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Personalized music therapy combined with medication as treatment for tinnitus

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Abstract. – OBJECTIVE: This study aimed to investigate the effects of personalized music therapy in combination with medication as a treatment for tinnitus.

PATIENTS AND METHODS: We retrospectively analyzed a total of 200 patients who were admitted to the Department of Otorhinolaryngology in our hospital from June 2018 to June 2019, with tinnitus as their primary complaint. Patients were divided into four groups based on their individual treatment methods: medication group (patients received medication only, n=40), tinnitus masking (TM) group (patients received medication plus TM, n=38), tinnitus re-training (TRT) group (patients received medication plus TRT, n=35), and personalized group (patients received medication plus personalized music therapy, n=30). The pure-tone audiometry (PTA), loudness visual analogue scale (VAS), and tinnitus handicap inventory (THI) for each patient were analyzed.

RESULTS: There were statistically significant differences in the THI and VAS scores of all groups before and after treatment ($p<0.05$). Following nine and twelve months of treatment, the THI and VAS scores of the TRT group and the personalized group were significantly lower than those of the other two groups ($p<0.05$). The THI and VAS scores of the personalized group were significantly lower than those of the TRT group ($p<0.05$). Additionally, THI and VAS scores were statistically different at various measurement time points in each group ($p<0.05$). The clinical effective rate (85.37%) of the personalized group was higher than that of the other three groups ($p<0.05$).

CONCLUSIONS: TM, TRT, or personalized music therapy, when combined with medication, are effective in treating patients with tinnitus. Among these methods, personalized music therapy may be the superior treatment after nine months of treatment.

Key Words:
Personalized music therapy, Medication, Tinnitus.

Introduction

Tinnitus refers to the perception of sound in the head or the ears, in the absence of any external source, and can be either subjective or objective[1]. It has been estimated that over 740 million individuals worldwide are affected by tinnitus, with over 120 million experiencing a severe form of the condition[2]. Subjective tinnitus is the more common form of tinnitus and accounts for 99% of all reported cases, according to the American Tinnitus Association[3]. Subjective tinnitus can lead to anxiety, depression, and insomnia, which can negatively affect patients' quality of life[4]. In extreme cases, some patients cannot bear the severe interference of tinnitus and the dual burden of physical and mental ailments and may even contemplate suicide[5]. Therefore, finding effective methods to diagnose and treat subjective tinnitus is one of the most pressing challenges in the medical field today.

Given the heterogeneity of tinnitus, there is currently no specific treatment modality available for all tinnitus patients[6]. Nonetheless, sound therapy has long been considered an effective treatment, owing to its non-invasive and easy-to-administer nature. Sound therapy involves the use of additional background sounds to modify a patient's reaction to tinnitus, which can effectively reduce its severity and alleviate the level of impairment and psychological distress[7,8]. Non-personalized sound therapies, such as tinnitus masking (TM) and tinnitus retraining therapy (TRT), are widely used treatment modalities. While they are effective in reducing tinnitus symptoms in some patients, they do have limitations. For example, some patients may find it difficult to adjust to the masking sound or just find it unpleasant overall, while TRT can be time-consuming, which may decrease treatment compliance. In this context,

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with the highly developed digital technology and the availability of precision medicine, personalized sound therapy for the different types of tinnitus patients has emerged[9].

Phase-shift tinnitus treatment, a personalized sound therapy, attempts to counteract the patient's perception of tinnitus by emitting a series of sounds with the same frequency, but logarithmic changes in phase, through headphones, based on the tone and loudness of the patient's tinnitus[10]. Studies[11,12] have shown promising results for phase-shift treatment in reducing tinnitus symptoms. However, the efficacy of phase-shift treatment has not been extensively investigated alone or in combination with other treatment options, such as medication. Thus, we aimed to provide individual interventions for tinnitus patients using personalized music therapy combined with medication, compared to treatment with TM and TRT, to understand the efficacy of this possible therapy.

