Use of MemoVigor 2 in the treatment of idiopathic Tinnitus

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ABSTRACT

Introduction: Tinnitus is an extremely common ear disorder. However, it is a phenomenon that is very poorly understood and has limited treatment options. The aim of this study was to recognize if the complex Supplement MemoVigor 2 provides relief from tinnitus and to identify if quality of life after treatment is accompanied by changes of objective audiological measures.

Material and methods: Forty-one patients with idiopathic tinnitus (23 females and 18 males with mean age 63.7±8.7 years) were included in the study. On initial evaluation a detailed history was taken and otolaryngologic clinical evaluation was performed. Conventional and high-frequency pure-tone audiometry, tympanometry and, occasionally, auditory brainstem response and otoacoustic emissions were conducted as well, whereas imaging studies were ordered in specific cases. Additionally, tinnitus measurement with specific audiologic tests was performed. All the patients were asked to fill questionnaire Tinnitus Handicap Inventory (THI). Repeat examination was performed after 3 months of treatment with MemoVigor 2 (one tablet/day).

Results: Puretone thresholds obtained on initial and on post-treatment session did not differ significantly. Specific tinnitus measurement tests showed significant decrease of frequency, change of minimal masking level and residual inhibition following masking of tinnitus. Improvement in THI scores was significant. Overall, 83% of the patients had objective or/and subjective improvement. Specifically, 58.5% patients had both objective and subjective improvement, 19.5% had only subjective improvement, probably due to placebo effect, and 5% had objective but not subjective improvement, which may attributed to to psychological comorbidities. Finally, 17% of the patients had no improvement at all. Recent onset tinnitus had better outcome.

Conclusions: MemoVigor 2, a compound that consists of phospholipids, Gingko biloba, Lacetylcar nitine, vitamins and several trace elements, reduces the severity of tinnitus hypothetically through its antioxidant, neurotrophic and vasoactive properties.

Key words: Tinnitus; MemoVigor 2; supplement; treatment; Tinnitus Handicap Inventory.

INTRODUCTION

Tinnitus continues to constitute, even today, a complex and multifaceted diagnostic and therapeutic problem which, due to its increasingly frequent occurrence among the general population (estimated to amount to 10%), has become a major daily concern for all otolaryngologists. The definition of Tinnitus is the subjective perception of sound without the presence of an auditory stimulus. Most Tinnitus cases are related to hearing impairment but it can occur to people with normal hearing. It can be separated into idiopathic or primary and secondary Tinnitus, with idiopathic Tinnitus being by far the most frequent form. Secondary Tinnitus is caused by a subjective disorder either of the auditory system, e.g. malfunction of the Eustachian, otosclerosis, earwax in the outer auditory meatus or a non-auditory disorder e.g. vascular anomalies, myoclony or intracranial hypertension. Idiopathic Tinnitus is usually due to cochlear pathology, or other areas of the auditory tract may be involved. In cases where the cochlea is...
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responsible for Tinnitus the most common diagnoses are presbyacusis, noise related hearing loss or disorders related to intra lymphatic sweat.

The lack of knowledge around the precise pathophysiological mechanism of idiopathic Tinnitus limits our ability to offer an effective treatment. Various therapeutic methods have been implemented on patients with Tinnitus over time including medication, tinnitus retraining therapy, sound masking, biofeedback therapy, intra-tympanic injections and various other therapies with specific devices. However, a consultation of medical literature indicates that results are contradictory for most of the aforementioned therapies with the inevitable consequence that most patients cannot have their condition treated effectively.

In recent years, a compound trading as Memovigor 2 circulated in the Greek market. It contains a combination of therapeutic ingredients. The objective of the present study is to evaluate the effectiveness of this compound in the treatment of idiopathic Tinnitus.

**MATERIAL AND METHODS**

It is a prospective study of a group of patients with Tinnitus. Patients had not received any previous medical treatment or had undergone therapy without success. Patients with otosclerosis, chronic otitis media, hypo- or hyperthyroidism, diabetes mellitus, hypertension, hypercholesterolemia were excluded. Patients with coagulation disorders as well as patients using anticoagulants regularly were also excluded due to potential side effects with the supplement (it contains Gingko biloba, that has antiplatelet properties).

