THE ROLE OF IMMUNE DISORDERS IN THE DEVELOPMENT OF EXUDATIVE MIDDLE OTITIS IN CHRONIC ADENOIDITIS IN CHILDREN.

[1]Salomov Kudrat Mengqobilovich
[2]Zokirova Mukhlisa Rustam kizi
[1]PhD, Assistant of the Department of Otorhinolaryngology, Pediatric Otorhinolaryngology. Tashkent State Medical University

[2] Resident of the Department of Otorhinolaryngology, Pediatric Otorhinolaryngology.

Tashkent State Medical University, Tashkent, Uzbekistan

Abstract
Background: Otitis media with effusion involves non-purulent fluid in the middle ear and conductive or mixed hearing loss. Eustachian tube dysfunction, often linked to chronic adenoiditis, is a key factor. The pharyngeal tonsil supports local immunity, and reduced secretory IgA may promote disease development.
Objective: This study will examine how various components of mucosal immune defense (including IgA, IL-6, IL-10, and IFN-γ) are reflected in the symptoms and progression of chronic adenoiditis (CA). In parallel, their role in the predisposition to developing otitis media with effusion (EOM) in the presence of CA will be investigated.
Materials and Methods: The study included children with chronic adenoiditis, with or without otitis media with effusion. Diagnosis was based on clinical data, otomicroscopy, nasopharyngeal endoscopy, tympanometry, and audiology. Nasal lavage fluid was analyzed for secretory IgA and cytokines, and results were compared with healthy controls.
Result: The study demonstrated that the imbalance of immune markers in nasal secretions reflects enhanced inflammation and impaired local immune homeostasis in children with chronic adenoiditis and otitis media with effusion.
Conclusion: In children with chronic adenoiditis, especially those complicated by otitis media with effusion, local levels of IgA, IL-6, and IL-10 are decreased, while the frequency of IFN-γ detection is increased. This indicates weakened protective mechanisms of the nasal and nasopharyngeal mucosa and a higher risk of involvement of the middle ear mucosa in the pathological process.

Keywords: exudative otitis media, adenoiditis, immunoglobulins, interleukin, immunity.

Introduction

Exudative otitis media (EOM) is a condition in which the middle ear inflames without suppuration, but with the formation of fluid of various compositions (serous, mucoid, or mucoid) in its cavity. This leads to hearing impairment manifested as conductive or mixed hearing loss. It is believed that auditory tube dysfunction, often caused by chronic adenoiditis (CA), plays a key role in the development of EOM[1]. In preschool and primary school-aged children, chronic adenoiditis (CA) is a fairly common problem affecting from 18% to 55% of upper respiratory tract diseases. This means that it plays a very important role among ENT diseases in this age

group. [4]. A characteristic feature of chronic adenoiditis is its prolonged nature, frequent exacerbations, and the inability to completely eliminate the pathological changes. Associated pathology encompasses various organs and systems and is represented by a wide range of comorbidities, the number of which can be counted by the tens. [3]. The pharyngeal tonsil is an important element of the lymphoepithelial pharyngeal ring and actively participates in the formation of local immunity of the upper respiratory tract. The pharyngeal tonsil, being a key component of the nasal-associated lymphoid tissue (NALT) in the nasal cavity and paranasal sinuses, plays a crucial role in attracting functionally active immune cells to the respiratory tract mucosa. In addition, it modulates the strength of immune responses and stimulates the production of secretory immunoglobulin A (sIgA). [2] Based on modern data, the ciliated epithelium of the pharyngeal tonsils of the nasal cavity and nasopharynx provides IgA synthesis to a greater extent than the palatine tonsils. [2]. The nasal cavity, being the entrance gateway to the respiratory tract, primarily experiences the maximum impact of pathogenic environmental factors. Immunoglobulin A (IgA) plays a central role in protecting the mucous membranes, especially the respiratory tract, acting as the first line of defense. When IgA levels decrease due to weakened local or general immunity, the protective barrier of the auditory tube's mucous membrane is disrupted. This may contribute to the development of exudative otitis media (ESO). [6, 7]. The process of secretory IgA formation involves the differentiation of B-lymphocytes into plasma cells under the influence of cytokines such as IL-6, IFN-γ, and IL-10, produced by T-helpers. [4]. Important it should be noted that IL-6 and IFN-γ primarily stimulate inflammation, whereas IL-10, in contrast, suppresses inflammatory reactions and controls the strength of the immune response.

