

Original Article

Dexamethasone injections through the eustachian tube using an electronic nasolaryngoscope in secretory otitis media patients

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Abstract: Objective: To study the effect of dexamethasone injections through the eustachian tube under an electronic nasolaryngoscope in the treatment of secretory otitis media (SOM) patients. Methods: 106 patients with SOM were randomly divided into a control group (n=53) and a study group (n=53). The patients in both groups were treated with dexamethasone, and the patients in the control group were given intratympanic injections of dexamethasone using a tympanic membrane puncture, while the patients in the study group were injected through the auditory tube under an electronic nasolaryngoscope. The clinical effects, the bone conduction threshold, the blood inflammatory response indexes (TNF- α , IL-6, IL-10), the seven-item Eustachian Tube Dysfunction Questionnaire (ETDQ-7) scores, the adverse reactions, and the recurrence rates were compared between the two groups before and after the treatment. Results: After the treatment, the study group's total effective rate was significantly higher than in the control group's total effective rate ($P<0.05$). The bone conduction thresholds of 1 kHz, 2 kHz, and 4 kHz in the two groups were all decreased, and the levels in the study group were significantly lower than the levels in the control group ($P<0.05$). The TNF- α , IL-6, and IL-10 levels in both groups were decreased, and the levels in the study group were significantly lower than they were in the control group ($P<0.05$). The ETDQ-7 scores were decreased in both groups, and the scores in the study group were significantly lower than the scores in the control group ($P<0.05$). The adverse reactions were mild, the otitis media recurrence rates were low in both groups, and there was no significant difference between the two groups ($P>0.05$). Conclusion: Injecting dexamethasone through the eustachian tube under an electronic nasolaryngoscope is effective in the treatment of SOM. It can effectively improve the eustachian tube function, reduce inflammatory reactions, and is very safe, so it is of clinical significance.

Keywords: Secretory otitis media, electronic nasolaryngoscope, eustachian tube injection of dexamethasone, inflammatory factors, bone conduction threshold

Introduction

Secretory otitis media (SOM) is a common disease in otorhinolaryngology. SOM patients often have middle ear effusion accompanied by decreased auditory function. Studies have found that the pathological process of the disease is often closely related to eustachian tube dysfunction, immune inflammatory injuries, ear canal infections, and other factors, among which eustachian tube dysfunction is the main cause [1, 2]. The eustachian tube is the only channel for the middle ear to communicate with the outside. Under normal circumstances, the air pressure inside and outside the middle ear is basically the same. However, when the

eustachian tube is blocked due to adenoid swelling, pharyngitis, rhinitis, or other factors, it will lead to damage to the ventilation function of the middle ear cavity in a negative pressure state. It will increase the mucosal permeability that causes the fluid exudation to accumulate in the middle ear, forming middle ear effusion eventually leading to SOM [3]. There are many conventional treatments, such as tympanic membrane puncture and drainage, tympanotomy and catheterization, oral administration, tympanic injection administration and so on. However, there is no gold standard treatment for this disease, so there still is controversy about the best treatment method, the clinical efficacy, and the safety [4, 5].

Table 1. Comparison of baseline data between the two groups ($\bar{x} \pm sd$)

Groups	Gender (male/female)	Age (years)	Course (months)	Tympanic curve			
				Left ear	Right ear	B Type	C Type
Control group (n=53)	30/23	20.4±8.3	9.42±1.28	24	29	36	17
Study Group (n=53)	28/25	19.9±8.2	9.51±1.37	26	27	39	14
t/ χ^2	$\chi^2=0.152$	t=0.312	t=0.350	$\chi^2=0.151$		$\chi^2=0.410$	
P	0.696	0.756	0.727	0.692		0.522	

