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Clear Tinnitus®, Middle-Ear Pressure, and Tinnitus Relief: A Prospective Trial

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Abstract: *Goal*. Our goal was to establish the efficacy, in a 12-week period, of Clear Tinnitus for tinnitus relief in patients with tinnitus of the severe, disabling type. *Hypothesis*. We hypothesized that tinnitus relief with Clear Tinnitus reflects improvement in the sensory component of the tinnitus complaint by controlling the factor of aeration of the middle ears and improving eustachian tube function. *Method*. In a prospective clinical trial of a homeopathic preparation—Clear Tinnitus—we attempted to identify in 15 tinnitus patients (14 male, 1 female; mean age, 47.6 years) its clinical efficacy for establishing tinnitus relief for a 3-month period. We employed a descriptive data analysis method across dimensions of risk to evaluate a base of multidimensional evidence and establish support for our hypothesis. A medical-audiological tinnitus patient protocol completed by each patient identified the clinical type of tinnitus as predominantly cochlear, with a central and middle-ear component bilaterally. We identified fluctuation in middle-ear pressure (MEP) via patients' clinical history, supported by physical examination and established with tympanometry, as a factor influencing the clinical course of the tinnitus in each patient. *Results*. Eleven of 15 patients completed the study. Seven responders reported tinnitus relief; four did not respond. Descriptive data analysis failed to detect any trends in a change in response with audiometric tests across the hearing spectrum; thus, we could derive no coefficients of hearing change. Evaluation revealed high-frequency tinnitus in 11 patients. The Feldmann masking curve comparison at the start and end of the study showed no significant change in the 11 patients. There was no significant alteration in the minimum masking levels or loudness discomfort levels before and after the study. Tympanometry and MEP measurement indicated a significant difference in MEP with an improvement on average of −58.18 in the right ear and −40.90 in the left ear for the 11 patients. Quantitative electroencephalography analysis revealed a marked difference in the number of significant abnormal recordings between the different frequency bands, with the delta band significantly higher than the theta, alpha, and beta bands for both the overall cohort of patients (n = 11) and those reporting tinnitus relief (n = 7). The tinnitus outcome questionnaires—the tinnitus intensity index, the tinnitus annoyance index, and the tinnitus reaction questionnaire—revealed a significant difference for the patients (7 of 11) obtaining tinnitus relief. Results of the tinnitus stress test , the tinnitus handicap index, and the measurement of depression scale before and after the study were not statistically significant. *Conclusions:* Patients who completed the study demonstrated with tympanometry a statistical and clinical significance in MEP improvement or maintenance of MEP (or both). Patients with tinnitus of the severe disabling type selected for this study and responding to Clear Tinnitus reported tinnitus relief accompanied by improvement in or maintenance of MEP of the middle ears. The statistical and clinical significance of Clear Tinnitus for establishing tinnitus relief remains to be established with a larger cohort of tinnitus patients.

Key Words: Clear Tinnitus; dimension of risk; medical-audiological tinnitus patient protocol; tinnitus relief; univariate

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We attempted in a prospective clinical trial of a homeopathic preparation—Clear Tinnitus—to identify in 15 tinnitus patients (14 male, 1 female; mean age, 47.6 years) its clinical efficacy for establishing tinnitus relief over a 12-week period. We employed a descriptive data analysis method across dimensions of risk to evaluate a base of multidimensional evidence to support our hypothesis.

We hypothesize that relief in the ear with the tinnitus complaint may result from oral intake of Clear Tinnitus for patients with severe disabling tinnitus in whom the factor of aeration of the middle ear and that of eustachian tube dysfunction is identified and treated. We clinically identified all patients in this study as having subjective idiopathic tinnitus of the severe type lasting at least 1 year.

Tinnitus is marked by its individuality and heterogeneity for each patient [1–3]. A focus on risk factors for each tinnitus patient provides an increased level of flexibility for interpretation of the clinical significance of the results of a treatment method and its future application for tinnitus relief. The benefits of a risk-stratified multivariate analysis across dimensions of risk, originally planned for this study, could not be achieved owing to an insufficient final sample size [4]. The designers of Clear Tinnitus have claimed that this blend of homeopathic remedies and herbal medicine, when taken on a daily basis for 3 months, has resulted in significant tinnitus relief [5].

Interference in aeration of the middle ears accompanying allergy and inflammation of the upper respiratory tract has been identified via a medical-audiological tinnitus patient protocol (MATPP) to be a factor that can influence the clinical course of subjective idiopathic tinnitus of the severe type [6–8].

Historically, the influence of aeration of the middle ear "effecting permeability of the eustachian tube" was reported by Politzer in 1863 [9]. Its application for hearing improvement and tinnitus relief has been reported in his classic textbook: "When there are accumulations of secretion in the middle ear, or anomalies of tension in the sound conducting apparatus which bring about an increased pressure in the labyrinth, it has been found inflations of air into the middle ear and rarefaction of air in the external meatus are often the most effectual means by which these subjective noises are overcome" [10].

Since 1979, the tinnitus clinic of the Health Science Center at Brooklyn, State University of New York, and the Martha Entenmann Tinnitus Research Center, Inc., have reported on more than 10,000 patients who had subjective idiopathic tinnitus (seen in neurotological consultation) and completed the MATPP. Significant tinnitus relief was obtained in approximately 10–15% of tinnitus patients in whom identification of and satisfactory treatment for the factor of aeration of the middle ear and of eustachian tube dysfunction was completed [6–8,11,12].

The prospect of a trial of Clear Tinnitus to attempt tinnitus relief in a selected cohort of patients who have subjective idiopathic tinnitus and exhibit objective evidence of interference in eustachian tube function provided a clinical opportunity to use our established experience to test the efficacy claimed for this preparation. Using multiple measures of analysis of risk factors, this study presents the results and conclusions of attempted tinnitus relief with Clear Tinnitus. We hypothesize in this study that relief occurs by identifying and treating the factor of aeration of the middle ear.

