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A randomised, placebo-controlled trial of manual and electrical acupuncture for the treatment of tinnitus

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Summary The aim of this study was to examine the effects of manual/electrical acupuncture treatment on tinnitus in a randomised, single-blinded, placebo-controlled design. Fifty patients (46 males, 4 females) suffering from tinnitus were investigated. The patients were randomly assigned to three groups: a manual acupuncture group (MA), an electrical acupuncture group (EA), and a placebo group (PL). The frequency of tinnitus occurrence, tinnitus intensity, and reduction of life quality were recorded before treatment (Baseline), after 6 treatments (After-Treatment), and 1 month after the completion of treatment (1-Month-After). Standard audiometric tests were conducted on each patient at Baseline and After-Treatment. The patients also provided an overall subjective evaluation of treatment effectiveness at each stage. Eight to ten acupoints were selected at each treatment by an experienced acupuncturist. Six treatments were performed, each separated by an interval of 1 week. Analysis of variance and *t*-tests were used to statistically compare the data. The frequency of tinnitus occurrence and the tinnitus loudness were significantly decreased After-Treatment compared with Baseline in the EA group ($P < 0.009$). Life quality was improved After-Treatment and at 1-Month-After compared with Baseline in both MA and EA groups ($P < 0.038$). However, no significant differences were detected among the three groups ($P > 0.079$). The audiogram did not show any significant changes after treatment in either group ($P > 0.091$). The overall subjective evaluation indicated significant improvements After-Treatment compared with Baseline in both MA and EA groups ($P < 0.011$). Furthermore, After-Treatment subjective evaluation was significantly better in the EA group compared with either the MA or PL group ($P < 0.011$). These results indicate that there is no statistically significant differential effect of manual or electrical acupuncture on tinnitus treatment efficacy, however, electrical acupuncture does confer some relative advantages.

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Introduction

Tinnitus is the perceived sensation of sound. It can be a nuisance or a severe debilitating disorder that can totally ruin a person's life.[1] Epidemiological data reports that tinnitus affects approximately 10% of adults in United Kingdom,[2] 14% in Sweden,[3] 17% in the United States.[4] Most tinnitus is associated with sensorineural hearing loss.[5] Its prevalence has been shown to increase with age, and it appears that males and females are affected equally.[6]

The pathophysiological mechanism of tinnitus is still unclear. Neurophysiological studies have determined that tinnitus can be caused by exposure to intense sound,[7] head injury[6] or ototoxicity from drugs such as aspirin[8] or quinine.[9] It has been demonstrated that these agents cause abnormal activity throughout the auditory system by acting peripherally to alter the normal function of the cochlea or auditory nerve, triggering changes at central levels of the auditory pathway.[10] In regarding to management of tinnitus, present non-surgical therapies include psychological counselling, biofeedback training,[4] and masking techniques.[11] There are also a number of drug treatments that have been applied.[12] However, no therapy has yet been effective in eliminating the symptoms of tinnitus.[13]

Acupuncture has been used to treat tinnitus for a long time. The rationale for the use of acupuncture is based on the grounds that it may influence the olivocochlear nucleus.[3] It has been reported that acupuncture can yield immediate relief, both from the loudness and the disturbing quality tinnitus, significant improvement in quality of life, less tension and better sleep.[14–17] Other experiments have failed to show any statistically significant advantage for acupuncture over placebo with respect to tinnitus loudness or annoyance.[18–20] A recent systematic review reported that the six eligible randomised controlled trials did not conclude that acupuncture was efficacious in the treatment of tinnitus.[3]

Electrical acupuncture for the treatment of tinnitus is a concept that is attracting attention from several sources. It was suggested that electrical stimulation is effective in treating cochlear tinnitus by influencing the polarity of the hair cells and inhibiting postsynaptic potentials.[21] Previous studies of electrical stimulation as a form of treatment for tinnitus have most commonly focussed on transcutaneous electrical stimulation.[22–25] Few studies have been performed using electrical stimulation through acupuncture needles. The effect of the electrical acupuncture on tinnitus needs further investigation.

