Improving quality of life in subjective tinnitus patients with Audistim®

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ABSTRACT

Objectives: *This study aims to improve the quality of life of chronic subjective tinnitus patients with Audistim®. Methodology It is a prospective study carried out in a Belgian target population, from one university and one regional hospital, suffering from chronic subjective tinnitus. Quality of life was measured by the Tinnitus Handicap Inventory (THI), the quality of sleep by the Pittsburgh Sleep Quality Index (PSQI) and stress by the Psychological Stress Mesure (MSP-9).* ***Results:*** *There is a significant improvement of the quality of life with Audistim® treatment when comparing the initial THI score and the THI score after 3 months of treatment (p-value 0.0000; p-value <0.0001). The initial PSQI score and the post treatment score show a significant improvement (T-test 8.7, p-value <0.01). Within the PSQI scores, especially the latency of sleep (T-test 15.1, p-value <0.001), and the daytime dysfunction (T-test 10.6, p-value <0.01) improved. There was also a slight improvement in sleep disturbance (T-test 4.0, p-value <0.05). The initial MSP-9 score (D0) and the score after Audistim® treatment (M3) show a significant improvement (T-test 7.6, p-value <0.01).* ***Conclusions:*** *There is a general improvement of quality of life when Audistim® is taken on a regular basis for 3 months.*

Keywords: Tinnitus – Quality of life – Drug therapy

INTRODUCTION

Tinnitus is a widespread problem that affects the quality of life of millions globally. According to the best estimates for Belgium, between 10 and 30% of the population experience either transient tinnitus or even persistent tinnitus[1]. One out of 6 of the patients (15%), rate their tinnitus very bothersome and distressing to the extent that it is affecting their quality of life.

Few treatments have been found to be effective for subjective tinnitus and to have a significant improvement on quality of life. In subjective tinnitus, neither an external nor endogenous sound source is present; instead, the tinnitus is caused by abnormal bioelectric, biomechanical, or biochemical activity in the inner ear and/or central nervous system.

The precise role of the numerous extra-auditory structures that contribute to the pathophysiology of tinnitus is difficult to establish. Some of them participate in the creation or in the chronification of tinnitus and some in the psychological reactions to the tinnitus[2]. Audistim® is a food supplement which contains ingredients with a specific composition based upon the multifactorial causal theory involving auditory, attentional, memory, and emotional systems[3]. These different systems are being targeted by the ingredients and their specific proportioning. The antioxidant theory is also involved in the creation of Audistim®, this theory states that the reactive oxygen species play an important microcirculatory role in the pathology of the inner ear and the peripheral and central pathways[4]. These components help to treat the multitude of causing factors and in that way improve the quality of life.

THIS PROSPECTIVE STUDY AIMS TO IMPROVE THE QUALITY OF LIFE OF CHRONIC TINNITUS PATIENTS IN A BELGIAN TARGET POPULATION WITH AUDISTIM®.

MATERIALS AND METHODS

Observational study of Audistim® carried out in one Belgian University Hospital and one regional hospital. Audistim® was created by Audistimpharma Laboratory in Pessac, France. Patients with ongoing tinnitus were included in this study upon the decision of the ear specialist. Patient selection was done at random. The first one hundred and ten patients who had a consultation at the outpatient clinic with the ear specialist with a main complaint of tinnitus were included in this study, even if they already had seen the specialist and received previous treatments. The patients must be between 18 and 75 years of age and suffering from tinnitus for at least 3 months. Tinnitus must be subjective. Patients were proposed the treatment and were at liberty to participate, they had to sign a consent. The exclusion criteria were limited to: *(I)* patients with major or ongoing diseases, *(II)* patients who have an actual or have had a treatment with psychotropic medication within the last 2 months, *(III)* patients who participate in another observational study or *(IV)* patients known to have a sensitivity to one of the components of the study product.

The patients were given 3 months of treatment and were then followed up. Monitoring was done by using the Tinnitus Handicap Inventory (THI)[5] questionnaire, psychological stress was measured by the Psychological Stress Mesure (MSP-9)[6] and the quality of sleep by the Pittsburgh Sleep Quality Index (PSQI)[7]. A tolerance test of the treatment was also done.

