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Original Research Article

Efficacy and safety of post-auricular injection of methylprednisolone sodium succinate and lidocaine in the treatment of acute tinnitus, and its effect on sleep quality

Bijun Liang[1], Xiaohua Feng[2], Rui Deng[1], Youli Liu[1], Ying He[1], Xiwu Zhang[3]*
[1]Department of Otolaryngology, Nanfang Hospital, Southern Medical University, [2]Department of Otolaryngology, [3]Department of Neurosurgery, General Hospital of Southern Theatre Command, Guangzhou, Guangdong, China

For correspondence: **Email: zihuangguansb@163.com, **Tel:** 86-13538989598*

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Abstract

Purpose: *To study the efficacy and safety of post-auricular injection of methylprednisolone sodium succinate plus lidocaine in the treatment of acute tinnitus, and its effect on sleep quality.*
Methods: *Eighty acute tinnitus patients admitted to Nanfang Hospital, Southern Medical University, Guangzhou, China from January 2020 to June 2021, served as subjects for this retrospective analysis. The patients were equally assigned to a reference group given postauricular injection of lidocaine, and a research group treated with post-auricular injection of methylprednisolone sodium succinate in combination with lidocaine. Treatment efficacy values in the two groups of patients were determined and compared.*
Results: *Total treatment effectiveness values in patients in the research group after one course of treatment, and at three months post-treatment, were significantly higher than the corresponding values in the reference group ($p < 0.05$). After treatment, the two groups had markedly improved Tinnitus Handicap Inventory (THI) scores, although patients in the research group had lower scores than those in reference group ($p < 0.05$). There were significant decreases in post-treatment pure tone threshold and Pittsburgh sleep quality index (PSQI) in the two groups of patients, with lower values in the research group than in the reference group ($p < 0.05$). There were no obvious adverse drug reactions during treatment and during 3-month follow-up period.*
Conclusion: *Post-auricular injection of methylprednisolone sodium succinate and lidocaine effectively improved the clinical efficacy and the sleep quality of acute tinnitus patients. It is a simple and highly safe operation which merits clinical application.*

Keywords: *Acute tinnitus, Methylprednisolone, Lidocaine, Sleep quality, Clinical efficacy*

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INTRODUCTION

Acute tinnitus is one of the common acute and severe diseases in otolaryngology, and it affects mostly the middle-age population. Although the affected patients receive a sensation of sound in the ear or the skull, they are unable to receive corresponding external stimulus or sound source [1-3]. A study has demonstrated that about 15 - 19 % of people have experienced or have been experiencing tinnitus [4]. Clinical data show that people with a predisposition to tinnitus frequently

manifest symptoms such as inattentiveness and poor sleep quality, and in severe cases, negative emotions such as irritability, depression and anxiety, all of which negatively affect quality of life and health [5]. The Nanfang hospital and the General hospital of Southern Theatre Command has achieved significant improvement in the treatment efficacy of acute tinnitus using post-auricular injection of the combination of methylprednisolone sodium succinate and lidocaine. This treatment has led to improvement of the physical and mental health of the affected patients. In the present study, the medical records of 80 patients with acute tinnitus who were admitted to these hospitals were retrospectively analyzed. This was aimed at assessing the efficacy and safety of post-auricular injection of methylprednisolone sodium succinate in combination with lidocaine in the treatment of acute tinnitus, as well as its effect on sleep quality.

PATIENTS AND METHODS

Inclusion criteria

Patients in the following categories were included in the study: those with primary complaint of unilateral persistent tinnitus; patients with normal functions of the external ear and middle ear, as determined using examinations such as acoustic impedance, ear endoscopy, and pure tone audiometry; and patients who had no history of ear surgery or history of trauma.

Exclusion criteria

The following categories of patients were excluded from the study: patients who had secondary tinnitus; those with history of otitis, worsening deafness in the previous three months; patients who were allergic to methylprednisolone sodium succinate and lidocaine; those with history of hypertension, diabetes, or cardiovascular disease, and patients who were breastfeeding or pregnant. Moreover, patients who had communication difficulties, cognitive impairments, or physical disorders, were excluded. All included patients signed informed consent form after being fully informed of the purpose of the study and the processes involved.

Screening of patients and grouping

A total of 80 acute tinnitus patients who were admitted to Nanfang Hospital, Southern Medical University, Guangzhou, China from January 2020 to June 2021 were included in this retrospective analysis. The patients were assigned to a reference group and a research group, based on treatment used. Each group had 40 patients. The study received approval from the ethics committee of the hospital, and followed international guidelines for human studies.