Thus, in the present study, a randomised, single-blinded, placebo-controlled trial was implemented to evaluate the effect of acupuncture, with and without electrical stimulation, as treatment for tinnitus.

Materials and methods

Subjects

Sixty patients, aged 30—70 years, who had all suffered from tinnitus for more than 3 months were recruited from the acupuncture clinic. The gender of the patients was not limited during the recruiting. No participating patients suffered from co-existent mental illness. Patients suffering from severe heart diseases were excluded. General information, history of symptoms, and related disorders were recorded from each subject. The local ethics committee approved the study (VN 2000/169). Patients were informed that they were going to be divided randomly between three different groups, including one group who would receive a placebo treatment. All patients gave written informed consent to participate in the study.

Experiment design

Patients were randomly allocated to one of three groups by the secretary of the clinic. One group was treated by manual acupuncture (MA) and another group was treated by acupuncture with electrical stimulations (EA). The control group was treated with placebo needles without any physical invasion (PL). The treatment took place once a week for 6 weeks. The patients were blinded to the identity of their treatment group and all treatments were performed by the same acupuncturist who has more than 10 years experience on treating the tinnitus by using acupuncture. Evaluations of tinnitus were performed before treatment (Baseline), after the last of the 6 treatments (After-Treatment), and one moth after the end of treatment (1-Month-After). Counselling was given for all subjects before treatment commencement by the same acupuncturist. This entailed education in basic tinnitus physiology, daily care of tinnitus, and information on the ongoing research protocol.

Assessment of tinnitus

Tinnitus occurrence frequency on a 5-point scale from 0 to +4, loudness on a 4-point scale from 0 to +3, and reduction of life quality on a 4-point scale from 0 to +3 were all reported subjectively by the patients at Baseline, After-Treatment and at 1-Month-After.[14] Finally, the patients also provided an overall evaluation of the treatment effect at each stage on a 6-point scale from −2 to +3 (−2: much worse; −1: a little worse; 0: no change; +1: a little better; +2: much better; +3: disappeared) After-Treatment and at 1-Month-After.

The best-match mimic frequency and intensity produced by an arbitrary waveform generator (Hewlett Packard 33120A, USA) was used to assess the frequency and intensity of ongoing tinnitus. The waveform generator can produce an arbitrary acoustic wave at the frequency of 0—20,000 Hz. Sound generated by this device was matched by patients to their tinnitus at Baseline, After-Treatment and 1-Month-After via an earphone. The frequency and the intensity of the ongoing tinnitus were assessed in this manner. Furthermore, an audiogram was recorded for each patient at Baseline and After-Treatment by a specialized ear doctor in his clinic.

Acupuncture/electrical acupuncture/placebo acupuncture

The manual acupuncture group received traditional Chinese acupuncture treatment for 25 min in each session. Patients were seated in an upright position in a chair and asked to focus their attention on the treatment task. Sterile single-