**Initial Check**

**a. Medical History**

The initial evaluation of the patients included taking a detailed medical history from every subject, recording, apart from the epidemiological data (age, sex, profession etc) the following information: (1) Presence of hearing loss, vertigo or saturation hearing, (2) ontological history, (3) neurological symptoms, (4) psychological problems (anxiety, depression, insomnia), (5) presence of systematic ailments, (6) drug intake, (7) history of exposure to noise.

As regards Tinnitus, the following data was recorded: (1) Total duration since its onset, (2) localization (left, right, bilateral, vague), (3) description (hissing, whistling, ringing etc.), (4) type (vibrant, breath concomitant, steady or erratic) (5) intensity (mild, moderate, acute).

**b. Clinical evaluation**

All patients underwent a clinical otolaryngological and a detailed neurological examination. The laboratory control included blood tests with Erythrocyte Sedimentation Rate (ESR) and biochemical control (electrolytes, blood sugar, cholesterol and triglycerides). In some cases a hormonal check for the function of the thyroid. Moreover, with the slightest indication of the possibility of posterior cochlear damage, a magnetic resonance of the inner acoustic canals/cerebellopontine angles (CPA).

**C. Audiologic control**

A complete audiologic evaluation was carried out including audiometry and tympanometry. Both standard pure tone audiometry and wide frequency range tests were conducted. An ultra-high frequency GSI 61 Clinical Audiometer (Grason Stadler, Madison, USA) was used. TDH-49 earphones for the frequency range 0.25–8 kHz. Sennheiser HDA200 earphones were used for the wider frequency range 9-20 kHz. Both Pure Tone audiometry and wide frequency range audiometry took place in an acoustic chamber. In Pure Tone Audiometry the auditory thresholds of every ear were measured at the frequencies of 0.25, 0.5, 1, 2, 4 and 8 kHz. In the wide frequency range audiometry the auditory thresholds of each ear were calculated at frequencies of 9, 10, 12, 15 and 18 kHz. Audiographs
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were measured and graded in decibels hearing level (dB HL) following the guidelines stipulated by the International Organization for Standardization and the American National Standard Institute. Measurements were made using the, ascending-descending technique in 5 dB steps, all auditory thresholds were calculated in dB HL. The maximum stimulus volume was 120 dB and when the auditory threshold surpassed this point (meaning that there was no positive reaction to this maximum stimulus) the hearing loss was registered at 120 dB, following standard current practice.

Standard one frequency tympanometry using the tympanometric device GSI Tymstar vs. 2, middle ear analyzer (Grason Stadler, Madison, USA) was performed. A tonal stimulus at 226 Hz, with sound pressure at 85 dB was used. In case of pathological tympanometric results, the patients were set for reassessment, after been given suitable treatment. If at reexamination the results remained pathological, subjects were excluded from the research. In some cases transient evoked otoacoustic emissions were performed via a ILO Otodynamics analyzer (ILO 292 DP Echoport) (Otodynamics, London, software version 3.94H) connected to a portable computer, as well as evoked potentials auditory brainstem response with the use of a Nihon Kohden Neuropak 2 device.

d. Specific Tinnitus Measurement check
1. Tinnitus frequency specification. Generally speaking, Tinnitus can be separated into two broad categories: Tone-resembling and Noise-resembling Tinnitus. In this specific trial and the following, either tones were utilized or narrow band noise (NBN), depending on the type of Tinnitus. Initially two separate frequency stimuli were given alternately (1 and 2 kHz) proportionate to the intensity of Tinnitus. The patient is then asked to choose the stimulus that better fits his case. We continue with successive pairs (e.g. 2 and 3 kHz), until the frequency of Tinnitus is determined.

2. Specification of Tinnitus volume. Again, either tone or NBN stimuli are applied. The frequencies used are the ones found on the previous trial on the one hand and 1 kHz on the other hand. Varied volumes of the stimulus are provided until the patient identifies the one that represents his Tinnitus more satisfactorily.

3. Minimal masking level (MML). White noise is delivered until the masking of Tinnitus or until the patient’s noise tolerance level. The result is described complete, partial or absence of masking.

