenius Faculty of Medicine, University Hospital in Martin, Slovakia.

Children with systemic or local antibiotics treatment within the 2 weeks before enrolment, recent respiratory infection, increased level of C-reactive protein and those with recurrent tonsillitis were excluded from the study. We excluded all children who used drugs that could compromise the reliability of the skin test for inhalant allergens, such as antihistamines and corticosteroids. Children with skin lesions that did not allow performing the skin test were also excluded from the study.

The presence of atopy was evaluated according to the results of skin prick tests. Differences in bacterial colonization of middle nasal meatus and nasopharynx according to the allergic status were analyzed.

The study was approved by the Ethics Committee of Jessenius Medical Faculty, Comenius University in Martin, Slovakia. An informed consent was signed by all parents of participating children.

Adenoid volume assessment

The children were evaluated by nasal endoscopy for adenoid hypertrophy. Children were divided into 3 groups according to the volume of adenoids: group I: less than 30% obstruction of the cavum in both nostrils, group II: 30% to 70% obstruction and group III: greater than 70% of cavum obstruction in at least one of the nostrils.

Skin-prick test

Skin-prick tests (SPT) were carried out in the pre-defined on the volar side of the left forearm, with a space of at least 2.5 cm between each prick with the following panel of allergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, mixed spring trees (*Betula verrucosa*, *Corylus avellana*, *Alnus glutinosa*), mixed grasses (*Avena sativa*, *Hordeum vulgare*, *Secale cereale*, *Triticum sativa*), wormwood, *Alternaria alternata*, *Aspergillus fumigatus*, birch, cat and dog dander (Stallergenes, France). A histamine dihydrochloride solution in distilled water (10 mg/mL) was used as positive control and the glycerol in saline solutions was used as negative control. We used 1-mm tip plastic lancets (Stallerpoint®, Stallergenes, France). The lancet was pricked vertically into the skin through each drop for 2 s with firm pressure. A new lancet was used for each prick tests. The tests were performed as stated by the European Academy of Allergy and Clinical Immunology [7]. The skin reaction was recorded after 15 min by evaluating the skin response in comparison with the wheal given by the positive and the negative control. A prick test was defined positive if the wheal was ≥ 3 mm in its longest dimension. The children with at least one positive SPT to common inhalant allergens were considered as atopic.

Bacteriology

Middle nasal meatus and nasopharyngeal swab specimens were obtained under endoscopic control by using sterile cotton-wool swabs and transported in Stuart's transport medium to the microbiological laboratory within 2-4 h. The swab was inoculated onto Sheep blood agar (Columbia Bio-Rad, Bratislava, Slovakia), Chocolate agar with bacitracin disc, Mac Conkey agar (Bio-Rad, Bratislava, Slovakia) and placed into a 7% CO₂ incubator at 37 °C. The plates were examined after 18-24 h of incubation. The incubation was further extended to 48 h to detect the slow-growing microbes. Identification of colonies to genus or species level was based upon typical colony morphology by subculture, Gram stain, standard rapid tests (catalase, pyrrolidonyl aminopeptidase - PYR and oxidase tests), identification by latex agglutination tests and biochemical tests. All pathogenic strains were tested for their susceptibility to antimicrobial agents by using the agar diffusion method (by EUCAST) with commercial discs (Oxoid).

Statistical analysis

Frequencies of categorical data were tabulated and evaluated with chi-square test using the Yates's correction. For other data, median and interquartile range was calculated and tested with Mann-Whitney test. The statistical analysis was performed with STATISTICA Cz 10. All conclusions were based on a significance level of $P < 0.05$.

Results

Forty children (26 male, 14 female, mean age 4 ± 2.6 years) were prospectively enrolled in the study. Demographic and

Table I – Demographic and clinical data of study population

	Total (n = 40)	Atopy (n = 30)	No atopy (n = 10)	P-value
Age (yr)	4 ± 2.6	4 ± 2.8	3.75 ± 1.8	0.433
Female	14 (35%)	11 (37%)	3 (30%)	0.305
Male	26 (65%)	19 (63%)	7 (70%)	0.305
AV	3 ± 0.5	3 ± 0.5	2.5 ± 0.5	0.323

yr – years, n – number of patients, AV – adenoid vegetation; data are shown as median ± SD.

clinical data of the study population are shown in Table I. Atopy was diagnosed by skin-prick tests in 30 (75%) children. House dust mite allergens (64%) and cat dander (32%) were the most common positive aeroallergens (Fig. 1).