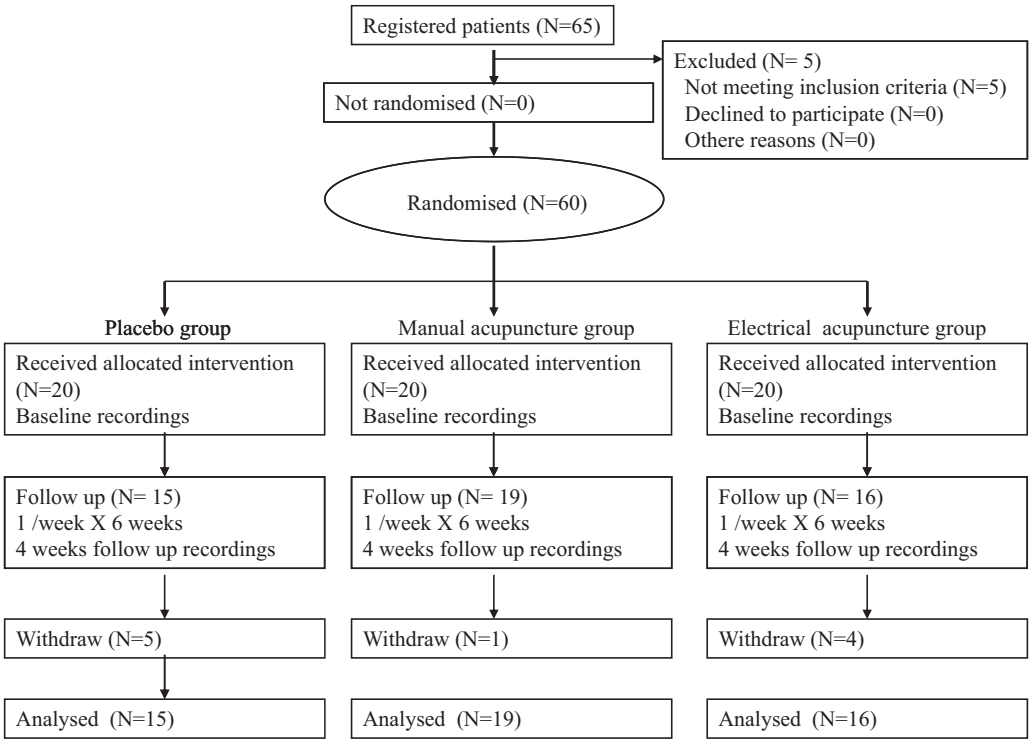

Figure 1 A flow diagram of the progression of the three groups through the phases of the randomised trial.

use acupuncture needles (0.26 × 40 mm, Hwato, Jiangsu, PR China) were used for all treatments. Acupoints described as being effective for tinnitus were selected according to Chinese medicine theory. These consisted of bilateral local points (GB 8, TE 17, GB 2, GB 20, GV 20,) and bilateral remote points (TE 3, ST 36). Fourteen points were selected for each treatment. After cleaning the skin over the acupoint with alcohol, the acupuncture needle was inserted into the deep tissue layer. During manual stimulation, the ''de qi'' sensation, a subjective feeling of numbness, tingle and deep muscle discomfort was obtained by turning the needle. After initial insertion, no stimulation of the needle was given throughout the treatment at intervals.

In the electrical stimulus session, procedures were the same as for manual acupuncture. The acupuncture needles were inserted into the same points to the same depth. Electrical stimulation was delivered by an electrical stimulator (HANS, Beijing China) through the needle to the local acupoints (bilateral GB8 and TE 17). The square burst pulse with 0.1 ms duration and an alternative frequency of 2/100 Hz at 3 s interval was applied. Stimulation was indicated with a green flash. The intensity was adjusted individually to maximum sensation below the pain threshold.[26]

In the placebo treatment session, placebo needles (half-cut, blunt-tip) were used. The half-cut needle was inserted through a cube-shaped piece of elastic foam to obscure the patients' vision of the insertion points (the same points as selected for the real treatment). The half-cut, blunt needle was inserted into the elastic foam and caused a pricking sensation when it touched the skin. The skin was not punctured.[27] Patients perceived that the needle was being inserted into their body.

Analysis

The sample size was calculated such that the risk of type I and type II errors was limited to 5% and 20% respectively, the expected standard residual deviation limited to 30% and the minimum detectable difference between means limited to 20%. A total of 45 subjects were required to meet these criteria.

A one-way analyses of variance (ANOVA) with repeated measures was performed and followed by pair-wise multiple comparison procedures (Student—Newman—Keuls, SNK) to compare the parameters Baseline, After-Treatment, and 1-Month. A *t*-test was used to compare between groups. The significance level was set at $P < 0.05$. Mean values ± SEM are presented in the text.