The intratympanic injection of dexamethasone through the tympanic membrane using electronic nasolaryngoscopy is also a traditional and widely used treatment. Dexamethasone injections are strongly associated with anti-inflammation and immunosuppression. With the cell-mediated immune response to reduce the tissue's response to inflammation, and a high local drug concentration, it is effective at reducing inflammation [6]. However, in recent years, studies have found that this treatment has the disadvantages of easily causing tympanic membrane perforation, secondary middle ear infections, and the like [7]. With the development of electronic nasolaryngoscope technology, the eustachian tube can be directly observed under a microscope, making it possible to inject drugs directly into the tympanic cavity through the eustachian tube under the microscope, effectively reducing the risk of infection and mucosal edema in the puncture. At the same time, the effusion in the eustachian tube can be effectively dredged under the microscope, and the risk of repeated tympanic membrane puncture caused by the blockage is effectively reduced [8]. At present, although some studies have been carried out to analyze the intratympanic injection of dexamethasone under an electronic nasolaryngoscope, their cohorts were small, and their observation indicators were incomplete, so their clinical application value remains to be determined [9]. Therefore, this study compares this treatment with transtympanic puncture under an electronic nasolaryngoscope to analyze the therapeutic effect of injecting dexamethasone into the eustachian tube using an electronic nasolaryngoscope on secretory otitis media patients. The report is as follows.

Materials and methods

Baseline data

106 patients with SOM treated at the Hebei Eye Hospital from December 2017 to Decem-

ber 2019 were randomly divided into a control group (n=53) and a study group (n=53). There were no significant differences in the baseline data in the two groups ($P>0.05$), so they were comparable, as shown in **Table 1**. This study was approved by the Medical Ethics Committee of Hebei Eye Hospital and all the patients signed an informed consent.

Selection criteria

Inclusion criteria: Patients who met the SOM diagnostic criteria in *Guidelines for Clinical Classification and Surgical Classification of Otitis Media* (2012) [10]. Patients whose clinical manifestations were earache, tinnitus, ear tightness, and hearing loss, patients whose hearing tests showed transmission deafness, patients with tympanic effusion and otitis media with limited movement and sticky effusions, patients who had not taken the study drug in the three months before their enrollment. Exclusion criteria: Patients with diabetes, hypertension, gastric or duodenal ulcers, thrombosis, myocardial infarction, osteoporosis, liver cirrhosis, hypothyroidism or renal dysfunction, Patients with a tendency to bleed, Patients with liver or kidney insufficiency, Patients with malignant tumors, Patients with a history of head trauma or a family history of deafness, patients who were allergic to adrenocorticosteroids.

Methods

Control group: The patients were given an intratympanic injection of dexamethasone through the tympanic membrane under an electronic nasolaryngoscope [11]. A supine position was taken, the exterior auditory canal was disinfected using iodophor, and 1% tetracaine hydrochloride (Jiangsu Jiuxu Pharmaceutical Co., Ltd., China, Specification: 5 mL) was instilled into the external auditory canal for the tympanic membrane infiltration anesthesia. The tympanic membrane was punctured with a no. 5

needle at 1 mm near the edge of the tympanic membrane in front of the tension part of the tympanic membrane. After drawing out the effusion, 5 mg of dexamethasone (Shaanxi Chunhui Pharmaceutical Co., Ltd., China, Specification: 5 mg) was injected once every 2 days.

Study group: The study group was administered an injection of dexamethasone through the eustachian tube under electronic nasolaryngoscopy [12]. The procedure before the anesthesia was identical to the procedure used in the control group, the anesthetic site was the mucosa of the nasal cavity and nasopharynx, and the amount of anesthesia used was the same that was used in the control group. A nasopharynx endoscope was placed into nasopharynx through the nasal passage to fully expose the pharynx mouth of eustachian tube. After clearing the surrounding secretion with a suction device, the eustachian tube was placed into the pharynx mouth of eustachian tube, and a Bols ball was used to inflate the tympanum to ensure that the tympanum was ventilated and unobstructed. A total of 5 mg of dexamethasone was injected into the tympanum at a slow and uniform speed, once every 2 days. The patients in the two groups were treated continuously for 2 weeks.

Observation indicators

Clinical efficacy: The clinical efficacy was evaluated after the treatment [13]. Significant effect: The clinical symptoms, such as hearing loss, ear tightness, and ear pain, disappeared, and the hearing returned to normal. Pure tone audiometry was improved >15 dB compared to before the treatment. The tympanic membrane returned to normal, the tympanic curve was type A, the eustachian tube was unobstructed, and the effusion disappeared. Effective: The clinical symptoms were significantly relieved and basically did not affect communication with other people. The tympanic curve was type C or AS, and the functions of the tympanic membrane and eustachian tube were improved. Compared with before the treatment, the pure tone audiometry increased less than 15 dB, and most of the effusion disappeared. Ineffective: There was no change in the clinical symptoms, no improvement in the hearing level, and no improvement in the effusion. Total effective rate = (significant effect + effective)/total number of cases * 100%.