PATIENT SELECTION

We selected 15 individuals with reported subjective, severe, disabling idiopathic tinnitus lasting at least 1 year. Of the 15 patients, 14 were male and 1 was female (mean age, 47.6 years; range, 25–58 years). The clinical history of each tinnitus patient reflected periods of tinnitus relief associated with fluctuation of tinnitus intensity and the location and degree of ear blockage.

The parameters of the patients' tinnitus included tinnitus intensity, location, masking characteristic, and duration. The 15 patients variously reported a bilateral tinnitus location (n = 12), a unilateral tinnitus in the right ear (n = 2), bilateral tinnitus in the head and ears (n = 1), a tonal quality to the tinnitus (n = 11), a noise band (n = 1), a combination tone and noise band (n = 3), and high frequency (n = 15; Table 1).

METHOD

All 15 subjects reported the tinnitus to be of the severe disabling type lasting for at least 1 year. All tinnitus patients completed an MATPP to identify the clinical type of tinnitus and factors influencing the clinical course of their tinnitus [6–8,11,12].

The homeopathic preparation for tinnitus relief—Clear Tinnitus—was taken on a daily basis. The specific regimen consisted of three capsules taken with food two times daily for 3 months.

Multiple Measures of Evaluation

The patients in this study completed multiple measures for evaluating the subjective idiopathic tinnitus and the hypothesized tinnitus relief.

Outcome Measures

Subjective outcome measures included visual analog indices: the tinnitus intensity index (TII); tinnitus annoyance index (TAI); tinnitus handicap inventory (THI); tinnitus stress test (TST); tinnitus reaction questionnaire (TRQ); and measurement of depression scale [13, 14].

Table 1. Parameters of Tinnitus Identification (Location, Frequency), Middle-Ear Pressure, and Tympanogram Results

Patient ID (N = 11)	Ear	MEP Initial	MEP End	Pre-treatment TYMP	Post-treatment TYMP	Pretreatment Frequency (kHz)	Posttreatment Frequency (kHz)
1 RL	Right	Normal −20	Normal −20	A	A	6,000 nb/t	6,000 nb
	Left	Normal −40	Normal −20	A	A	6,000 nb/t	
2 RL	Right	Abnormal −150	Normal −40	C	A	16,000 t	16,000 t
	Left	Abnormal −150	Normal/borderline −50	C	A	16,000 t	16,000 t
4 RL	Right	Abnormal −100	Normal −30	C	A	6,000 nb/t	6,000 nb
	Left	Normal 0	Normal 0	A	A	6,000 nb	6,000 nb
6 R	Right	Normal/borderline −50	Normal 0	A	A	4,000 t	4,000 t
	Left	Normal/borderline −50	Normal −30	A	A		
11 RL	Right	Abnormal −250	Normal/borderline −80	A	A	6,000 t	6,000 t
	Left	Abnormal −120	Abnormal −120	C	C	6,000 t	6,000 t
12 R	Right	Normal −20	Normal 0	A	A	8,000 t	No tinnitus
	Left	Normal −30	Normal −30	A	C		
13 RL	Right	Normal/borderline −50	Normal 0	A	A	8,000 nb	8,000 nb
	Left	Normal/borderline −80	Normal 0	A	C	8,000 nb	8,000 nb
3 RL	Right	Normal −30	Normal 0	A	A	12,000 t	12,000 t
	Left	Abnormal −100	Normal −10	C	A	12,000 t	11,000 t
7 RL	Right	Normal 0	Normal −40	C	A	16,000 t	16,000 t
	Left	Normal/borderline −80	Normal/borderline −80	A	A	16,000 t	16,000 t
9 RL	Right	Abnormal −100	Normal −20	C	A	6,000 t	
	Left	Abnormal −100	Normal 0	C	A	6,000 t	
15 RL	Right	Abnormal −100	Normal 0	C	A	10,000 t	
	Left	Normal/borderline −50	Normal −10	A	C		

MEP = middle-ear pressure; nb = noise band; t = tone; t/nb = combined tone and noise band; TYMP = tympanogram type.
Note: Heavy line separates responders (above) from nonresponders (below).

The answer to the final question was whether the reported tinnitus relief was considered significant to the patient.

We identified for each patient multiple risk dimensions known to influence the clinical course of subjective, idiopathic, severe, disabling tinnitus, with a focus on fluctuation of aeration of the middle ear and eustachian tube dysfunction. Risk dimensions for each tinnitus patient included noise exposure; stress; associated cochleovestibular complaints of hearing loss; vertigo; ear blockage; hyperacusis; metabolic-cardiovascular complaints; central nervous system complaints highlighting interference in speech expression or memory (or both), headache, nausea, and gait; and affect behavioral alterations of anxiety and depression. Such an analysis provided information of both the sensory and affect components of the tinnitus complaint [15]. We used quantitative electroencephalography (QEEG) as a monitor at the start and conclusion of the study to identify patterns of electrical activity of brain function hypothesized to reflect tinnitus relief [16].

Objective Measures

We used multiple objective measures to evaluate the risk dimensions for each tinnitus patient. We originally planned to use the data obtained to provide a base for a multivariate risk-benefit stratified analysis of the significance of the reported tinnitus relief. We hoped to focus on a single variable (i.e., fluctuation of aeration of the middle ears and eustachian tube dysfunction).