Audistim® is composed of different nutritional supplements. It should be taken orally in the morning (day capsule: red pill) and in the evening (night capsule: blue pill) 30-60 minutes before going to bed.

Day capsule ingredients include: Marine magnesium oxide, maltodextrin, hawthorn leaf and flower extract (Crataegus monogyna and Crataegus laevigata), L-Theanine, Ginkgo biloba leaf extract, Quercetin, nicotinamide (vit B3), anti-caking agents: magnesium salts of fatty acids, cyanocobalamine (vit B12), Pyridoxine hydrochloride (vit B6), Thiamin hydrochloride (vit B1). Capsule: gelatine, colouring agents: E171, E172, E122. Night capsule ingredients include: Maltodextrin, Tryptocetine® (L-Tryptophan, Quercetin complex), marine magnesium oxide, lemon balm leaf extract (Melissa officinalis), California poppy extract (Eschscholzia californica) aerial parts, zinc citrate, Ginkgo biloba leaf extract, anti-caking agents: magnesium salts of fatty acids, silica, melatonin.

RESULTS

One hundred and seven patients were included in the study. One person did not take the treatment and was excluded and 5 others did not complete the THI at the end of the treatment. Sixty patients were male (59.4%) and the mean age was 53.3 years (23 - 75 years). The mean duration of tinnitus was 7.5 months (4 – 420 months) *(table 1)*.

Seventy-three (73.3%) patients received a treatment for their tinnitus in the past; this treatment could be pharmaceutical drugs (78.5%), relaxation therapies (1.8%), acupuncture (1.2%), manual therapies (1.8%), electromagnetic procedures (11.9%), white noise generators (1.8%), hyperbaric oxygen (1.8 %) and miscellaneous (dental treatment, ventilation tubes)(1.2%).

The pharmaceutical drugs used by the patient population were betahistine (3.0%), antidepressant drugs (3.7%), anxiolytics (1.5%), oral corticosteroids (5.3%), antiepileptic drugs (1.5%), piracetam (11.3%), Ginkgo biloba (37.6%), magnesium (31.6%), non-steroidal anti-inflammatory drugs (0.8%) and zinc (3.7%). Inefficacy was the major reason to stop treatments in the past (94.5%). The mean initial THI score was 49.8 out of 100 (8-98). The mean end THI score was 39.9 out of 100 (0-100). The distribution of the THI before and after Audistim® treatment can be found in the first figure *(Fig. 1)*. There is a significant improvement of the quality of life with Audistim® treatment when comparing the initial THI score (D0) and the THI score after 3 months of treatment (M3) (p-value 0.0000; p-value <0.0001). More than 50% of the patients had an improvement of their THI score after 3 months of treatment *(table 2)*. The initial PSQI score (D0) and the post treatment (M3) score show a significant improvement (T-test 8.7, p-value <0.01). Within the PSQI scores, especially the latency of sleep (T-test 15.1, p-value <0.001), and the daytime dysfunction (T-test 10.6, p-value <0.01) improved. There was also a slight improvement in sleep disturbance (T-test 4.0, p-value <0.05) *(Fig.2)*. There was no significant improvement for the other individual components of the PSQI. A significant correlation can be found between the evolution of the THI score and the evolution between the PSQI score at DO and M3 (r 0.06, p-value <0.01) *(Fig. 3)*.

The initial MSP-9 score (D0) and the score after Audistim® treatment (M3) show a significant improvement (T-test 7.6, p-value <0.01) *(Fig.4)*. The reported adverse effects of Audistim® were temporomandibular joint pain (1%), increase of tinnitus (1%), benign positional paroxysmal vertigo (1%) and facial erythema (1%).

DISCUSSION

Various treatments have been trialled and errored for the treatment of chronic tinnitus. Various drugs including antihistamines, barbiturates, anaesthetics, calcium channel blockers, vasodilators, muscle relaxants, anticonvulsants and also various methods of psychotherapy and tinnitus masking agents have been used to reduce the tinnitus severity. However, they have little effects and their results are not different from those of placebo[4].

