

Effects of dexamethasone combined with ambroxol hydrochloride on T-Cell subsets and hearing in patients with secretory otitis media

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Abstract: The aim of the study was to investigate the effect of dexamethasone combined with ambroxol hydrochloride on T cell subsets and hearing in patients with secretory otitis media. Eighty-six cases of patients with secretory otitis media admitted to “Gansu Provincial Hospital, Lanzhou, China” from September 2016 to September 2018 were regarded as subjects of the study. The patients were divided in two groups according to the digital table method. Among them, the control group was treated with ambroxol hydrochloride, while the study group was treated with dexamethasone combined with ambroxol hydrochloride. The clinical efficacy, T cytokines before and after treatment, auditory threshold and middle ear resonance frequency were observed and compared between the two groups of the patients. SPSS 18.0 software was used to statistically analyze the data. The therapeutic efficacy of the study group was better than that of the control group and the levels of CD4⁺, CD4⁺/CD8⁺ after treatment of the study group were higher than that of the control group (P<0.05), while the content of CD8⁺ in the study group was lower than that in the control group (P<0.05). In addition, the auditory threshold of the study group was lower than that of the control group (P<0.05), whereas the middle ear resonance frequency was higher than that of the control group (P<0.05). The application of dexamethasone combined with ambroxol hydrochloride improved the clinical symptoms and restored hearing in the clinical treatment of patients with secretory otitis media and the therapeutic efficacy was ideal.

Keywords: Dexamethasone, ambroxol hydrochloride, Secretory otitis media, T cell.

INTRODUCTION

One of the most common diseases in clinical otolaryngology is secretory otitis media, which is an inflammatory disease. The clinical standard of patients is mainly characterized by a significant decrease in hearing and accumulation of fluid in the ear (Passali & Zavattini, 1987). There are many factors inducing patients with secretory otitis media, such as immune response, Eustachian tube dysfunction and infection. If the patient cannot be given timely and effective intervention, the patient's disease may even lead to complete loss of hearing ability with the development of the disease, which seriously affects the normal life and work of the patient (Sanjew *et al.*, 2017). The secretory otitis media is deceptive in onset and usually runs long course. The clinical appearance differs accordingly. The condition happens in childhood as hearing loss, as an educational or behavioral problem. In younger children it may present as speech and language, delay, or as pronunciation defect. Often the hearing loss is first detected on routine screening examinations before 3 to 5 years of age, or later at pre-school testing. Sometimes attention is drawn to it by frequent episodes of otalgia which specify an exacerbation of acute suppurative otitis media superimposed on the middle ear effusion. Occasionally, presentation is with complication such as otorrhoea, secondary to perforation of the tympanic membrane

(Sanjeev & Sayed, 2017). A total of 86 cases with secretory otitis media were enrolled in the study. Half of the patients were treated with dexamethasone combined with ambroxol hydrochloride, with satisfactory efficacy.

MATERIALS AND METHODS

General data

A total of 86 cases of patients with secretory otitis media admitted to “Gansu Provincial Hospital, Lanzhou, China” from September 2016 to September 2018 were studied in the present work.

Inclusion criteria

- Patients who met the clinical diagnosis of secretory otitis media.
- Patients aged 20-60 years old.
- Patients who did not use any drugs that might affect the results of the research 30 days before the study.
- Those Patients and their families who were informed and had signed informed consent.

Exclusion criteria

- Patients who were complicated with mental disorders.
- Patients who were complicated with perforation of femoral membranes.
- Patients with hearing loss caused by other causes.
- Patients during pregnancy or lactation.
- Patients who used hormone drugs for a long time.

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- Patients who were complicated with severe diabetes mellitus.

The control group consisted of 43 cases, 64 ears, aged 20-60 years, with an average age of (41.2±1.1) years. Among them, 20 were male and 23 were female. The average course of disease was (14.6±2.1) days. Among them, 21 cases were binaural and 22 cases were monaural. The study group consisted of 43 patients, 66 ears, aged 20-60 years, with an average age of (14.2±1.6) years, including 21 male and 22 female, with an average course of disease (13.9±2.3) days. Among them, 23 were binaural patients and 20 were monaural patients. There was no significant difference in the general data between the two groups ($P>0.05$), were comparable and approved by the ethics committee of the corresponding hospital.

