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Original Research

Effects of Qing Qiao Capsule in the treatment of chronic secretory otitis media and the levels of serum inflammatory factors

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Abstract: To explore the effects of Qing Qiao Capsule in the treatment of chronic secretory otitis media and the levels of serum inflammatory factors, a total of 50 chronic secretory otitis media patients in the control group were subjected to caefaclor capsule, while the total of 50 cases in the observation group were treated with Qing Qiao Capsule. The traditional Chinese medicine (TCM) syndrome scores, therapeutic effects, and the levels of inflammatory factors were evaluated. After treatment, the scores of deafness, hearing loss, dizziness, soreness and weakness of the waist and knees, and fever is hens in palms and soles were significantly decreased in both groups (all P value <0.05). However, each score in the observation group was markedly less than that of the control group (all P value <0.05). Moreover, the C-reactive protein (CRP), procalcitonin (PCT) and tumor necrosis factor-α (TNF-α) levels measured after treatment were significantly lowered than those before treatment (all P value <0.05). Also, the levels of CRP, PCT and TNF-α in the observation group were obviously less than that of the control group (all P value <0.05). And the total therapeutic efficacy of the observation group was significantly higher than that of the control group (P<0.05). But no significant difference was observed in the rates of adverse reactions between both groups (P>0.05). Application of Qing Qiao Capsule in the treatment of chronic secretory otitis media yields better results, lowers TCM syndrome scores, and alleviates the body's inflammatory response, which is a safe drug in clinical use.

Key words: Qing Qiao Capsule; Caefaclor capsule; Chronic secretory otitis media; Inflammatory response.

Introduction

As one of the common diseases in the otology department, secretory otitis media (SOM) is a kind of middle ear disease that mainly characterized by conduction hearing loss, ear fullness and blockage, and tympanic cavity effusion. With improper treatment, the course of the disease would be protracted, and the disease would develop into adhesive otitis media, tympanosclerosis and the like. Those with a course of more than 8 weeks are called chronic secretory otitis media (1), which is often resulted from late and ineffective treatment of acute secretory otitis media or protracted course of the disease. The pathogenesis of the disease is rather complicated, and its underlying mechanisms are not yet defined. In the view of modern Western medicine, numerous factors would cause increased negative pressure in the middle ear, mucosal edema in the middle ear, angiotelectasis and increased capillary permeability. The exuded liquid filled the tympanic cavity, leading to effusion in the middle ear, which cause relevant clinical symptoms (2-3). Research has demonstrated that chronic secretory otitis media is closely related to eustachian tube insufficiency, infection, body immune response, inflammation and the like, which would lower the patient's life quality (4). It has been years of history in the treatment of chronic secretory otitis media with Chinese medicine. The disease falls into the category of "ear blockage", which believes that it is caused by retention of a pathogenic toxin. And it is related to weakness of viscera, mostly symptoms with mixed excessiveness and deficiency. In the view of modern Chinese medicine, chronic secretory otitis media is mainly caused by the accumulation of phlegm-dampness in Auris, which blinds the Qing Yang or resulted from the evil of phlegm-dampness days after the invasion of exogenous evil, which causes the retention of phlegm-dampness in the ear and obstruction of the Qi movement. However, long-term blockage of evil Qi in the Auris could definitely result in Qi-stagnation and blood stasis in the ear. Blood flow disturbance and loss of nutrition inside the ear would aggravate "ear blockage", hearing loss and presentation of relevant clinical symptoms (5-6). The spleen governs the transportation and transformation of the water-dampness and is also the source of phlegm. Therefore, clinical treatment mainly involves invigorating the spleen, eliminating the phlegm and dampness, promoting Qi, activating blood and dredging orifices. On that basis, we observe the effects of Qing Qiao Capsule in the treatment of chronic secretory otitis media and the levels of serum inflammatory factors from January 2016 to January 2018, which is reported as follows.