The measures included audiological testing via pure-tone audiometry and speech audiometry performed using a Beltone 2000 audiometer. We performed tympanometry using a Madsen ZO71. Tinnitus evaluation included pitch and loudness matching, masking curves, and loudness discomfort levels (LDLs). We performed ultra-high-frequency audiometry using the Tonndorf audiometer for electrical high-frequency audiometry and the Beltone 2000 audiometer for air-conduction high-frequency audiometry. At the start and conclusion of the study, we performed QEEG testing using a Neurosearch 24 Instrument (Lexicor Medical Technology, Inc., Colorado) to measure objectively a spectral analysis of electrical activity of the brain. We placed an electrode array (consisting of 19 electrodes) on the scalp in a standard international 10–20 pattern [16]. At the conclusion of the 12-week period, we repeated all the audiological tests administered on the initial visit.

Tympanometry values for normal range of MEP were 0–50 mm H_2O. Borderline values were −50 to 100 mm H_2O. Abnormal values were −100 mm H_2O

and above. We correlated the physical examination of the tympanic membrane with the tympanometry result.

THE CLEAR TINNITUS PREPARATION

The Clear Tinnitus preparation is a blend of homeopathic remedies and herbal medicines. manufactured by a certified current good manufacturing practices (cGMP) company [17,18]. A copy of the manufacturer's cGMP certification and standard operating procedures used in the production of Clear Tinnitus is maintained by Clear Products, Inc. The homeopathic remedies have been reported to influence the following [17]:

- Calcarea carbonica: crackling noise in the ear
- Cinchona officinalis: ringing in the ears and hearing that is sensitive to noise
- Chininum sulphuricum: ringing and roaring in ears sometimes associated with deafness
- Graphites: hissing in the ears
- Kali carbonicum: crackling, ringing, and roaring noise
- Kalil iodium: crackling in ears, ringing and buzzing, sounds of a river or rain falling on the roof
- Lycopodium: humming, noise echoes in the ear, roaring, difficulty in hearing
- Salicylicum acidum: roaring and ringing in the ears

Extensive scientific research has been carried out on the preparation's chemical composition, and pharmacological and clinical research has focused on its individual herbs. The herbal contents of the formula include the following [18]:

- Pueraria root (Ge Gen): treats tinnitus, headache, dizziness, hypertension, and pain; relaxes muscles
- Platycodon root (Jie Geng): directs the effects of other herbs upward
- Angelica root (Bai Zhi): unblocks sinus passages; reduces swelling; expels dampness; alleviates pain; has an antimicrobial effect
- Ligustici root (Chuan Xiong): alleviates all types of headaches, dizziness, and pain; reduces blood pressure; increases blood flow; has antiinflammatory and antibiotic effects
- Peony root (Bai Shao): nourishes blood to the head; stops spasms, headaches, and dizziness; reduces blood pressure; increases blood flow; has antiinflammatory and antibiotic effects
- Coix seed (Yi Yi Ren): drains mucus and phlegm from sinus canals
- Magnolia flower (Xin Yi Hua): unblocks the ear and sinus canals; eliminates headaches; reduces secretions in the nasal mucosa; reduces blood pressure; has a strong antifungal effect
- Notoptergii root (Qiang Huo): alleviates pain and any type of ear and nasal congestion
- Scutallaria root (Huang Qin): analgesic; alleviates headache and nasal discharge; has an antibiotic effect; lowers blood pressure
- Tangerine peel (Chen Pi): improves the transporting functions of digestion; expels dampness; eliminates fatigue; alleviates loose stools; has an antiinflammatory effect
- Cinnamon bark (Gui Zhi): breaks up or eliminates stagnation; increases blood circulation; has an antibiotic effect
- Ginger root (Sheng Jiang): calms the stomach, nausea, and vomiting
- Licorice root (Gan Cao): regulates the stomach; acts as an expectorant and an analgesic; harmonizes and moderates the characteristics of other herbs; has antiinflammatory and antiallergic effects

STATISTICAL ANALYSIS

We performed all statistical analyses using the Statistical Package for the Social Sciences (SPSS Release 14) [19]. We planned the analysis to include the use of both univariate and multivariate procedures. We modeled recordings of audiometric tests across the hearing spectrum using nonlinear regression. We used within-group repeated-measures analysis of variance (RMANOVA) to assess the differences in the TAI, the TST, the TII, the THI, the stress test, and the depression scale. Both within-group and interaction effects also were measured. We analyzed recordings from the QEEG analysis for power. The analysis compared changes over time in the number of abnormal recordings from the main locations of the scalp recordings (frontal, temporal, parietal, and occipital). We used the RMANOVA to test changes in the number of abnormal recordings for the 12-week period of the study for the EEG band frequencies delta, theta, alpha, and beta.

RESULTS

All 15 patients completed their initial visit, but 4 patients did not complete the study. Three of those four terminated the study because they had adverse reactions. The adverse reactions included gastrointestinal complaints (one with gastroesophageal reflux disease and one with bloating and constipation) and ear complaints (one with "ear spasms"). The remaining patient dropped out after 1 week in the study because of difficulty in adhering to the regimen, even though subjectively reporting tinnitus relief through the use of Clear Tinnitus.

Seven of the 11 patients who completed the study reported tinnitus relief. No tinnitus patient reported a worsening of the tinnitus. Four patients did not respond.

STATISTICAL PROCEDURES

Audiometric Tests

Regression analysis failed to detect any trends in the change in response to audiometric tests across the hearing spectrum; thus, we could not derive coefficients of change for testing. Conventional pure-tone audiometry conducted at 250–8,000 Hz (including 3,000 and 6,000 Hz) showed no significant difference in thresholds for either ear at any of the frequencies before and after testing all 11 subjects. Likewise, speech audiometry did not show any significant difference for speech reception threshold or word discrimination scores before and after testing.