Bacterial growth was present in 31 of the 40 samples (77.5%) from middle nasal meatus and 40 of the 40 samples (100%) from nasopharynx. Microorganisms isolated from the middle nasal meatus and nasopharynx are presented in Tables II and III. Coagulase-negative *Staphylococcus* species, *Corynebacterium* species, *Streptococcus viridans* and *Nisseria* species are considered as commensals of upper respiratory tract. Other species of identified bacteria in our study were considered as pathogens. We found significantly more intense colonization by pathogenic bacteria in middle nasal meatus in children with atopy compare to non-atopic children ($P=0.045$). In nasopharynx, there were no significant differences in the presence of commensals or pathogenic bacteria according to the presence of atopy (Fig. 2). In children with atopy, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae* and *Moraxella catarrhalis* were significantly more often isolated from middle nasal meatus ($P=0.047$, $P=0.031$, $P=0.041$, $P=0.023$, respectively) (Table II). Those differences were not observed in

nasopharynx. Identification of pathogenic bacteria in middle nasal meatus did not correlate with isolation of pathogenic bacteria in nasopharynx in both groups of children (Fig. 3).

Discussion

Upper airways symptoms are very common in the paediatric population. Airflow limitation during childhood is frequently attributed to enlarged adenoids, but also other causes such as choanal atresia, polyps, and tumour must be considered [8].

Atopy

Allergy is frequent in children, affecting up to 40% of the general population, and may cause the open-mouth posture [9]. Well-established opinion assumes that children with AV also frequently may have AR [10]. The possible correlation between atopy and adenoid hypertrophy has been investigated by some studies that reported a positive association between the 2 disorders [11–14]. One of the possible explanations in this relationship is the overstimulation of

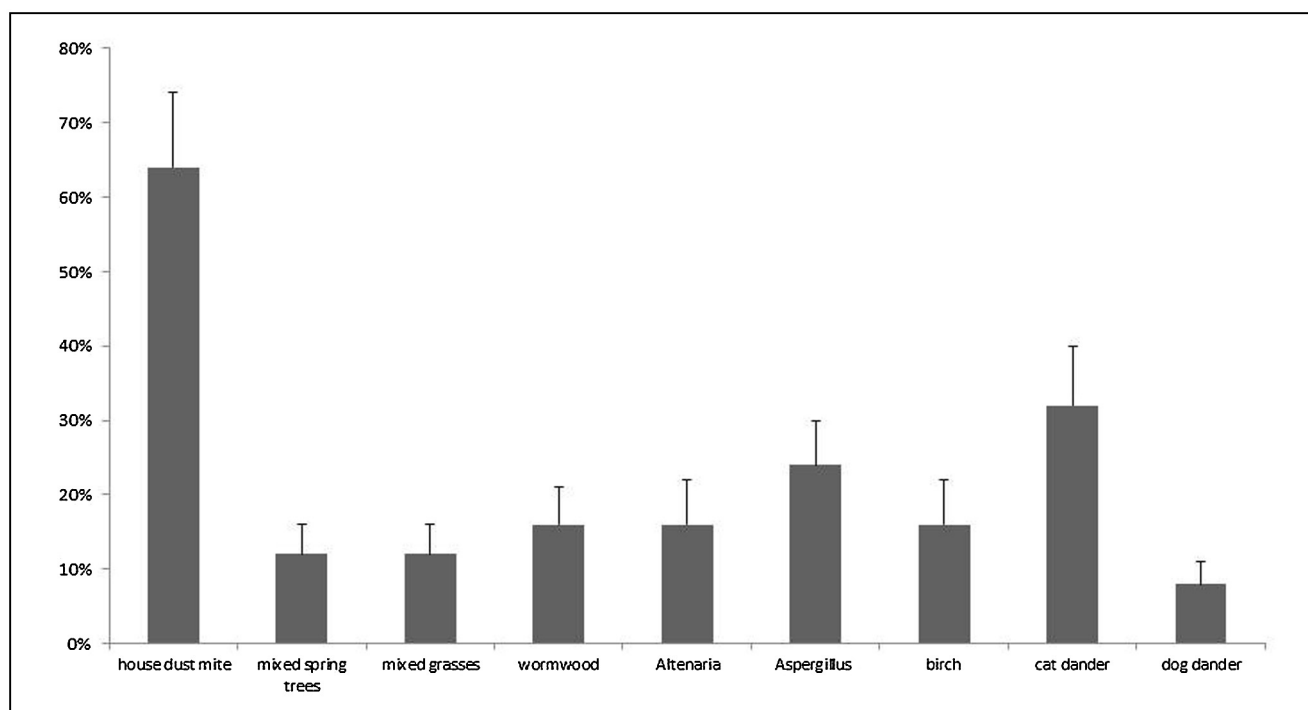


Fig. 1 – Aeroallergens identified in atopic children. Data are shown as median ± SD