Patients And Methods

We retrospectively analyzed a total of 200 patients who were admitted to the Department of Otorhinolaryngology in our hospital from June 2018 to June 2019, with tinnitus as their primary complaint. Patients were divided into four groups based on their prescribed treatment: medication group (patients received medication only, n=40), TM group (patients received medication plus TM, n=38), TRT group (patients received medication plus TRT, n=35), and personalized group (patients received medication plus personalized music therapy, n=30). The medication group received basic drug treatment only, while the TM, TRT, and personalized groups received sound therapy and basic drug treatment based on the frequency and loudness of their tinnitus. The study was approved by the Ethical Committee of our Hospital (Date: June 9th, 2023), and informed consent was received from all patients.

Inclusion Criteria

- Patients aged 18 - 70 years.
- Patient diagnosed with subjective tinnitus and primarily experiencing a pure tone[13,14].
- Patients with disease duration ≥6 months.
- Patients with tinnitus frequency within the range of 1.0 kHz - 8.0 kHz.
- Patients with hearing threshold of the affected ear ≤70 dB HL.
- Patients with complete clinical data.

Exclusion Criteria

- Patients with ear diseases with definite etiology, such as otitis externa, furuncle in the ear canal, cerumen embolism, otitis media, traumatic perforation of the tympanic membrane, Meniere's disease, tympanosclerosis, acoustic neuroma, and otosclerosis.
- Patients with objective tinnitus, such as tinnitus caused by intracranial arteriovenous fistula, jugular spheroid tumor, vascular malformation, jaw muscle spasm, stapedius muscle spasm, and tensor tympani muscle spasm.
- Patients whose pure-tone audiometry test results indicate conductive or mixed hearing loss.
- Patients suffering from systemic diseases and tinnitus caused by cardiovascular and cerebrovascular diseases, such as high blood pressure, diabetes, and kidney disease.
- Patients with severe mental illness.
- Patients who are receiving another type of sound therapy or taking drugs.

Treatment Methods

All patients were evaluated by pure-tone audiometry (PTA), loudness visual analogue scale (VAS), and tinnitus handicap inventory (THI) before treatment. Loudness VAS is a 10-point self-graded scale ranging from 0 - 10, with a score of 0 indicating the absence of symptoms, while a score of 10 represents extremely loud tinnitus[15]. THI has 25 items with a total score ranging from 0 - 100. The response options for each item were categorized into three choices: "yes" (4 points), "sometimes" (2 points), and "no" (0 points)[16]. The total score was calculated by adding up all individual scores, with higher scores indicating more severe tinnitus[17].

The treatment methods of each group were as follows:

(1) Medication group – The patients in this group took 80 mg Ginkgo tablets (Shenzhen Neptunus Pharmaceutical Co., Ltd., Guangdong, China; Approval No.: Z20027956) three times a day. Three months was considered a course of treatment, and all patients received continuous treatment for 4 courses.

(2) TM group – In addition to drug therapy, patients also received TM therapy. The doctor selected a masking sound based on the results of the patient's tinnitus assessment and communicated with the patient to ensure that the chosen masking sound provided a comfortable sensation[18]. A narrow-band noise or white noise was selected to

match the pitch and center frequency of the tinnitus, and the intensity was set to completely mask the tinnitus at 10 dB above the tinnitus threshold. This was then recorded and stored in a storage device, and the patient was instructed to listen to it once a day for 30 minutes.

(3) TRT group[19] – In addition to drug therapy, patients also received TRT. TRT consists of psychological intervention, relaxation training, attention diversion, and partial masking therapy. Psychological intervention: Doctors outlined the basic knowledge, treatment methods, and treatment effects related to subjective tinnitus and answered any patient questions. Patients were encouraged to face tinnitus with a positive attitude to alleviate any negative emotions. Relaxation training: Doctors guided patients to master the correct method of sitting with eyes closed or lying down, enabling patients to control the nerves and muscles of their whole body using their own thoughts, keeping the body in a relaxed state. Training should last for 10-20 minutes per session and be completed 1-2 times per day. Attention diversion: Patients were informed that when tinnitus occurs, they should divert their attention by engaging in other activities. Partial masking therapy: Doctors collected naturally simulated sounds from nature, and the intensity was mixed or slightly lower than the mixed point, while the frequency was selected based on the patient's tinnitus pitch. Patients underwent partial masking therapy for two hours per session once per day.