4. Transient Tinnitus suppression. That is what the phenomenon of Tinnitus disappearing after exposure to noise is called. This trial is performed by implementing masking with broad band noise (BBN). The volume of the delivered stimulus is determined by the minimum masking level determined through the preceding trial augmented by 10 dB. The duration of delivery is 60 sec. The suppression, if existent, is recorded as complete or partial, as complete followed by partial or as lack of suppression.

E. Questionnaire

All patients participating in the research were asked to complete a questionnaire, known in international bibliography as “Tinnitus Handicap Inventory” (THI). Despite the fact that this questionnaire has been used for a number of years in our clinic and has proved exceptionally useful it has not as yet been officially validated for use in the Greek language. THI comprises of a list of 25 questions pertaining to the conditions that are influenced by the patient’s Tinnitus. Possible answers “Yes”, “Sometimes”, “No”. Depending on the answers, a grading list is extracted based on which Tinnitus is classified in 5 categories according to intensity.

Therapy
Patients partaking in the research group were given 1 tablet 900mg of Memovigor 2 (Bionat, Athens, Greece) daily for 3 months. Patients were advised to record and
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report any complication. The intake of any medication capable of interfering with Memovigor’s action and altering the study’s results was interrupted.

Repeat Check
During the repeat session the clinical, audiologic and specific Tinnitus measurement tests were performed again. All patients were asked to complete the THI questionnaire at new.

Statistical analysis
Research data was entered using the statistical software SPSS into a personal computer for further evaluation and analysis (SPSS Inc., Release Version 21.0, Chicago II, USA. To study potential variations of the auditory thresholds during the treatment the repeated measures analysis of variance (RANOVA) was used. Separate comparisons for the thresholds of Standard and High-Frequency Pure-Tone Audiometry were made. Thus, two separate tripartite RANOVA of auditory thresholds were performed. The comparison was made between the initial and the final (after the 3-month treatment) measurements. As a within group factor the frequency (F) was used divided by ear (Right or Left) and session (Initial or Final). The frequency was used as the dependent variable and was measured in frequency zones per octave. Therefore, in conventional audiometry the factor frequency F of RANOVA had 6 levels of measurement: 0.25, 0.5, 1, 2, 4 and 8 kHz. Respectively, in ultrahigh-frequency audiometry factor frequency F had 4 levels of measurement: 10, 12, 15 and 18 kHz. For compensating for the breach of the roundness and the complex symmetry of the within-group factors the Greenhouse and Geisser method was used.

The in tandem t-test method was used to compare the initial with the final specific measurements of Tinnitus as well as the questionnaire scores. Also, the x² method was used to compare the percentage of ears with complete, partial or lack of masking or suppression of Tinnitus before and after the treatment.

Finally, the correlations between the duration and the specific audiometric parameters of Tinnitus and the decrease in the questionnaire’s scores between the initial and final measurements were calculated using the Pearson correlation coefficient. 0.05 was considered, following established practice, as the point of statistical significance.

RESULTS

a. Material
Fifty five patients with idiopathic Tinnitus participated in the study. Among them 14 (25.45%) didn’t appear for reappraisal. In our phone communications 4 were not found, 6 reported improvement and 4 insignificant change. All claimed increased professional burden, change of domicile or inability to attend. Therefore, there were 41 patients left. From the patients remaining 23 (56%) were female with mean age 63.9 (±9.6) years old (age range 40 to 77 years). The remaining 18 (44%) were male with mean age 63.5 (±7.6) years (age range 52 to 78 years).

b. Qualitative evidence
In 16 (39%) patients Tinnitus was located in their Left Ear whereas 9 (22%) it appeared in both ears or they were unable to locate its provenance. The average duration of Tinnitus amounted to 2 years and 3 months, when the value range was between 1 month and 5 years. No case of vibrant or breathe concomitant Tinnitus were located. 31 (74%) described their Tinnitus “whistling”, whereas the rest used other terms such as “hissing” with “hissing” being the most often. For 33 patients (80.5%) Tinnitus was continuous and 8 (19.5%) had intervals without Tinnitus. Furthermore, in 30 (73%) patients Tinnitus was stable throughout the day, when in 11 (27%) it had fluctuations. The epidemiological data is presented summarily on Table 1.

