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TREATMENT OF RECENT ONSET TINNITUS-SUBJECTIVE RELIEF WITH INTRAVENOUS AND INTRATYMPANIC REGIMENS

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Abstract

Tinnitus is phantom auditory sensation felt in one or both ears without external sound stimulus. It can be continuous or pulsatile. Among the most accepted hypothesis of pathophysiology is the one relating to the production of electrical impulses adjacent to the area of loss of outer hair cells of cochlea. Innumerable methods of treatment for tinnitus are described in the literature with variable results of cure and control. Few among them are Intratympanic injection of steroids and lignocaine; infusions of Piracetam in addition to supportive therapy. To evaluate the therapeutic effect of drugs formulated into three schedules on the subjective relief of tinnitus.

MATERIALS AND METHODS: 138 patients 80 males and 58 females, selected randomly from among the patients attending the ENT department. Divided into three groups; A: Intratympanic lignocaine, Alprazolam 0.5mg, injection of B1,B6 and B12; B: Intratympanic Dexamethasone, Alprazolam 0.5 mgs, Gingko Biloba 40 mgs, C: Intravenous Piracetam, Alprazolam 0.5mgs, vinpocetin.

RESULTS: The effective treatment among the three groups was the combination of intravenous infusion of Piracetam, Alprazolam and Vinpocetin regimen in treating moderate to severe grades of recent onset tinnitus.

CONCLUSION: All patients showed significant response to their respective regimens for mild grade of tinnitus. I.V. Piracetam gave significant response to subjective relief of tinnitus in intolerable, severe and moderate grades.

INTRODUCTION

Tinnitus is defined as subjective sensation of sound, in the absence of external sound stimulus (1). It is one of the most common ENT medical symptoms. Transient and short duration tinnitus is more common and persistent form occurs in 10% to 15% of the adult population; 2% of the patients may develop a severely restricted quality of life (2). Tinnitus can occur continuously, intermittently or in pulsatile manner. It can be heard in one ear or both ears or can be heard in the head. The intensity of the tinnitus may vary from low to a very high frequency, which cannot be masked with any external noise. Tinnitus is more common in males than in females (3). Tinnitus may be due to noise trauma, inner ear damage or related to somatic system of cervical spine or TM joint (2). Tinnitus is heterogeneous clinically because of its etiology, nature of perception associated symptoms. In addition to the

physical noise, it involves cognitive, emotional and memory components. The important risk factor for tinnitus is old age. Tinnitus due to cervical spine degenerative changes is explained by connections between the dorsal column of the spinal cord and the cochlear nuclei (CN) which have been found in several animal studies (4, 5). These axons of the dorsal column originate from the C1-C8 dorsal roots of the spinal cord. In particular, stimulation of the C2 dorsal root ganglion generates responses from cells in the CN (6). Partial or complete remission is possible, but tinnitus usually becomes chronic (7). Controlled studies on ultimate therapeutic results for tinnitus are lacking except to control of tinnitus. Among those available they do not take the symptom duration into consideration; majority of the patients having tinnitus for more than one year are studied. Hence the present study is conducted to know the therapeutic effect of the medicines used and subjective improvement from tinnitus in the patients with recent onset of tinnitus (3 days to 3 months).