Table II – Bacterial species isolated from middle nasal meatus

Bacteria	Atopy present	Atopy absent	P-value
Gram-positive			
Coagulase-negative <i>Staphylococcus</i>	7 (24%)	2 (20%)	0.601
<i>Corynebacterium</i> species	5 (17%)	2 (20%)	0.572
<i>Streptococcus viridans</i>	4 (13%)	2 (20%)	0.314
<i>Streptococcus pneumoniae</i>	3 (10%)	0	0.047
<i>Staphylococcus aureus</i>	5 (17%)	0	0.031
<i>Staphylococcus aureus</i> MRSA	0	0	NA
Gram-negative			
<i>Neisseria</i> species	0	0	NA
<i>Haemophilus influenzae</i>	7 (23%)	1 (10%)	0.041
<i>Moraxella catarrhalis</i>	11 (36%)	2 (20%)	0.023

NA – not applicable.

Table III – Bacterial species isolated from nasopharynx

Bacteria	Atopy present	Atopy absent	P-value
Gram-positive			
Coagulase-negative <i>Staphylococcus</i>	2 (7%)	1 (10%)	0.589
<i>Corynebacterium</i> species	0	0	NA
<i>Streptococcus viridans</i>	22 (73%)	7 (70%)	0.568
<i>Streptococcus pneumoniae</i>	8 (27%)	3 (30%)	0.334
<i>Staphylococcus aureus</i>	10 (33%)	3 (30%)	0.524
<i>Staphylococcus aureus</i> MRSA	0	0	NA
Gram-negative			
<i>Neisseria</i> species	3 (10%)	5 (50%)	0.023
<i>Haemophilus influenzae</i>	12 (40%)	3 (30%)	0.243
<i>Moraxella catarrhalis</i>	9 (30%)	2 (20%)	0.279

NA – not applicable.

immune system caused by airborne allergens with subsequent enlargement of adenoid lymphatic tissue [15, 16]. Furthermore, intranasal corticosteroids used in treatment of allergic rhinosinusitis, improve nasal obstruction symptoms

in children and this improvement may be associated with a reduction in adenoid size [17–19].

In this study, atopy was diagnosed in 75% of children with adenoid hypertrophy. Similarly to our results,

