Outcomes of Triple-Combination Therapy for Chronic Tinnitus

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Abstract. Background/Aim: Patients with tinnitus suffer not only from auditory dysfunction but also physical, mental, and social difficulties. Our aim was to investigate the outcomes of our triple-combination therapy for chronic tinnitus, which includes narrow-band noise masking, auricular acupuncture and cognitive behavioral therapy. Patients and Methods: The tinnitus handicap inventory (THI) scores of 78 adults with chronic tinnitus who received triple-combination therapy for 12 weeks were analyzed retrospectively. Results: There were 39 females and 39 males in this study. The mean age was 60.5 years [standard deviation (SD)=13.0, range=27-88 years] for all subjects. Mean pure tone average=39.5 decibel hearing level (SD=23.09). Pre-treatment mean THI score was 41.4 (SD=21.13), functional (F) subscore was 17.9 (SD=10.69), emotional (E) subscore was 10.6 (SD=6.87), and catastrophic (C) subscore was 12.9 (SD=4.85). Post-treatment THI total score was significantly lower compared to pre-treatment THI total score. Also, post-treatment subscores were significantly lower compared to pre-treatment subscores in F and C subscores, but not in E subscore. In addition, multivariate logistic regression analysis showed that coffee and tea consumption was significantly positively associated with a reduction of THI total score. Conclusion: Triple-combination therapy could be helpful for chronic tinnitus patients. It seemed that coffee and tea consumption may elicit increased improvement in conjunction with combined therapy for chronic tinnitus.

Tinnitus is a phantom sensation of non-speech sound in the absence of acoustic stimulation. Dysfunction in the cochlea, auditory and non-auditory cortices have been reported to be associated with auditory tinnitus (1). Patients with tinnitus suffer from not only auditory dysfunction, but also physical, mental, and social difficulties. Patients with tinnitus also often have symptoms consistent with vagal withdrawal and sympathetic overactivity (2). Many factors have been reported to be related with the occurrence and/or severity of auditory tinnitus. For example, age, gender, hearing loss and tinnitus duration were associated with tinnitus-related loudness and/or distress (3, 4). Increased caffeine intake has been demonstrated to be associated with a lower risk of tinnitus in women (5). Any individual treatment for this complex disease may not achieve a satisfactory result. Thus, combined therapy, including tinnitus retraining therapy (TRT), sound therapy, acupuncture and/or psychotherapy, are applied in patients with chronic tinnitus (2, 6-8). TRT, which includes directive counseling and sound therapy, is used by patients with chronic tinnitus with success (8). It has been suggested that sound therapy could mask symptoms associated with tinnitus, acupuncture may improve the autonomic nervous dysfunction of tinnitus patients, and psychotherapy could relieve tinnitus-related emotional distress (2, 6-8).

In this study we aimed to investigate the outcomes of our triple-combination therapy (narrow-band noise masking, coffee and tea consumption was significantly positively associated with a reduction of THI total score. Conclusion: Triple-combination therapy could be helpful for chronic tinnitus patients. It seemed that coffee and tea consumption may elicit increased improvement in conjunction with combined therapy for chronic tinnitus.

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auricular acupuncture and cognitive behavioral therapy) in adult patients with chronic tinnitus.

Patients and Methods

Clinical data of 78 adult patients with chronic auditory tinnitus (duration >6 months) receiving combined tinnitus therapy between 2013 and 2016 at Dalin Tzu Chi Hospital were retrospectively investigated. The study was conducted in accordance with the Declaration of Helsinki (9) and was approved by The Research Ethics Committee of Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation (No. B10503006). Informed written consent was waived because the study was a retrospective data analysis.

The triple-combination therapy included: i) narrowed-band noise masking, ii) acupuncture, and iii) cognitive behavioral therapy. The narrowed-band noise was generated by a sound generator, depending on the frequency of each patient’s tinnitus, which was determined by frequency matching. The narrowed-band noise with the loudness of a minimal masking level was given binaurally via a headset for 15 minutes. Auricular acupuncture was applied at three points: i) SJ 21, ii) SI 19, and iii) GB2, preauricularly (Figure 1) for 20 minutes by a traditional Chinese medicine doctor. SJ21 (Ermen) was indicated for tinnitus, deafness, otitis media, and toothache (10), SI19 (Tinggong) was indicated for tinnitus, deafness, otorrhea, toothache, and dysfunction of the temporomandibular joint (11), and GB2 (Tinghui) was indicated for tinnitus, deafness, and toothache (12). The cognitive behavioral therapy included an introduction to tinnitus and its related distress, as well as relaxation training, auto suggestion, and mindfulness. This was conducted as part of a group therapy for 30 minutes by a clinical psychotherapist.