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MATERIALS AND METHODS

From March 2010 to July 2012 a prospective study of patients with complaints of tinnitus, attending the Government General hospital attached to Kakatiya Medical College, Warangal was conducted. The patients with recent onset of tinnitus within 3 months period were included in the study. Complaints in unilateral or bilateral tinnitus were included. Following inclusion and exclusion criteria were used to select the patients. As persistent tinnitus for more than 6 months is considered to be chronic, the present study included patients presenting with complaints between 3 days to 60 days as tinnitus of recent origin. Informed consents from the patients were obtained and ethical committee approval was taken before starting the study. **Inclusion criteria:** 1. Persistent subjective peripheral tinnitus for more than 3 days and less than 60 days. 2. Patients age above 20 years. 3. Patients with hearing loss in one or both ears bilateral. 4. Patients with sudden onset of Hearing loss. **Exclusion Criteria:** 1. Patients with fluctuating tinnitus. 2. Patients age below 20 years. 3. Patients complaining of intermittent tinnitus. 4. Patients with tinnitus resulting from traumatic head or neck injury. 4. Patients with presence of chronic tinnitus. 5. Patients with suspected or diagnosed Meniere's disease or vertigo 6. History of repeated idiopathic sudden sensorineural hearing loss (defined as at least two events of ISSNHL in the last 24 months) or history of acoustic neuroma. 7. Patients with acute or chronic otitis media or otitis Externa. 8. Abnormality of the tympanic membrane in the affected ear(s). 8. Subjects with current unilateral or bilateral hearing loss of 90 dB or more in one or more test frequencies (250 Hz, 500 Hz, 1 kHz, 2 kHz, 3 kHz, 4 kHz, 6 kHz, and 8 kHz). 138 patients were randomly divided into 3 groups each consisting of equal number of 46 patients. The mean duration of tinnitus symptom was 32 days. The mean age was 53 years. All the patients underwent thorough ENT clinical examination, otomicroscopy, audiometry and clinical vestibular tests before and after the completion of the regimens. **Group A regimen:** Intratympanic injection of 0.3 to 0.5 ml of Injection 2% xylocaine once a week for 4 weeks, Tab Alprazolam 0.5mgs twelfth hourly daily for 4 weeks, Inj B1+B6+B12 commercial preparation Intramuscularly on

alternate days for 4 weeks. **Group B regimen:** Intratympanic injection of 0.5 ml of Injection Dexamethasone 0.3 to 0.5 ml of 4mg/ml weekly once for 4 weeks, Tab Alprazolam 0.5 mgs twelfth hourly for 4 weeks, Tab Gingko Biloba 40mgs 8th hourly for four weeks. Tab Vinpocetin. **Group C Regimen:** Intravenous Injection Piracetam 10 g/day diluted in 250 ml of saline solution and administered in a 15-minute intravenous infusion for three days consecutively followed by Tab Piracetam 800 mgs twelfth hourly for 4 weeks, Tab Alprazolam 0.5 mgs twelfth hourly for 4 weeks, Tab Vinpocetin (cavinton) 10 mgs 8th hourly daily for 4 weeks, There was no objective method of measuring the relief in tinnitus. The improvement was measured by a VAS with 0 to 10 points of subjective expression of the symptom tinnitus. **FOLLOWUP:** After 4 weeks of initial therapy with the prescribed regimens, all the patients were followed up at 6 weeks, 3 months, 6 months 9 months and 15 months. Patients not responding to the regimens were treated as chronic tinnitus with other modalities not included in the study. In the present study the maximum follow up till the submission of the paper is 15 months and the minimum follow up is 9 months. At the end of 6 months VAS score was used to record subjective improvement from tinnitus and the statistical analysis was done using Mann Whitney U value calculator. **CRITERIA FOR RELIEF OF TINNITUS:** Subjective improvement from tinnitus described by the patient as mild, moderate and maximum relief. In a VAS score of 0-10, 0 is absence of tinnitus, mild is 1-3, moderate is 4-6 and severe is 7-9; 10 is taken as intolerable tinnitus. Similarly the relief or regression of tinnitus at the end of the 6 months period is recorded on VAS score. Reliefs of accompanying symptoms like anxiety, depression are recorded. Associated symptoms like loss of hearing, vertigo, ear blockage and increase in tinnitus following therapy are also recorded. Duration of persistence of relief after 6 months is noted. Patients reported relief based on their symptom of tinnitus before and after the completion of the regimens. If there was no tinnitus it indicated 100% improvement and if there was change in tinnitus then the improvement is taken as 0%.

OBSERVATIONS

138 patients included in the present study were randomly selected from the patients attending the ENT department of Government General Hospital attached to the Kakatiya Medical College, Warangal between March 2010 and July 2012. The total OPD turn out in this regional Hospital was 479876 during that period. 9246 were patients attending the ENT department in that period. The prevalence of tinnitus calculated from the above data in this study was 0.74%. The youngest patient was aged 21 years and the eldest patient was 80 years. The mean age was 52.52 with SD 16.98 **(Table 1).** Present study included 80 (57.97%) males and 58 females (42.02%). Sex ratio was 1:1.37 with male preponderance **(Table 2).**

Table 1: Showing the Age related statistics; Mean, Median and Mode with SD values (n=138).

Observation	Total Patients (138)	Group A (46)	Group B (46)	Group C (46)
Mean	52.52	52.78	53.23	51.54
Standard deviation	16.98	15.56	17.76	17.83

Table 2: Showing the incidence of sex in the study (n=138).