For 15 (36.5%) patients an imaging check via magnetic resonance or angiography which proved negative for pathological findings. For the rest due to evidence from their medical history, clinical check through lab tests and especially due to the findings of the
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brainstem response to evoked potentials, no further imaging test was deemed necessary.

c. Audiometry findings

The tympanograms of all patients were normal (Type A), either at the initial examination (39 patients, 95%), or at the final examination after suitable treatment (2 patients, 5%). Six patients had normal hearing during the initial check in all frequencies, except for a %\text{=}10 dB exceedance of the maximum normal value of 20 dB in one or two frequencies. The remaining patients had neurosensory hearing loss, mainly in high frequencies. The average auditory thresholds are depicted in Image 1, separately for the Left and for the Right ear. The summary results of the repeated measures of variance analysis (RANOVA) are presented in Table 2. The analysis indicated that the main effect of Frequency, were statistically (Frequency: F=175.59, p<0.001). All other measured factors, i.e. Ear (left/right) and Session (initial/final) didn’t show statistically significant changes. The effect of the Frequency is obviously caused by the significant differences of auditory thresholds in low frequencies, where they are almost normal and the high frequencies where significant elevation is observed. Finally, all measured interactions proved statistically insignificant. The average auditory thresholds during the repeat session, after three months, appear on Image 1, and do not present important differences with the initial as mentioned before.

Equivalent measurements and analyses were performed for ultra-high frequencies too, presented on Table 3, whereas average auditory thresholds are depicted on Image 2. Here too a significant effect of the Frequency (Frequency F=43.75, p<0.001) is noticed due to important differences between auditory thresholds in varied frequencies. All other measured factors and interactions were statistically insignificant.
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Image 1. Average auditory thresholds of conventional Pure Tone audiometry (0.25 to 8 kHz) during initial check and final check, after 3 month treatment.

Upper Panel. Right Ear  Lower panel. Left Ear

The average auditory thresholds of ultra-high frequencies during the repeat session, after 3 months, are shown on Image 2. As well and do not present essential differences with the initial. In the ultra-high frequency measurements, the average auditory thresholds were especially low (10 kHz 65 dB, 12 kHz 77.2 dB, 15 kHz 84 dB, 18 kHz 86.6 dB). The 20 kHz frequency was not measured, because according to previous studies, it is not particularly reliable.

d. Findings from the specific audiologic Tinnitus check

Frequency: During the initial check an average Tinnitus frequency of 9030 Hz was identified. During the repeat check after three months, a decrease in the frequency of Tinnitus was observed, which is a positive prognostic sign from 9030 Hz to 6425 Hz (t=3.51, p<0.0010.)
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Volume: Tinnitus volume in its usual frequency was reduced from 64 dB to 52 dB, a difference however that is not statistically significant.

| Table 2. Repeated Measures Analysis of Variance (RANOVA) by Session, Ear, Frequency, for variation in the auditory thresholds in Conventional Pure Tone Audiometry during the 3 month treatment. |
|-----------------|---|-----------------|---|---|
|                  | Square Total | df | Average Square | F   | p   |
| Frequency        | 105166.01    | 2.5| 41038.24       | 175.59 | < 0.001 |
| Ear              | 8.33         | 1  | 8.33           | 0.00  | 0.936 |
| Session          | 81.38        | 1  | 81.38          | 0.06  | 0.803 |
| Frequency * Session | 661.19    | 2.5| 258.01         | 1.10  | 0.343 |
| Ear * Session    | 312.63       | 1  | 312.63         | 0.24  | 0.625 |
| Session * Ear    | 876.43       | 2.5| 342.00         | 1.46  | 0.229 |
| Frequency * Ear * Session | 223.69    | 2.5| 87.29          | 0.37  | 0.740 |

Minimum Masking Level (MML): During the initial check, the Tinnitus masking was complete in 25 patients, partial in 15 patients where in 1 patient masking was not possible. During the repeat check Tinnitus masking was complete in 35 patients, partial in 5 patients and not possible for the same 1 patient (Im. 3). The difference in these results is statistically significant (x=6.97, p<0.05). The MML with the use of white noise was 46.3 dB in the initial check and was reduced to 36 dB in the repeat check, a statistically insignificant change.