Audistim®'s goal is to treat a variety of causes and contributing factors of tinnitus, the components have different effects following the multifactorial origin of tinnitus *(table 3)*.

In our study, 37.5% of the population received Ginkgo biloba, the majority with an association of a form of oral magnesium. According to previous studies, Ginkgo biloba can be considered as a promising option to improve tinnitus[25]. Since tinnitus is multifactorial, the association of other components could be key to a good natural treatment option.

Several of the components of Audistim® have antioxidant effects and vascular modulator effects improving the microcirculation of the endothelium of the inner ear[4].

Pyridoxine chlorhydrate, thiamine chlorhydrate and L-trypthophan aim to support the non-auditory neuronal networks involved in tinnitus[2].

Insomnia and stress are both causing and contributing factors of tinnitus[26].By implementing relaxing and sleep inducing components, Audistim® aims to take this into account. The MSP-9 and PSQI improvements reflect this ability. Also the significant correlation between improvement of quality of life in the THI and the improvement of sleep in the PSQI shows an important role of treating sleep problems.

Of the adverse effects reported by the patients, the erythema of the face could be a sensitivity to one of the components. The increase of tinnitus could have a multifactorial origin, but we cannot exclude one of Audistim® components. The other adverse effects are thought not to be linked to Audistim®.

A similar study with Audistim® was carried out in France and also showed improvement in the quality of life, stress and sleep of the examined patient group[27].

CONCLUSION

There is a general improvement of quality of life when Audistim® is taken on a regular basis for 3 months. Several theories can be applied to this effect. Especially the improvement of sleep that leads to an improvement in quality of life should be noted. The different questionnaires all suggest this conclusion. This is the second study showing these results. The next step should be a double blind study.

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TABLES AND TABLE LEGENDS

	N	%
6 months or less	2	2.0
Between 6 months to 2 years	25	24.8
Between 2 and 10 years	55	54.5
More than 10 years	19	18.8
Total	101	100.0

TABLE 1: **DURATION OF TINNITUS**

	N	%
Decrease of THI score of at least 20 points (<=-20)	23	22.8
Decrease of THI score of at least 10 points (] -20 ; -10])	21	20.8
Decrease of THI score of at least 5 points (] -10 ; -5])	13	12.9
Stability of THI score (] -5 ;5[)	31	30.7
Increase of THI score (>=5 points)	13	12.9
Total	101	100.0

TABLE 2: **IMPROVEMENT OF THI SCORE**

Component	Dosage	Effect
Ginkgo biloba	31.5 mg (63 mg in total)	Improves ischemia; has antiplatelet and vascular modulator effects; there is also an antioxidant and protective effect on nerve cells in the brain[9]
Magnesium	75 mg (morning) 37.5 mg (evening)	In a comparative study with patients suffering from subjective tinnitus and patients without tinnitus the serum magnesium level was significantly lower in patients suffering from tinnitus. This suggests a causal relationship between a magnesium deficiency and tinnitus[10]
Hawthorn	37.5 mg	Is a natural antioxidant, has anti-inflammatory and vasodilatation effects[11,12]
L-Theanine	50 mg	Has relaxation effects, can improve concentration and learning abilities[13]
Quercetin	25 mg (50 mg in total)	Is a flavonoid, increases the levels of antioxidant enzymes, ameliorates the cognitive impairment induced by chronic unpredicted stress, partially reversed the learning and memory impairment induced by ischemia in rats[14]
Nicotinamide	16 mg	Reduced intake of vitamin B2 and B3, water and protein may be associated with tinnitus and tinnitus-related annoyance[15]
Cyanocobalamin	2.5 µg	There is a link between cobalamin deficiency and tinnitus thereby suggestive of a therapeutic role of B12 in cobalamin-deficient patients of tinnitus[16]
Pyridoxine chlorhydrate	1.4 mg	Pyridoxine surplus can lead to auditory neuropathy[17]
Thiamin chlorhydrate	1.1 mg	Neonatal thiamine deficiency can cause auditory neuropathy in humans[18]
L-tryptophan	40 mg (in Tryptocetin)	A deficiency can lead to cognitive impairment[19]
Melissa Officinalis	60 mg	High amount of antioxidant activity[20],treatment of insomnia[21]
Eschscholzia californica	40 mg	Has a mild sedative effects on mice[22]
Zinc citrate	10 mg	There is a significant correlation between zinc level and the severity and loudness of tinnitus; zinc deficiency was also associated with impairments in hearing thresholds[23]
Melatonin	0.3 mg	Insomnia treatment[20], has a protective effect against cochlear damage induced by acoustic trauma and ototoxic agents and clinical studies report the ability of melatonin to minimize the severity of tinnitus[24]

