Clinical Trial/Experimental Study

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A Pilot Randomized Controlled Trial of Transcutaneous Electrical Nerve Stimulation for Patients With Acute Tinnitus

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Abstract

Background: This pilot study aimed to evaluate the feasibility effectiveness and safety of transcutaneous electrical nerve stimulation (TENS) for patients with acute tinnitus.

Methods: A total of 46 eligible patients with acute tinnitus were entered and included in this randomized controlled trial. All the included patients were equally and randomly divided into a verum TENS group and a sham TENS group, each group 23 participants. All patients received parenteral intramuscular therapy of 1 ml Vitamin B12 weekly for a total of 4 weeks. In addition, they also underwent verum or sham TENS 30 min daily, 3 times weekly for 4 weeks. The primary efficacy endpoint was measured by the Tinnitus Severity Scale (TSS) and Tinnitus Questionnaire (TQ) sum score. The secondary efficacy endpoints were assessed by the Tinnitus Handicap Inventory (THI), 12-Item Short Form Health Survey (SF-12) questionnaire, and adverse events. All outcome efficacy endpoints were measured at baseline and after 4 weeks of treatment.

Results: After 4-week treatment, the patients undergoing verum TENS showed statistically efficacy of symptoms relief, as measured by the scales of TSS ($P < .01$), TQ ($P < .01$), and THI ($P < .01$), and improvement of quality of life, as assessed by the SF-12 ($P < .01$), compared with patients receiving sham TENS. In addition, no adverse events related to the treatment were recorded in either group.

Conclusions: The results of this study showed that verum TENS may benefit patients with acute tinnitus after 4 weeks of treatment.

Abbreviations: SF-12 = 12-Item Short Form Health Survey, TENS = transcutaneous electrical nerve stimulation, THI = Tinnitus Handicap Inventory, TQ = Tinnitus Questionnaire, TSS = Tinnitus Severity Scale.

Keywords: acute tinnitus, effectiveness, safety, transcutaneous electrical nerve stimulation

1. Introduction

Tinnitus is a common and disturbing condition.[1–2] It characterizes as the perception of sound or noise that has no external source.[3–4] It has been reported that about 5 to 10 percent of patients suffer from such condition.[5–6] This rate can increase up to 30% among the elderly,[5] and often becomes chronic condition, which may result in the anxiety, depression, insomnia, and poor quality of life in patients with such condition.[7–10]

Presently, no highly effective management was recommended for tinnitus, although a variety of therapies are utilized to treat this condition. These therapies consisted of medications, hearing aids, retraining therapy, behavioral therapy, cochlear implant therapy, acupuncture, and electrical stimulation, such as transcutaneous electrical nerve stimulation (TENS).[11–21] Of these managements, TENS is regarded as one of the most potential candidates with safe, non-invasive, and effective intervention.[19–21] However, there is still insufficient data to effectively support that TENS can manage acute tinnitus specifically.

In the present study, we hypothesized that verum TENS therapy for acute tinnitus specifically after 4 weeks treatment would be superior to the effectiveness of sham TENS intervention. Thus, we designed this pilot randomized sham-controlled trial to evaluate the feasibility effectiveness of verum TENS therapy for the treatment of patients with acute tinnitus.

2. Methods/design

2.1. Study design

This pilot study was approved by the Medical Ethics Committee of The People's Hospital of Yanan and Yanan University Affiliated Hospital. It was conducted from June 2017 to May 2018 at both centers. A total of 46 patients with acute tinnitus were recruited from 2 centers in this study. The first center of The People's Hospital of Yanan recruited 20 patients, and the second center of Yanan University Affiliated Hospital included 26 patients. All patients in both centers were randomly allocated to a

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verum TENS group and a sham TENS group at a 1:1 rate. They all received parenteral intramuscular therapy of 1 ml Vitamin B12 weekly for a total of 4 weeks. Moreover, subjects in the verum TENS group underwent real TENS therapy. The participants in the sham TENS group received sham TENS intervention. Patients in both groups were treated 30 min daily, 3 times weekly for a total of 4 weeks.