Materials and Methods

General data

A total of 100 patients with chronic secretory otitis media treated in our hospital from January 2016 to January 2018 were enrolled. All patients met the Chinese medicine diagnostic criteria for chronic secretory otitis media described in "Guiding Principles for Clinical Research of New Drugs in Traditional Chinese Medicine" (7): The main symptoms are ear fullness and blockage, hearing loss or the symptoms could be temporarily alleviated at the supine position, autophonia and tinnitus. And the secondary symptoms are dizziness, head heaviness, body heaviness and weakness, abdominal distention and anorexia, pale tongue with greasy coating, slippery pulse. Moreover, the patients also met the Western medicine diagnostic criteria for chronic secretory otitis media: (a) The patient has a history of external infection or insidious onset, with a course of more than 8 weeks. (b) The patient presents with hearing loss, accompanied by autophonia, ear blockage or fullness, tinnitus which is mostly intermittent, with or without earache. (c) Unoticeable congestion in the eardrum, or otopiesis, protruding of the short process of malleus, the eardrum lose its normal reflex when tympanic cavity effusion occurred and presents with faint yellow, orange-red or amber, and the fluid level could be seen through the eardrum. (d) Pure tone audiometry showed conduction deafness to a varying degree, part of whom were mixed deafness. Acoustic immittance showed type B or type C tympanogram. The age of these 100 patients ranges from 32 to 69. And the consent was obtained from the patient or their guardians. The exclusion criteria were as follows: those complicated with the severe primary disease in the acute cardiac-cerebral vascular system, liver, kidney and hematopoietic system, those complicated with peptic ulcer and gastrointestinal bleeding, those suffered from inferior turbinate hypertrophy, nasal polyp, severe deviation of the nasal septum, nasopharyngeal mass or second-degree or above tonsil hypertrophy, those allergic to the drugs used in this research. This study was approved by the ethics committee of our hospital. These 100 patients were randomized into two groups. There were 50 cases in the control group, with 26 male patients and 24 female patients. The average year of the control group was (42.5 ±11.4) years, ranging from 32 to 68. The average disease course was (21.1±5.7) weeks, ranging from 9 to 29 weeks. And the auditory threshold of the control group was (42.5±9.4) dB, with 28 cases of type B curves and 22 cases of type C curves. Moreover, there were 50 cases in the observation group, with 27 male patients and 23 female patients. The average year of the observation group was (43.8±11.1) years, ranging from 33 to 69. The average disease course was (21.8±5.4) weeks, ranging from 10 to 31 weeks. And the auditory threshold of the observation group was (42.0±9.7) dB, with 26 cases of type B curves and 24 cases of type C curves. These data of both groups were of no significant difference, which was comparable (P>0.05).

Therapeutic methods

The control group was treated with cefaclor capsule (H10983030, 0.25g/pill ×12 pills, Lilly Suzhou Pharmaceutical Co., Ltd.) based on routine Eustachian tube insufflation, which was orally administered, 1 pill/time, 3 times/d for 10 days. The treatment group was subjected to Qing Qiao Capsule (each pill weight 0.4g, containing 2.2g of crude drug, mainly consisted of Scrophularia ningpoensis, the rhizome of Rehmannia, Danshen, medicinal cyathula root, stiff silkworm, angelicasinensis, semen coicis, Cardamine and other components) based on routine Eustachian tube insufflation treatment, which was orally administered, 1 pills/time, 3 times/d, with continuous administration for 1 month.

Observation indicators

(a) TCM syndrome scores: the scores of deafness, hearing loss, dizziness, soreness and weakness of the waist and knees, and feverishness in palms and soles were evaluated before and after treatment. (b) The levels of inflammatory factors: The levels of CRP, PCT and TNF-α were tested with enzyme-linked immunosorbent assay (ELISA) before and after treatment. (c) Clinical efficacy: The therapeutic efficacy of both groups were analyzed according to the standards in reference (7). Clinical recovery: The TCM clinical symptoms and signs disappeared or basically disappeared, and the syndrome scores were reduced by≥90%. Excellent effect: The TCM clinical symptoms and signs were significantly improved, the syndrome scores were reduced by ≥70% but<90%. Valid: The TCM clinical symptoms and signs were improved, the syndrome scores were reduced by ≥30% but<70%. Invalid: No significant improvement of the TCM clinical symptoms and signs, or even worse, and the syndrome scores were reduced by <30%. The total efficacy was calculated by adding basic recovery, excellent effect and valid cases. (d) Adverse reactions: The incidence of adverse reactions during the treatment of these two groups was recorded.

Statistical analysis

The data were analyzed and processed with SPSS20.0 software. The quantitative data were expressed as x±s, and the comparison was performed by t-test. The enumeration data were expressed as a percentage, and the comparison was performed by the $\chi 2$ test. The test level was set as $\alpha=0.05$.

Results

Comparison of the TCM syndrome scores before and after treatment between both groups

No significant difference was observed in the scores of deafness, hearing loss, dizziness, soreness and weakness of the waist and knees, and feverishness in palms and soles between both groups (all P value >0.05). However, the above scores were significantly decreased in both groups after treatment (all P value <0.05), and each score in the observation group was markedly less than that of the control group (all P value <0.05). The details were listed in Table 1.