TABLE 3: **COMPONENTS OF AUDISTIM® AND THEIR RESPECTIVE EFFECTS**

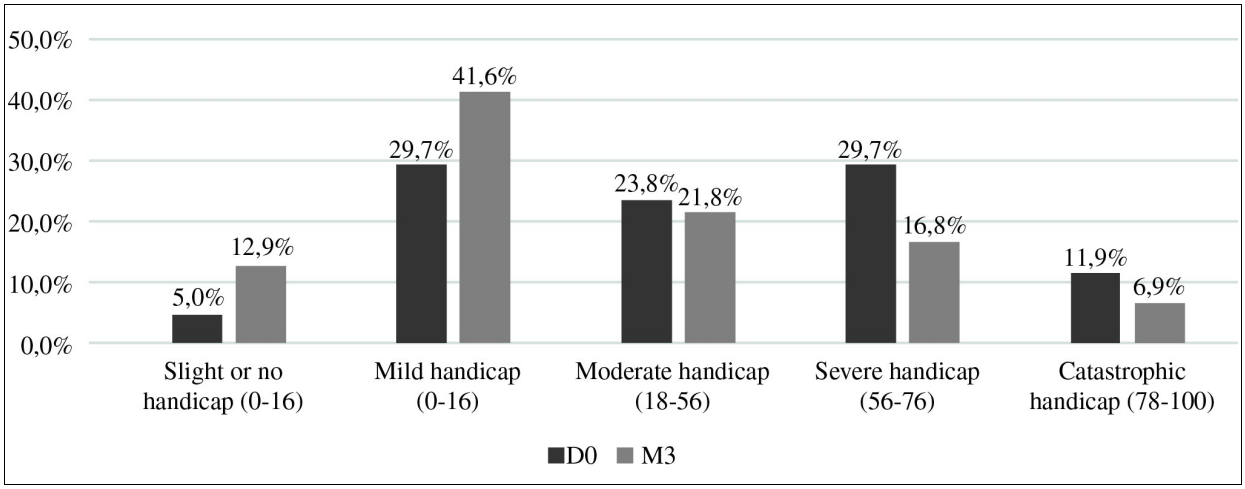


Figure 1: **Evolution of the general THI-score between D0 and M3**

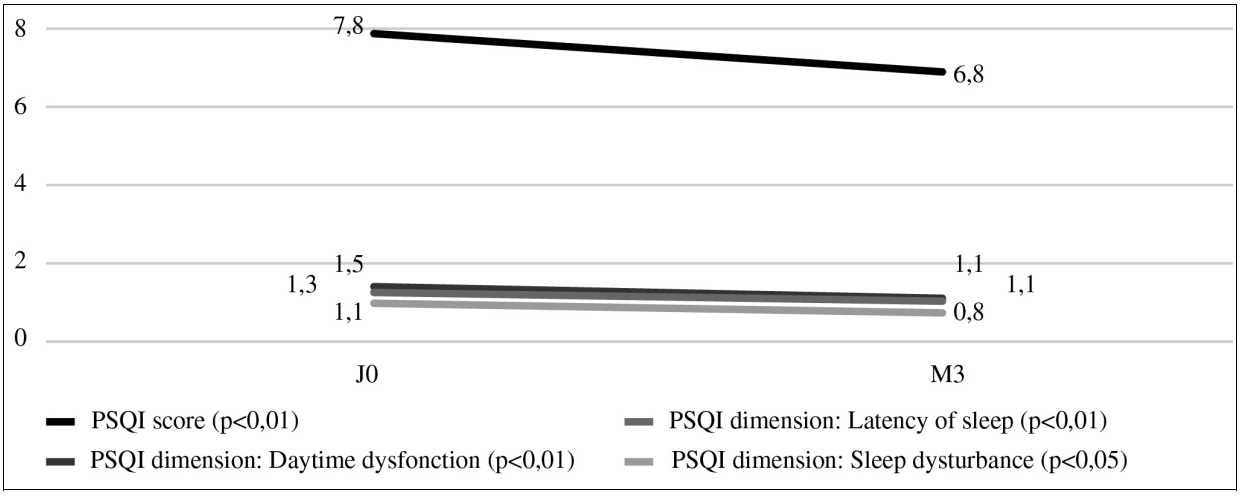
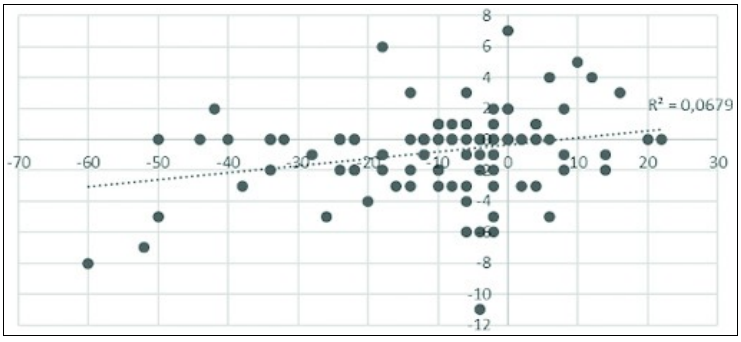


Figure 2: **Evolution of the PSQI score between D0 and M3**