Sex	Males	Percentage	Females	Percentage
Number	80	57.97	58	42.02

The incidence of tinnitus in the age group of 21-30 was 14 (11.5%), in group 31-40 it was 17 (12.31%), in 41-50 it was 25 (18.11%), in 51-60 years 24 (17.39%), in 61-70 group 30 (21.73%) and in 71-80 it was 26 (18.84%)-(Table3). The incidence of tinnitus between ages of 41 to 70 years accounted for more than 50% of the study group **(Table 3).**

Table 3: Showing the incidence according to Age group and sex (n=138).

Age Group	Group A	Group B	Group C	Group A-46		Group B-46		Group C-46	
	(46)	(46)	(46)	Male-(29)	Female-(17)	Male-(26)	Female-(20)	Male-(25)	Female-(21)
21-30 Yrs	04	06	06	02	02	04	02	03	03
31-40 Yrs	05	04	08	03	02	02	02	05	04
41-50 Yrs	09	08	08	06	03	05	03	03	03
51-60 Yrs	08	10	06	05	03	05	05	03	04
61-70 Yrs	12	08	10	07	05	04	04	06	04
71-80 Yrs 0	08	10	08	06	02	06	04	05	03

The incidence of tinnitus in both ears was 67 (48.55%) and only in one ear were 71 (51.44%). The incidence of tinnitus in females was equal in affection to single ear or both ears 29 (21.01%) **(Table 4).**

Table 4: Showing the incidence of unilateral or bilateral tinnitus in both sexes (n=138).

Observation	Percentage %		Group A-46		Group B-46		Group C-46	
	Male	Female	Male	Female	Male	Female	Male	Female
Unilateral	58.75	67.24	18	10	12	10	12	09
Bilateral	41.25	32.75	11	07	14	10	13	12

In the present study the duration of symptom prior to starting the treatment was ranging from 3 days to 60 day with a mean duration of 31.28 and SD 17.56. Similarly the mean is calculated for all the three groups of A, B and C **(Table 5).**

Table 5: Showing the mean duration before starting treatment (n=138).

Duration before Treatment	Total Patients-138	Group A	Group B	Group C
Mean	31.28	31.80	30.13	31.8
Std deviation	17.56	17.13	16.16	19.09

Tinnitus was graded according to the subjective quantification by the patients on a VAS scale of 0 to 10 points. The tinnitus was graded as Mild for VAS score between 1 and 3, Moderate grade with VAS score between 4 and 6 and severe grade with VAS score between 7 and 9. Vas score 0 is taken as no tinnitus and VAS score 10 is regarded as intolerable tinnitus. Mild tinnitus was seen in 21.73% of the patients, moderate in 34.05% and severe grade in 37.67% of total patients (**Table 6**).

Table 6: Showing Grading of tinnitus on VAS score (n=138).

Grading Tinnitus	Percentage		Group A-46		Group B-46		Group C-46	
VAS	Male	Female	Male	Female	Male	Female	Male	Female
Mild (VAS 1-3)	13.04	8.69	07	04	06	04	05	04
Moderate (VAS 4-6)	18.11	15.94	09	06	09	07	07	09
Severe (VAS-	23.18	14.49	11	06	10	08	11	06

7-9)								
Intolerable (VAS 10)	3.62	2.89	02	01	01	01	02	02

Hearing assessment with pure tone audiometry done and PTA calculated for all the patients, showed mild HL in 14.49%, moderate in 23.91%, moderate to severe in 23.18%, severe in 25.36% and profound HL in 13.04% of patients **(Table 7).** Severe (71-90 B HL) Air conduction loss was seen in frequencies of 4, 6 and 8KHZ in all the groups. It ranged between 13.04% and 28.26%. Normal PTA was seen in 7.24% of the patients. **(Table 8).**

Table 7: Showing the PTA values in the patients with tinnitus (n=138).