(4) Personalized group: In addition to drug therapy, patients also received personalized music therapy. Doctors selected music from the computer database that overlapped with the patient's tinnitus frequency range. By matching the frequency and intensity of the tinnitus sound, the doctors edited the music so that the phase changed logarithmically, and the edited music contained segments with frequencies and intensities that tended to be similar to the patients' personal tinnitus sound, with logarithmic phase changes. By establishing a WeChat platform, a remote treatment system was built. The personalized therapeutic music was uploaded to the WeChat platform, which patients could access at any time outside the hospital. The patients were instructed to listen to the music continuously or intermittently for a total of two hours or more per day, and to record the treatment time and duration. A daily check-in function was set up, and nurses and audiologists provided online training, timely supervision, and professional psychological counseling and support.

Efficacy Evaluation

THI and loudness VAS were used to evaluate the severity of tinnitus at 1, 3, 6, 9, and 12 months after treatment, respectively. Effective treatment was defined as a reduction in THI of at least 7 points after treatment[20].

Statistical Analysis

SPSS 19.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Measurement data were presented by X±SD, and comparisons between the groups were performed by One-way ANOVA. Counting data were presented by n (%), and Chi-square analysis was used for comparison between groups. Multiple time points were compared using repeated ANOVA. $p<0.05$ was considered statistically significant.

Results

Patient Characteristics

In the medication group, there were 25 males and 16 females, with an average age of 44.7±7.8 years and an age range of 27 to 68 years. In the TM group, there were 25 males and 13 females, with an average age of 46.8±12.3 years and an age range of 19 to 70 years. In the TRT group, there were 26 males and 9 females, with an average age of 46.3±10.7 years and an age range of 25 to 63 years. In the personalized group, there were 17 males and 13 females, with an average age of 43.1±13.1 years and an age range of 25 to 65 years. There was no statistically significant difference in the baseline characteristics between the four groups ($p>0.05$) (Table I).

THI and VAS Assessment

There were no significant differences in the THI or VAS scores of the four patient groups before treatment ($p>0.05$) (Table II and Table III). There were statistically significant differences in the THI and VAS scores of the four patient groups following 1, 3, 6, 9, and 12 months of treatment ($p<0.05$) (Table II and Table III). At 9 and 12 months after treatment, the THI and VAS scores of the TRT group and the personalized group were significantly lower than those of the other two groups ($p<0.05$), and the THI or VAS scores of the personalized group were significantly lower than those of the TRT group ($p<0.05$). In addition, there were also statistical differences in the THI or VAS scores at different measurement time points in each group ($p<0.05$), indicating that the

Table I. Patient baseline characteristics.

Characteristics	Medication group (n=41)	TM group (n=38)	TRT group (n=35)	Personalized group (n=30)	F/χ^2	p
Age (year)	44.7±7.8	46.8±12.3	46.3±10.7	43.1±13.1	0.792	0.501
Male/Female	25/16	25/13	26/9	17/13	2.520	0.472
Tinnitus duration (year)	4.78±1.86	4.84±2.11	4.54±1.65	4.33±2.25	0.473	0.702
Main frequency (Hz)	5,167±1,180	5,300±1,232	5,058±1,401	4,939±1,550	0.458	0.712
Loudness of tinnitus (dB HL)	56.9±23.8	51.9±21.2	56.2±22.8	59.2±22.8	0.627	0.599
Tinnitus localization (One/Both)	31/10	31/7	29/6	22/8	1.283	0.733

TM, tinnitus masking; TRT, tinnitus retraining therapy.

Table II. Tinnitus handicap inventory (THI) changes before and after treatment.