Materials and Methods

The study included 44 children of both sexes, aged 2 to 7 years, diagnosed with chronic adenoiditis in remission. The first group consisted of 24 patients with isolated chronic inflammation of the pharyngeal tonsil, while the second group comprised 20 children who were diagnosed with otitis media with effusion secondary to chronic adenoiditis. The diagnosis was verified based on clinical and anamnestic data, otomicroscopy results using an operating microscope, and endoscopic examination of the nasopharynx using a 2.7 mm rigid endoscope with a 0° viewing angle (Karl Storz, Germany). The functional state of the middle ear was assessed by tympanometry (type B or C) using an Interacoustics tympanometer (Denmark). To assess auditory function, an audiological examination was conducted, which included pure-tone audiometry. This examination, performed using an Interacoustics audiometer (Denmark), diagnosed grade I or II conductive hearing loss. For laboratory analysis, samples were collected from the nasal cavity. These samples consisted of nasal lavage fluid obtained by irrigating the nasal passages with 2-4 milliliters of sterile isotonic sodium chloride solution. The resulting fluid was centrifuged at 3000 rpm, after which the supernatant was separated and frozen at -18°C until further analysis. The level of secretory immunoglobulin A (IgA) was measured by enzyme-linked immunosorbent assay (ELISA) using commercially available kits from Human GmbH (Germany), which are widely used in laboratory practice in Central Asian countries. A solid-phase enzyme-linked immunosorbent assay with commercial reagent kits from DRG International (Germany) was used to measure IL-6, IFN-γ, and IL-10. Cytokine concentrations

were calculated in picograms per 1 g of protein in the nasal lavage fluid. The total protein level in the study samples was determined by the biuret method using reagents from Human GmbH (Germany). To process the clinical and anamnestic information in both cohorts, a questionnaire was used to systematically assess the key manifestations of chronic adenoiditis: impaired nasal breathing, nocturnal snoring, rhinolalia, pathological nasal discharge, and cough. The severity of each symptom was rated on a five-point scale, where 1 point corresponded to the complete absence of the symptom and 5 points to its maximum severity. Intermediate values (2, 3, 4) reflected minimal, moderate, and above-average symptom intensity, respectively. To assess mucosal immunity parameters, a control group of 15 apparently healthy children of a corresponding age was included. Statistical analysis of the data was performed using the Statistica 8.0 software package. The median (Me) and interquartile range (Q25-Q75) were calculated as part of the descriptive statistics. Quantitative indicators between independent samples were compared using the non-parametric Wilcoxon rank-sum test. Differences were considered statistically significant at $p < 0.05$.

Results

The evaluation of patient complaints demonstrated that the severity of nasal breathing difficulty and snoring during sleep did not differ statistically between the groups. However, symptoms such as rhinorrhea, cough, and nasal voice were significantly less pronounced in children from the first group (CA) compared to children from the second group (CA with EOM). Clinical and anamnestic data are presented in Diagram 1. A comparative analysis of the questionnaires revealed that the second group of patients had a statistically significant higher total score for all symptoms than the first group ($p = 0.017$, Diagram 1). In the samples taken from the control group participants, secretory immunoglobulin A was present in every case (100%). Moreover, its concentration was significantly higher than in patients from both clinical groups. Detailed data on the concentration of secretory IgA and cytokines in nasal washes are provided in Table 1. Severity of Clinical Symptoms in Children with Chronic Adenoiditis and with EOM. The diagram displays the median (Me) and interquartile range (Q25-Q75) for five clinical symptoms in two patient groups: CA (n=24) and CA+EOM (n=20).