Ultra-high-frequency audiometry (UHFA) did not show any clinically significant change in threshold at 10,000–20,000 Hz before and after testing with air-conduction high-frequency or electrical high-frequency audiometry. A statistically significant change in UHFA at 14 kHz occurred in the left ear at 3.33 dB and in the right ear at 4.5 dB; we also recorded a change of 4.28 dB at 17 kHz in the right ear. None of these changes is considered statistically and clinically significant. RMANOVA demonstrated no overall significant difference. The results included the following: right ear, 14 kHz, 4.5 dB ($t = -2.377$; $p = .041$); left ear, 14 kHz, 4.2 dB ($t = -2.521$; $p = .045$); right ear, 17 kHz, 3.3 dB ($t = -2.828$; $p = .022$).

Tinnitus evaluation identified the parameters of tinnitus (i.e., intensity, location, masking characteristic, and duration). Among our 15 patients, 12 originally reported tinnitus in the ears bilaterally, 2 originally reported unilateral tinnitus in the right ear, and 1 reported tinnitus in the head and ears bilaterally. The quality was reported as tonal in 11 patients, as noise band in 1, as combined tone and noise band in 3, and as high-frequency in all 15. For 10 of the 11 patients who completed the study, tinnitus location was unchanged; the remaining patient had no tinnitus at the end of the study. All had tinnitus at 4 kHz or higher: one at 4 kHz, four at 6 kHz, two at 8 kHz, one at 10 kHz, one at 12 kHz, and two at 16,000 kHz (Table 1).

In the 11 patients completing the study, all masking curves were either type I or type IV according to Feldmann's classification system. Five were type I before the study, four were type IV before the study, and two were mixed (type I for one ear and type IV for the other ear). After the study, five with type I remained unchanged, and three of the four with type IV remained unchanged. Of the remaining three, one with type IV went to type I for both ears; the other two with type IV in both ears went from type IV to type I for one ear and remained at type IV for the other. Type I masking curves are considered consistent with peripheral tinnitus and type IV with central tinnitus (Table 2).

Minimum masking level (MML) changes for the right ear before and after the study are reported for 10 individuals, as 1 had no tinnitus at the end of the study. The MML was reduced at 2,000 Hz by −10.50 dB; by −11 dB at 4,000 Hz; and by −12 dB at 8,000 Hz. For the left ear, the eight patients who had tinnitus after the study exhibited a reduction in the masking level of −11.25 dB at 8,000 Hz (Tables 3 and 4).

We established LDLs at 250–8,000 Hz for the right and left ears before and after the study (Table 5). No clear trend in the data for either ear was demonstrated by the mean change in LDL before and after the study.

Tympanometry and MEP

All 11 patients who finished the study recorded a negative bilateral MEP (see Table 1). A normal MEP was recorded in 3 of the 11. Improvement in MEP was recorded in 8 patients. In the nonresponders, MEP was normal in one and changed in three. Of the seven responders, two reported no MEP change; one nonresponder also reported no MEP change. All three had normal MEPs.

Tympanometry recorded a significant decrease in MEP for both ears in the 11 patients. Tympanometry showed an improvement of MEP (59.18 right ear and 40.91 left ear) in the 11. Mean right-ear MEP change for the 11 patients who completed the study ranged from −70.09 to −20.91 ($t = 3.36$; $p = .007$). Mean MEP in the left ear changed from −72.73 to −31.82 ($t = 3.155$; $p = .010$). At the conclusion of the study, 10 of the 11 patients had

Table 2. Tinnitus Masking Curves, Before and After Treatment

	Right		Left	
Patient ID (N = 11)	Pre-treatment Masking Curve	Post-treatment Masking Curve	Pre-treatment Masking Curve	Post-treatment Masking Curve
1	I	I	I	I
2	IV	IV	IV	IV
3	IV	I	IV	I
4	I	I	I	I
6	IV	IV	—	—
7	IV	IV	IV	IV
9	I	I	IV	I
11	IV	IV	I	IV
12	I	I	—	—
13	I	I	—	—
15	I	I	I	I

Table 3. Minimum Masking Levels, Right Ear

Patient ID (N = 11)		250 Hz	500 Hz	1,000 Hz	2,000 Hz	3,000 Hz	4,000 Hz	6,000 Hz	8,000 Hz
1	Pre	75	75	75	80	75	60	55	40
	Post	50	55	60	40	40	45	45	40
2	Pre	85	80	>85	70	75	75	70	90
	Post	>80	80	75	>80	>80	>80	>80	>85
3	Pre	85	>85	>80	>75	>75	75	70	55
	Post	60	70	50	30	30	30	30	30
4	Pre	55	60	70	65	55	55	55	60
	Post	75	75	75	65	70	70	60	60
6	Pre	70	65	70	60	65	75	70	70
	Post	80	80	75	65	60	60	60	50
7	Pre	55	60	60	60	60	60	50	50
	Post	55	55	55	55	55	60	60	55
9	Pre	85	90	80	80	75	70	70	55
	Post	80	75	80	65	75	60	60	55
11	Pre	>80	>80	>85	>85	>90	90	85	85
	Post	55	60	60	55	55	55	55	45
12	Pre	65	65	60	70	65	65	65	60
	Post	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
13	Pre	40	30	35	35	30	45	40	40
	Post	20	15	20	20	30	35	40	40
15	Pre	30	20	15	5	20	35	35	35
	Post	50	45	25	35	35	35	35	0

N/A = not applicable (no tinnitus); Pre = pretreatment; Post = posttreatment.

