

## Original Research Article

# Balloon dilation of Eustachian tube combined with triamcinolone acetonide therapy for secretory otitis media

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### Abstract

**Purpose:** To determine the effect of combining Eustachian tube balloon dilatation with triamcinolone acetonide on inflammatory response and immune function in secretory otitis media patients.

**Methods:** Seventy-six (76) patients diagnosed with acute secretory otitis media in the Ninth People's Hospital Affiliated with Shanghai Jiao Tong University, Shanghai, China were randomly assigned to study group (SG) and control group (CG). Patients in CG received 40 mg triamcinolone acetonide injections in the tympanic membrane weekly for 4 weeks, while SG patients were administered Eustachian tube balloon dilatation in addition to triamcinolone acetonide injection. Pre- and post-treatment assessments in the two evaluated groups included the proportion of T lymphocytes, serum inflammatory molecules and Eustachian Tube Score (ETS).

**Results:** The study group exhibited a significantly higher efficacy (92.1 %) than the control group (68.4 %;  $p < 0.05$ ). In addition, the study group exhibited higher  $CD8^+$ ,  $CD4^+$ ,  $CD4^+/CD8^+$  ratio and T cells proportion after treatment ( $p < 0.05$ ). Furthermore, the concentration of serum inflammatory cytokines (PCT, IL-2, IL-4, TNF- $\alpha$ ) in SG was significantly lower than that in CG ( $p < 0.05$ ). Also, the ETS score in CG was lower ( $3.53 \pm 2.40$ ) compared to SG ( $5.25 \pm 2.02$ ) after treatment ( $p < 0.05$ ).

**Conclusion:** The combination of triamcinolone acetonide and Eustachian tube balloon dilatation demonstrates enhanced efficacy in alleviating symptoms, diminishing inflammatory responses and re-establishing immune balance in the treatment of acute secretory otitis media, underscoring its significant promise. Longer follow-up and larger sample size prospective studies are, however, warranted.

**Keywords:** Balloon dilation, Eustachian tube, Triamcinolone acetonide, Secretory otitis media, Inflammatory reaction, Immune function

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## INTRODUCTION

Secretory otitis media is a prevalent ear disease characterized by middle ear effusion, increased mucous membrane secretion and hearing impairment, affecting children and adults [1]. Multiple factors could cause secretory otitis media including upper respiratory tract infection, immune dysregulation, allergy and Eustachian

tube dysfunction. Eustachian tube serves to maintain normal middle ear ventilation and drainage. Dysfunctional Eustachian tube may result in fluid accumulation in the middle ear, creating an environment conducive to inflammation and infection [2]. The main symptoms of secretory otitis media include ear fullness, with some patients also experiencing tinnitus and earache. These symptoms

significantly impact patients' life quality, especially impairing children's speech and cognitive development.

Conservative treatment is the first choice for secretory otitis media, especially for patients with initial diagnosis or mild symptoms. At present, therapeutic options for secretory otitis media include antibiotics, anti-inflammatory medications and surgery, but their efficacy varies. For some patients, allergy and immunotherapy may help to relieve symptoms [3]. This involves the identification and management of allergic factors that may lead to secretory otitis media and the corresponding allergic treatment. Some patients experience persistent or recurrent symptoms, necessitating more effective treatment options. Surgical treatment may be considered when conservative treatment is ineffective or symptoms last for a long time. When choosing surgical treatment, a comprehensive evaluation should be made according to the specific situation and etiology of patients [4]. Eustachian tube surgery and tympanic membrane catheterization are common choices, but the choice should be based on the severity of the disease and the needs of patients.

As an innovative treatment, Eustachian tube balloon dilation is gaining increasing attention. It is anticipated to enhance its ventilation function, as well as decrease the possibility of middle ear effusion. Relative to traditional Eustachian tube surgery, Eustachian tube balloon dilatation is less invasive and gentler. It is now widely performed due to its minimal anesthesia-associated complications and minor surgical trauma, which make it more readily accepted by patients. Balloon dilation of Eustachian tube shows promising application potential and the technology and equipment are constantly improved [5].

Triamcinolone acetonide is a topical corticosteroid that inhibits inflammatory responses, and reduces local congestion and body fluid extravasation [6]. It has been widely administered to various middle ear diseases due to its anti-inflammatory and immunomodulatory effects [7]. Studies have shown that long-term use of triamcinolone acetonide is safe for children and adults and will not cause obvious hormone-related side effects [8]. This provides a feasible choice for patients with secretory otitis media for long-term treatment. This study aimed to investigate the impact of eustachian tube balloon dilation combined with triamcinolone acetonide on inflammatory and immune reactions in secretory otitis media patients.