Comparison of the levels of inflammatory factors between both groups

No significant difference was observed in the CRP, PCT and TNF-α levels measured before treatment between both groups (all P value >0.05). However, the levels of CRP, PCT and TNF-α measured after treatment

Table 1. Comparison of the TCM syndrome scores before and after treatment between both groups (x±s, score).

Groups	n	Time	Deafness	Hearing loss	Dizziness	Soreness and weakness of the waist and knees	Feverishness in palms and soles
Observation group	50	Before treatment	2.3±0.7	2.7±0.6	3.4±0.4	2.2±0.6	3.0±0.4
	50	After treatment	0.7±0.4*#	0.5±0.5*#	0.7±0.3*#	0.8±0.4*#	0.6±0.5*#
Control group	50	Before treatment	2.4±0.8	2.8±0.7	3.5±0.5	2.3±0.6	2.9±0.5
	50	After treatment	1.8±0.6*	1.7±0.6*	1.8±0.4*	1.6±0.5*	1.6±0.6*

Note: * as compared with those before treatment, # as compared with those in the control group P<0.05.

Table 2. Comparison of the levels of inflammatory factors between both groups (x±s).

Groups	n	Time	CRP/(mg/L)	PCT/(ng/L)	TNF-α/(ng/L)
Observation group	50	Before treatment	4.05±1.15	0.98±0.13	78.75±11.04
	50	After treatment	1.30±0.46*#	0.20±0.09*#	32.40±8.96*#
Control group	50	Before treatment	4.06±1.22	0.97±0.17	79.64±12.53
	50	After treatment	3.11±0.64*	0.34±0.08*	43.66±8.94*

Note: * as compared with those before treatment, # as compared with those in the control group P<0.05.

were significantly lowered than those before treatment (all P value <0.05). Also, the values of those indicators in the observation group were obviously less than that of the control group (all P value <0.05) (Table 2 and Figure 1).

Comparison of the therapeutic efficacy between both groups

The total therapeutic efficacy of the observation group was significantly higher than that of the control group (P<0.05). And the details were listed in Table 3.

Comparison of the adverse reactions between both groups

No significant difference was observed in the rates of adverse reactions between both groups (P>0.05). And the details were listed in Table 4.

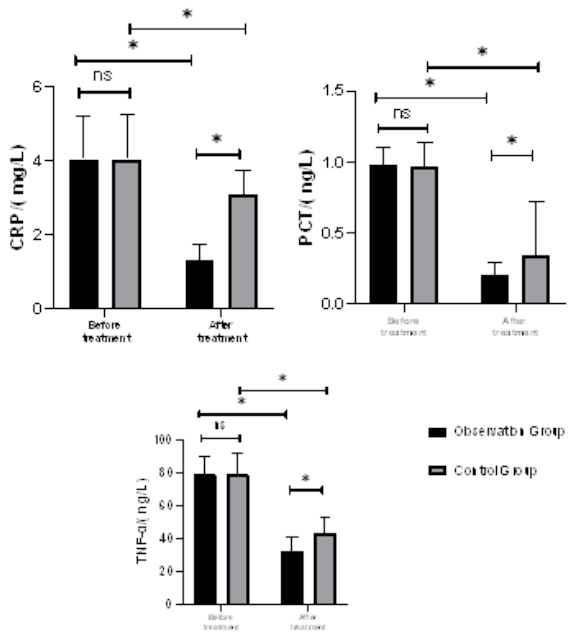

Figure 1. Comparison of the levels of inflammatory factors between both groups (x±s). Note: * P<0.05.

Discussion

In the view of Modern Western medicine theory, the occurrence of chronic secretory otitis media is closely related to a variety of factors, including Eustachian tube dysfunction such as glue ear, Eustachian tube cleaning and defensive dysfunction that can cause Eustachian tube insufficiency, which increases the chances of invasion of bacteria, viruses, chlamydia, etc., and leads to the onset of the disease. Moreover, allergens deposition on the surface of the nose and nasal mucosa could have resulted from the immune response. And these allergens could combine with mast cells and release bioactive substances, causing congestion of the Eustachian tube and increased secretion of mucus, which then leads to Eustachian tube blockage and occurrence of secretory otitis media. In addition, allergens can be directly released into the middle ear cavity, causing inflammation response and related symptoms (8-10). Researches have shown that both pathogen invasion and immune response injury can lead to the release of inflammatory mediators, which then causes inflammatory damage. As the important indicators of inflammation in clinical, the serum levels of CRP, PCT and TNF-αin patients with

Table 3. Comparison of the therapeutic efficacy between both groups (cases (%)).