| Table 3. Repeated Measures Analysis of Variance (RANOVA) by Session, Ear, Frequency, for variations in the auditory thresholds in ultra-high frequency audiometry during the 3 month treatment |
|-----------------|---|-----------------|---|---|
|                  | Square Total | df | Average Square | F   | p   |
| Frequency        | 66244.28     | 1.6| 41432.78       | 43.75 | < 0.001 |
| Ear              | 1671.14      | 1  | 1671.14        | 0.69  | 0.406 |
| Session          | 81.38        | 1  | 81.38          | 0.06  | 0.803 |
| Frequency * Session | 434.13     | 1.6| 271.52         | 0.28  | 0.701 |
| Ear * Session    | 260.20       | 1  | 260.20         | 0.10  | 0.743 |
| Session * Ear    | 3218.89      | 1.6| 2013.27        | 2.12  | 0.132 |
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| Frequency * Ear * Session | 791.55 | 1.6 | 495.08 | 0.52 | 0.553 |

**Image 2.** Average auditory thresholds of ultra-high frequency Pure Tone Audiometry (10 to 18 kHz) during the initial and the final check, after 3 months of treatment.

| Upper panel. Right Ear | Lower Panel. Left Ear |

**Transient suppression of Tinnitus:** During the initial check, suppression of Tinnitus was complete in 19 patients, partial in 17 patients and in 5 patients it was not possible. During the repeat check, suppression was complete in 30 patients, partial in 9 and for 2 patients it was not attainable (im. 4). This difference in results was statistically significant ($x=6.21$, $p<0.05$)

**Image 3.** Percentages of MML in patients, complete, partial or absence thereof, during initial check (above) and final check (below)

e. **Questionnaire and Qualitative control**

The THI questionnaire’s has a maximum potential score of 100, when the patient answers “Yes” in all 25 questions and a minimum score of 0. The average
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Image 4. Percentages of Transient Suppression of Tinnitus, complete, partial or absence thereof, during the initial check (above) and the final check (below)

value of the patients’ answers at the initial check was 44 (value range 6-100), whereas the average value at the repeat check was 28 (value range 0-100), a statistically significant change ($x=6.12$, $p<0.001$). The above are depicted on Image 5.

The combination of the objective findings and of the questionnaire’s findings along with the patients’ personal opinion concerning the treatment’s success yielded 4 categories of patients: 1) objective improvement and subjective opinion of improvement - cure: 24 (58.5%) patients 2) objective improvement but subjective opinion of lack of improvement through treatment: 2 (5%) patients 30 lack of both objective and subjective improvement: 7 (17%) patients 4) lack of objective improvement but claim of subjective improvement: 8 (19.5%) patients.

A Pearson statistical correlation control was performed where the presence of correlation between the drop in THI scores and, firstly, the duration of Tinnitus (negative

Image 5. Average values with stable deviations of the initial and the final THI score.

Maximum score is 100 in very heavy forms of Tinnitus, whereas the lowest score is 0, in the absence of symptoms.

DISCUSSION

At times various pharmacological treatments and nutritional supplements or other therapeutic means have been proposed for the treatment of tinnitus, including tinnitus maskers, sound stimulation, transcutaneous electrical stimulation, low-level laser, vibrations treatments, internal drum infusions, cochlear implants, hyperbaric oxygen or transcranial magnetic stimulation. Moreover, psychological or behavioral therapies, the tinnitus retraining therapy and psychological support have been applied. 25-31

Regarding the pharmacological treatment of tinnitus, drugs from different categories have been proposed, such as antidepressants, lidocaine, prostaglandins, antiepileptics, antiglutaminergic, dopaminergic and antidopaminergic, melatonin, misoprostol, atorvastatin, vaso-actives, furosemide, osmotic drugs, scopolamine, vetaistin, baclofen, antihistamines, various metals, etc. However, no drug has yet been approved for the treatment of tinnitus, neither from
the Food and Drug Administration of the USA, nor from the European Medicines Agency.\(^{30,32}\)