## METHODS

### General information

Seventy-six (76) acute secretory otitis media patients in the Ninth People's Hospital Affiliated with Shanghai Jiao Tong University, Shanghai, China were recruited. Study population was assigned to a study group and control group, each with 38 patients. This study received approval from the Ethics Committee of the Ninth People's Hospital affiliated with Shanghai Jiao Tong University (approval no. SH9H-2023-T316-5) and was conducted in line with the guidelines of Helsinki Declaration [9].

### Inclusion criteria

Patients between 16 and 75 years old; clinically and audiological diagnosed with otitis media; intact tympanic membrane with no significant structural abnormalities; Preoperative Ear, Throat, and Speech (ETS) score  $\leq 5$  and patients with Acoustic immittance tympanogram results showing type B or C were admitted into study.

### Exclusion criteria

Patients younger than 16 years or older than 75 years old; who have undergone neck or head surgery in the past three months; in whom there was the presence of tympanic membrane perforation or other significant abnormalities; with acute upper respiratory tract infection and severe systemic diseases or malignant tumors and patients who were unwilling to comply with study were excluded.

### Treatment process

Patients in control group (CG) were treated with triamcinolone acetonide. Before administration, the external auditory canal of all patients was thoroughly disinfected. Next, a 1-gram tetracaine patch was applied to the surface of the tympanic membrane for 5 min after which 40 mg of triamcinolone acetonide (Kunming Jida Pharmaceutical Co. Ltd, National Medicine Standard no. H53021604) was injected into the tympanic membrane and maintained for 30 minutes. The treatment regimen was once a week for 30 days.

On the other hand, patients in study group (SG) received Eustachian tube balloon dilatation based on triamcinolone acetonide injection. Eustachian tube balloon dilation surgery was conducted using a specific kit (Spiggle & Their Medicine Technik GmbH, Germany). The surgery was performed under local anesthesia combined

with sedation, with the assistance of laryngoscopes. A guide wire was carefully inserted into the entrance of the patient's Eustachian tube, followed by the advancement of a balloon catheter through the guiding catheter to enter Eustachian tube.

The balloon was inflated to gradually expand the Eustachian tube without causing tissue damage. The permeability and ventilation of the Eustachian tube were determined and patients' sensations during the procedure were monitored to avoid discomfort or complications.

**Evaluation of parameters/indices**

**Flow cytometry**

Patients' blood samples were collected before and after treatment, and the human peripheral blood mononuclear cells (PBMC) were isolated using Ficoll density gradient centrifugation method. The proportion of CD8+ T cells, CD4+ T cells and CD4+/CD8+ ratio was analyzed by NovoCyte Flow Cytometer (ACEA Biosciences, Hangzhou, China) and Flowjo software.

**Enzyme-linked immunosorbent assay**

Serum inflammation-associated molecules such as procalcitonin (PCT), IL-2, IL-4 and tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) were determined with a commercial ELISA kit.

**Treatment efficacy**

The therapeutic effects in the two groups of patients (CG + SG) were evaluated as follows: The disappearance of symptoms such as tinnitus and earache was considered a significant improvement (Is); an obvious alleviation of tinnitus and earache was regarded as effective (Ie); no change in symptoms was considered invalid. Therefore, the total effective rate (TE) was calculated using Eq 1.

$$TE = (I_s + I_e) / (CG + SG) \times 100 \dots\dots\dots (1)$$

**Eustachian tube function**

The Eustachian tube function was assessed using the Eustachian Tube Score (ETS). It includes five items: Eustachian tube opening delay index (R) assessed through objective Eustachian Tubomanometry (TMM), and the Valsalva action and click scores in subjective assessment. Each item has a maximum score of

2, with a total possible score of 10. An ETS of  $\leq 5$  indicates impaired Eustachian tube function.

**Statistical analysis**

Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM, Armonk, NY, USA) was utilized for data analysis. Data were described as mean  $\pm$  standard deviation (SD) or n (%) according to the distribution type. The differences between SG and CG were assessed using student's *t*-test. Statistical significance was determined with a *p*-value threshold of less than 0.05.