Examination and treatment

All patients were examined by the same physician who inquired about their conditions and completed the Tinnitus Disability Inventory (THI). All patients were orally administered *Ginkgo biloba* extract tablets (Dr. Willmar Schwabe GmbH & Co. KG, NMPA approval number = HJ20140768; specification: 40 mg) and mecobalamin tablets (Eisai China Pharmaceutical Co. Ltd, NMPA approval number = 20051440; specification: 0.5 mg) at doses in accordance with the doctor's advice [6-9].

Then, each patient in the reference group was given a post-auricular injection of 0.3 mL of lidocaine (Shanghai Zhaohui Pharmaceutical Co. Ltd, NMPA approval number = H41022244; specification: 5 mL). After routine sterilization, the injection was administered subcutaneously in the mastoid region, once every 2 days, 5 times continuously. Patients in the research group received post-auricular injection of methylprednisolone sodium succinate (Pfizer Co. Ltd., NMPA approval number H20170197; specification: 40 mg) in combination with lidocaine. The injection comprised 40 mg of methylprednisolone sodium succinate and 0.3 mL of lidocaine. After routine sterilization, the mixture was administered subcutaneously in the mastoid region with a 2-mL syringe configured with a 1-mL syringe needle. The injection was given once in 2 days, for 5 continuous times. In both groups of patients, one course of treatment was taken as 10 days.

Evaluation of treatment indicators

The age, gender, affected ears, tinnitus grade, education level, and other general information on the two groups of patients were recorded. Due to lack of standard efficacy evaluation methods, this study employed the tinnitus grading method for assessment of treatment efficacy [10]. Efficacy was categorized as cured, markedly effective, effective or ineffective. If tinnitus disappeared completely, the patient was regarded as cured. Treatment was markedly effective if tinnitus was mitigated by more than two grades; or effective if tinnitus was improved by one grade. On the other hand, if tinnitus grade remained static or if the patient’s condition became worsened, the treatment was ineffective. The total treatment effectiveness was obtained as shown in Eq 1.

TTE (%) = (CC + MEC + EC) / TNC * 100 …… (1)

where TTE = Total treatment effectiveness, TNC = Total number of cases, CC = cured cases, MEC = Markedly effective cases and EC = effective cases

The modified version of the THI scale was used to assess the severity of tinnitus in patients (Table 1).

The GSI61 dual-channel diagnostic pure tone audiometer was used for pure tone hearing threshold test. The pure tone hearing threshold test was performed in a standard soundproof room.

The Pittsburgh Sleep Index (PSQI) was used to assess quality of sleep before and after treatment. The scale contained 9 self-rated parameters and 5 parameters rated by others, with a total score of 21 points. The higher the score, the lower the quality of sleep. Incidence of adverse reactions in the patients during the treatment were recorded in detail.

Statistical analysis

The data processing software used in this research was SPSS 22.0, while GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used for graphics. Counting data are expressed as numbers and percentages {n (%)} and were analyzed with chi square (χ^2) test. Measurement data are expressed as mean ± standard deviation (SD), and were analyzed with *t*-test. Values of $p < 0.05$ were taken as indicative of statistically significant differences.

RESULTS

Baseline data of patients

There were no significant differences between the two groups, with respect to basic information such as age, gender, affected ear, tinnitus grades, and educational level ($p > 0.05$). These data are presented in Table 2.

Treatment efficacy

Total treatment effectiveness values in patients in the research group after one course of treatment,

Table 1: Treatment indicators and scoring criteria in the THI scale

Evaluation indicator	0 point	1 point	2 points	3 points
Environment where tinnitus occurred	No tinnitus	Quiet environment	Daily environment	Anywhere
Tinnitus duration	No tinnitus	Intermission time>duration	Intermission time<duration	Persistent tinnitus
Impact on sleep	No tinnitus	Occasionally	Often	Always
Impact on work	No tinnitus	Occasionally	Often	Always
Impact on emotions	No tinnitus	Occasionally	Often	Always

Table 2: Comparison of general information on the two groups of patients

Parameter	Reference group	Research group	t/χ^2	*P*-value
Age (years)	36.15±6.22	37.01±6.58	0.601	0.550
Gender			0.474	0.491
Male	17（42.5）	14（35）		
Female	23（57.5）	26（65）		
Affected ear			0.450	0.502
Left	21（52.5）	18（45）		
Right	19（47.5）	22（55）		
Tinnitus grade				
I	0（0）	0（0）		
II	10（25）	8（20）	0.287	0.592
III	18（45）	20（50）	0.201	0.654
IV	10（25）	12（30）	0.251	0.617
V	2（5）	0（0）	2.051	0.152
Educational level			0.739	0.390
Middle school and below	9（22.5）	6（15）		
High school and above	31（77.5）	34（85）		

and at three months post-treatment, were significantly higher than the corresponding values for patients in the reference group (p < 0.05). These results are shown in Figure 1 and Figure 2.