Characteristics	Medication group (n=41)	TM group (n=38)	TRT group (n=35)	Personalized group (n=30)	F	p
Before treatment	42.7±6.0	43.4±6.5	43.0±6.8	44.2±5.9	0.375	0.771
1 month of treatment	40.7±5.9	38.1±5.6[a]	37.8±5.5[a]	36.7±4.6[a]	3.510	0.017
3 months of treatment	36.9±5.0	34.5±4.7[a]	34.3±4.7[a]	33.7±4.6[a]	3.304	0.022
6 months of treatment	32.8±4.9	30.7±4.4[a]	29.5±4.8[a]	28.7±4.3[a]	5.445	0.001
9 months of treatment	30.5±4.5	28.4±3.9[a]	23.9±2.7[a,b]	21.0±2.8[a,b,c]	49.378	<0.001
12 months of treatment	28.3±3.3	25.4±3.0[a]	18.0±2.2[a,b]	15.9±1.8[a,b,c]	167.096	<0.001
F						
p	<0.05	<0.05	<0.05	<0.05		

TM, tinnitus masking; TRT, tinnitus retraining therapy. [a]$p<0.05$, compared with medication group; [b]$p<0.05$, compared with TM group; [c]$p<0.05$, compared with TRT group.

Table III. Loudness visual analogue scale (VAS) changes before and after treatment.

Characteristics	Medication group (n=41)	TM group (n=38)	TRT group (n=35)	Personalized group (n=30)	F	p
Before treatment	5.29±1.54	5.13±1.58	5.31±1.47	5.67±1.75	0.663	0.576
1 month of treatment	4.73±1.40	4.10±1.33[a]	4.06±1.21[a]	3.93±1.31[a]	2.798	0.042
3 months of treatment	4.66±1.32	3.95±1.33[a]	3.91±1.25[a]	3.83±1.29[a]	3.355	0.021
6 months of treatment	4.41±1.32	3.71±1.23[a]	3.69±1.02[a]	3.63±1.16[a]	3.716	0.013
9 months of treatment	3.98±0.99	3.47±1.29[a]	2.97±0.89[a,b]	2.43±0.97[a,b,c]	13.899	<0.001
12 months of treatment	3.21±0.98	2.71±0.80[a]	2.17±0.79[a,b]	1.73±0.74[a,b,c]	20.721	<0.001
F						
p	<0.05	<0.05	<0.05	<0.05		

TM, tinnitus masking; TRT, tinnitus retraining therapy. [a]$p<0.05$, compared with medication group; [b]$p<0.05$, compared with TM group; [c]$p<0.05$, compared with TRT group.

treatment was effective, and the effect was better with the increase of the course of treatment.

Clinical Effect

There was a statistically significant difference in the clinical curative effect within all four groups ($p<0.05$). The clinical effective rate (85.37%) of the personalized group was higher than that of the other three groups, and the difference was statistically significant ($p<0.05$) (Table IV).

Discussion

Sound therapy for tinnitus has evolved from TM to TRT, and then personalized music therapy in recent years[7]. Personalized music therapy is considered a cutting-edge method that is at the forefront of tinnitus treatment. In this study, we found that after nine and 12 months of treatment, the THI and VAS scores of the personalized group were lower than those of the other treatment groups, and the

Table IV. Clinical effective rate.

Groups	Effective	Non-effective	χ^2	*p*
Medication group (n=41)	16 (39.0)	25 (61.0)	16.383	0.001
TM group (n=38)	22 (57.9)	16 (42.1)		
TRT group (n=35)	25 (71.4)	10 (28.6)		
Personalized group (n=30)	26 (83.3)	6 (16.7)		

TM, tinnitus masking; TRT, tinnitus retraining therapy.

clinical effect was better as the course of treatment increased. In addition, the overall clinical effective rate of the personalized group was higher than any of the other treatment groups.