Hearing Loss	**Group A-46**		**Group B-46**		**Group C-46**		**Percentage**	
PTA	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**n=138**	
Normal	**02**	**01**	**01**	**01**	**03**	**02**	**7.24**	
26-40 dB	**04**	**02**	**04**	**03**	**04**	**02**	**13.76**	
41-55 dB	**06**	**04**	**06**	**04**	**05**	**04**	**21.01**	
56-70 dB	**06**	**05**	**06**	**06**	**05**	**05**	**23.91**	
71-90 dB	**08**	**05**	**06**	**05**	**05**	**05**	**24.63**	
91- >90 dB	**03**	**00**	**03**	**01**	**03**	**03**	**09.42**	

Table 8: Showing the High frequency loss of hearing in Tinnitus patients (n=138).

Frequency	**Group A**		**%**	**Group B**		**%**	**Group C**		**%**
AC:71-90 dB	**Male**	**Female**		**Male**	**Female**		**Male**	**Female**	
4000KHZ	**04**	**04**	**17.39**	**03**	**03**	**13.04**	**06**	**04**	**21.73**
6000KHZ	**07**	**08**	**32.60**	**06**	**07**	**28.26**	**08**	**05**	**28.26**
8000KHZ	**06**	**05**	**23.91**	**08**	**08**	**34.78**	**08**	**05**	**28.26**

Post treatment subjective evaluation on VAS scoring at specified intervals showed persistence of tinnitus or relief from tinnitus from higher grade to lower grades. The efficacy of the treatment schedules of three regimens is shown in **Table 9, 10 and 11**. A comparative analysis of these results was done using Mann Whitney P value calculator. It showed that patients of group C regimen showed better control of tinnitus compared to other group patients. Group C therapeutic regimen was efficient in relieving the tinnitus of Intolerable, severe, moderate grades VAS scores when compared to group A and B (P- value less than 0.05). But there was no statistical significance between groups A, Band C in controlling tinnitus of mild grade. There was no statistical significance between Group A and B in controlling any of the grades of tinnitus. There was statistical significant between group B and C in controlling the severe and moderate grades of tinnitus **(Table 10).**

Table 9: Showing the post treatment results (VAS score) in patients of Group A (n=46).

Time of recording VAS	**Group A**			
	Persistence of score 10	**Severe to Moderate 17**	**Moderate to Mild 15**	**Mild to normal**
2 Weeks	**3**	**3**	**05**	**04**
6 Weeks	**3**	**09**	**07**	**07**
3 Months	**2**	**09**	**08**	**09**
6 Months	**1**	**11**	**10**	**10**
9 Months	**1**	**10**	**10**	**10**

15 Months	**1**	**09**	**08**	**11**

Table 10: Showing the post treatment results (VAS score) in patients of Group B (n=46).

Time of recording VAS	Group B			
	Persistence of score 10	Severe to Moderate 17	Moderate to Mild 15	Mild to normal
2 Weeks	**02**	**04**	**06**	**05**
6 Weeks	**02**	**10**	**09**	**05**
3 Months	**02**	**10**	**09**	**05**
6 Months	**02**	**09**	**08**	**03**
9 Months	**01**	**08**	**09**	**03**
15 Months	**01**	**06**	**09**	**03**

Table 11: Showing the post treatment results (VAS score) in patients of Group C (n=46).

Time of recording VAS	Group C			
	Persistence of score 10	Severe to Moderate 17	Moderate to Mild 15	Mild to normal
2 Weeks	**0**	**15**	**10**	**08**
6 Weeks	**0**	**16**	**11**	**08**
3 Months	**0**	**15**	**11**	**07**
6 Months	**0**	**13**	**12**	**06**
9 Months	**0**	**13**	**12**	**07**
15 Months	**0**	**13**	**12**	**09**

Table 12: Showing the comparison between the three groups in their efficacy and their statistical significance.

Comparison of efficacy between groups	VAS score conversion	Z score	P value	U value	Statistical significance
Group A and C At 2 weeks, 6 weeks, 3 months, 6 months ,9 months and 15 months period	VAS 10	2.8022	0.00512	0	Significant
	Severe to Moderate	-2.8022	0.00512	0	Significant
	Moderate to Mild	-2.6421	0.0083	1	Significant
	Mild to Normal	1.1209	0.2627	10.5	Not significant
Group A and B At 2 weeks, 6 weeks, 3 months, 6 months ,9 months and 15 months period	VAS 10	0.0801	0.936	17	Not significant
	Severe to Moderate	0.4804	0.6312	14.5	Not significant
	Moderate to Mild	-0.3203	0.7489	15.5	Not significant
	Mild to Normal	1.1209	0.2627	10.5	Not significant
Group B and C	VAS 10	1.8415	0.06576	6	Not significant