Bone conduction threshold for each frequency: The hearing thresholds of 1 kHz, 2 kHz, and 4 kHz in the two groups were measured using a Danish International AD226 audiometer before and at two weeks after the treatment.

Indicators of the inflammatory response: Before the treatment and at two weeks after the treatment, fasting venous blood was taken from the patients, and their serum was taken using centrifugation with a centrifugal radius of 13.5 cm for 5 min, then frozen for later inspection. With the aid of a gc-2010 radioimmune counter (Anhui USTC Zonkia Scientific instrument Co., Ltd., China), the interleukin-6 (IL-6) and interleukin-10 (IL-10) levels were measured using enzyme-linked immunoassays (ELISA). The tumor necrosis factor (TNF- α) levels was measured using an enzyme linked immunosorbent assay (ELISA) with Beckman IAMMGE. The kits were purchased from Shanghai Jingkang Biological Engineering Co., Ltd., China.

Seven-item eustachian tube dysfunction questionnaire (ETDQ-7) score: The ETDQ-7 was used to evaluate the eustachian tube function before and after the treatment [14]. There were seven questions in the questionnaire, and the total possible score was 49. Grades 1-2 (7-14 points) indicated almost unaffected, grades 3-5 (15-35 points) indicated moderate, and grades 6-7 (36-49 points) indicated serious.

Adverse reactions and recurrence: The adverse drug reactions during the treatment, including digestive tract ulcers, osteoporosis, diabetes, and infections, were recorded. Following the recommendations in *Guidelines for the Clinical Application of Secretory Otitis Media* (2004 Edition), the recurrence of the patients at six months after their operations was determined [15]. The main follow-up methods were telephone follow-up and outpatient follow-up.

Statistical methods

SPSS 21.0 software was used for the data analysis. The measurement data were expressed as the mean \pm standard deviation ($\bar{x} \pm sd$). Independent sample t tests were used for the comparisons between two groups, and paired t tests were used for the before and after comparisons within a group. The count data were expressed as percentages, and χ^2 tests and log-rank tests were used for the

Table 2. Comparison of clinical efficacy between the two groups (n, %)

Groups	Significant effect	Effective	Ineffective	Total effective
Control group (n=53)	30 (56.60)	16 (30.19)	7 (13.21)	46 (86.79)
Study group (n=53)	41 (77.36)	11 (20.75)	1 (1.89)	52 (98.11)
Z/ χ^2		Z=2.463		$\chi^2=4.867$
P		0.014		0.027

ranked data, and $P<0.05$ indicated that a difference was statistically significant.

Results

Baseline data

There was no significant differences in the sexes, ages, courses of the disease, pathological sites, or tympanic curves of the patients in the two groups ($P>0.05$). Therefore, the two groups were comparable. See **Table 1**.

Clinical efficacy

The total effective rate in the study group was significantly higher than it was in the control group ($P<0.05$). It is clear that injecting dexamethasone through the eustachian tube using an electronic nasolaryngoscope can improve the clinical effect of SOM. See **Table 2**.

Bone conduction threshold at each frequency

Before the treatment, there was no significant difference in the bone conduction threshold at each frequency between the two groups. After the treatment, the bone conduction thresholds of 1 kHz, 2 kHz, and 4 kHz in the two groups were decreased, and the threshold in the study group was significantly lower than it was in the control group ($P<0.05$). It is clear that the injection of dexamethasone through the eustachian tube using an electronic nasolaryngoscope is better at improving the bone conduction threshold at each frequency. See **Table 3** and **Figure 1**.

Inflammatory factors

Before the treatment, there was no significant difference in the inflammatory factors levels in the two groups ($P>0.05$). After the treatment, the TNF- α , IL-6, and IL-10 levels in the two groups decreased, and the level in the study

group was significantly lower than the level in the control group ($P<0.001$). It is clear that the injection of dexamethasone through the eustachian tube using an electronic nasolaryngoscope is better at inhibiting patients' inflammatory reactions. See **Table 4** and **Figure 2**.