2.2. Patients

Patients were included if they met the following criteria:

1. all included patients were diagnosed as acute tinnitus;
2. male or female aged between 18 to 75 years old;
3. have a history of tinnitus less than 6 consecutive months;
4. not caused by any kinds of medications; and
5. written informed consent was provided by each individual.

Patients were excluded if they had received TENS, acupuncture, or electroacupuncture 3 months before this study; cardiac peacemaker; diseases that can cause tinnitus, such as otosclerosis; severe psychiatric disorders; cancer or severe mental disorders; pregnancy and lactation. They were also excluded if they had received medications for the treatment of acute tinnitus 3 months before the study, or during the study period.

2.3. Randomization and blinding

Forty-six patients with acute tinnitus were randomly allocated to the verum TENS group and sham TENS group in a 1:1 ratio. Randomization is conducted by a block randomization using a computerized number generator with SAS package 8.1 (SAS Institute Inc., Cary, NC, USA). The allocation information was concealed in sequentially numbered, opaque, sealed envelopes. The researchers, outcome assessors, and data analysts were masked to the treatment allocation information.

2.4. Intervention schedule

In this study, patients in both groups received parenteral intramuscular therapy of 1 ml Vitamin B12 (2500 mcg) weekly for a total of 4 weeks, according to the previously published study.[22]

Additionally, TENS therapy is performed by a LH202H Han Electrostimulator (Jinghua Wei Industry Development Company, Beijing, China). A pair of electrodes was placed on the left and right C2 nerves dermatomes. The negative electrode was placed at the opposite to the tinnitus side. If patients suffered from acute tinnitus on both sides, then the negative electrode was placed on the left side. It can generate pulses of disperse-dense wave and a frequency of 2/100 Hz. Each individual was treated 30 min daily, 3 times weekly for a total of 4 weeks. Sham TENS intervention was applied by the same electrostimulator at the same location, session, and total treatment duration, but without electrical power.

2.5. Outcome measurements

The primary efficacy endpoint was severity of tinnitus. It was measured by the Tinnitus Severity Scale (TSS)[23] and Tinnitus Questionnaire (TQ) sum score.[24] TSS consists of 6 numeric rating scales. Of these, scale 1 ranges from 0 to 5, and scales 2 to 6 vary from 0 to 10, with a higher score, indicating a severer tinnitus. TQ sum score range from 0 to 84, with a higher score, indicating a severer distress. The secondary efficacy endpoints were measured by the Tinnitus Handicap Inventory (THI),[25] the 12-Item Short Form Health Survey (SF-12) questionnaire,[26] and adverse events during the treatment period. The THI scale ranges from 0 to 100; with a higher score, indicating a greater handicap. The SF-12 includes physical and mental components; each item ranges 0 to 100, with a higher score, indicating a better quality of life. All the outcomes were measured at baseline and after 4 weeks of treatment.

2.6. Statistical analysis

The outcome values were conducted by using SAS package 8.1 (SAS Institute Inc., Cary, NC, USA). The minimum size of each group was estimated at 20 participants with $\alpha = 0.5$, $\beta = 0.8$. Assuming a 15% drop-out rate, the required sample size of this study was therefore estimated to be 46 patients, with 23 assigned to each group.

All outcome data were analyzed by intention-to-treat (ITT) principle. The Mann-Whitney *U* test or Fisher two-tailed exact test was used to compare the primary and secondary outcome measurements. The value of $P < .05$ was set to have the statistical significance.

3. Results

In total, 57 patients with acute tinnitus were admitted and entered the study (Fig. 1). Of these participants, 11 did not meet the inclusion criteria. Thus, 46 patients were randomly divided into the verum TENS group or sham TENS group in a ratio of 1:1. ITT approach was utilized to analyze all the primary and secondary efficacy outcomes. No patients withdraw or lost to follow-up visit (Fig. 1).