A wide range of medications is presently employed in the treatment of tinnitus, encompassing antidepressants, antiarrhythmics, muscle relaxants, and anxiolytics, among others[21]. However, medication alone is not effective in treating chronic tinnitus. It is important to note that the US Food and Drug Administration (FDA) has not yet approved any medications specifically for the treatment of tinnitus[22]. The present study showed that medication combined with TM, TRT, or personalized music therapy was more effective than medication alone, which was generally consistent with the findings by Liu et al[8]. TM was developed based on the concept of distraction. By introducing sound, typically referred to as "white noise", it aims to divert the patient's attention away from their tinnitus noises while simultaneously masking or covering up the sounds of their tinnitus[23]. TRT combines counseling and sound therapy to facilitate the gradual habituation to the sound of tinnitus, where habituation refers to the process of becoming accustomed to a sound to the extent that it no longer remains the primary focus of attention[24]. There are many types of personalized music therapy, including neuromonics tinnitus therapy (NTT), phase-shift treatment, tailor-made notched music training (TMNMT), the Heidelberg model of music therapy (HMMT), and five lines of music therapy. Phase-shift treatment was used with a follow-up platform in this study. TM, TRT, or personalized music therapy all have been widely used in tinnitus management.

Interestingly, we found that within six months after treatment, there was no difference in THI and VAS changes between TM, TRT, and personalized music therapy. However, after nine and 12 months of treatment, the THI and VAS scores were lower in the TRT and personalized groups compared to the medication and TM groups, and those patients experienced a greater clinical effect as the course of treatment increased. Furthermore, THI and VAS scores in the personalized group were lower than in the TRT group after nine and 12 months of treatment. A clinical trial by Henry et al[18] reported that TM yielded the most significant benefit after three months of treatment, with similar results between the TM and TRT groups after six months, while TRT was substantially greater at the 12-month mark, and additional progress was noted at the 18-month assessment. These results are partially in line with our study, in that no differences were observed between the groups six months after treatment, suggesting that TRT became significantly effective after six months of treatment.

The personalized group was found to be more effective than the TRT group after nine and 12 months of treatment. Phase-shift treatment has long been introduced in tinnitus management, but controversy continues regarding its clinical effectiveness. A double-blind crossover randomized controlled trial by Heijneman et al[25] found that phase-shift sound therapy did not show a significant effect on tinnitus management, while a pilot study by Rodrigues et al[26] showed promising results. Our findings appeared consistent with the latter, and it is possible that follow-up with the WeChat platform significantly contributed to this positive result. In most studies, sound therapy focuses only on the patient listening to music, with little interaction with the doctor. In this study, we established a WeChat platform for patients to have daily check-ins. Nurses and audiologists provided patients with online training, timely supervision, and professional psychological counseling and support. They were kept informed of any changes in patients' tinnitus treatment, so as to implement matching phase-shift interventions for them, which helped to improve the clinical efficacy.

There were a couple of limitations associated with this study. This was a retrospective study with a small sample size, and the findings of this study should be further demonstrated by a prospective study with a larger sample size. The follow-up period was up to 12 months after

treatment, and as TRT and music therapy usually become significantly more effective after long-term treatment, a longer follow-up period could result in more clinically significant results. Finally, there are many types of personalized music therapy, and we focused on phase-shift treatment in this study, as such, an exploration of other personalized music therapies is warranted.

Conclusions

TM, TRT, or personalized music therapy, when combined with medication, demonstrate clinical effectiveness in treating patients with tinnitus. Among these methods, personalized music therapy exhibits superior outcomes after nine months of treatment.

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Availability of Data and Materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' Contributions
YD conceived and designed the study. SG, DL, RH, and QX collected the data and performed the analysis. YD was involved in the writing of the manuscript. YL Edited the manuscript. All authors have read and approved the final manuscript.

Ethics Approval
The study was approved by the Ethical Committee of The First Affiliated Hospital of Hebei North University (No.: 20230609; Date: June 9th, 2023).

Informed Consent
Informed consent was obtained from all patients.

Conflict of Interest
The authors declare that they have no competing interests.

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