Results

General information of patients

Sixty patients were recruited to the present study. Ten of the patients withdrew during the study for personal reasons. Fifty patients received all six sessions of treatment and were unaware of which group they were in. A flow of the study protocol is illustrated in Fig. 1.[28]

General information and tinnitus characteristics of the patients are shown in Table 1. Please note that the frequency of the ongoing tinnitus was assessed by the patients by using the waveform generator. Intensity of the ongoing tinnitus are not reported in the present study since the patients all had different levels of hearing losing. There were no sig-

Table 1 General information from participating patients.

Participates in three groups (male, female)	Age (mean ± SEM)	Tinnitus years (mean ± SEM)	Tinnitus in both ears	Hearing loss	Matched frequency of the ongoing tinnitus (Hz)	Quality reduction of daily life (0–3)
EA: 16 (12 M, 4 F)	51.06 ± 3.54	12.19 ± 2.02	12/16	13/16	5304 ± 598	1.91
MA: 19 (M)	51.79 ± 2.68	13.71 ± 2.64	12/19	16/19	5442 ± 871	1.87
PL: 15 (M)	56.50 ± 2.31	9.67 ± 2.53	9/15	13/15	4909 ± 403	1.79
Total: 50 (46 M, 4 F)	53.12 ± 2.84	11.86 ± 2.40	33/50	42/50	5218 ± 624	1.86

EA: electrical acupuncture group; MA: manual acupuncture group; PL: placebo group. There were no significant differences among the three groups on any of the general Baseline measures.

Table 2 Subjective evaluation of the treatments between groups.

Evaluations	After-Treatment	1-Month-After
EA	0.087 ± 0.206	0.438 ± 0.185
MA	0.421 ± 0.154	0.316 ± 0.159
PL	0.105 ± 0.070	0.079 ± 0.079
P-value	$P < 0.001$	$P = 0.110$

EA: electrical acupuncture group; MA: manual acupuncture group; PL: placebo group. There was a significantly better evaluation of the treatment by the EA group compared to the MA or PL group ($P < 0.001$).

nificant differences among the three groups concerning age (*t*-test: $P = 0.410$), years of tinnitus suffering ($P = 0.508$), or frequency of tinnitus occurrence ($P = 0.502$).

Tinnitus occurrence

The daily tinnitus occurrence was significantly decreased After-Treatment compared with Baseline in the EA group ($P = 0.009$). There were no significant time effects in the MA ($P > 0.153$) or in PL ($P > 0.641$) group. No significant differences were detected among the three groups at any stage ($P > 0.111$).

Tinnitus loudness

Tinnitus intensity was significantly lower After-Treatment and at 1-Month-After compared with the Baseline in the EA group ($P < 0.001$). There was no significant time effect in the MA ($P > 0.063$) or in PL ($P > 0.967$). Again no significant differences were detected among the three groups at any stage ($P > 0.079$).

Quality reduction of daily life

The influence on quality of daily life was significantly decreased After-Treatment and at 1-Month-After compared with Baseline in the EA and MA ($P < 0.002$) groups. No significant time effect was observed in the PL group ($P = 0.768$). Again there was no significant treatment effect among the three groups at any stage ($P > 0.108$).

Subjective general evaluation of the treatments

From the subjective evaluation on the effects of the treatments, it is evident that the patients felt significantly better After-Treatment compared with Baseline in the EA ($P < 0.001$) and MA groups ($P = 0.011$). No significant treatment effect was indicated in PL group. The evaluation of treatment was a significantly better in the EA group compared to either the MA or PL group ($P < 0.001$) (Table 2).