**RESULTS**

**Patients' baseline information**

The demographic information for study and control groups is presented in Table 1 below. The characteristics of the two groups were statistically comparable (*p* > 0.05).

**Table 1:** Baseline characteristics of SG and CG

Variable		Control group	Study group
Age (years)		34.75 $\pm$ 7.21	34.68 $\pm$ 6.95
Gender	Male	21	19
	Female	17	19
Ear side	Left	21	19
	Right	17	19
Acoustic immittance	B	24	22
	C	14	16

**Therapeutic effects of patients in both groups**

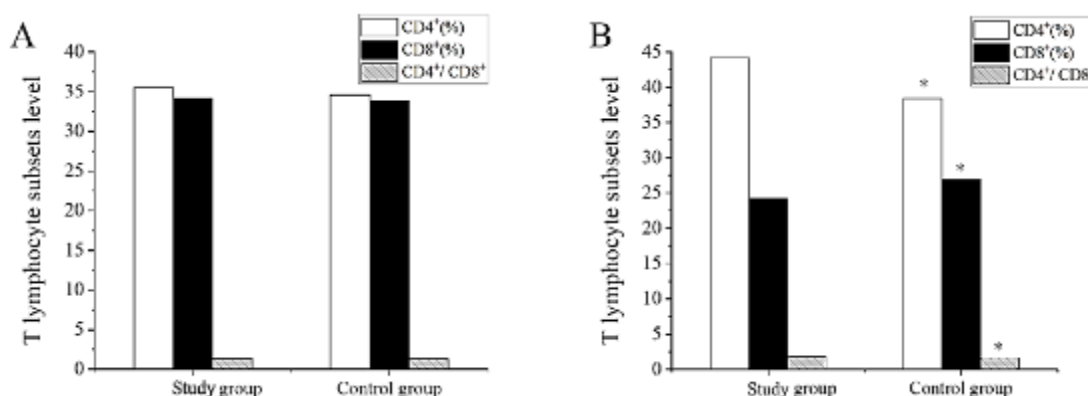
The Curative effects of the two groups are shown in Table 2 below. The gross effective rate of the two groups showed a statistically significant difference, with 92.1 % in SG and 68.4 % in CG (*p* < 0.05).

**T lymphocyte subpopulation levels**

Pre- and post-treatment T lymphocyte subset levels are displayed in Figure 1. The percentages and ratios of T cells in the two groups were comparable before treatment (*p* > 0.05). After treatment, however, CD8+, CD4+ and CD4+/CD8+ ratio in SG were 24.24  $\pm$  3.39, 44.21  $\pm$  6.02, and 1.74  $\pm$  0.82, respectively. In CG, the values were 26.93  $\pm$  3.25, 38.44  $\pm$  5.70, and 1.65  $\pm$  0.78, respectively. The results indicated that patients in study group displayed more CD4+, CD8+ T cells and higher CD4+/CD8+ ratio (*p* < 0.05).

**Table 2:** Efficacy in the study and control groups

Group	Significant	Effective	Invalid	Total effective rate
Control	15 (39.5%)	11 (28.9%)	12 (31.6%)	26 (68.4%)
Study	22 (57.9%)	13 (34.3%)	3 (7.9%)	35 (92.1%)



**Figure 1:** T lymphocytes percentage and ratio in two groups before and after treatment. **Note:** A = pre-treatment; B = post-treatment

### Serum inflammatory levels

The concentration of inflammatory molecules in the two groups, pre-and post-treatment, are shown in Figure 2. The concentration of IL-2, IL-4, TNF- $\alpha$  and PCT in SG and CG showed no statistical differences before treatment ( $p > 0.05$ ). However, after treatment, the concentrations in SG were  $4.31 \pm 0.74 \mu\text{g/mL}$ ,  $3.20 \pm 0.37 \mu\text{g/mL}$ ,  $4.67 \pm 0.31 \text{ pg/mL}$  and  $1.16 \pm 0.69 \text{ ng/mL}$  respectively. The values of the above serum inflammatory molecules decreased compared with CG ( $p < 0.05$ ).