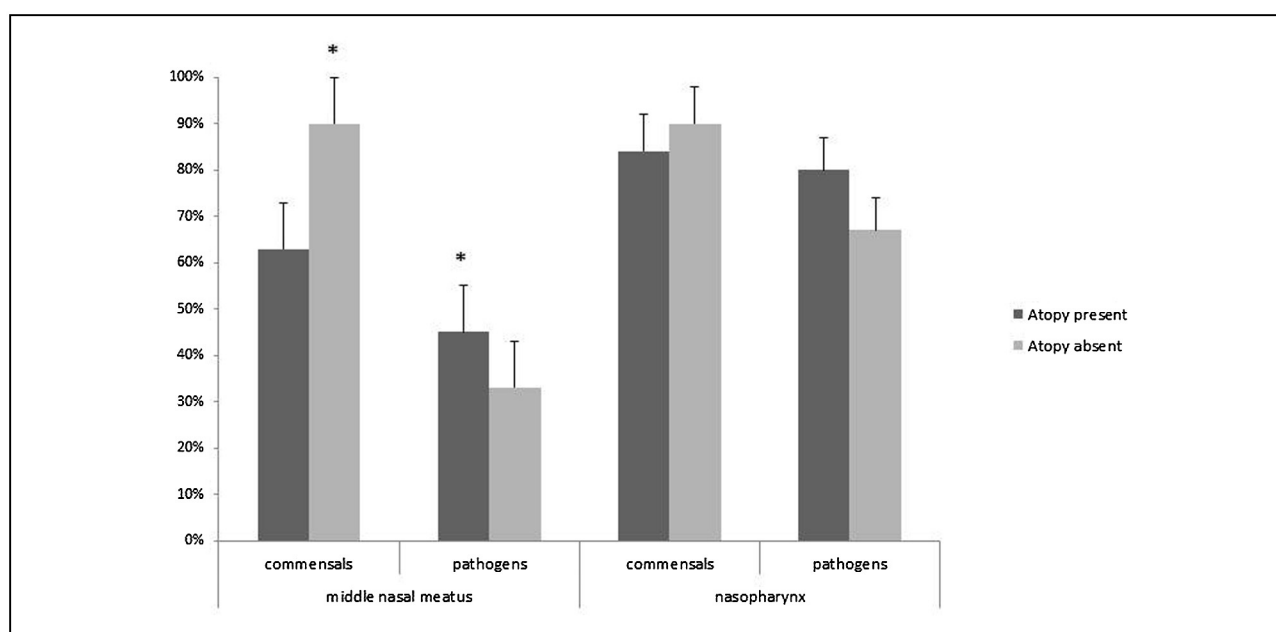


Fig. 2 – Differences in microbial isolation and presence of atopy. Data are shown as median $\pm$ SD, *P < 0.05