Each of the three individual therapies was administered on the same day once per week for 12 weeks. Before therapy was administered, a questionnaire to collect clinical data, habits and pure tone audiometry was acquired. Severity of tinnitus was evaluated using the Tinnitus Handicap Inventory (THI) (13) before and immediately after therapy was administered. Taken together, there were 25 questions with three possible responses: i) yes, ii) sometimes, iii) no. Answers were scored as follows: i) 4 points for an answer of “yes”, ii) 2 for an answer of “sometimes”, and iii) 0 for an answer of “no”. Thus, the total scores of the THI ranged between 0 and 100 (13). The higher the THI score were, the higher as severity of tinnitus. The reduction of THI score was defined and calculated from pre-treatment data minus post-treatment data for each patient.

Exclusion criteria included: i) subjects aged younger than 20 years, ii) with external or middle ear disease, iii) conductive hearing loss (presenting with an air-bone gap on audiogram), iv) arteriovascular malformation, v) brain tumor or vestibular schwannoma, cancer, vi) Parkinson’s disease, vii) dementia, viii) liver cirrhosis, ix) stroke, or x) head and neck radiation exposure.

Statistical analysis. In this study, sex, hypertension, diabetes mellitus, dyslipidemia, coronary artery disease (CAD), chronic kidney disease (CKD), insomnia, smoking, alcohol drinking, coffee, tea, and high noise exposure were treated as the category variables. Furthermore, we also categorized the habits of coffee and/or tea consumption into four groups: i) without coffee and tea, ii) with coffee, iii) with tea, and iv) with coffee and tea. Age, body mass index (BMI), and pure tone average (PTA) were treated as the numerical variables. Student’s t-test was used to test the differences of THI total score and subscores before and following therapy. Univariate linear regression analysis was used to test for the initial effects of individual variables on the reduction of THI total score. Multivariate logistic regression analysis was used to test the odds of prominent clinical factors on the reduction of THI total score (≥10), with adjustment variables of p-Value<0.2 from the univariate linear regression analysis. All analyses were performed using STATA 10.0 software (Stata Corp, College Station, TX, USA).

Results

Subjects’ clinical characteristics are shown in Table I. There was a total of 78 subjects (39 women and 39 men) included in the study. The mean subject age was 60.5 years (SD=13.0; range: 27-88 years old) for all subjects, 58.6 years (SD=13.0) for women and 62.4 years (SD=12.9) for men. The mean body mass index (BMI) was 23.2 kg/m² (SD=3.0) for all subjects, 22.6 kg/m² (SD=3.2) for women, and 23.9 kg/m² (SD=2.6) for men. The mean pure tone threshold on audiometry (PTA) was 39.5 decibel hearing level (dBHL) (SD=23.1) for all subjects, 36.3 dBHL (SD=24.8) for women, and 42.7 dBHL (SD=21.1) for men.

Figure 2 shows comparisons of the THI scores before and after treatment. The mean pre-treatment THI total score was 41.4 (SD=21.1), the functional (F) subcore was 17.9 (SD=10.7), the emotional (E) subcore was 10.6 (SD=6.9), and the catastrophic (C) subcore was 12.9 (SD=4.9). The mean post-treatment THI total score was 30.9 (SD=17.0), the F subcore was 13.6 (SD=8.1), the E subcore was 9.6 (SD=6.5), and the C subcore was 7.7 (SD=4.1). Following treatment, the mean reduction of the THI score was 10.5 (SD=21.0), the F subcore was 4.3 (SD=10.5), the E subcore was 1.0 (SD=6.8), and the C subcore was 5.2 (SD=5.1).

The post-treatment THI total score was significantly lower compared to the pre-treatment THI total score (Student’s t-test, p<0.0001). Also, post-treatment subscores were significantly lower compared to pre-treatment subscores in F (Student’s t-test, p=0.0005) and C (Student’s t-test, p<0.0001) subscores, but not in E subcore (Student’s t-test, p=0.1996).

Table II shows the effects of individual variables on the THI total score by univariate linear regression analysis. Among all the tested variables, only hypertension and dyslipidemia were significantly positively associated with the pre-treatment THI total score. Otherwise, coffee and tea consumption was significantly positively associated with the reduction in the THI total score.

Multivariate logistic regression analysis on the significant reduction (≥10) of the THI total score by prominent clinical factors is shown in Table III. Coffee and tea consumption [odds ratio (OR)±SE=2.01±0.47, p=0.003], but not sex (OR±SE=0.54±0.28, p=0.255) or dyslipidemia (OR±SE=1.27±0.87, p=0.732), was significantly positively associated with the reduction in the THI total score.
Discussion

This retrospective study showed that our triple-combination therapy of narrow-band noise masking, auricular acupuncture and cognitive behavioral therapy for 12 weeks, could reduce the severity of chronic tinnitus in the Taiwanese population.