Table 4. Minimum Masking Levels, Left Ear

Patient ID (N = 11)		250 Hz	500 Hz	1,000 Hz	2,000 Hz	3,000 Hz	4,000 Hz	6,000 Hz	8,000 Hz
1	Pre	60	70	60	50	50	40	40	45
	Post	60	60	60	35	40	45	40	40
2	Pre	80	80	80	75	>85	>85	90	85
	Post	70	75	>80	>70	>80	>80	70	65
3	Pre	—	—	60	—	—	—	65	60
	Post	70	—	65	—	—	—	—	25
4	Pre	>80	75	>85	>85	75	75	75	75
	Post	80	75	75	70	65	70	70	70
6	Pre	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Post	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
7	Pre	70	70	75	65	65	60	60	55
	Post	65	70	75	65	60	60	60	55
9	Pre	>85	>85	75	80	85	85	80	70
	Post	60	65	65	65	65	70	55	55
11	Pre	25	35	60	50	55	55	35	30
	Post	50	55	55	55	50	50	50	45
12	Pre	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Post	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
13	Pre	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Post	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
15	Pre	15	10	0	0	25	35	30	60
	Post	50	35	35	25	25	35	30	35

N/A = not applicable (no tinnitus); Pre = pretreatment; Post = posttreatment.

Table 5. Loudness Discomfort Level (N = 11)

Frequency	Mean	SEM
Right change at 250 Hz	2.27	1.236
Right change at 500 Hz	.91	2.002
Right change at 1,000 Hz	1.36	1.664
Right change at 2,000 Hz	4.09	1.626
Right change at 3,000 Hz	3.18	2.161
Right change at 4,000 Hz	4.09	2.318
Right change at 6,000 Hz	2.73	2.465
Right change at 8,000 Hz	−.45	1.423
Left change at 250 Hz	3.18	2.161
Left change at 500 Hz	.91	2.002
Left change at 1,000 Hz	2.27	1.408
Left change at 2,000 Hz	1.82	1.939
Left change at 3,000 Hz	.45	2.817
Left change at 4,000 Hz	3.64	3.377
Left change at 6,000 Hz	3.64	2.531
Left change at 8,000 Hz	−1.82	1.394

normal to borderline MEPs, and 1 had an abnormal MEP. These results indicate a statistical and clinically significant decrease in MEP.

For the tympanogram type, using −100 mm H_2O as abnormal, three of the seven responders went from type C tympanogram to type A. The four nonresponders had type A to start with and finished with type A. Of the four who did not report improvement, three went from type C to type A (one on both ears, the other two on one of the two ears; see Table 1).

Categories of Tinnitus Relief

Both responders and nonresponders (N = 11) correlated to recorded MEPs before and after the study (see Table 1). Two patients with a normal starting MEP that remained unchanged reported a positive tinnitus relief outcome, whereas one patient with a normal starting MEP that remained unchanged reported negative tinnitus relief. Two patients whose MEP was abnormal to start but changed to normal reported positive tinnitus relief, whereas three patients whose MEP was abnormal to start but changed to normal reported negative tinnitus relief. Two patients with a borderline MEP at the outset that changed to normal reported a positive tinnitus relief outcome, and a single patient with an originally abnormal MEP that changed to borderline also reported positive tinnitus relief.

SUMMARY

We found improvement in aeration of the middle ear, as established by tympanometry and supported by physical examination of the tympanic membranes, in

eight patients. Three patients had normal to normal-borderline MEPs.

Five of the seven patients reporting subjective tinnitus abatement recorded MEP improvement at the start and conclusion of the study. Two reported normal MEPs before and after the study.

No alteration in subjective tinnitus was reported by four patients. MEP improvement was recorded in three patients and remained unchanged in one, who had a normal MEP both before and after the study. Outcomes of the TII and the THI indicated no significant change in all four individuals. One individual reported a significant improvement of 2 units on the TAI.

We analyzed the QEEG for the four EEG bands: delta, theta, alpha, and beta (Table 6; Figs. 1 and 2). The number of significant abnormal power recordings was identified with a normative database and analyzed by the Lexicor Corporation. In a general linear model, a RMANOVA reported a significant difference in frequency bands ($F = 12.33$; $p < .0005$).

A nonsignificant difference occurred over time when testing for a quadratic change over the course of the study, with a lowering of the total significant abnormal recordings. A post hoc test using the Bonferroni correction indicated that the delta band was significantly higher and differed from two of the other three EEG frequency bands (i.e., alpha and beta): delta versus theta, $p = .061$; delta versus alpha, $p = .023$; delta versus beta, $p = .025$, for both responders and nonresponders ($N = 11$; see Figs. 1 and 2). Comparison QEEGs of the seven responders and four nonresponders demonstrated similar patterns. No significant main effects arose for either changes in the number of abnormal QEEGs over time or the interaction of the EEG band by time. The delta band did display an observable drop over the course of the study, from a mean of 4.45 to 2.72 at its conclusion. This difference, when analyzed by a general linear RMANOVA, was not significant owing to the low power and small sample size. This lack of significance, due to low power (.336), estimates that there was approximately a 66% chance of missing a significant result for the change in the number of significant recordings over time. These results indicate that a slightly larger sample size might have changed the outcome of this analysis. No significant relationship appeared with the number of reductions of significant QEEG recordings over time and MMLs or LDLs.

Table 6. Qualitative Electroencephalography Average Change in the Number of Significant Recordings

Patient ID (N = 11)	Delta	Theta	Alpha	Beta
1	−12	0	0	0
2	−2	+9	0	0
3	−2	0	0	0
4	0	0	0	−1
6	+3	0	0	0
7	−1	0	−1	0
9	−6	−2	−5	0
11	−1	−1	−3	0
12	+6	0	0	+1
13	−2	0	−1	0
15	−2	0	0	0

Minus (−) = number of reduced abnormal significant recordings; plus (+) = number of increased abnormal significant recordings; zero (0) = no change in number of abnormal significant recordings.