The severity of clinical symptoms in children with chronic adenoiditis and concurrent exudative otitis media.(Me.Q25-Q75)

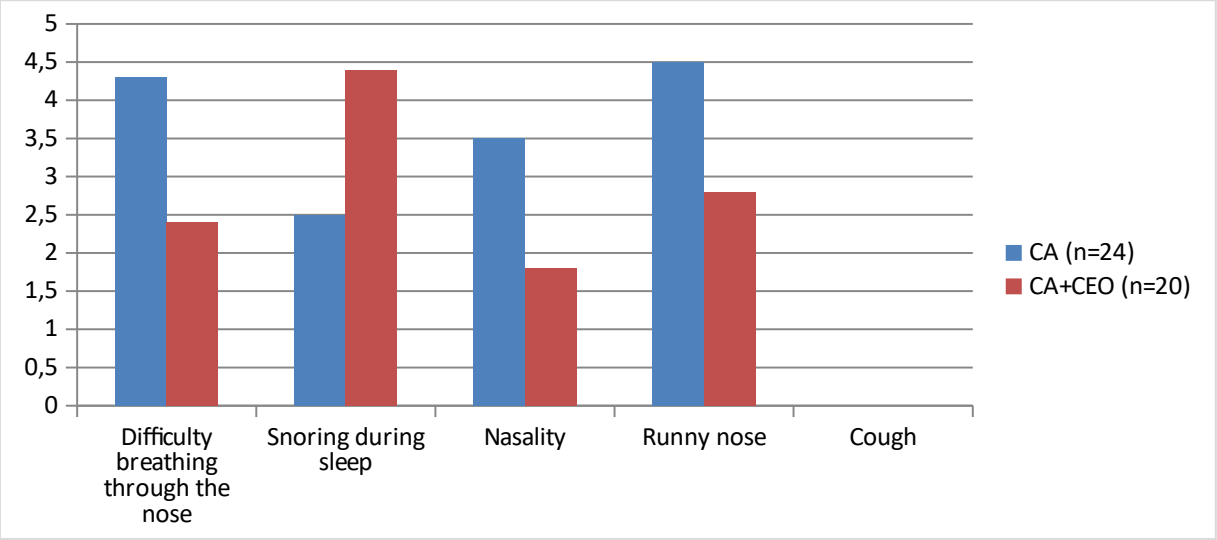

Table 1. IgA and cytokine levels in nasal washings in patients with chronic adenoiditis and OME, pg/g protein (Me, Q25-Q75).

Parameter	Control group (n=15)	CA (Group 1, n=24)	CA + OME (Group 2, n=20)	p1	p2
IgA	40,2 (28,0–65,0)	23,5 (18,0–35,0)	12 (4,0–20,0)	0,03 / 0,05	0,0005 / 0,008
IL-6	42,0 (5,0–240,0)	7,5 (4,0–21,0)	7,25 (2,5–12,0)	0,03 / 0,02	0,006
IL-10	0 (0–0)	0 (0–0)	0 (0–4,0)	—	—
IFN-γ	0 (0–0)	0 (0–1,0)	0 (0–3,8)	0,07 / 0,09	—
Note: Me - median, Q25-Q75 - interquartile range; p1 - significance level of differences compared to the control group; p2 - significance level of differences between the two groups.					

In the group of patients with isolated chronic adenoiditis (CA), IgA was detected in nasal wash samples in 92% of cases. A similar detection rate for this immunoglobulin (92%) was also noted in children with CA complicated by otitis media with effusion (EOM).

According to the results of statistical analysis, IgA levels in patients of the first group showed a downward trend compared to the control group. However, despite this trend, the observed differences were not statistically significant ($p = 0.006$). At the same time, children in the second group had a significant decrease in IgA concentration relative to control values (12 [4.0-20.0] pg/g of total protein; $p = 0.0005$). Additionally, the IgA level in patients with a combination of CA and EOM was found to be statistically significantly lower compared to the values in children with uncomplicated CA ($p = 0.008$).