Although a previous study has shown that caffeine could reduce the risk of tinnitus in women (5), we found that only hypertension and dyslipidemia, but not coffee or tea consumption, were positively related with the severity of chronic tinnitus prior to treatment. Furthermore, subjects who consumed coffee or tea, compared to subjects without these two habits, showed greater improvement following the combined treatment for chronic tinnitus.

Tinnitus is a complex disease with multiple adverse effects for patients, not only concerning the accompanying sound but also the related psychological disturbances (2). Several studies have shown that the severity and/or risk of tinnitus would be related with some clinical factors. For example, loudness and annoyance of tinnitus were generally higher in older subjects, those with binaural or centrally perceived tinnitus, those with persistent tinnitus, and those who had coexisting hearing loss, vertigo, and hyperacusis (14). Annoying tinnitus was also increased in patients with a history of smoking, those reporting less sleep, those with increased stress levels, those in smaller households, those with a history of hypertension, hyperlipidemia, osteoarthritis,

Table I. Baseline patient characteristics (N=78).

| Variables                                      | Values |
|-----------------------------------------------|--------|
| Age (mean±SD, yr)                             | 60.5±13.0 |
| Gender (n, M/F)                               | 39/39  |
| BMI (mean±SD, kg/m²)                          | 23.3±3.0 |
| PTA (mean±SD, dBHL)                           | 39.5±23.1 |
| Pre-treatment THI total score (mean±SD)       | 41.4±21.1 |
| Pre-treatment F subscore (mean±SD)            | 17.9±10.7 |
| Pre-treatment E subscore (mean±SD)            | 10.6±6.9 |
| Pre-treatment C subscore (mean±SD)            | 12.9±4.9 |
| Post-treatment THI total score (mean±SD)      | 30.9±17.0 |
| Post-treatment F subscore (mean±SD)           | 13.6±8.1 |
| Post-treatment E subscore (mean±SD)           | 9.6±6.5 |
| Post-treatment C subscore (mean±SD)           | 7.7±4.1 |
| Reduction of THI total score (mean±SD)        | 10.5±21.0 |
| Reduction of F subscore (mean±SD)             | 4.3±10.5 |
| Reduction of E subscore (mean±SD)             | 1.0±6.8 |
| Reduction of C subscore (mean±SD)             | 5.2±5.1 |
| Hypertension (%)                              | 18.0   |
| Diabetes mellitus (%)                         | 9.0    |
| Dyslipidemia (%)                              | 14.1   |
| Coronary artery disease (%)                   | 11.5   |
| Chronic kidney disease (%)                    | 5.1    |
| Insomnia (%)                                  | 41.0   |
| Smoking (%)                                   | 6.4    |
| Alcohol drinking (%)                          | 23.1   |
| Coffee (%)                                    | 52.6   |
| Tea (%)                                       | 70.5   |
| High noise exposure (%)                       | 46.8   |

BMI: Body mass index; dBHL: decibel hearing level; F: female; M: male; PTA: pure tone threshold on audiometry; SD: standard deviation; THI: tinnitus handicap inventory.
rheumatoid arthritis, asthma, depression, thyroid disease, an abnormal tympanic membrane, and increased noise exposure (3, 15-18). Hyperinsulinemia (17, 19), drug abuse in boys and exposure to second hand smoke in girls (20), obesity, and diabetes mellitus (17), have also been identified as risk factors of tinnitus. However, the role of the sex difference on tinnitus loudness and annoyance is still inconclusive (14, 15). Also, higher caffeine intake may reduce the risk of tinnitus in women (5). On the contrary, the acute effects of caffeine withdrawal may add to the burden associated with tinnitus (21).

In the aspect of tinnitus treatment, various sound therapies have demonstrated significant benefit for patients with tinnitus (6, 7). Some authors have reported that acupuncture alone (22) or combined with Qi-training (2) could modulate cardiac autonomic functions and reduce tinnitus-related symptoms in patients with chronic tinnitus. However, a meta-analysis has concluded that the beneficial effect of traditional Chinese acupuncture remains inconclusive for patients with tinnitus (23, 24). In this study, we found that the F and C subscores, but not the E subscore, were significantly decreased following our triple-combination therapy. These findings raised an interesting issue around sound therapy, acupuncture, and especially cognitive behavioral therapy, which could not relieve tinnitus-related emotional distress effectively. We suggest that other types of psychologic therapy should be employed in the future to help reduce tinnitus-related emotional problems.