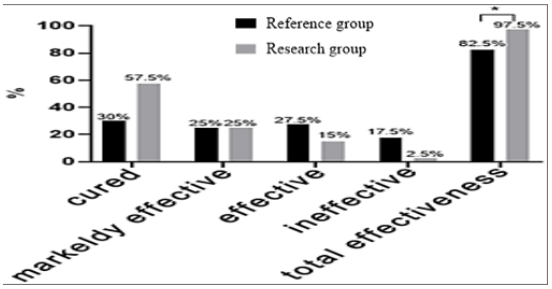

Figure 1: Comparison of total treatment effectiveness between the two groups of patients after a course of treatment (%)

In the reference group, the number of patients in the cured, markedly effective, effective and ineffective categories were 12, 10, 11 and 7, respectively, resulting in treatment effectiveness in a total of 33 patients. The number of patients in the cured, markedly effective, effective and ineffective categories in the research group were 23, 10, 6 and 1, respectively, accounting for treatment effectiveness in 39 patients. *P = 0.025; χ^2 = 5.000, research group vs reference group.

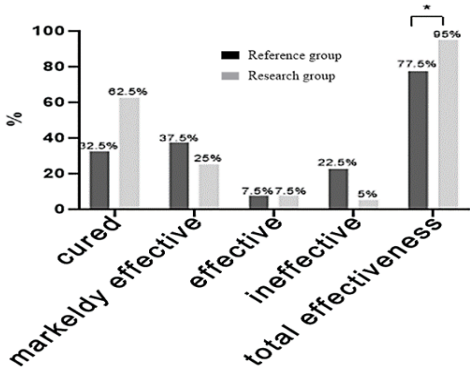

Figure 2: Comparison of efficacies in the two groups of patients three months after treatment (%)

In the reference group, the number of patients in the cured, markedly effective, effective and ineffective categories after 3 months were 13, 15, 3 and 9, respectively, giving rise to treatment effectiveness in a total of 31 patients. The number of patients in the cured, markedly effective, effective and ineffective categories in the research group after 3 months were 25, 10, 3 and 2, respectively, giving rise to treatment effectiveness in a total of 38 patients. *P = 0.023; χ^2 = 5.165, research group vs reference group.

THI scores

After treatment, the THI scores of the two groups of patients were markedly reduced, but THI score was lower in the research group than in the reference group (p < 0.05; Table 3).

Table 3: Comparison of THI scores of the two groups of patients (mean ± SD, n = 40)

Group	Before treatment	After treatment
Reference	12.97±3.15	9.57±3.61
Research	13.14±3.42	6.53±4.02
t		3.559
P-value		<0.001

Pure tone hearing thresholds

The pure tone threshold values of the two groups of patients were significantly decreased post-treatment, with lower value in the research group than in the reference group (p < 0.05). These results are presented in Table 4.

PSQI scores

Figure 3 shows that, following treatment, there were decreases in the Pittsburgh sleep quality index (PSQI) scores of the two groups of patients, but PSQI scores were lower in the research group than in the reference group (p < 0.05).

Incidence of adverse reactions

There were no obvious adverse drug reactions during treatment period and after three months of follow-up. However, 2 patients in the research group experienced slight local swelling during the injection, but the symptoms spontaneously subsided without any special treatment after 3 - 6 h.

Table 4: Comparison of pure tone hearing threshold values of the two groups of patients (mean ± SD, n = 40)

Group	Before treatment	After treatment	△before and after treatment
Reference	64.23±13.67	55.46±11.25	11.02±2.28
Research	63.97±14.18	45.59±9.87	18.25±14.27
t		4.171	3.164
P-value		<0.001	0.002

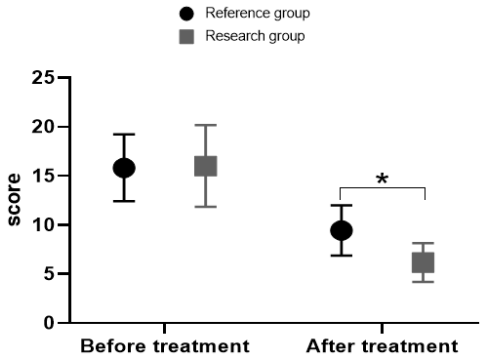

Figure 3: Comparison of PSQI scores of the two groups of patients. The PSQI scores of the reference group before and after treatment were 15.83 ± 3.41 and 9.44 ± 2.56, respectively, while PSQI scores of the research group before and after treatment were 16.02 ± 4.15 and 6.17 ± 1.93, respectively. *P < 0.001, research group vs reference group