The characteristics of all included patients at baseline are listed in Table 1. In addition, the primary and secondary efficacy outcomes were also measured at baseline (Table 1). There were no significant differences in all characteristics, as well as the primary and secondary outcome measurement at baseline between 2 groups.

Results of all primary and secondary efficacy endpoints are summarized in Tables 2 and 3. They showed that patients in the Verum TENS group exerted better outcomes in TSS ($P < .01$, Table 2), TQ ($P < .01$, Table 2), THI ($P < .01$, Table 3), and SF-12 ($P < .01$, Table 3), compared with patients in the Sham TENS group.

During the 4-week treatment period, no adverse events related to the verum TENS or sham TENS intervention occurred in either group.

4. Discussion

It has been reported that tinnitus can greatly impact the quality of life in patients with it.[1] Many therapies are suggested to treat such condition. Of these, electrical stimulation is reported to treat tinnitus for more than 30 years.[27–29] It was gradually confirmed by several clinical studies.[20,29] TENS is one of the most important interventions of electrical stimulation. Previous studies found that TENS can treat tinnitus condition.[19–21] They found that TENS of the median nerve could not only modulate the tinnitus percept in some patients,[30] but also had an inhibitory effect by acting to the temporomandibular joint in patients with tinnitus.[31] Unfortunately, almost all of those studies provided quite low level of evidence to support this therapy. In the present