The incidents of tinnitus are originally attributed usually to peripheral damage e.g. in cases of cochlear hearing loss, or on exposure to noise that damages to the outer hair cells of the cochlea, but subsequently the problems are focused, attributed particularly to the reorganization of various neural circuits of lemniscus. However, it is not known exactly what population of neurons in the cerebral cortex and subcortical structures are involved in the creation of tinnitus. It is also equally unknown what neurotransmitter systems are involved pathophysiologically.\(^{33-35}\)

Therefore, it is clear that the tinnitus are still an important therapeutic problem, the treatment of which is hampered by the lack of sufficient knowledge of its pathophysiology. Due multifactorial etiology, and based on the principles of competitive and synergistic action, a treatment that interacts with more than one receptors, could cause a greater decrease in tinnitus, compared to a treatment that would act with a single actions mechanism.\(^{36}\)

In the present study we used a relatively new drug, MemoVigor 2, that contains a combination of substances, such as phospholipids, L-acetylcarnitine, Gingko Biloba extract, vitamin B, E and C, as well as trace minerals as selenium, magnesium and potassium. Most of them have been previously used for tinnitus, and other peripheral and central vestibular syndromes as well as for treating lesions of the acoustic and the facial nerve. We noted a significant reduction of tinnitus after 3-month treatment with the intake of one pill of this drug per day, to a significant proportion of patients.

**Ginkgo biloba**

Extracts from the leaves of the plant Gingko, which is native to China and East Asia in general, have been used for many years in various neurological and other disorders, such as dementia, cognitive disorders, headaches, dizziness, mood disorders, cardiovascular diseases and coronary heart disease. Ginkgo biloba has also been used for the treatment of tinnitus. Its major components are flavonoids and terpenoids, it has been proven to possess antioxidant activity, increases tolerance to hypoxia, improves blood flow, increasing the flexibility of the cellular elements of blood and improving microcirculation.

It also affects the levels of neurotransmitters, increases neuroplasticity, provides neuroprotection and prevents cerebral oidima.\(^{37-40}\) Such action mechanisms may help in the treatment of tinnitus, reducing damage caused by free radicals to the cochlea, or by increasing the blood flow and health of the inner ear. Various studies as well as several systematic reviews have also been conducted for its usefulness in the treatment of tinnitus. The German Commission E. Blumenthal, recommended the systematic use of Ginkgo biloba to counter-act tinnitus.\(^{41}\) In a previous review, Holstein ascertained a significant effect of the drug, both in acute and chronic tinnitus.\(^{42}\) Also, in a review of randomized researches with a control group, where Ginkgo biloba was used as a treatment of tinnitus, where Jadad\(^{43}\) scale was used to assess each research, the authors found that the results were positive to the use Ginkgo.\(^{44}\) On the contrary, some studies and reviews found non-activity of the drug,\(^{45, 46}\) but these studies have received criticism for methodological errors.\(^{47,48}\) There are two recent reviews,\(^{49}\) of the Cochrane Database, to one of which the activity of the drug in not confirmed,\(^{50}\) but in the second there are positive results. In the latter of these reviews, von Boetticher, in a review of double blind-studies with placebo control,\(^{47}\) found that only 3 of the numerous studies fulfilled the necessary criteria for inclusion in the review, the ones that studied the efficacy of the drug in tinnitus treatment and S more that studied efficiency not only in tinnitus but also in other agnosia disorders and dementia. According to the author, all 8 studies showed statistically significant superiority of active treatment versus placebo. Therefore, he concluded that the extracts of Gingko biloba are suitable for the treatment of tinnitus, as either a single symptom, or in combination with dementia or age-related cognitive disorders.
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L-acetylcarnitine

Carnitine has strong antioxidant activity and is essential for the mitochondrial function while it may enhance the mitochondrial Bioenergy and biogenesis, restoring mitochondrial function.\textsuperscript{51} L-Carnitine, a form of carnitine used pharmacologically, may inhibit the nerve activity of the receptors by activation of the gamma-aminobutyric acid receptor system (GABA).\textsuperscript{52} This is important, because a widely accepted mechanism of tinnitus procreation is nerve hyperexcitability, particularly through GABA systems glycine.\textsuperscript{53} This is the reason why L-carnitine has been successfully used in the treatment of tinnitus.\textsuperscript{54-55}