ETDQ-7 scores

Before the treatment, there was no significant difference in ETDQ-7 scores in the two groups. After the treatment, the ETDQ-7 scores in both groups decreased, and the scores in the study group were significantly lower than the scores in the control group ($P<0.001$). It is clear that the injection of dexamethasone through the eustachian tube using an electronic nasolaryngoscope is better at improving patients' eustachian tube function. See **Table 5**.

Adverse reactions and recurrence

The adverse reactions in the two groups were mild, the otitis media recurrence rates were low, and there was no significant difference between the two groups ($P>0.05$). It is clear that the injection of dexamethasone through the eustachian tube using an electronic nasolaryngoscope is safe and reliable. See **Table 6**.

Discussion

Dexamethasone is a class of adrenocortical hormone drugs that are the commonly-used drugs in the treatment of SOM. It has strong anti-inflammatory and immunosuppressive effects. It can inhibit the accumulation of white blood cells and macrophages at the site of the inflammation, inhibiting the synthesis and release of the inflammatory factors and reducing the vascular permeability to prevent the tissue's response to the inflammation, reducing the inflammation [16, 17]. Cytokines that regulate the inflammatory response play an important role in the pathogenesis and pathological evolution of SOM. High concentrations of TNF- α , IL-6, and IL-10 are mainly produced by the middle ear cavity, which is an important factor causing middle ear mucosal damage and fibroblast proliferation. When the ventilation function of the middle ear cavity is impaired and

Table 3. Comparison of the bone conduction threshold at each frequency between the two groups ($\bar{x} \pm \text{sd}$, dB)

Groups	1 kHz		2 kHz		4 kHz	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=53)	11.95 \pm 2.52	10.69 \pm 2.23**	14.85 \pm 3.17	12.85 \pm 2.68**	18.98 \pm 6.17	16.67 \pm 4.28*
Study group (n=53)	11.77 \pm 2.59	9.27 \pm 1.92***	15.06 \pm 3.38	11.04 \pm 2.25***	18.55 \pm 6.11	14.22 \pm 3.10***
t	0.363	3.513	0.330	3.766	0.361	3.375
P	0.717	0.001	0.742	<0.001	0.719	0.001

Note: Compared with this group before the treatment, *P<0.05, **P<0.01, ***P<0.001.