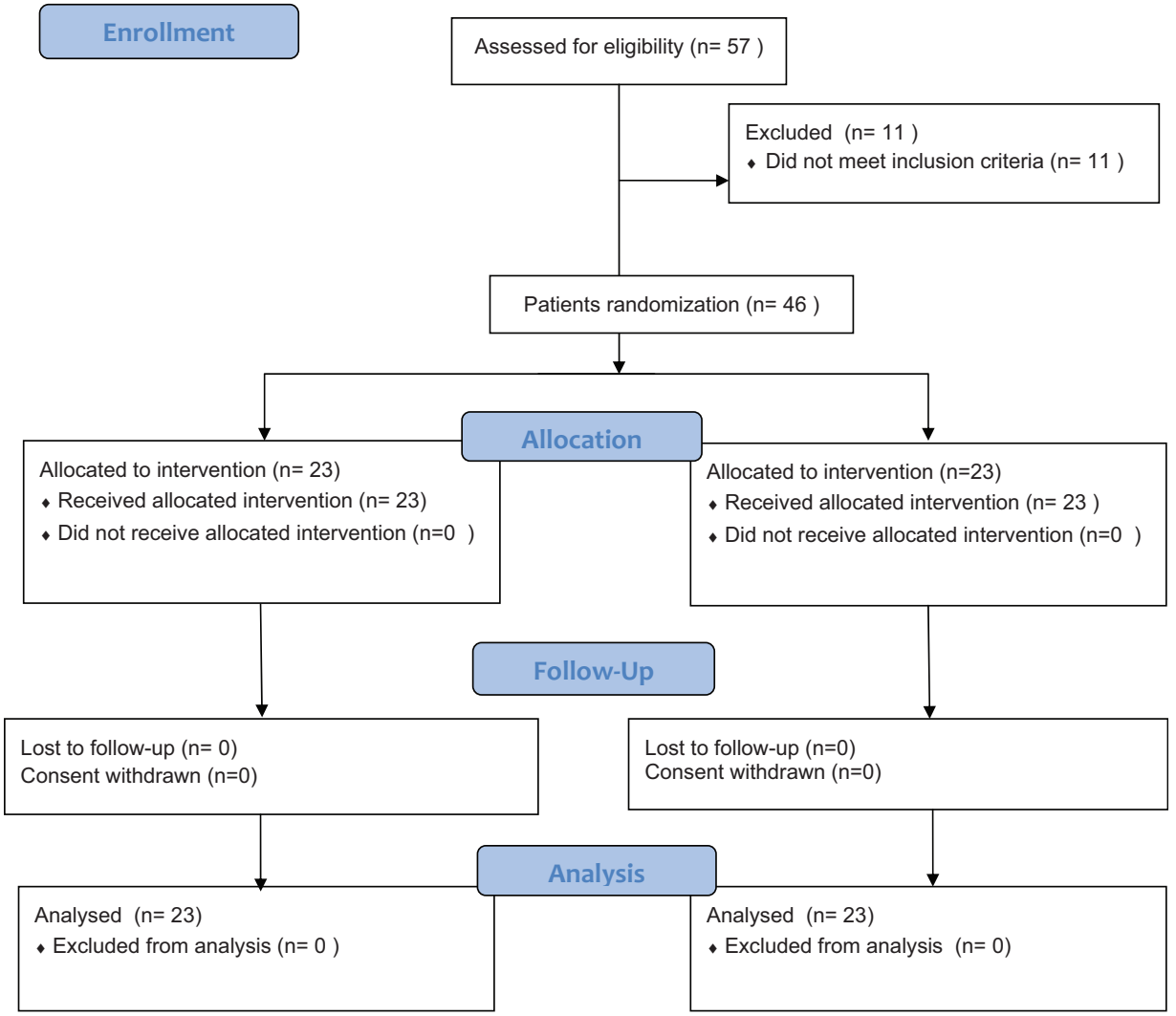

Figure 1. Flowchart of participant selection.

Table 1

Patient characteristic at baseline.

Characteristics	Verum TENS group (n = 23)	Sham TENS group (n = 23)	*P* value
Mean age (year)	46.8 (11.6)	48.4 (13.1)	0.66
Sex			
Male	14 (60.9)	17 (73.9)	0.35
Female	9 (39.1)	6 (26.1)	0.35
BMI (kg/m^2)	22.5 (2.0)	21.9 (2.4)	0.36
Tinnitus duration (months)	3.7 (1.4)	4.0 (1.6)	0.50
Location of tinnitus			
Left	5 (21.8)	7 (30.4)	0.50
Right	3 (13.0)	4 (17.4)	0.68
Both	15 (65.2)	12 (52.2)	0.37
Primary endpoint measurements			
TSS	22.8 (7.7)	21.1 (6.9)	0.43
TQ	20.1 (9.5)	19.3 (8.4)	0.76
Secondary endpoint measurement			
THI	31.8 (12.6)	30.2 (14.3)	0.69
SF-12 (physical)	77.6 (16.2)	79.3 (17.0)	0.72
SF-12 (mental)	80.1 (15.4)	81.6 (14.4)	0.73

Data are present as mean ± standard deviation or number (%). BMI = body mass index, SF-12 = 12-Item Short Form Health Survey questionnaire, TENS = transcutaneous electrical nerve stimulation, THI = Tinnitus Handicap Inventory, TQ = Tinnitus Questionnaire, TSS = Tinnitus Severity Scale.

Table 2

Primary efficacy endpoint at the end of 4-week intervention (change from baseline).

Outcome Measurements	Verum TENS group (n = 23)	Sham TENS group (n = 23)	Difference	*P* value
TSS	−9.3 (−12.2, −6.9)	−3.1 (−5.8, 1.9)	−6.2 (−8.7, −4.6)	<.01
TQ	−13.8 (−17.3, −9.2)	−3.5 (−7.1, −2.0)	−10.3 (−16.9, −8.7)	<.01

Data are present as mean change ± standard error. TENS = transcutaneous electrical nerve stimulation, TQ = Tinnitus Questionnaire, TSS = Tinnitus Severity Scale.

Table 3

Secondary efficacy endpoints at the end of 4-week intervention (change from baseline).