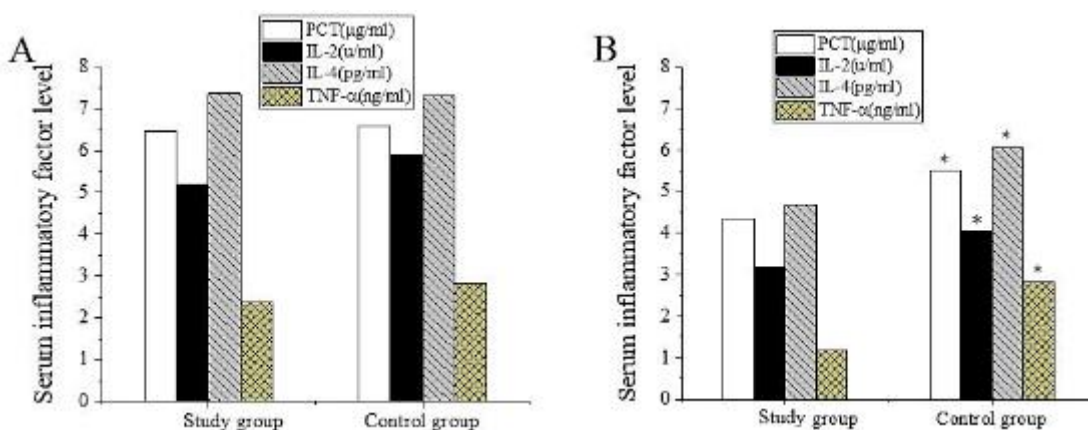
### Postoperative Eustachian tube scores

Figure 3 displayed the EST scores for study and control groups before and after treatment. The EST scores were comparable in SG and CG

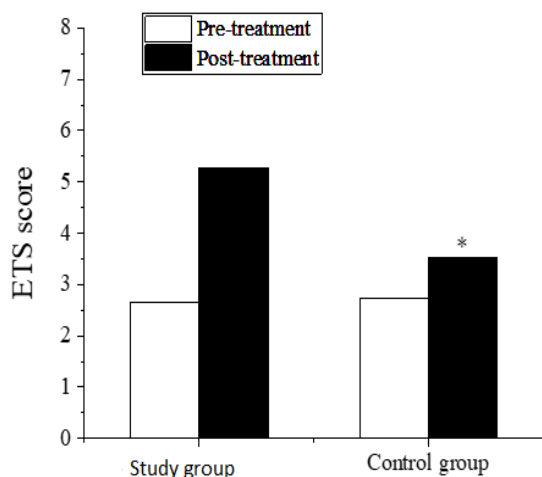
before therapy ( $p > 0.05$ ). However, the post-treatment scores were significantly elevated in SG ( $5.25 \pm 2.02$ ) compared to CG ( $3.53 \pm 2.4$ ), with the difference being statistically significant ( $p < 0.05$ ).

### DISCUSSION

Secretory otitis media is characterized as effusion in the middle ear cavity which may hinder sound wave transmission and cause hearing damage [10,11]. This is especially important for children with otitis media and effusion (OME), because hearing impairment may affect language and learning development. Even for adults, hearing impairment may lead to social and professional problems and reduce the quality of life [12].



**Figure 2:** Serum inflammatory molecules in two groups before and after treatment. **Note:** A = pre-treatment; B = post-treatment



**Figure 3:** ETS values in the two groups before and after treatment

Secretory otitis media may be accompanied by repeated middle ear infections, which not only lead to pain and discomfort but also require repeated antibiotic treatment, which increases the risk of antibiotic resistance. Patients with secretory otitis media usually experience inflammation and dysregulated immune function. Therefore, it is crucial to explore the impact of different treatment options on these aspects [13]. This study sought to investigate the effect of combining Eustachian tube balloon dilatation with triamcinolone acetonide on inflammatory response and immune function among secretory otitis media patients.

The treatment options in children and adult patients vary due to anatomic and multiple factors [14]. In addition, the causes of this disease are varied, which may include Eustachian tube dysfunction, adenoid hypertrophy, sinus problems and so on. It is imperative to identify the etiology for optimizing appropriate treatment methods. For example, Eustachian tube surgery may be suitable for Eustachian tube dysfunction, while adenoidectomy may be suitable for adenoidal hypertrophy. The final surgical decision should be based on the professional opinions of doctors, taking into account the specific situation and etiology of patients. Doctors will provide advice based on medical history, physical examination, hearing test, imaging examination and other information [15].