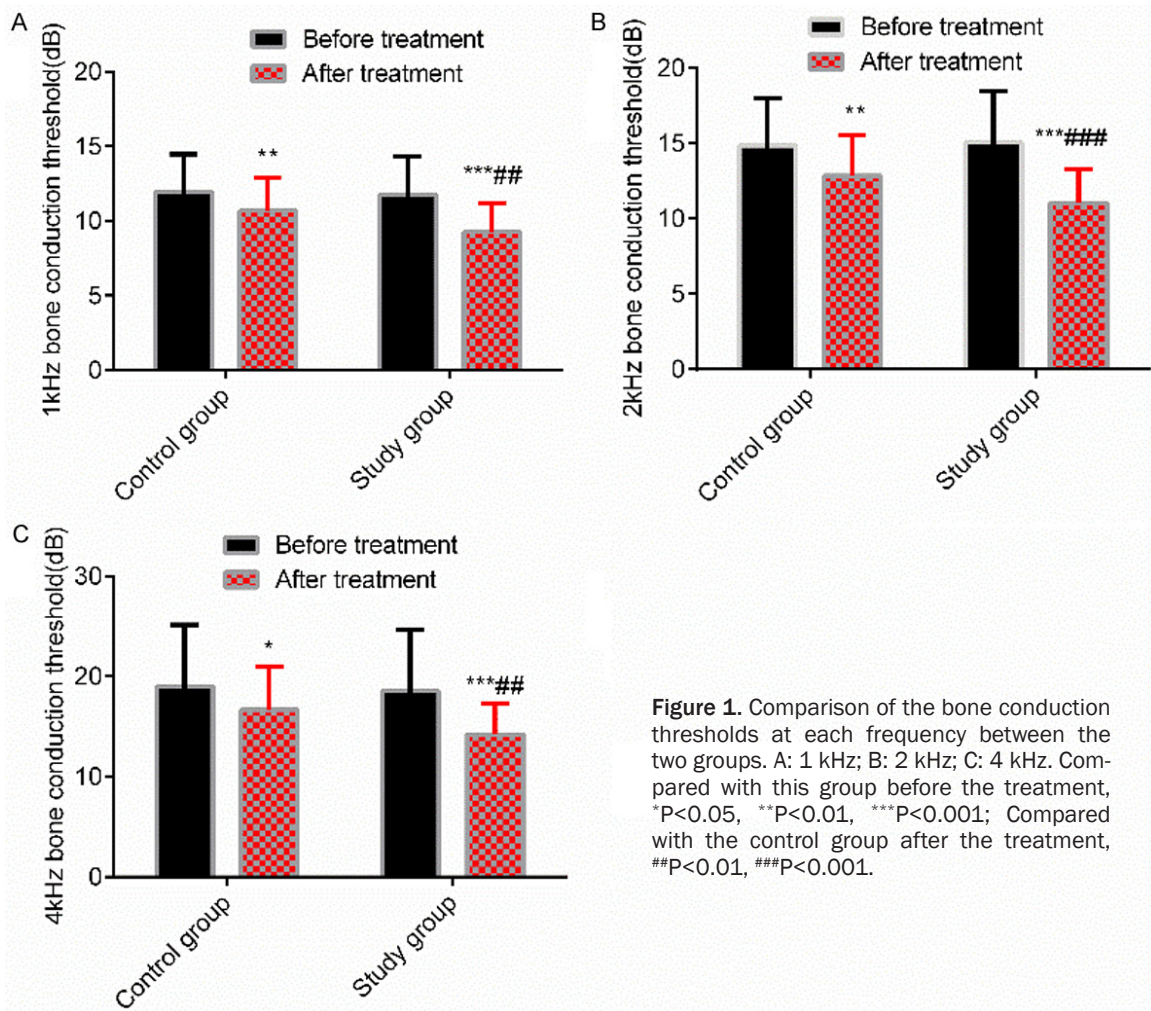


Figure 1. Comparison of the bone conduction thresholds at each frequency between the two groups. A: 1 kHz; B: 2 kHz; C: 4 kHz. Compared with this group before the treatment, *P<0.05, **P<0.01, ***P<0.001; Compared with the control group after the treatment, ##P<0.01, ###P<0.001.

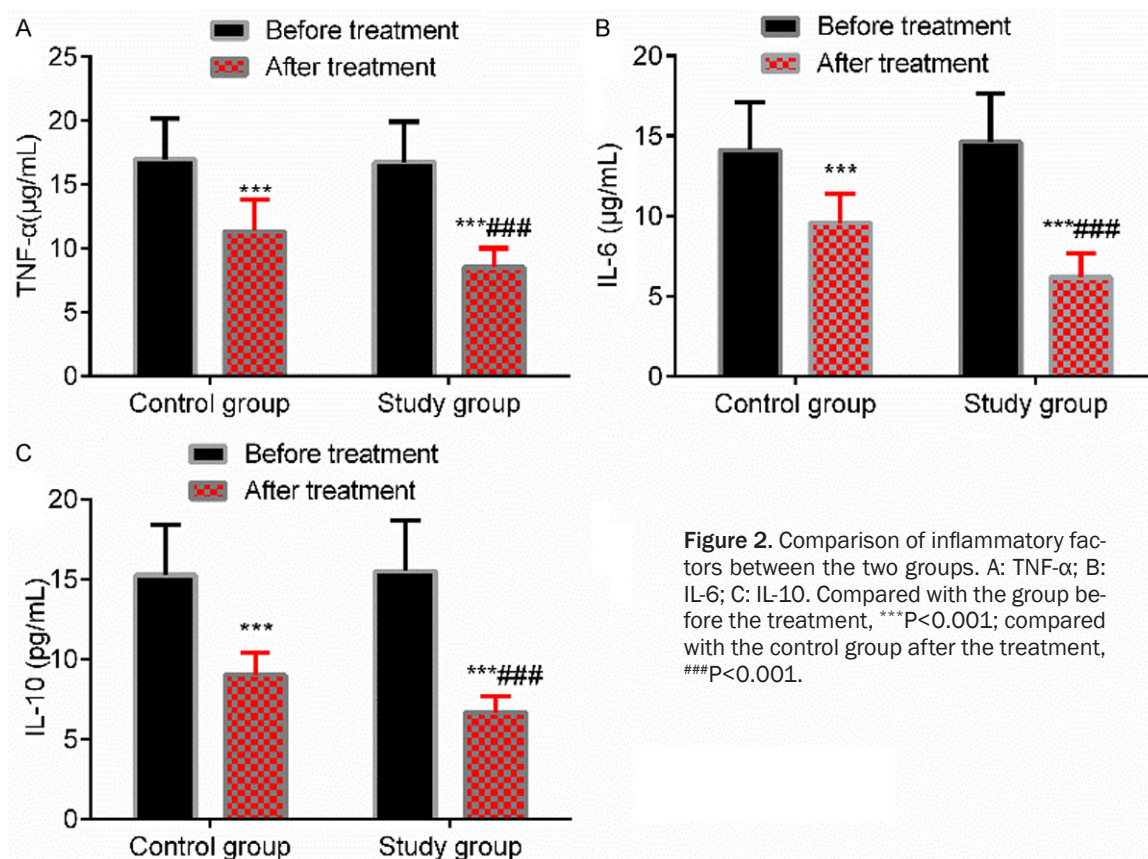
there are infection factors, a large number of inflammatory mediators, such as TNF- α , IL-6, and IL-10, will be secreted, which damage the middle ear mucosa and increase mucosal permeability, resulting in middle ear fluid retention or eustachian tube edema [18]. Therefore, clarifying the inflammatory factors levels in the ear mucosa can better reveal the pathogenesis of