Effect on the hearing improving

The audiograms for both ears at Baseline and After-Treatment from all three groups are shown in Fig. 2. There

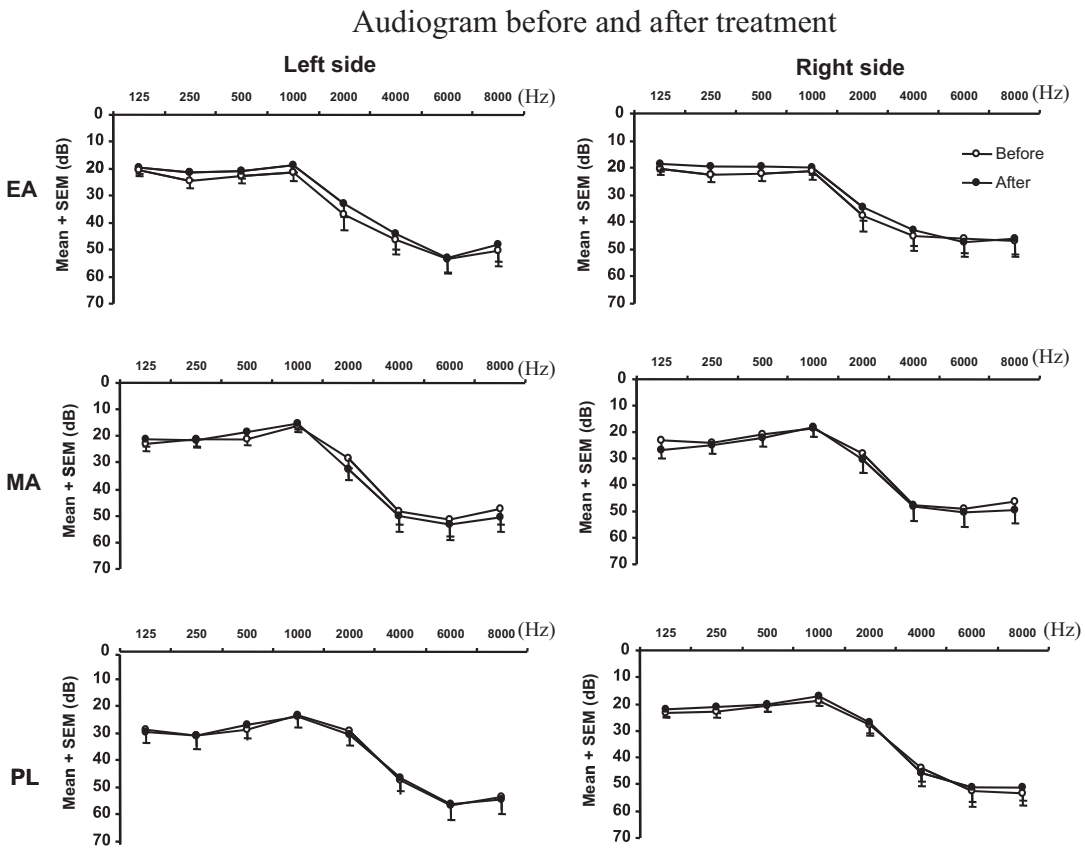

Figure 2 Audiogram of both ears at Baseline and After-Treatment (mean + SEM). EA: electrical acupuncture; MA: manual acupuncture; PL: placebo acupuncture. No significant differences were detected among the three groups.

was no significant time effect on hearing ($P > 0.091$) in any group.

Discussions

Controls and limitations

This study was designed as a randomised, single-blinded and placebo-controlled trial. The recruited patients were randomised into three groups. The three groups did not show any significant differences in age, gender, tinnitus history, or tinnitus symptom parameters. To standardize the method, the same acupuncture points were selected, and the same stimulation intensity was used for all patients. The results from the study did not show a significantly specific effect among the three groups for frequency of tinnitus occurrence or tinnitus loudness.

The first limitation of this study was the relatively small sample size. Only 50 patients were finally recruited into the three groups (19 EA, 16 in MA, 15 in PL). A placebo-controlled study on a larger sample to assess the effectiveness of electrical acupuncture or acupuncture on tinnitus is expected.

The second limitation is that use of a standardized between-subject treatment method is contrary to the theory of traditional Chinese acupuncture. Traditional acupuncture emphasises individualized treatment. Different points and different stimulation should be used individually according to the individual difference of the patients.[29] From this point of view, the results of the study may not present the real effect of traditional Chinese acupuncture. The specific treatment (e.g., specific choice of acupuncture points, intensity, and frequency) for specific individuals should be considered as a basic acupuncture principle in future research and clinical treatment.