Groups	n	Clinical recovery	Excellent	Valid	Invalid	Total efficacy
Observation group	50	23(46.0)	12(24.0)	11(22.0)	4(8.0)	46(92.0)#
Control group	50	6(12.0)	13(26.0)	18(36.0)	13(26.0)	37(74.0)

Note: # as compared with those in the control group, P<0.05.

Table 4. Comparison of the adverse reactions between both groups (cases (%)).

Groups	n	Nausea and vomiting	Liver and kidney function injury	Diarrhea	In total
Observation group	50	1(2.0)	2(4.0)	1(2.0)	4(8.0)
Control group	50	2(4.0)	1(2.0)	0(0.0)	3(6.0)

chronic secretory otitis media are markedly elevated (11-12).

Currently, the treatments of chronic secretory otitis media in modern Western medicine mainly involve antibiotics, allergy treatment and surgery. Certain effects could be obtained through these methods. However, some patients respond poorly. In Chinese medicine, the treatments of chronic secretory otitis media have years of history. And the disease is categorized into "ear fullness and blockage". Also, there is a saying of "wind deaf" in ancient times, which was believed to be caused by the invasion of wind evil. At the early stage of the disease, it presents with ear fullness, or with an earache. Those being sick for a long time present with ear blockage. That is, it feels like something is obstructing inside the ear and blocking the orifices, obvious hearing loss, mostly recurrent ear fullness. And it has resulted from protracted retention of pathogenic toxin inside the Auris. In ancient medicine, there are numerous causes accounted for chronic secretory otitis media. In "Su Wen – Viscera theory", it is recorded that "those with lung disease…suffered from deficiency and insufficient qi, which cause them unable to breathe smoothly, leading to deafness." Later, doctor Li Dong-yuan explained that "the lung collaterals were gathered inside the ear, resulting in deafness." He believes that lung disharmony is an important reason for ear blockage. However, doctor Fang Yu in the Ming dynasty pointed out that "those aged people suffered from weakness and insufficiency of qi and blood, which cause them to be unable to listen clearly, thus called ear blockage." He believes that viscera weakness is the reason for ear blockage. In the view of modern Chinese medicine, it is caused by improper diet and injured spleen and stomach. The essence of water and grain could not be transformed properly, which gathers dampness that forms into phlegm. The phlegm-dampness is stagnated and steamed in the lower part, which then flows upwards and streams into the Auris. Besides, the internal dampness would be generated as the spleen qi is deficient. Meanwhile, the yang of spleen fails, which couldn't warm the essence of water and grain. Then the essence of water and grain becomes phlegm instead of body fluid, leading to spleen deficiency and difficult improvement of yang qi. The lucid yang fails to increase, the Auris is full of yin dampness, and the phlegm is stagnated inside the tympanic cavity, resulting in ear blockage (13). Qing Qiao Capsule is an agreed formula that concluded from decades of clinical experience. Of this prescription, the Scrophularia ningpoensis and rhizome of Rehmannia could clear heat and cool blood, nourish yin and generate body fluid, as well as decrease internal fire and detoxify. The angelica sinensis, Danshen and medicinal cyathula root could activate blood and remove stasis as well as eliminate dampness and treat stranguria. The tiff silkworm could dispel the wind and relieve the spasm. These men coicis and Cardamine could strengthen the spleen and remove dampness. Combined with Liquorice that could nourish spleen and benefit qi, the above medicines are in harmony. Together they could clear heat and toxic materials, activate blood and remove stasis, dispel the wind and relive spasm, strengthen the spleen and remove dampness, remove turbidity and free the orifice (14,15).

The results of our study proved that the TCM syndrome scores were significantly decreased in both groups, and the scores in the observation group were markedly less than that of the control group. After treatment, the levels of CRP, PCT and TNF-α in both groups were lower than those measured before treatment in both groups. Also, the levels of these indicators in the observation group were obviously less than that of the control group. And the total therapeutic efficacy of the observation group was significantly higher than that of the control group. But no significant difference was observed in the rates of adverse reactions between both groups. The above findings indicate that the application of the Qing Qiao Capsule in the treatment of chronic secretory otitis media yields better results significantly improves the TCM syndrome scores and lowers the levels of inflammatory factors, which is a safe drug in clinical use.

Interest conflict

None.

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