Method

Periosteum puncture was performed in both groups for intra tympanic injection. The patient was instructed to sit on the hospital bed so that the affected side could face the implementer. Then the patient's head was kept slightly forward and the external auditory canal was sterilized by routine procedure. The syringe (10mL size, with tympanic puncture needle) was inserted into the middle ear cavity about 1mm-2mm away from the edge of the tympanic membrane at the front and lower quadrant of the tense part of the eardrum. Then the effusion in the middle ear was pumped back with the syringe until the liquid with bubbles was sucked out (Massimo *et al.*, 2017). If there was a gelatinous or viscous secretion that was difficult to withdraw from the ear, the syringe would be replaced by a long needle (size 9 needles) and connected to a negative pressure suction device, thereby sucking out the stubborn substance. The liquid was then perfused into the middle ear cavity.

The control group was treated with 15mg of ambroxol hydrochloride and slowly injected into the middle ear cavity at one time. The study group received a combination of dexamethasone and ambroxol hydrochloride i.e., dexamethasone (5mg) and ambroxol hydrochloride (15mg) were thoroughly mixed and the mixed drug solution was slowly injected into the middle ear cavity at one time (Long *et al.*, 2016).

Once the drug bolus was completed, the patient's head was biased to one side, and the ear canal was sealed with the air otoscope or pressed against the tragus, until the patient felt the liquid inside the throat (Roditi *et al.*, 2016). The dry cotton ball was placed in the patient's external ear canal for about 30 minutes and the patient was advised to pay attention to the cleanness of the external auditory canal. After 7 days, the patients who did not cured were treated again according to the above-mentioned plan, and they could not be repeated more than 5 times at most (Dong *et al.*, 2016). Both groups of

patients were treated with ephedrine nasal drops for nasal drops and antibiotics were also appropriately used as adjuvant therapy during the treatment period.

Observational index

The clinical efficacy of the two groups of patients was observed and compared. The efficacy was evaluated on the basis of patient's clinical symptoms and hearing recovery. The specific classification was as follows.

Significant effect

The patient's clinical symptoms (such as ear nausea, tinnitus, etc.) completely disappeared, the hearing ability returned to the pre-onset and the pure tone hearing threshold test results suggested that the air conduction and bone conduction difference <10db and tympanogram represented as A type.

Valid

The clinical symptoms of the patients were significantly improved. Although the hearing did not return to the pre-onset, the improvement was obvious. The pure tone hearing threshold test results showed that the air conduction and bone conduction difference was $\geq 10\text{db}<15\text{db}$ and tympanogram represented as AS type.

Invalid

Patients who did not meet the above criteria (Flasche *et al.*, 2016). The levels of T cytokines before and after treatment were compared between the two groups. The fasting venous blood samples of about 3ml for 8 hours were taken from the two groups before and after treatment for flow cytometry (Gates *et al.*, 1989).

Changes in the hearing threshold and middle ear resonance frequency before and after treatment were observed and compared between the two groups.

STATISTICAL ANALYSIS

The data was analyzed by SPSS18.0 statistical software, in which the count data was subjected to Chi-square analysis (%), while the measurement data was performed by t test ($\bar{x} \pm s$).

Ethical approval

This study was approved by the institutional ethical committee of Gansu Provincial Hospital, Lanzhou, Gansu, PR China. All the experiments were conducted as per Helsinki's declaration for Human volunteers. The reference No. is 1003/IEC-GP/2017.

RESULTS

Clinical efficacy

The efficacy of the study group was better than that of the control group. When statistical tool was applied then these effects were significant at 5% p value i.e ($P<0.05$), as shown in table 1.