At 2 weeks, 6 weeks, 3 months, 6 months ,9 months and 15 months period	Severe to Moderate	-2.8022	0.00512	0	significant
	Moderate to Mild	-2.8022	0.00512	0	significant
	Mild to Normal	-2.8022	0.0512	0	significant

Evaluation of associated symptoms showed in 83% of patient's significant relief in group C patients compared to other groups. 76% of the group C patients showed 5 to 10 dB improvement in thresholds in higher frequencies. Whereas 47% of patients belonging to group A and 51% of patients of group B showed improved Air conduction thresholds in higher frequencies. 46% Patients of group A experienced vertigo following Intratympanic injection of xylocaine. There were no complaints exaggerations of tinnitus in any of the patients of three groups. No complications or side effects noted

DISCUSSION

As the etiology of tinnitus is markedly varied, so is the variability in the treatment outcome seen in the different clinical trials. Clinical diagnosis and confirmation of purely cochlear type of tinnitus is the key to achieve a high degree of efficacy in the therapies selected (8). Evaluating the intensity and pitch of tinnitus is critical in diagnosing the etiology and to study the therapeutic response to different drugs used. Tinnitus can also be assessed by psychoacoustic methods and by subjective rating scales (VAS) (9). In the present study VAS is used to evaluate the patients with tinnitus before and after treatment. There are many diversified protocols of treatment are available for tinnitus. The important are counseling, cognitive behavioral therapy and various types of sound therapies. These may be used as a single or in combination (10). Even though there is no single approved drug in the market for the treatment of tinnitus over 4 million prescriptions are written every year for tinnitus relief in Europe (11). In few patients tinnitus causes depression, anxiety, irritability, insomnia and interferes with normal life leading to suicidal tendencies, so even a drug that produces a small and significant effect will have a huge therapeutic effect (12). Sudden onset of Tinnitus may be for short duration (temporary) of few days to weeks or prolonged (permanent) over few months to one year or more. Prognosis is good in patients with early treatment. In majority of the patients tinnitus is associated with hearing loss; suggesting common cochlear pathology, even though few cases of tinnitus take origin from somatic innervations. The intensity and the pitch of tinnitus are usually similar to the hearing loss frequency of the lesion or just below the actual loss of frequency. Reduction in the signal intensity from the damaged hair cells results in reduced lateral inhibition at the dorsal cochlear nucleus or inferior colliculus into a characteristic frequency, leading to hyperactivity in the neurons of the auditory nerve at the edge of the frequency site, experienced as tinnitus by the individual (6). Tinnitus is produced by cochlear damage at the initial stage, when it remains reversible and treatable. The pathophysiology of tinnitus shows that the tinnitus is an altered neuronal activity hence transmitted through neuromodulators or neurotransmitters and hence can be treated pharmacologically. Among the many medical treatment protocols described for tinnitus in the literature, Intratympanic steroids is a promising modality similar to their use in the treatment of sudden hearing Loss (13). Another drug is voltage-gated sodium channel blocker lignocaine, when used intravenously showed transient dose dependent relief in tinnitus. The drug was unstable biologically given orally. The effect was short lasting and side effects were many (14). Intra dermal injection of lignocaine is also described as having produced good results (15). There is no clear cut border described in the literature defining acute and chronic tinnitus. In the present study an approximate distinction is made to consider less than 3 months duration as acute. Majority of clinical cases of tinnitus resolve spontaneously especially those patients having associated loss of hearing. The treatment regimens directed towards loss of hearing have also beneficial effect on the tinnitus recovery. The treatment strategies include systemic and Intratympanic steroids (16). Glucocorticoid receptors are found on the walls of cochlea and also the enzymes Na, K-ATPase involved in production and regulation of endocochlear potentials and regulation of fluid-ion flow in the cochlea necessary for normal function of cochlea (17). In the present study Injection Dexamethasone 4mgs/ml concentration is used through Intratympanic route. Alprazolam acts as GABA agonist causing increased permeability if chloride ions leading to hyper polarization and diminished excitability (18). Its role is studied in