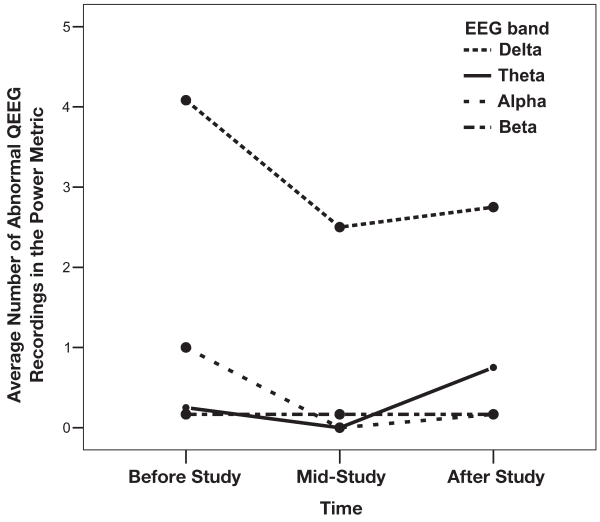

Figure 1. Results of quantitative electroencephalography (*QEEG*) recordings of the four EEG frequency bands for the 11 patients completing the study.

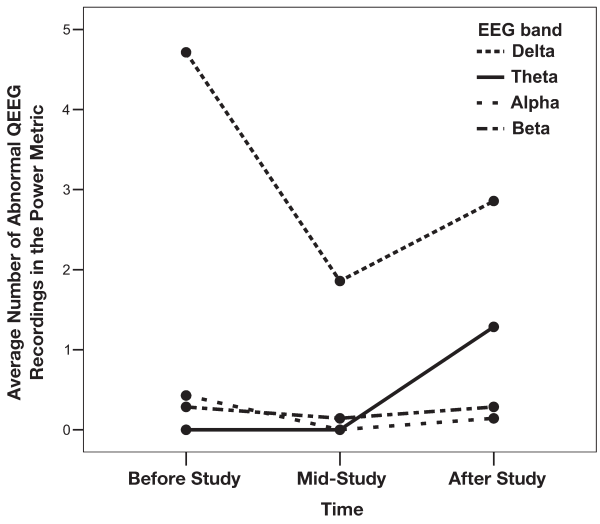

Figure 2. Results of quantitative electroencephalography (*QEEG*) recordings of the four EEG frequency bands for the seven responders.

Tinnitus Outcome Questionnaires

We analyzed the results of the outcome questionnaires as an average for all patients who completed the study (N = 11) and separately for the responders (n = 7) and nonresponders (n = 4; Table 7). A general linear model for repeated measures demonstrated a significant change for the tinnitus outcome questionnaires (TII, TAI, THI, TST, and TRQ; F = 6.605; p = .034). When tested by a paired Student's t-test for change over the course of the study, only the TII, the TAI, and the TRQ demonstrated a significant decrease in the patients' responses. The TII showed a significant decrease from 4.91 to 3.77 (t = 3.76; p = .004); the TAI showed a significant decrease from 3.82 to 3.68 (t = 4.34; p = .001); and the TRQ showed a significant decrease from 64.09 to 48.91 (t = 2.75; p = .020). In a comparison of the change in response between responders (n = 7) and nonresponders (n = 4), we observed no significant differences. The clinical significance to the patient of reported and recorded tinnitus relief was positive in five patients.

Among the 11 patients who completed the study, the TII showed a significant decrease in intensity from 4.91 to 3.77 (−1.136 for seven responders; t = 3.76; p = .004). The TAI showed a significant decrease in annoyance from 3.82 to 3.68 (1.136 for seven responders; t = 4.34; p = .001). The TRQ demonstrated a significant decrease in a mean pre-study score of 64.09 and a post-study score of 48.91 (t = 2.75; p = .0200). The TST indicated a mean change before and after the study of −4.18, which was not statistically significant. The THI indicated a mean pre- and post-study change of −11.73, which was not considered to be statistically significant.

The measurement of depression test (Zung) indicated a mean change of −2.27 before and after the study, which also was not considered statistically significant. Five responders reported positive significance of the tinnitus relief, and two reported it as negative (see Table 6).

In summary, a statistically significant improvement in one or more of the outcomes (TII, TAI, TRQ) was identified in six of seven patients reporting tinnitus relief. An improvement in the TII and TAI scores of 2 units or more was reported by four of the seven. One patient reported tinnitus relief, improvement in MEP, and no improvement in outcome measures.

DISCUSSION

This study differentiated between the efficacy of the Clear Tinnitus preparation for maintenance and improvement of MEP and the correlation of the MEP improvement with reported tinnitus relief. All patients who completed the study demonstrated via tympanometry a statistical and clinical significance in MEP improvement (n = 8) or maintenance of MEP (n = 3) or both (see Table 1).

Seven of the 11 patients reported relief from severe, disabling-type tinnitus after oral intake of Clear Tinnitus. As identified with tympanometry, five demonstrated a significant improvement in MEP, and two showed maintenance of a normal MEP (see Table 1).

Side effects of Clear Tinnitus were occasional and primarily gastrointestinal (n = 2). No patient reported an increase in the original tinnitus. None of the 11 patients who completed the study reported significant side effects.