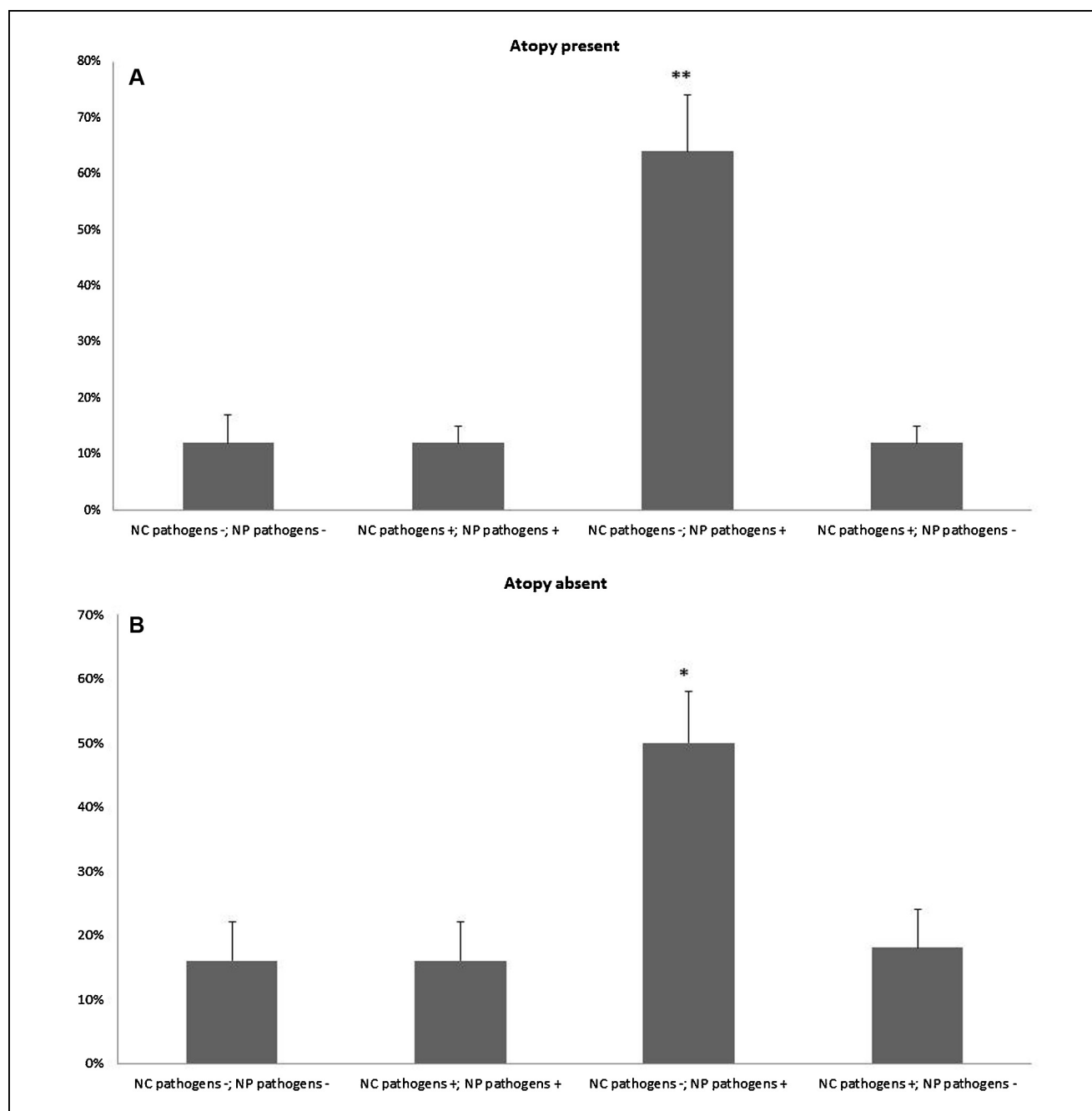


Fig. 3 – Correlation in microbial isolation from middle nasal meatus and nasopharynx. NC – nasal cavity, NP – nasopharynx, pathogens– – no pathogens present, pathogens+ – pathogens present; data are shown as median $\pm$ SD, * $P < 0.05$, ** $P < 0.005$

Sadeghi-Shabestari et al. [20] found 70% positive skin reactions to aeroallergens and food antigens in a group of 117 children with adenotonsillar hypertrophy and only 10% were positive in a control group of children of the same age, but without adenotonsillar hypertrophy. Taken together, atopy and allergic rhinitis can be considered as a risk factor for the development of adenoid hypertrophy in children with atopic sensitization to respiratory allergens. Moreover, atopy significantly contributes to the increase respiratory tract infections and chronic stimulation of upper airways mucosal lymphatic tissue [6].

Bacterial colonization

Colonization of organisms is the first step towards development of respiratory diseases. Therefore, recognition of the risk factors for colonization is important. However, data are sparse with regard to the influence of atopy on rates of nasal and nasopharyngeal colonization with these organisms in children and adults.

In the present study, we demonstrated that children with atopy had a significantly higher rate of pathogenic bacteria (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella*

catarrhalis and *Staphylococcus aureus*) carriage than non-atopic children. The increased carriage rate in children with atopy was seen in the middle nasal meatus but not nasopharyngeal specimens. One explanation for this finding is the study population. All children in the present study underwent surgical treatment due to adenoid vegetation. Pathogens, such as *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* are most commonly detected bacteria in adenoid tissue [21, 22]. Therefore we assume that colonization by pathogens was up-regulated due to the adenoid vegetation (enlarged adenoid tissue), thus, the possible differences between the presence of atopy and pathogens in nasopharynx in children with adenoid vegetation could not be manifested.

Furthermore, identification of bacteria from the middle nasal meatus did not correlate with isolation of pathogenic bacteria from nasopharynx. Pathogens were significantly more often isolated from nasopharynx than nasal cavity. Therefore we assume that bacteriological swab from nasopharynx is more reliable for diagnosis of focal infection in children. On the other hand, colonization of pathogenic bacteria was influenced by the presence of atopy only in middle nasal meatus not nasopharynx, where the possible differences could not be manifested according to the up-regulation of pathogens in adenoid vegetation.

The mechanism by which atopy is associated with the carriage of potentially pathogenic bacteria is not fully understood. One of the possible explanations is based on remodelling of respiratory mucosa. Several studies showed that atopy is associated with airway changes including epithelial damage, goblet cell hyperplasia and smooth muscle hypertrophy [23–25]. Increased mucous secretion and reduced ciliary beat of respiratory epithelial cells leads to alterations of mucociliary transport. As a consequence, more intense colonization of upper respiratory tract by the pathogenic bacteria might be a result of impaired local defence mechanisms of respiratory mucosa. Moreover, the increased nasal colonization by pathogenic bacteria may be a predisposing factor to additional spread, resulting in lower respiratory tract infections. This could be further increased during coinfection with respiratory viruses, such as influenza viruses in children [26].

Conclusion

There is a high incidence of atopy in children with adenoid hypertrophy. Atopy is related to increased colonization by pathogenic bacteria in middle nasal meatus but not in nasopharynx.

The high prevalence of atopy and adenoid hypertrophy emphasize the importance of a complete ENT and immunoallergologic investigations, because proper treatment lead to improvement of quality of life for these patients, avoiding functional and structural changes.

Authors' contributions/Wkład autorów

According to order.

Conflict of interest/Konflikt interesu

None declared.

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Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

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