double blind studies show that it reduces tinnitus loudness, measured with a tinnitus synthesizer (18). The active principle in Gingko Biloba, bioflavonoid glycoside is known to be vasodilator and to decrease viscosity and both of them improve blood supply to the cochlea 19). Gingko Biloba is antagonist to platelet activating factor and prevents damage caused by free radicals (20). Vinpocetin (cavinton) is known to increase the blood flow to brain by decreasing the viscosity of blood, platelet aggregation and intravascular coagulation and by increasing the RBC deformability. It has also an anti oxidant property and neuroprotective properties (21). Piracetam increases neuronal transmission and cell metabolism in cellular hypoxia. It has favorable action on neuronal glucose and oxygen metabolism. It has several vascular effects on microcirculation, capillary perfusion and platelet aggregation. It decreases red blood cell perfusion and increase red cell deformability (22). In a study by Solanellas Soler J et al, Intravenous administration of 10Gms/day Piracetam diluted in 250 ml of saline administered in 15 minutes, as a three day course showed no side effects. 50% of the ears showed improved hearing. Eight (89%) patients had vestibular symptoms (23). García Callejo et al studied using Piracetam and steroids and compared vasodilators with steroids in the treatment of sudden deafness with tinnitus and found usefulness of rheoactive properties of Piracetam (24). Gutmann R, Mees K conducted a study on patients with sudden HL with acute tinnitus treated with intravenous Piracetam and Naftidrofuryl; "The improvement in tinnitus amounted 27 dB (Piracetam) and 19.9 dB (naftidrofuryl). Both the differences were not significant" (25). The present study is conducted to evaluate the response to three different regimens formulated, after going through the literature for their mode of action and reviewing the results of their efficacy. Intratympanic injection of Dexamethasone and Lignocaine and intravenous Piracetam were considered as the first line drugs in acute tinnitus as they are known to produce immediate relief. In all the regimens Alprazolam is added keeping in view of the associated symptoms in the patients with tinnitus like anxiety and depression. Gingko Biloba, Vinpocetin and B1, B6 and B12 are used as anti oxidants and to give supportive therapy. Patients assorted to the three groups are randomly picked up from among the patients attending the ENT OPD for tinnitus of less than 3 months duration. After completion of the regimens the patients are assessed for improvement with the help of VAS. Analysis of the data was done with the help if Mann Whitney U value calculator to know the P value and significance between the groups of regimen administered to the patients. Efficacy of the three regimens was compared for significance at the end of 2 weeks, 6 weeks, 3 months, 6 months 9 months and 15 months periods. When the two groups of A and C are compared, Patients of group C with VAS score 10 showed significant relief (Total relief) compared to group A. The Z-score was 2.8022. The P-value was 0.00512. (The result was significant at $P \leq 0.05$). The U- value is 0. The critical value of U at $P \leq .05$ is 5. Therefore, the result was significant at $P \leq 0.05$. Similar comparison of efficacy for other grades of tinnitus showed statistical significance for severe to moderate, moderate to mild grades also. But there was no significance for mild group between A and C groups (Table 10). Similar comparison between B and C groups showed relief of tinnitus which was statistically significant for severe to moderate and moderate to mild groups. There was no significance in group A and B for >10 VAS score group and mild groups (Table 10). Follow up at 6 months, 9 months and 15 months also showed no recurrence of tinnitus in patients showing significant response. Associated symptoms like anxiety, depression and insomnia also showed improvement.

CONCLUSION

Intravenous therapy with Piracetam in combination with oral Alprazolam and Vinpocetin showed significant relief from tinnitus for patients selected randomly with similar demographic features in comparison with Intratympanic administration of xylocaine, Alprazolam and B1, B6 and B12 supplementation. The study also showed significant response to I.V. Piracetam in combination with Vinpocetin when compared to Intratympanic steroids and oral Gingko Biloba. Relief from associated symptoms of anxiety, depression and insomnia was seen in. There were no untoward effects of the treatment regimens used in the present study except to vertigo in patients treated with Intratympanic xylocaine.

REFERENCES

1. *Landgrebe M, Azevedo A, Baguley D, Bauer C, Cacace A, Coelho C, Dornhoffer J, Figueiredo R, Flor H, Hajak G, van de Heyning P, Hiller W, Khedr E, Kleinjung T, Koller M, Lainez JM, Londero A, Martin WH, Mennemeier M, Piccirillo J, De Ridder D, Rupprecht R, Searchfield G, Vanneste S, Zeman F, Langguth*

B: Methodological aspects of clinical trials in tinnitus: a proposal for an international standard. J Psychosom Res 2012. 73. 112-121.