The third limitation is that the investigation of the present study followed only 1 month after termination of the treatment. Therefore, the results show only short-lasting effects. Long-lasting effects were not investigated.

Evaluation of the treatment effect of acupuncture is part of the general problem of evaluating various physical forms of treatment.[30] Placebo acupuncture has been defined as a mock acupuncture procedure without physical invasion. Therefore, placebo acupuncture is considered a physiologically inert control. This may create suspicion among the patients regarding the authenticity of the therapy.[31]

Effects of treatments

The results of the present study showed that acupuncture with electrical stimulation was the most effective treatment modality. Tinnitus occurrence and tinnitus loudness were significantly decreased After-Treatment compared with Baseline although statistical significance could not be detected in comparison to the other groups.

The therapeutic modality of electrical stimulation is most commonly used for pain relief.[32] Electrical stimulation for

the treatment of tinnitus is a concept that is attracting attention from several sources. The alleviation of tinnitus by direct electrical stimulation of the inner ear has also been described.[33,34] Advantages in electronic technology appear to make this treatment more effective than other treatments.[23,35] It was suggested that electrical stimulation is effective in treating cochlear tinnitus by influencing the polarity of the hair cell and inhibiting postsynaptic potentials.[21] The effectiveness of electrical stimulation depends upon the characteristics of the electrical stimulus and the anatomical area of stimulation.[34] The method most used for electrical stimulation in previous studies has been transcutaneous electrical stimulation.[22–25] Few studies have been conducted using electrical stimulation through acupuncture needles and the long-lasting effects of the electrical acupuncture on tinnitus needs further investigation. The most recent researches shows that low-frequency repetitive transcranial magnetic stimulation is a promising treatment modality that can transiently diminish tinnitus in some individuals.[36,37]

The alternate stimulation of low (2 Hz) and high (100 Hz) frequency with an interval of 3 s was utilised for the stimulation protocol in the current study. It has been demonstrated that low frequency electrical stimulation (2 Hz) induces the release of encephalin and endorphin, and that the antinociceptive effect is mediated by both mu and delta opioid receptors; high frequency stimulation (100 Hz) evokes a release of dynorphine in the central nervous system, and the antinociceptive effect is mediated primarily by the kappa receptor.[38] Reports demonstrate that this dense-and-dispersed design has the largest effects in experiments and clinical applications.[39,40]

The present results showed that the general effects of the treatment were more profound than the specific effects. The ''reduction of life quality'' data and the ''subjective evaluation'' of the treatment indicated that the patients felt significantly better After-Treatment in both the EA and MA groups.

Pericranial muscle tenderness can be found in a lot of tinnitus sufferers. A recent study suggested that strong muscle contractions of the head and neck could modulate tinnitus perception in approximately 80% of people with ongoing tinnitus, and could elicit a sound percept in approximately 50% of people with no tinnitus.[41] Likely neural pathways underlying both the induction and modulation of tinnitus have been revealed in animal studies. Stimulation of acupuncture points could elicit a local effect: improved blood circulation and relaxation of local tender points in the muscles.[42,43] Neurophysiological studies in animal and humans provide evidence that acupuncture increases pain threshold and works through activation of an endogenous analgesic system by increasing the levels of certain endogenous opioids and/or other neurotransmitters.[40] Patients may feel better subjectively on the general conditions since the muscle tension is decreased and the sleep quality is improved.[14–17]

In conclusion, the specific effects of reducing the tinnitus occurrence and tinnitus loudness were not detected. The treatment effects of the manual and electrical acupuncture were difficult to differentiate from the placebo control in the present study. However, electrical acupuncture showed some promising short-term general effects on tinnitus. Further carefully controlled research with bigger sample sizes and longer treatment periods are required.

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