Vitamins

MemoVigor 2 contains vitamins of groups B, E and C. Vitamins of groups E and C are known for their antioxidant action. The complex of vitamin B is a family of compounds which have been grouped because of their interaction to the functions of the human enzyme systems, and because of their allocation in natural food sources. Deficiency of vitamin B complex has been shown to result to the procreation of tinnitus, while intake may improve symptoms .\textsuperscript{56-57} Coadministration of vitamins is useful since, in case of administration of a single antioxidant the endogenous antioxidant defense system may block its action, while the combination prevents the disturbance of the balance of the antioxidant system.\textsuperscript{58}

Minerals (magnesium, potassium, selenium)

Magnesium is essential for the activity of many enzymes in the brain cells and serves as a major regulator of calcium channels involved in neurotransmission.\textsuperscript{59} Therefore, magnesium plays a significant role in nerve and central acoustic paths. It is proven that magnesium supplement facilitates nerve regeneration after hearing loss following exposure to noise, or sudden idiopathic hearing loss.\textsuperscript{60} It has also been used successfully in the treatment of tinnitus.\textsuperscript{61-62}

Potassium is the major electrolyte of the intracellular liquid. Potassium channels Kv7 regulates the excitability of the nerve, sensory and muscle cells. It has been denoted in animals that the noise exposure causes tinnitus due to an increase of automatic excitation of spindle cells in the dorsal cochlear nucleus, which is caused by reduction of potassium currents via the channels Kv7.\textsuperscript{63-64}

Finally, selenium is associated with activity of glutathione peroxidase, which is the only enzyme in the cochlea, that deactivates reactive oxygen species (ROS) and reactive nitrogen species (RNS).\textsuperscript{65} Deficiency of selenium reduces the effectiveness of glutathione peroxidase, and for this reason it has been used in combination with B and E vitamin complexes in the treatment of idiopathic sudden hearing loss.\textsuperscript{66}

Phospholipids

Phospholipids partake in the formation of cell membranes and are oxidized from the oxygen free radicals into OH or COH, thus compromising the integrity of the cell membrane. Therefore, a phospholipid sufficiency is essential because they constitute membrane stabilizers especially in patients with idiopathic Tinnitus whose blood count has yielded increased ROS values. The administered compound of this study, containing a combination of all these ingredients, that also have antioxidant, vasoactive and neurogenic properties, had a positive outcome for a large percentage of our patients. It appears that therapy with antioxidant ingredients in patients with idiopathic Tinnitus reduces oxidation stress which harms the inner ear tissues. Its vasoactive and neurogenic properties improve the circulation and structural integrity of nerve circuits. Moreover, it seems to reduce the subjective tolerance of patients vis-à-vis their symptoms.

In the present study we distinguished 4 groups of patients. The most numerous group, representing 58.5% of the total was comprised of patients with both an objective and a subjective improvement. The second group representing a percentage of 19.5% were patients who claimed subjective improvement that could not be supported by our objective findings. We can legitimately deduce that the compound had the, very common in any treatment “placebo” effect.
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The third group, representing 5% showed significant improvement in all objective indexes, but personally claimed no improvement of their condition. This can be attributed to the psychological background of these patients, who have been greatly influenced by their Tinnitus and merit psychological support and auxiliary treatment such as alprazolam type stress relievers that have proven helpful in cases of Tinnitus.

The last group, 17% of patients presented neither objective nor subjective improvement. A closer look to these traits of these patients showed that they were cases where the onset of Tinnitus spans over a number of years. They indicated significant pathological factors and scored high at the questionnaires. They had already tried, unsuccessfully, a number of drugs in the past. In the statistical review of the results, a negative correlation between the improvement of Tinnitus based on the questionnaires and the duration of their affliction. This revealed that, because of the fact that improvement was greater in cases of recent onset of Tinnitus, we should not delay treatment and leave Tinnitus unchecked and untreated for a long time.

Finally, we must mention that this study has two disadvantages. There was no control group and the material was incongruous. Both chronic and recent onset patients were included. Most importantly, though, our patients had more severe Tinnitus than the mean of patients. For example, the average volume of Tinnitus was 64 dB, whereas other studies have shown that only 3% of the total of patients has a Tinnitus volume of over 20 dB. Moreover, the average Tinnitus frequency was over 9000 Hz, whereas in a number of other studies it is 6000 Hz. That can be explained by the fact that our department is a Third-stop reference point for audiologic/neuro-otologic disorders. Consequently, there is a bias against the true therapeutic value of the compound, which could prove even greater for the general population.