The completion by each patient of an MATPP established an accurate diagnosis for the tinnitus symptom by identifying the clinical type of tinnitus and focused on a particular factor influencing the clinical course of the tinnitus (i.e., fluctuation in MEP). This clinical medical-audiological approach provided a basis for objective interpretation of the reported subjective tinnitus relief with the

Table 7. Tinnitus Subjective Outcome Questionnaires

Patient ID (N = 11)	TII		TAI		THI		TST		TRQ		Subjective Relief	Significant to the Patient?
	Pre	Post*	Pre	Post*	Pre	Post	Pre	Post	Pre	Post*		
1 RL	5	3	5	3	46	41	10	13	70	73	Improved	Yes
2 RL	4	3.5	4	3	70	26	9	7	100	51	Improved	Yes
3 RL	5	4	5.5	5	80	64	8	13	89	87	No change	No
4 RL	4	4	4	4	50	42	8	8	61	49	Improved	Yes
6 R	5	3.5	5.5	3.5	28	30	9	9	48	42	Improved (transient)	No
7 RL	4	3.5	3	3	56	54	9	9	64	53	No change	No
9 RL	6	5.5	6	4.5	38	30	7	7	54	36	No change	No
11 RL	7	4.5	5	3.5	42	38	9	9	69	63	Improved (minimal)	No
12 R	5	4	6	4	70	10	8	8	95	43	Improved	Yes
13 RL	6	3	6	4	28	42	8	8	45	39	Improved	Yes
15 RL	3	2	3	3	2	4	6	6	10	2	No change	No

* Statistically significant at $p < .05$.
L = left ear; Pre = pretreatment; Post = posttreatment; R = right ear; TAI = tinnitus annoyance index; THI = tinnitus handicap inventory; TII = tinnitus intensity index; TRQ = tinnitus reaction questionnaire; TST = tinnitus stress test.

Clear Tinnitus treatment. A multidimensional method of analysis across dimensions of risk is recommended for all clinical studies attempting to evaluate the efficacy of therapeutic modalities attempting tinnitus relief. Owing to small sample size, statistical analysis was limited to univariate and repeated-measures statistical procedures.

The clinical course of the tinnitus patients selected for this study was identified, by their clinical history and physical examination, to have been influenced by fluctuation of MEP. The MATPP electrodiagnostic cochleovestibular test battery identified the tinnitus to be predominantly a cochlear type, bilateral and unilateral, with a middle-ear and central component. The clinical type of this tinnitus correlates with the patients' reports of tinnitus relief in five of seven. The correlation of the nonresponders (n = 4) and the responders with the recorded fluctuation in MEP is considered significant. In both groups, MEP fluctuation or maintenance of normal pressure was and was not (respectively) correlated with positive tinnitus relief. This dichotomy in correlation of positive response and MEP fluctuation suggests that the factor of MEP fluctuation is outweighed by the central component of the tinnitus or by additional factors (e.g., stress, anxiety) or by both.

The patients' clinical history was positive for the association of tinnitus intensity fluctuation with the subjective report of ear blockage—specifically, increased tinnitus intensity with increased ear blockage and vice versa. Physical examination of the tympanic membranes before and at the conclusion of the study identified mild to moderate scarring of the tympanic membranes consistent with eustachian tube dysfunction. The reported improvement in MEP with tympanometry was associated with reported subjective abatement in ear blockage in the tinnitus ear and with evidence of increased aeration of the middle ear on physical examination of the tympanic membrane.

The regression analysis failed to detect any trends in a change in response with audiometric tests across the hearing spectrum; thus, we could not derive coefficients of change from testing. Clinically, this suggests to the limits of examination that the site of Clear Tinnitus action is not cochlear in location. Otoacoustic emission tests in the future may provide a basis for audiological coefficients of change. The tympanogram findings of improvement in MEP function in responders is considered to support the hypothesis that improvement in MEP underlies Clear Tinnitus resultant efficacy for tinnitus relief by influencing the transduction mechanism of the middle and inner ear.

The tinnitus evaluation of all 11 subjects completing the study indicated high-frequency tinnitus: 10 had a pitch match from 6,000 Hz to 16,000 Hz; 1 had a pitch match of 4,000 Hz; 8 were tonal, 1 was narrow-band, and 2 were a combination of tonal and noise band. Pitch match did not correlate with outcome measurements, masking curve type, MMLs, or LDLs. In the 11 patients completing the study, all masking curves were either type I or type IV, according to Feldmann's classification system. Five were type I before the study, four were type IV before the study, and two were mixed (type I for one ear and type IV for the other ear). After the study, five with type I remained unchanged, and three of the four with type IV remained unchanged. Of the remaining three, one with type IV went to type I for both ears, and the other two who were type IV for both ears went from IV to I for one ear and remained type IV for the other. Type I masking curves are considered consistent with peripheral tinnitus and type IV with central tinnitus. We found no statistically or clinically significant correlation of masking curve type to outcomes.

LDLs had positive and negative changes before and after the study. We saw no statistically significant change or clear trend in the data. The Clear Tinnitus preparation did not significantly influence the tinnitus evaluation measures consisting of pitch match, masking curves, MMLs, or LDLs.

The range of normal and abnormal MEP varies in reports from different investigators (from -25 mm H_2O to -100 mm H_2O) [20–26]. Clinically for this study, tympanometry values for a normal range of MEP were established to be from 0 to -50 mm H_2O. Borderline normal values were -50 to 100 mm H_2O. Abnormal values were -100 mm H_2O and higher. Significant for this study is the correlation of -100 mm H_2O as abnormal with the tympanogram results: Of the seven patients who reported subjective improvement, three went from type C tympanograms to type A. The other four had type A to start and finished with type A. Of the four who did not report subjective improvement, three went from type C to type A (one in both ears, the other two in one ear). Nonresponders with normal MEP and responders with no MEP change provide an inconsistency surrounding the hypothesis. This inconsistency leads us to consider that, although MEP activity is influenced by Clear Tinnitus, other factors to be considered influence the clinical course of the tinnitus in these patients (e.g., the central component of clinical-type tinnitus, anxiety, stress, and depression). In the patients reporting tinnitus relief when a tympanogram type A was identified at the start of the study and remained unchanged at the conclusion of the study, the tinnitus relief correlated more with the improvement in appearance of the tympanic membrane and the reported reduced negative MEP than with the tympanogram type (see Table 1).