X= Difference of THI between D0 et M3

Y= Difference of PSQI between D0 et M3

Figure 3: **Difference of THI between D0 and M3 in function of the difference of the PSQI between D0 and M3.(p-value <0.01)**



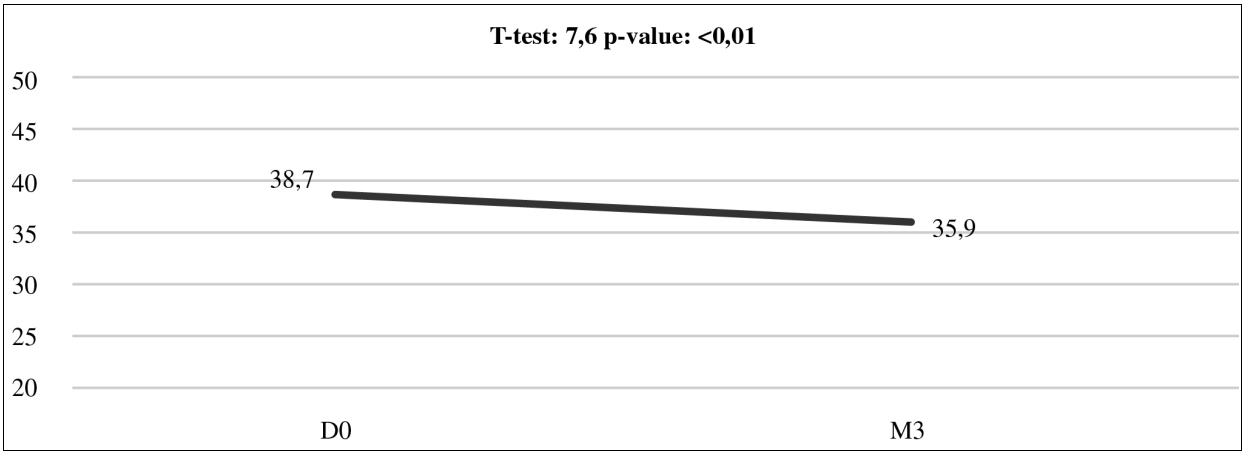


Figure 4: **Evolution of the MSP-9 score between D0 and M3 (p-value <0.01)**