It appears, therefore, that the greatest percentage of patients showed improvement, largely objective and in a small percentage placebo. Though most patients showed improvement and not absence of Tinnitus, even if the mean results of the therapeutic treatment of Tinnitus were limited in size, given the annoying nature of Tinnitus that often leads to an important handicap, even moderate improvements can have an substantial positive effect on the quality of life of patients. It is the medical expert’s responsibility to offer advice, support and the best possible alternative treatment to the patient. Therefore, the results of this study must be appreciated accordingly.

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APPENDIX
TINNITUS HANDICAP INVENTORY

INSTRUCTIONS:
- This questionnaire aims to allocate the problems caused by your tinnitus
- Circle "Yes" or "Sometimes" or "No" in each question
- Answer all questions

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
<th>Sometimes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Does Tinnitus hinder your concentration?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Does the intensity of your Tinnitus impede your hearing other people talking to you?</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Does Tinnitus make you angry?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Does Tinnitus make you confused?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Does Tinnitus cause frustration?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Do you constantly complain about your Tinnitus?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Does Tinnitus influence your ability to sleep?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Do you feel that you can never rid yourself of Tinnitus?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Is Tinnitus an obstacle to enjoying social activities, such as going out for dinner or watching a movie?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Does Tinnitus irritate you?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Does your Tinnitus make you believe that you are suffering from a serious illness?</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Does Tinnitus make it hard to enjoy life?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Does Tinnitus intrude in your professional or family obligations?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Do you think that your often touchy because of your Tinnitus?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Does Tinnitus make it difficult to read a book?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Does Tinnitus upset you?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Does Tinnitus influence negatively your relationship with your family and your friends?</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Use of MemoVigor 2 in the treatment of idiopathic Tinnitus

Do you find difficult to focus on anything other than your Tinnitus?  
18 Yes Sometimes No

Do you feel that you have lost control of your Tinnitus?  
19 Yes Sometimes No

Does Tinnitus cause you fatigue?  
20 Yes Sometimes No

Does Tinnitus cause you depression?  
21 Yes Sometimes No

Does Tinnitus cause you anxiety?  
22 Yes Sometimes No

Do you feel that you can no longer face Tinnitus?  
23 Yes Sometimes No

Is your Tinnitus worse when you are under stress?  
24 Yes Sometimes No

Does Tinnitus make you insecure?  
25 Yes Sometimes No

TO BE COMPLETED BY THE DOCTOR

Total per column

\[ \begin{array}{ccc}
\text{Total Score} & + & + & = \\
\times 4 & \times 2 & \times 0 \\
\end{array} \]

Tinnitus severity index based on the Tinnitus Handicap Inventory

<table>
<thead>
<tr>
<th>Grade</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0-16</td>
<td>Light: Perceived only in quiet surroundings and is masked easily. It does not disturbed the day's activity or the ability to sleep.</td>
</tr>
<tr>
<td>2</td>
<td>16-36</td>
<td>Mild: Is masked easily by ambient sounds and is easily forgotten throughout the day's activities. Ocasionally, it disturbs sleep but not the day's activities</td>
</tr>
</tbody>
</table>
### Use of MemoVigor 2 in the treatment of idiopathic Tinnitus

<table>
<thead>
<tr>
<th>Level</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>38-56</td>
<td>Moderate: Can be perceived, despite the presence of ambient and other noise. Neverthess, it does not bear upon daily activities.</td>
</tr>
<tr>
<td>4</td>
<td>58-76</td>
<td>Severe: Is always perceivable and can rarely, if at all, be masked. It leads to troubled sleep and may influence the ability to perform daily activities. The activities carried out in quiet surroundings are influenced the most.</td>
</tr>
<tr>
<td>5</td>
<td>78-100</td>
<td>Catastrophic: Is always perceivable, hinder the ability to sleep and make all activities hard to perform.</td>
</tr>
</tbody>
</table>