Table 1: Clinical Efficacy of ambroxol HCl between two groups (Cases, %)

Groups	Cases	Significant Effect	Valid	Invalid	Efficiency
Control group	43	16 (37.2)	17 (39.5)	10 (23.3)	76.7%
Study group	43	22 (51.2)	18 (41.9)	3 (7.0)	93.0%
X ²	---	5.218	0.519	6.172	5.427
P	---	<0.05	>0.05	<0.05	<0.05

Table 2: T Cytokine Levels before and after treatment ($\bar{x} \pm s$)

Groups	Time	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Control group	Prior Treatment	37.6±2.9	32.7±4.1	1.0±0.2
	Post Treatment ^a	40.8±3.0	30.9±2.9	1.3±0.3
Study group	Prior Treatment	37.9±3.1	33.2±4.2	1.0±0.4
	Post Treatment ^{ab}	45.1±3.4	27.8±3.0	1.6±0.4

Table 3: Auditory Threshold and Middle Ear Resonance Frequency before and after Treatment (decibel, ($\bar{x} \pm s$))

Groups	Time	Auditory Threshold (db)			Middle Ear Resonance Frequency (Hz)
		500Hz	1000Hz	2000Hz	
Control Group	Prior Treatment	22.9±3.1	21.4±4.2	22.4±2.5	529.7±43.7
	Post Treatment ^a	12.2±1.4	9.5±1.1	10.4±1.3	635.7±61.4
Study Group	Prior Treatment	22.8±3.3	21.2±3.6	22.5±2.3	531.2±52.8
	Post Treatment ^{ab}	7.6±0.9	4.4±0.7	6.3±0.8	809.1±75.2

Note: Comparison within the group showed ^aP<0.05; comparison between groups showed ^bP<0.05.

T Cytokines

After treatment, the levels of CD4⁺, CD4⁺/CD8⁺ of the study group was statistically higher (P<0.05) than that of the control group, while the content of CD8⁺ in the study group was lower than that in the control group (P<0.05), as depicted in table 2.

Auditory threshold and middle ear resonance frequency

Auditory threshold of the study group was lower than that of the control group. Statistically these findings were significant (P<0.05) between the groups, whereas the middle ear resonance frequency was statistically higher (P<0.05) than that of the control group, as depicted in table 3.

DISCUSSION

Dexamethasone is a hormonal drug, which possess the main effects of immunosuppressive and anti-inflammatory functions. Dexamethasone can also alleviate the stress response of body tissues to inflammation, thereby relieving inflammation (Xiang *et al.*, 2016). At the same time, dexamethasone can also inhibit and prevent the immune response mediated by cells, reduce the amount of eosinophilic, mononuclear and T lymphocytes secreted by tissues, thereby blocking the ability of the immunoglobulin to bind to the cellular receptor, thus reducing the conversion of T lymphocytes into lymphoblast and ultimately mitigating the immune response (Dagan *et al.*, 2016).

The characteristic of ambroxol hydrochloride is that it can dissolve and eliminate mucus. It can increase the secretion of more active substances on the surface of the ear Eustachian tube, which has a positive effect on the smooth opening of the Eustachian tube (Deng and Li, 2017). It can regulate the viscous secretions in the Eustachian tube, stimulate the active substances on the mucosal surface, inhibit the excessive release of inflammatory mediators and alleviate the inflammatory response (Liuyin and Yana, 2017). Ambroxol hydrochloride can improve the elimination of bacteria (Xiang *et al.*, 2016; Kaur *et al.*, 2016). Ambroxol hydrochloride can improve ciliary movement and keep the Eustachian tube clean. The intra tympanic injection method was applied in the process. The drug can directly affect the mucosa, tympanic cavity and Eustachian tube of the mastoid cavity in the affected ear, so that the edema and inflammation in the ear can be relieved more quickly and recovery of mucosal secretion of active substances can be further promoted (Li *et al.*, 2018).

CONCLUSION

Results of this work demonstrated the application of dexamethasone combined with ambroxol hydrochloride in improving the clinical symptoms and restoring hearing in the clinical treatment of patients with secretory otitis media, and the therapeutic efficacy was proved to be ideal, which is worthy of application and promotion.

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