T lymphocytes are indispensable component in the immune system and are divided into two main subgroups: CD4<sup>+</sup> and CD8<sup>+</sup>. CD4<sup>+</sup> T cells facilitate antibody production by B cells and participate in humoral immune response, while CD8<sup>+</sup> T cells are cytotoxic that directly kill cancer

cell or infected cells. The CD4<sup>+</sup>/CD8<sup>+</sup> ratio was reported to represent immune function, a higher ratio usually reflects favorable prognosis. Results from this study show that both CD4<sup>+</sup> and CD8<sup>+</sup> T cells increased significantly in SG after treatment, with a more pronounced increase in CD4<sup>+</sup> T cells, leading to an elevated CD4<sup>+</sup>/CD8<sup>+</sup> ratio.

These results suggest that Eustachian tube balloon dilatation combined with triamcinolone acetonide may improve the immune response by regulating the levels of T lymphocyte proportion, particularly by increasing the number of CD4<sup>+</sup> cells in secretory otitis media patients. This improvement may help to enhance the resistance of patients to infection and inflammation and is expected to reduce the symptoms and disease progression of patients with OME. The percentage of T lymphocyte subsets serves as an ideal indicator in judging the therapeutic effect. The change in T lymphocyte subsets reflects the regulation of the immune system, especially the increase of CD4<sup>+</sup> cells may represent the enhanced immune function [16].

The concentration of serum inflammatory molecules positively correlates with the inflammatory response. Therefore, reducing their concentration may help protect against tissue damage and disease progression. Serum inflammatory molecules are critical in regulating and transmitting inflammatory signals in the immune system [17]. Procalcitonin (PCT) is widely used to represent the severity of bacterial infection, while TNF- $\alpha$  is an important mediator in the inflammatory response. Interleukins (IL-4 and IL-2) participate in regulating the immune cells' function and cell signal transduction. The concentration of serum inflammatory molecules in the two groups before treatment were comparable, which indicated the immune status of patients in the initial stage of the disease might be similar. However, comparing with CG, the concentration of PCT, TNF- $\alpha$ , IL-2 and IL-4 were significantly decreased in SG.

The findings suggest that the combination of Eustachian tube balloon dilatation and triamcinolone acetonide reduces the release of inflammatory molecules, thereby decreasing the inflammatory response. In addition, the decrease in IL-2 and IL-4 levels represented depressed immune reaction. This regulation of inflammatory factors may help to protect patients from tissue damage and promote the immune status.

Eustachian Tube Score (ETS) system is a powerful tool to evaluate Eustachian tube function. By comparing the ETS results before

and after treatment, it is easy to assess the treatment efficacy and determine the extent the symptoms and Eustachian tube function of patients are improved. Triamcinolone acetonide is widely used to treat otitis media and Eustachian tube dysfunction. It may improve ETS by reducing inflammation and improving the permeability of Eustachian tube [18,19]. Therefore, the comparative study evaluates the relative effect of Eustachian tube balloon dilatation and drug therapy on ETS. Tympanic catheterization is a technique used to ventilate the middle ear cavity by placing a small catheter through the tympanic membrane. It may affect ETS, especially by improving middle ear ventilation, but it needs to be compared with balloon dilatation of Eustachian tube. Balloon dilation of Eustachian tube improves middle ear ventilation, decreases its pressure and alleviates symptoms, consequently improving the subjective score of ETS.

### Limitations of this study

Although this study has achieved positive preliminary results, there are some many limitations. Given that it is a retrospective study, selection bias is a concern.

### CONCLUSION

The combination of Eustachian tube balloon dilation and triamcinolone acetonide demonstrates a very high efficacy on acute secretory otitis media, indicating its potential for clinical application. However, longer follow-up and larger sample size prospective studies are needed. In addition, more in-depth studies to reveal the precise mechanism of the combined treatment on the immune system would be required.

### DECLARATIONS

#### Acknowledgement

None.

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None provided.

#### Ethical approval

This study received approval from the Ethics Committee of the Ninth People's Hospital affiliated with Shanghai Jiao Tong University (approval no. SH9H-2023-T316-5).

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Conflict of Interest

No conflict of interest associated with this work.

### Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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### REFERENCES

1. Liu X, Sun J, Yin G. Expressions of MUC5AC and TNF- $\alpha$  in middle ear mucosa, and influence of anti-TNF- $\alpha$ ; McAb treatment on rat model of acute otitis media with effusion. *Trop J Pharm Res* 2019; 18(8): 1621-1625 doi: 10.4314/tjpr.v18i8.8
2. Roditi RE, Caradonna DS, Shin JJ. The Proposed Usage of intranasal steroids and antihistamines for otitis media with effusion. *Curr Allergy Asthma R* 2019; 19(10): 47.
3. Shevchik E, Svistushkin V, Nikiforova G, Zolotova A. Eosinophilic otitis media: modern aspects of pathogenesis, clinical features, diagnosis and treatment. *Indian J Otolaryngol* 2022; 74(Suppl 1): 132-140.
4. Polunin MM, Chernova OV. Treatment of exudative (secretory) otitis media in young children taking into account the anatomical features of the auditory tube. *Vestn Otorinolaringol* 2020; 85(1): 10-13.
5. Plaza G, Navarro JJ, Alfaro J, Sandoval M, Marco J. Consensus on treatment of obstructive Eustachian tube dysfunction with balloon Eustachian tuboplasty. *Acta Otorinolaringol Esp (Engl Ed)* 2020; 71(3): 181-189.
6. Rahman S, Tayyab H, Siddiqui M. Suprachoroidal triamcinolone acetonide injection to treat macular edema: a review. *J Vitreoretin Dis* 2024; 2053452167.
7. Li Y, Tu Q, Xie D, Chen S, Gao K, Xu X, Zhang Z, Mei X. Triamcinolone acetonide-loaded nanoparticles encapsulated by CD90(+) MCSs-derived microvesicles *Trop J Pharm Res*, November 2024; 23(11): 1922

- drive anti-inflammatory properties and promote cartilage regeneration after osteoarthritis. *J Nanobiotechnol* 2022; 20(1): 150.
8. Gulati D, Saini A, Dhingra AK. Analytical methods for triamcinolone acetonide: an exploratory literature review. *Antiinflamm Antiallergy Agents Med Chem* 2023; 22(2): 71-78.
  9. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 310(20): 2191-2194.
  10. Webster KE, Mulvaney CA, Galbraith K, Rana M, Marom T, Daniel M, Venekamp RP, Schilder AG, MacKeith S. Auto-inflation for otitis media with effusion (OME) in children. *Cochrane Db Syst Rev* 2023; 9(9): CD15253.
  11. Yin X, Liu L, Luo M, Liu Y, Duan M. Association between secretory otitis media and laryngopharyngeal reflux in adults. *Acta Oto-Laryngol* 2023; 143(11-12): 946-950.
  12. Hidaka H, Ito M, Ikeda R, Kamide Y, Kuroki H, Nakano A, Yoshida H, Takahashi H, Iino Y, Harabuchi Y, et al. Clinical practice guidelines for the diagnosis and management of otitis media with effusion (OME) in children in Japan - 2022 update. *Auris Nasus Larynx* 2023; 50(5): 655-699
  13. Oehlandt H, Pulkkinen J, Haavisto L. Balloon dilation of eustachian tube in chronic eustachian tube dysfunction: a retrospective study of 107 patients. *J Int Adv Otol* 2022; 18(6): 495-500.
  14. Urik M, Slapak I, Machac J. Chronic secretory otitis media and tympanoplasty in children. *Cas Lek Cesk* 2019; 158(6): 240-242.
  15. Aboueisha MA, Attia AS, McCoul ED, Carter J. Efficacy and safety of balloon dilation of eustachian tube in children: Systematic review and meta-analysis. *Int J Pediatr Otorhi* 2022; 154: 111048.
  16. Ramakrishnan N, D'Souza R, Kadambi P. A systematic literature review of the safety and efficacy of eustachian balloon tuboplasty in patients with chronic eustachian tube dysfunction. *Indian J Otolaryngol* 2019; 71(3): 406-412.
  17. Yeghaneh MA, Talaei R, Nikoueinejad H, Akbari H. Studying the Serum as Well as Serous Level of IL-17 and IL-23 in Patients with Serous Otitis Media. *Iran J Allergy Asthm* 2017; 16(6): 520-524.
  18. Koumpa FS, Moraitis I, Bowles P, Saunders N. Eustachian tube balloon dilatation: a cross-sectional, survey-based study of 137 UK consultants. *J Laryngol Otol* 2020; 134(1): 41-45.
  19. Moneir W, El-Kholy NA, Ali AI, Abdeltawwab MM, El-Sharkawy A. Correlation of Eustachian tube function with the results of type 1 tympanoplasty: a prospective study. *Eur Arch Oto-Rhino-L* 2023; 280(4): 1593-1601.