DISCUSSION

In recent years, the incidence of tinnitus has been on a gradual increase due to changes in people's lifestyles and living environment, thereby constituting a serious threat to life and health. Clinically, treatment methods for tinnitus vary widely due to the multiplicity of risk factors associated with the disease. This results in poor certainty and variability in the overall treatment efficacy. Statistics have shown that the total effectiveness of drug treatment for acute tinnitus is 68.6 %, with only 18.6 % cure, which underlines the importance of early treatment of the disease [11]. Glucocorticoids, lidocaine, and some Chinese patent medicines are currently applied in the treatment of tinnitus, with the main treatment target being the repair of nerves and improvement of microcirculation in the inner ear. Methylprednisolone sodium succinate injection is a synthetic glucocorticoid with rapid onset, long action time, and anti-inflammatory, anti-edema, and anti-toxic effects. In addition, it enhances microcirculation, suppresses immune response, and regulates the synthesis and metabolism of the three major nutrients. Methylprednisolone sodium succinate is widely used in the treatment of deafness, ear inflammatory diseases, and tinnitus, due to the presence of glucocorticoid receptors in the inner ear tissue. The drug directly regulates signal transduction in the inner ear lymph, and indirectly regulates the hearing nerve.

Previously, methylprednisolone sodium succinate was administered through intravenous injection and oral route. These routes of administration result in decreased drug efficacy due to the blood brain barrier which critically reduces the blood concentration of the drug, leading to low drug levels in the inner ear. Moreover, relatively high concentrations of drug residues in various organs may easily trigger adverse reactions such as disorder in drug metabolism, gastrointestinal irritation, disorder in water and mineral metabolism, and infections. In particular, uncontrollable increases in blood sugar level are extremely likely to occur in diabetic patients during the treatment process, a situation which may result in ketoacidosis [12].

The selection of post-auricular injection in this study is attributed to the fact that due the presence of a network of arteries behind the ear, locally injected drugs can be rapidly absorbed into the blood through the posterior auricular artery. The drugs subsequently enter the inner ear, where the blood supply is improved. This method of administration increases the concentration of drug in the target area, reduces the drug dose used, and mitigates side effects of the drug. This study implemented a combined administration method for the patients in the research group. The results showed that values of total effectiveness of treatment in the research group after one course of treatment, and after three months of treatment, were significantly higher than those of the reference group. This is consistent with a previous finding which showed that after treatment, there were markedly improved THI scores in the research group and reference group, but with lower scores in the research group [13]. In this study, after treatment, the pure tone threshold and PSQ1 scores of the two groups of patients were significantly decreased, with lower outcomes in the research group than in the reference group. Thus, post-auricular injection of methylprednisolone sodium succinate in combination with lidocaine was more effective than single therapy of lidocaine in the treatment of acute tinnitus, mitigation clinical symptoms, and improvement of sleep quality. No obvious adverse drug reaction was seen after three months of follow-up, and during the treatment. Only 2 patients in the research group experienced slight local swelling during the injection, but the symptoms spontaneously subsided after 3 - 6 h without special treatment. This further confirmed the high safety and low adverse effect of post-auricular injection of methylprednisolone sodium succinate and lidocaine in the treatment of acute tinnitus, which is in line with the results of Langguth *et al* [15].

In recent years, the clinical application of lidocaine has received considerable attention in academia. Lidocaine, a membrane stabilizer, inhibits the activity of Na^+ channels and blocks

information transmission, thereby reducing pathological irritation of the cochlea, and mitigating the symptoms of tinnitus. In addition, lidocaine produces promising regulatory effects on blood supply to the cochlea and central nervous system, thereby ameliorating the discharge activity of the outer hair cells of organ of Corti, resulting in suppression of tinnitus [15]. The effect of lidocaine on tinnitus varies remarkably with different administration methods. In most cases, intravenous injection and tympanic administration, which produce short durations of efficacy, are mainly used as auxiliary measures in clinical practice to shorten the adaptation time to tinnitus for patients.

In a previous study [16], the total effectiveness of post-auricular lidocaine injection was 82.7 %, which is similar to 82.5 % seen in the control group in the present study. A careful analysis has shown that lidocaine can only exert a significant short-term efficacy, but fails to sustain a long-term effect. Accordingly, in this study, the treatment regimen for the patients in the research group involved combined administration of methylprednisolone sodium succinate and lidocaine, which ultimately produced a satisfactory long-term curative effect, with lidocaine as a therapeutic drug and a local anesthetic [17].

CONCLUSION

Post-auricular injection of methylprednisolone sodium succinate in combination with lidocaine effectively results in improved clinical efficacy in the treatment of acute tinnitus, and enhances the sleep quality of patients. It is also a facile operation with a high level of safety. Therefore, this treatment strategy has promise for application in clinical practice.

DECLARATIONS

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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