The factors that affect the outcomes associated with chronic tinnitus treatment are poorly reported in the literature. For example, prognosis of sudden sensorineural hearing loss, due to tinnitus, is poor in cases of severe hearing loss or long-lasting tinnitus (25). Pre-treatment tinnitus severity has been negatively associated with the TRT outcome (26, 27). Baseline tinnitus severity and duration have also been found to influence repetitive transcranial magnetic stimulation (rTMS) outcomes (28). On the other hand, higher levels of education have been reported to be associated with increased improvement in a habituation-based training for patients with tinnitus (29). A diabetic diet might result in a significant improvement in complaints associated with tinnitus in patients with hyperinsulinemia (19). Improvement in the THI score have been positively correlated with pre-treatment activities of the left insula and the left rostral and pregenual anterior cingulate cortices, which control parasympathetic activity (30). However, improvement in loudness was negatively correlated with the activities of the right auditory cortices and parahippocampus (30). In the current study, we found that coffee and tea consumption was positively associated with a good prognosis of the tinnitus treatment.

| Variables | Before treatment | After treatment | Reduction |
|-----------|-----------------|----------------|-----------|
| Age       | –0.17±0.19 (0.380) | 0.04±0.15 (0.787) | –0.21±0.19 (0.268) |
| Gender (M versus F) | –6.85±4.75 (0.154) | 2.00±3.88 (0.607) | –8.85±4.68 (0.062) |
| BMI       | 0.07±0.85 (0.934) | –0.04±0.69 (0.955) | 0.11±0.87 (0.900) |
| PTA       | 0.18±0.10 (0.085) | 0.19±0.09 (0.029) | –0.01±0.10 (0.907) |
| Hypertension | 18.84±5.89 (0.002) | 13.39±4.82 (0.007) | 5.45±6.21 (0.382) |
| Diabetes mellitus | –6.09±8.40 (0.471) | 0.93±6.79 (0.892) | –7.01±8.33 (0.403) |
| Dyslipidemia | 13.82±6.74 (0.044) | 4.59±5.55 (0.411) | 9.23±6.79 (0.178) |
| CAD       | –0.07±7.54 (0.992) | 7.93±6.01 (0.191) | –8.00±7.43 (0.285) |
| CKD       | –2.26±10.92 (0.836) | –9.88±8.73 (0.261) | 7.61±10.82 (0.484) |
| Insomnia  | 7.27±4.83 (0.136) | 1.28±3.94 (0.747) | 6.00±4.82 (0.217) |
| Smoking   | –6.41±9.81 (0.515) | –13.11±7.78 (0.096) | 6.70±9.74 (0.493) |
| Alcohol drinking | –2.54±7.51 (0.658) | –2.00±6.60 (0.665) | –0.54±5.68 (0.925) |
| Coffee    | 0.19±4.82 (0.969) | –9.70±3.73 (0.011) | 9.90±6.66 (0.037) |
| Tea       | 6.79±5.22 (0.198) | –4.13±4.23 (0.332) | 10.92±5.10 (0.035) |
| High noise exposure | 1.84±4.88 (0.708) | 6.15±3.87 (0.116) | –4.31±4.83 (0.375) |

Table III. The effects of coffee and tea, and prominent variables on significant reduction (≥10) of THI scores (multivariate logistic regression analysis). "Coffee and Tea" was treated as a category variable with four groups, as mentioned in our method.

| Variables | Odds ratio | Standard error | p-Value |
|-----------|------------|----------------|---------|
| Sex (M versus F) | 0.54 | 0.28 | 0.255 |
| Coffee and Tea* | 2.01 | 0.47 | 0.003 |
| Dyslipidemia | 1.27 | 0.87 | 0.732 |

Pseudo R square=0.1026.
As previously reported, neural inflammation and/or damage resulting from oxidative stress might represent novel mechanisms of tinnitus (31-35). Furthermore, caffeine has been demonstrated to have an anti-oxidative effect, providing possible benefits to patients with tinnitus (36), despite its possible involvement with the increase in sympathetic tone (37). Taken together, previously published reports (18, 21), suggest that caffeine-containing coffee and tea may be beneficial for the prevention of tinnitus and as part of a treatment regimen. These results might also encourage patients with tinnitus to maintain their consumption of coffee and/or tea during their treatment, with no need to withdraw, as Claire et al., have previously suggested (21).

Herein we report that our triple-combination therapy was helpful for our patients with chronic tinnitus. Patients who consumed coffee and tea had improved outcomes during the therapy, and thus they should be encouraged to maintain this habit. These findings provide important insight and nutritional options for supplementing tinnitus treatment. However, additional large-scale, prospective, clinical trials should be conducted in order to provide additional and more convincing data in the future.

Conflicts of Interest

The Authors declare no conflicts of interest.

Authors’ Contributions

YHJ performed the treatment and wrote the manuscript. CTH performed the study, performed the treatment, analyzed data, wrote manuscript and supervised the study.

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