2. *Baguley D, McFerran D, Hall D: Tinnitus. Lancet 2013. 382. 1600-1607.*

3. *Ahmad N, Seidman M. Tinnitus in the older adult: epidemiology, pathophysiology and treatment options.Drugs Aging. 2004. 21. 5. 297–305.*

4. *Zhan X, Pongstaporn T, Ryugo DK: Projections of the second cervical dorsal root ganglion to the cochlear nucleus in rats. J Comp Neurol. 2006. 496. 335-348.*

5. *P faller K, Arvidsson J. Central distribution of trigeminal and upper cervical primary afferents in the rat studied by anterograde transport of horseradish peroxidase conjugated to wheat germ agglutinin. J Comp Neurol. 1988. 268. 91-108.*

6. *Kanold PO, Young ED. Proprioceptive information from the pinna provides somatosensory input to cat dorsal cochlear nucleus. J Neurosci. 2001. 21. 7848-7858.*

7. *Eggermont JJ, Roberts LE. The neuroscience of tinnitus. Trends Neurosci. 2004. 27. 11. 676–682.*

8. *Shulman A. Medical Audiologic Tinnitus Protocol. In A Shulman, JM Aran, H Feldman, et al. (eds), Tinnitus Diagnosis and Tretment. Philadelphia: Lea& Febger. 1991. 319-321.*

9. *Adamchic I, Langguth B, Hauptmann C, Tass PA. Psychometric evaluation of Visual Analog Scale for the assessment of chronic tinnitus. Am J Audiol. 2012. 21. 2. 215- 25.*

10. *Cima RF, Maes IH, Joore MA, et al. Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. Lancet. 2012. 379. 1951-9.*

11. *Vio MM, Holme RH. Hearing loss and tinnitus: 250 million people and a US $10 billion potential market. Drug Discov Today 2005. 10. 1263-5.*

12. *Langguth B. Tinnitus: the end of therapeutic nihilism. Lancet. 2012. 379. 1926-8.*

13. *Thomas Meyer. Intratympanic treatment for tinnitus: A review. Noise and Health. 2103. 15. 63. 83-90.*

14. *Melding PS, Goodey RJ, Thorne PR. The use of intravenous lignocaine in the diagnosis and treatment of tinnitus. J Laryngol Otol. 1978. 92. 115-21.*

15. *Rauschecker JP, Leaver AM, Muhlau M. Tuning out the noise: limbic-auditory interactions in tinnitus. Neuron. 2010. 66. 819-26.*

16. *Slattery WH, Fisher LM, Iqbal Z, et al. Intratympanic steroid injection for treatment of idiopathic sudden hearing loss. Otolaryngol Head Neck Surg. 2005. 133. 251-9.*

17. *Salt A, Melichar I, Thalmann R. Mechanisms of endocochlear potential generation by stria vascularis. Laryngoscope. 1987. 97. 984- 991.*

18. *R. Salvi, E. Lobarinas, and W. Sun. Pharmacological treatments for tinnitus: New and Old. Drugs Future. 2009. 34. 5. 381–400.*

19. *Kajsa –Mia Holgers, Alf Axelsson, Inger Pringle. Gingko Biloba extracts for the treatment of Tinnitus. Audiology. 1994. 33. 85-92.*

20. *Hoffman F, Beck C, Schultz A, Offerman P. Ginkgo extract EGb 761 (tenobin)/HAES versus naftidrofuryl (Dusodril)/HAES. A randomized study of therapy of sudden deafness. 1994. 73. 3. 149-52.*

21. *Szirmai A. Experiences with complex vestibular rehabilitation. Int Tinnitus J. 2012. 17. 2. 112-116.*

22. *Packard B, Debetdt W, Vleymen BV. Nootropil monograph. 1996.Budapest. Pharma press.*

23. *Solanellas Soler J, Esteban Ortega F, Soldado Patiño L, Jiménez Morales JM. Sudden hearing loss. Treatment with Piracetam Acta Otorrinolaringol Esp. 1997 . 48. 1. 21-5.*

24. *García Callejo FJ, Velert Vila MM, Morant Ventura A, Orts, Alborch MH, Marco Algarra J, Blay Galaud L. Acta otorrinolaringológica española. 2000. 51. 4. 319- 26.*