SOM and provide symptomatic treatment. Dexamethasone has a significant effect on the anti-inflammatory mechanism, so it can effectively inhibit the activation of the inflammatory cells to reduce the inflammatory response, reduce mucosal permeability, alleviate symptoms such as middle ear fluid retention or eustachian tube edema, and promoting a recur-

Table 4. Comparison of inflammatory factors between the two groups ($\bar{x} \pm sd$)

Groups	TNF- α ($\mu\text{g/mL}$)		IL-6 ($\mu\text{g/mL}$)		IL-10 (pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=53)	16.98 \pm 3.18	11.34 \pm 2.51***	14.12 \pm 2.98	9.58 \pm 1.85***	15.27 \pm 3.16	9.04 \pm 1.39***
Study group (n=53)	16.77 \pm 3.16	8.54 \pm 1.47***	14.65 \pm 3.01	6.17 \pm 1.49***	15.50 \pm 3.20	6.67 \pm 1.02***
t	0.341	7.008	0.911	10.451	0.372	10.007
P	0.734	<0.001	0.364	<0.001	0.711	<0.001

Note: Compared with this group before the treatment, ***P<0.001.


Table 5. Comparison of ETDQ-7 scores between the two groups ($\bar{x} \pm sd$, score)

Groups	Before treatment	After treatment	t	P
Control group (n=53)	36.18 \pm 6.17	11.29 \pm 1.54	28.494	<0.001
Study group (n=53)	35.98 \pm 6.08	9.65 \pm 0.88	31.202	<0.001
t	0.168	6.731		
P	0.867	<0.001		

Note: ETDQ-7, the seven-item Eustachian Tube Dysfunction Questionnaire.

rence of the disease [19, 20]. Wang et al. pointed out that the treatment of SOM with glucocorticoids can reduce the recurrence rate, improve

the hearing level, and reduce patients' inflammatory reactions [21].

On the other hand, the middle ear itself has immune activity, so when the organ is infected by bacteria or viruses, it will increase the immune activity of its mucosal cells, and the exudate contains a large number of antigen-specific IgA and IgG antibodies, which bind to the IgAE of the mucosal mast cells, inducing an inflammatory reaction, activating the central nervous signal pathway, and changing the vascular permeability [22]. On the other hand,

Table 6. Comparison of adverse reactions and recurrence between the two groups n (%)