The study of the cytokine profile of nasal lavage in healthy children demonstrated that interleukin-6 (IL-6) was detected in the vast majority of samples (over 80%) and was characterized by the highest concentrations compared to both clinical groups, reaching 42.0 [5.0-240.0] pg/g of total protein.

Regarding interleukin-10 (IL-10) and interferon-γ (IFN-γ), the median values in the control group were zero. Nevertheless, IL-10 was detected in 21% of the examined children, and in the positive samples, its concentration was 20.5 [5.0-34.0] pg/g of protein. Interferon-γ was detected

only in isolated cases (6.3%), and its content was at a minimal level, not exceeding the sensitivity threshold of the test systems used.

Table 3. Analysis of the prevalence and levels of IL-10 and IFN-γ in positive nasal wash samples from patients with CA and EOM.

Group	IL-10, Me (Q25-Q75), pg/g protein	Frequency of positive samples, %	IFN-γ, Me (Q25-Q75), pg/g protein	Frequency of positive samples, %
Control (n=15)	20,5 (5,0–34,0)	22	–	6
CA (Group 1, n=24)	17,0 (12,5–40,0)	13	16,5 (15,0–21,0)	17
CA + OME (Group 2, n=20)	–	9	26,0 (4,0–120,0)	31

In children with chronic adenoiditis without concomitant otitis media with effusion, a statistically significant deficiency of IL-6 in the nasal secretion was recorded compared to their healthy peers (median 7.5 pg/g protein; p = 0.03). Notably, the median values of IL-10 and IFN-γ in this group were zero. The analysis showed that IL-10 was present in 13% of the samples studied, which is approximately half its detection frequency in the control group. However, in the samples where IL-10 was detected, its concentration did not differ from the control values. At the same time, IFN-γ was detected in 17% of samples, which is almost three times more frequent than in healthy children, with a median concentration of 16.5 pg/g of protein in positive samples.

The study results indicate that children with CA and EOM have a marked decrease in IL-6 concentration (7.5 [4.0-21.0] pg/g protein; p = 0.02) (Table 1), which is a statistically significant difference from the control group. Regarding IL-10 and IFN-γ, their median values generally did not differ from the control and the CA without EOM groups, remaining at zero. However, despite this, a trend toward an increased IFN-γ level was recorded compared to the control group (p = 0.09). A more detailed analysis showed that IL-10 was detected very rarely (in 9% of cases), whereas IFN-γ was detected significantly more often (in 31% of cases), and its concentrations in these positive samples were quite high (26.0 [4.0-120.0] pg/g protein, Table 3). A more detailed analysis showed that IL-10 was detected extremely rarely (9% of cases), while IFN-γ was detected significantly more frequently (31% of cases), and in these positive samples, its concentrations were quite high. (26.0 [4.0-120.0] pg/g protein, table.

The comparative analysis established that IFN-γ levels in positive samples did not show statistically significant fluctuations between the clinical groups. At the same time, the interpretation of the IL-10 data is limited, as its concentration in the second group was minimal (trace amounts), which prevents a full comparison.

Discussion

The findings of the present study confirm that chronic adenoiditis, particularly when complicated by otitis media with effusion, is associated with impaired local mucosal immunity. Children with these conditions demonstrated decreased levels of secretory IgA and IL-6 in nasal secretions, along with rare detection of IL-10 and relatively frequent presence of IFN-γ, indicating a shift

toward a pro-inflammatory Th1 response. These results highlight the critical role of local immune factors in maintaining the protective function of the nasopharyngeal mucosa and preventing the spread of inflammation to the middle ear.

The study emphasizes the importance of monitoring immune markers in children with chronic adenoiditis to identify those at higher risk for otitis media with effusion. Supporting local mucosal immunity, for example through targeted interventions or immunomodulatory strategies, may help reduce disease progression. Despite these findings, ongoing evaluation of mucosal immune status remains essential, as fluctuations in immune responses can influence susceptibility to middle ear pathology over time.

This approach aligns with previous research demonstrating that local immune deficiencies contribute to the development and persistence of otitis media with effusion in children with adenoid hypertrophy.