Outcome Measurements	Verum TENS group (n = 23)	Sham TENS group (n = 23)	Difference	*P* value
THI	−11.6 (−15.3, −8.2)	−2.9 (−5.8, −1.5)	−8.6 (−11.5, −5.7)	<.01
SF-12 (physical)	11.3 (8.9, 14.5)	2.5 (1.4, 4.2)	8.8 (6.3, 9.9)	<.01
SF-12 (mental)	12.6 (8.3, 16.6)	3.0 (1.9, 5.1)	9.7 (7.1, 11.3)	<.01

Data are present as mean change ± standard error; SF-12 = 12-Item Short Form Health Survey questionnaire, TENS = transcutaneous electrical nerve stimulation, THI = Tinnitus Handicap Inventory.

study, we applied the TENS to the location of the external pinna and tragus of each ear.

The results of the present pilot study confirmed our hypothesis that the effectiveness of verum TENS treatment is superior to the sham TENS for the treatment of patients with acute tinnitus after 4 weeks treatment. The results found that verum TENS may either significantly reduce the severity of acute tinnitus, as measured by the TSS, TQ, and THI, or greatly improve the quality of life in patients with acute tinnitus. These positive results indicated that verum TENS may have encouraging effectiveness for the treatment of acute tinnitus.

The present pilot study has 2 limitations. First, the sample size of this study is quite small, which may affect the results of this study. Second, this study only included 4 weeks treatment duration, which may quite short to assess the effectiveness of TENS. However, its effectiveness showed significantly positive after 4 weeks treatment, it may be because of the acute tinnitus with quite short disease duration.

5. Conclusion

The results of this study found that verum TENS may effectively treat acute tinnitus after 4-week treatment.

Author contributions

Conceptualization: Li Li, Hao Shi, and Min Wang.
Data curation: Li Li, Hao Shi, and Min Wang.
Formal analysis: Li Li.
Investigation: Min Wang.
Methodology: Li Li.
Project administration: Min Wang.
Resources: Hao Shi and Min Wang.
Software: Li Li.
Supervision: Hao Shi.
Validation: Hao Shi and Min Wang.
Visualization: Hao Shi and Min Wang.
Writing – original draft: Li Li, Hao Shi, and Min Wang.
Writing – review & editing: Li Li, Hao Shi, and Min Wang.