Groups	Amyasthenia	Osteoporosis	Fural fullness	Infection and other	Total incidence rate	Recurrence rate
Control group (n=53)	0 (0.00)	2 (3.77)	0 (0.00)	1 (1.89)	3 (5.66)	3 (5.66)
Study group (n=53)	1 (1.89)	0 (0.00)	1 (1.89)	0 (0.00)	2 (3.77)	2 (3.77)
χ^2	0.000	0.510	0.000	0.000	0.210	0.210
P	1.000	0.475	1.000	1.000	0.647	0.647

dexamethasone has a strong immunosuppressive effect, so it can reduce the number of T lymphocytes and eosinophils, reduce the immunoglobulin content such as IgA and IgG, and enter the nucleus in the form of a glucocorticoid receptor complex by binding to the cell surface receptors, activating the MAD-3 gene, increasing the I κ B α synthesis, and blocking the protein complex signal pathway, so as to inhibit the activation of the target genes and control the synthesis and release of the inflammatory factors to achieve the immunosuppression [23, 24]. In addition, dexamethasone can also promote the excretion of effusion in the middle ear cavity and the release of surfactants from the eustachian tube by regulating the sodium transport channel of the middle ear epithelial cells, to enhance the contraction of lymphatic vessels and lymphoid tissue, reduce the viscosity of the middle ear fluid, and improve the function of the eustachian tube [25]. However, it is worth noting that because the drug is absorbed quickly and the action time is short after each dexamethasone injection, it needs to be injected repeatedly, which may increase the risk of tympanic adhesion and fibrosis.

Although the effect of dexamethasone injections by tympanocentesis is considerable, it needs to be injected repeatedly because of the duration of the drug action. During the tympanocentesis recovery period, it is not recommended to allow water into the ear canal, otherwise it will easily cause an infection and lead to complications such as tympanic membrane perforation. Prolonged otitis media is difficult to heal. And if the needle puncture is too deep, it can easily cause vertigo, nausea, vomiting, and other conditions, thus affecting the therapeutic effect [26]. The results of this study showed that after treatment, the clinical effect of the study group was significantly higher than the clinical effect in the control group, and the improvement of the bone conduction threshold

at each frequency and the inflammatory factors in the study group were better than they were in the control group, suggesting that the injection of dexamethasone into the eustachian tube using an electronic nasolaryngoscope is effective at improving the clinical effect, inhibiting inflammatory reactions, and improving the bone conduction threshold of patients at all frequencies. Sheng et al. reported that the injection of hormones through the eustachian tube under endoscopy has a higher cure rate than injection of hormones by tympanocentesis in the treatment of chronic SOM, that the recurrence rate of both the two methods is equal, and that both can reduce patients' air conduction thresholds [27]. Yang et al. reported that the endoscopic administration of dexamethasone through the eustachian tube in the treatment of chronic SOM is superior to tympanocentesis administration in terms of its effect, alleviating the clinical symptoms, improving the bone conduction threshold, and reducing the risk of relapse [28]. However, the safety of the two administration methods is equal, and they are also consistent with the results of this study. The reason is that the injection of dexamethasone into the eustachian tube under an electronic nasolaryngoscope can effectively dredge the eustachian tube and resolve the eustachian tube blockage. At the same time, the injection can reach the tympanum directly, be fully absorbed by the focus, have a high concentration and a strong effect. To a certain extent, it can prolong the injection interval, reduce the number of injections, further alleviating the eustachian tube edema and negative pressure, improving the inflammatory reaction, and preventing tympanic effusion. In addition, the endoscopic technology has a clear field of vision, which can fully expose the eustachian tube and the nasopharynx, allowing doctors to quickly inject dexamethasone. At the same time, injection through the eustachian tube can also avoid the discomfort caused by puncture, thus reducing the patients' pain. According to

the data gathered during the treatment period, the adverse reactions of the two groups were mild and resolved without intervention, and the postoperative recurrence rate was also low, indicating that the drug has a reliable efficacy, safety and high application value in the treatment of SOM.

To sum up, the effect of injecting dexamethasone into the eustachian tube using an electronic nasolaryngoscope is considerable, it is better at improving the clinical efficacy, inhibiting inflammatory reactions, improving patients' bone conduction thresholds at each frequency, and the adverse drug reactions are small, safe, and reliable. However, because this study was limited to a small sample size, and because the samples were all from the same hospital, the results may not be convincing. In addition, SOM often occurs in children, but the patients included in this study were at least 10 years old. Although the ETDQ scores used in the study have no age restrictions, it does not rule out that some children's subjective expressions are vague, resulting in score errors. Therefore, more extensive research and more evaluation indicators will be needed in the future.

Disclosure of conflict of interest

None.

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