Conclusion

The intensification of chronic adenoiditis symptoms in patients of the second group (with exudative otitis media) statistically confirms a more active inflammation. The study of immune markers in nasal rinse water revealed similar trends in both groups of patients compared to the control group: a decrease in the level of immunoglobulin A (IgA) and a decrease in the production of interleukin-6 (IL-6). In this case, interleukin-10 (IL-10) was detected rarely, and interferon-γ (IFN-γ) was detected relatively frequently. Low IgA levels, and in some cases its complete absence, indicate the key role of this protective protein in maintaining the immune homeostasis of the nasopharyngeal mucosa and nasopharynx, which is provided by the local immune system (NALT).

The detection of IFN-γ in nasal secretions reflects the shift in immune balance towards the predominance of type 1 T-helpers in chronic inflammation of the pharyngeal tonsils. This imbalance was most pronounced in patients with EOS, which corresponds to data presented in the works of S. Matkovic and co-authors [6]. The presence of IFN-γ, on the one hand, indicates its pro-inflammatory effect when inflammation spreads to the middle ear, and on the other hand, confirms its participation in the regulation of local IgA production in the nasopharynx.

Consequently, a decrease in local IgA, IL-6, and IL-10 levels, along with the appearance of IFN-γ in nasal flush, indicates a weakening of the mucous membrane's protective mechanisms and the depletion of its local reserves. This can contribute to the spread of the pathological process to the mucous membrane of the middle ear.

Thus, a decrease in the local production of IgA, IL-6, and IL-10, along with the detection of IFN-γ in nasal flushing water, indicates a weakening of the mucous membrane's protective mechanisms and the depletion of its functional capabilities. This, in turn, can contribute to the development of a pathological process in the mucous membrane of the middle ear.

References

1. Hasanov S.A., Amonov Sh.E. // Chronic purulent otitis media in children. Monograph. 2010.

2. Amonov Sh.E., Karabayev Kh.E., Nurmukhamedova F.B., Abdullayev Kh.N., Salomov K.M., Egamberdiyeva Z.D., // Anatomy, physiology and methods of studying the ear. Study Guide. 2022.
3. Karaboeva, Z. K., Nasretdinova, M. T., Egamberdieva, Z. D., & Karabaev, H. E. (2024). Optimization of treatment methods for chronic allergic rhinitis in workers producing glass-plastic structures. Central Asian Journal of Medical and Natural Science, 5 (4), 871-875.
4. Salomov, K., & Jabbarova, D. (2023). Dysphonia is a sign of laryngeal diseases. Pediatrics, 1 (1), 164-167.
5. Amonov, S., Alimova, D., Nurmukhamedova, F., Umarov, K., & Salomov, K. (2020). Treatment optimization of chronic odontogenic maxillary sinusitis. European Journal of Molecular & Clinical Medicine, 7 (2), 2419-2422.
Ergashev, J., Santos, S., Rasulova, N., Yakubov, M., & Salomov, K. (2019). Clinical picture of vestibular schwannomas in a series of 106 patients who underwent various treatment methods. A New Day in Medicine, (4), 369-373.
7. Yeo S.G., Park D.C., Choo J.H. et al. Squamous metaplasia and BCL-6 in pediatric adenoid accompanied by otitis media with effusion // Yonsei Med. J. 2007. V. 48, No. 3. P. 449-456.
8. Alimova, D. D., & Sagidullaeva, D. B. (2025). Clinical characteristics of patients and treatment of chronic polypoid rhinosinusitis. Central Asian journal of medicine, (2), 32-41.
9. Rajabov A.H., Yakubboev B.R.// Modern approaches to the diagnosis and treatment of chronic rhinosinusitis in children. Science and innovation international scientific journal volume 3 issue 9 September 2024. P. 257-263.
10. Nasyrov V.A., Izayeva T.A., Ismailova A.A. // "Actual problems in the treatment and speech rehabilitation of congenital deafness in Kyrgyzstan," article, Bulletin of KGMA named after I.K. Akhunbayev, 2019, No2, pp. 10-15.