The QEEG testing was recommended in this study to improve the accuracy of the tinnitus diagnosis. It could function as a monitor for establishing the efficacy

of the therapeutic modality—Clear Tinnitus—attempting tinnitus relief and aid in understanding the clinical course of the tinnitus as reflected in brain function of memory, consciousness, attention, and affect [3,12]. The QEEG results are considered to be electrophysiological brain function responses hypothesized to reflect a synchrony of responses at the cortex in the central nervous system (see Fig. 1). In general, it was hypothesized for this study that an alteration in an original dyssynchronous auditory signal from the peripheral auditory system, resulting from improvement in MEP, and its subsequent effect on the transduction processes of the middle and inner ear, when received by the thalamus, would be synchronized at brain cortex in the form of different brain rhythms. Alterations in the brain rhythms may reflect the efficacy of the Clear Tinnitus for tinnitus relief. Efficacy of treatment was hypothesized to be reflected by a reduction in the delta or beta frequencies (or both), a minimal or unchanged theta frequency, and an increase in the alpha frequency.

We analyzed the QEEG data as an average of the significant number of abnormal recordings for the power metric of each of the four frequencies of synchronous brain rhythms (i.e., delta, theta, alpha, and beta) for both the responders and nonresponders (N = 11) and for only the responders (n = 7) and reported as an average for all participants in the study at this time. The low power of the analysis for the nonresponders (n = 4) precluded any conclusion or clinical correlation. The delta band was significantly higher than the alpha and beta bands both for the overall cohort of 11 patients and for the 7 reporting tinnitus relief (see Table 5; see Figs. 1 and 2). A reduction in the number of significant delta band recordings occurred over the time course of the study; however, the reduction was not statistically significant. The beta frequency was unchanged. The reduction in the delta response was accompanied by a small increase in the theta response in one patient (not statistically significant at this time).

Clinically, when interpreted in terms of the tinnitus dyssynchrony-synchrony theory, the QEEG data in this study are considered to provide an understanding of the clinical course of the tinnitus in the patients in this study and of the efficacy of the Clear Tinnitus therapy attempting tinnitus relief [2]. Specifically, one can hypothesize that the increase in delta recorded at the start of the study and its overall decrease over the time of the study, the relative lack of increase-decrease in the "ground state" brain activity (i.e., the alpha rhythm), and the relative lack of the beta rhythm are considered to reflect persistence of the tinnitus. In only one patient in this study, demonstration of the theta and its increase may reflect the persistence of the tinnitus and the ongoing development of a paradoxical memory for the dyssynchronous auditory signal—tinnitus [2,3,27–29]. The similarity of the mean delta QEEG response in the 11 patients and the 7 individual responders and the relative lack of correlation of the delta response to the remaining theta, alpha, and beta find clinical support for consideration that the action of the Clear Tinnitus preparation is predominantly its peripheral MEP effect, with secondary tinnitus relief as reported by the responders, and not specifically its effect on the tinnitus. We recommend a larger patient sample over a longer interval of Clear Tinnitus treatment to determine whether the delta rhythm data, although not significant at this time, may reflect a trend of a positive response to therapy when correlated with the remaining theta, alpha and beta frequencies. The QEEG data suggest that a slightly larger sample size might have changed the outcome of this analysis.

The outcome results reflect the dilemma of all professionals involved in attempting to evaluate modalities of therapy attempting tinnitus relief: specifically, how a subjective response becomes one of affect and how a subjective response might be objectified [1,13]. To determine patients' baseline responses, we administered questionnaires to record subjective tinnitus at the outset of the study and again at the conclusion. Of the six outcome measures, only the TII, TIA, and TRQ reported the data to be statistically significant (as noted by the asterisk in the top row of Table 7). No significance appeared in comparing the results of responders to those of nonresponders but, again, this could be owing to the small sample size when separating the patients into independent groups. For the tinnitus outcome tests that were statistically significant, the key question to be asked is whether the reported tinnitus relief is clinically significant to the patients. Of interest was the response of the seven patients who reported tinnitus relief: When asked whether their relief was "significant," the response was negative for two and positive for five.

The outcome results highlight the need for answers to the questions of what the criteria of tinnitus relief are (as identified by the investigators) and what expectations and goals of treatment each tinnitus patient has established (i.e., cure or relief). If the reality of the absence of a tinnitus cure at this time is accepted and tinnitus relief is the goal, is relief expected for the tinnitus sensation or for the annoyance and intrusion into one's lifestyle, as manifested in the behavioral response of affected patients to the presence of the tinnitus? For some, a decrease in only the intensity or annoyance (or both) is significant. For others, the feeling of being less handicapped is significant. For still others, a combination of these factors or other issues are the goals of treatment. In any case , the outcome results of this study emphasizes the need for a battery of outcome measures to be included in the evaluation of therapeutic modali-

ties attempting tinnitus relief [13]. Such a battery of outcome measures should be completed at least at the start and end of the study. Furthermore, the duration of clinical studies evaluating therapeutic modalities for tinnitus relief should be long-term (at least 6–12 months).

CONCLUSIONS

The 11 tinnitus patients who completed the study demonstrated with tympanometry a statistical and clinical significance in MEP improvement (n = 8) or maintenance of MEP (n = 3) or both. Of the 11 patients, 7 with severe, disabling tinnitus and fluctuation of aeration of the middle ears (diagnosed with the MATPP as a factor influencing the clinical course of their tinnitus) reported tinnitus relief with Clear Tinnitus.

The subjective report of tinnitus relief in those seven patients was supported by objective measures of analysis in five patients; the remaining two responders recorded normal MEP before and after the study. These results indicate that a slightly larger sample size might have changed the outcome of this analysis. This study supports the hypothesis that identifying and treating the MEP fluctuation factor may provide tinnitus relief from a predominantly cochlear-type tinnitus.

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