References

[1] Wu V, Cooke B, Eitutis S, et al. Approach to tinnitus management. Can Fam Phys 2018;64:491–5.
[2] McCormack A, Edmondson-Jones M, Somerset S, et al. A systematic review of the reporting of tinnitus prevalence and severity. Hear Res 2016;337:70–9.
[3] Bauer CA. Tinnitus. N Engl J Med 2018;378:1224–31.
[4] Hertzano R, Teplitzky TB, Eisenman DJ. Clinical Evaluation of Tinnitus. Neuroimaging Clin N Am 2016;26:197–205.
[5] Nondahl DM, Cruickshanks KJ, Wiley TL, et al. Prevalence and 5-year incidence of tinnitus among older adults: the epidemiology of hearing loss study. J Am Acad Audiol 2002;13:323–31.
[6] Sindhusake D, Golding M, Wigney D, et al. Factors predicting severity of tinnitus: a population-based assessment. J Am Acad Audiol 2004;15:269–80.
[7] Ziai K, Moshtaghi O, Mahboubi H, et al. Tinnitus patients suffering from anxiety and depression: a review. Int Tinnitus J 2017;21:68–73.
[8] Wakabayashi S, Saito H, Oishi N, et al. Effects of tinnitus treatments on sleep disorders in patients with tinnitus. Int J Audiol 2018;57:110–4.
[9] Aazh H, Moore BCJ. Thoughts about suicide and self-harm in patients with tinnitus and hyperacusis. J Am Acad Audiol 2018;29:255–61.
[10] Bartels H, Pedersen SS, van der Laan BF, et al. The impact of type D personality on health-related quality of life in tinnitus patients is mainly mediated by anxiety and depression. Otol Neurotol 2010;31:11–8.
[11] Seidman MD, Babu S. Alternative medications and other treatments for tinnitus: facts from fiction. Otolaryngol Clin North Am 2003;36:359–81.
[12] Kimball SH, Johnson CE, Baldwin J, et al. Hearing aids as a treatment for tinnitus patients with slight to mild sensorineural hearing loss. Semin Hear 2018;39:123–34.
[13] Henry JA, McMillan G, Dann S, et al. Tinnitus management: randomized controlled trial comparing extended-wear hearing aids, conventional hearing aids, and combination instruments. J Am Acad Audiol 2017;28:546–61.
[14] Berry JL, Brozoski TJ. The effect of tinnitus retraining therapy on chronic tinnitus: a controlled trial. Laryngoscope Investig Otolaryngol 2017;2:166–77.
[15] Jun HJ, Park MK. Cognitive behavioral therapy for tinnitus: evidence and efficacy. Korean J Audiol 2013;17:101–4.
[16] Wang Q, Li JN, Lei GX, et al. Interaction of tinnitus suppression and hearing ability after cochlear implantation. Acta Otolaryngol 2017;137:1077–82.
[17] Naderinabi B, Soltanipour S, Nemati S, et al. Acupuncture for chronic nonpulsatile tinnitus: a randomized clinical trial. Caspian J Intern Med 2018;9:38–45.
[18] Doi MY, Tano SS, Schultz AR, et al. Effectiveness of acupuncture therapy as treatment for tinnitus: a randomized controlled trial. Braz J Otorhinolaryngol 2016;82:458–65.
[19] Moon YK, Kim MH, Nam HJ. Comparison of the effectiveness between transcutaneous electrical nerve stimulation, manual acupuncture, and electroacupuncture on tinnitus: study protocol for a randomized controlled trial. Trials 2018;19:342.
[20] Vanneste S, Plazier M, Van de Heyning P, et al. Transcutaneous electrical nerve stimulation (TENS) of upper cervical nerve (C2) for the treatment of somatic tinnitus. Exp Brain Res 2010;204:283–7.
[21] Aydemir G, Tezer MS, Borman P, et al. Treatment of tinnitus with transcutaneous electrical nerve stimulation improves patients' quality of life. J Laryngol Otol 2006;120:442–5.
[22] Singh C, Kawatra R, Gupta J, et al. Therapeutic role of Vitamin B12 in patients of chronic tinnitus: a pilot study. Noise Health 2016;18:93–7.

[23] Meikle MB, Stewart BJ, Griest SE, et al. Assessment of tinnitus: measurement of treatment outcomes. Prog Brain Res 2007;166:511–21.
[24] Goebel G, Hiller W. The tinnitus questionnaire. A standard instrument for grading the degree of tinnitus. Results of a multicenter study with the tinnitus questionnaire. HNO 1994;42:166–72.
[25] Newman CW, Jacobson GP, Spitzer JB. Development of the tinnitus handicap inventory. Arch Otolaryngol Head Neck Surg 1996;122: 143–8.
[26] Salyers MP, Bosworth HB, Swanson JW, et al. Reliability and validity of the SF-12 health survey among people with severe mental illness. Med Care 2000;38:1141–50.
[27] Steenerson RL, Cronin GW. Treatment of tinnitus with electrical stimulation. Otolaryngol Head Neck Surg 1999;121:511–3.
[28] Graham JM, Hazell JW. Electrical stimulation of the human cochlea using a transtympanic electrode. Br J Audiol 1977;11:59–62.
[29] Cazals Y, Negrevergne M, Aran JM. Electrical stimulation of the cochlea in man: hearing induction and tinnitus suppression. J Am Audiol Soc 1978;3:209–13.
[30] Moller AR, Moller MB, Yokota M. Some forms of tinnitus may involve the extralemniscal auditory pathway. Laryngoscope 1992;102:1165–71.
[31] Herraiz C, Toledano A, Diges I. Trans-electrical nerve stimulation (TENS) for somatic tinnitus. Prog Brain Res 2007;166:389–94.