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Original Article

Clinical management of tinnitus

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Abstract

Aim: Tinnitus is defined as the perception of sound or sounds without any external audible source. Unknown ethiopathological mechanisms with lack of standardized protocol in symptom evaluation, causes difficulties in clinical management. Therefore, we aimed to evaluate the efficacy of magnesium, misoprostol and lidocaine treatments in patients with tinnitus.

Material and Methods: The 58 tinnitus cases, were evaluated retrospectively. A total number of 40 patients who were able to comply with the scheduled therapy were received two staged therapy. As first line therapy, 20 patients with sensorineural hearing loss and acoustic trauma history were received oral magnesium, while remaining 20 cases without hearing loss were received oral misoprostol. Tinnitus handicap inventory (THI) was applied to all patients before and one month after the therapy. As second line therapy, 1.5mg/kg intravenous lidocaine was administered to the patients who had ineffective treatment results according to the THI.

Results: The 40 patients included in this study were 10 female (25%), and 30 male (75%) and the mean age of all patients was 41,47 years. In both magnesium and misoprostol group, the mean scores of post-treatment THI were significantly lower than pre-treatment THI scores (p-values=0,001 and 0,007, respectively). No statistically significant difference was found between pre - and post treatment scores of the THI in lidocaine group.

Conclusion: In present study, it was demonstrated that magnesium treatment is effective on tinnitus cases with acoustic trauma and misoprostol is effective on normal hearing tinnitus group, whereas intravenous lidocaine treatment was not found to be effective in tinnitus.

Keywords: Lidocaine; magnesium; misoprostol; tinnitus; tinnitus handicap inventory; tinnitus management

INTRODUCTION

Tinnitus is the perception of sound(s) by only patient in the absence of any external audible source. It is accepted widely as a symptom rather than a disease (1). Various types of perceived sounds (ringing, buzzing, humming etc.) may manifest as continuously or intermittently, unilaterally or bilaterally, or in the head (2). Prevalence of tinnitus among general adult population is approximately 10-15%, while 1-3% of them are reported as severely and disturbing (1). As a heterogeneous disorder tinnitus is frequently associated with varying degrees of hearing loss and older age. In addition, some studies reported higher incidence of older age-related tinnitus and hearing loss in male gender (3).

Although pathophysiology of tinnitus has been tried to explain by possible mechanisms such as 'hair cell' damage or auditory neuronal dysfunction, no consensus was reached and numerous etiological approaches were emerged up to now (2,4). Exposure to loud noises, ototoxic agents, head traumas, otitis media, otosclerosis, alcohol consumption and hypertension are frequently reported causes (4,5). Moreover magnesium, mostly reported as a beneficial therapeutic agent for noise induced hearing loss and tinnitus, is recently indicated to play an important role in tinnitus pathology. Furthermore, application of lidocaine which provides a temporary relief in subjective tinnitus cases is shown to decrease magnesium levels, and it is also demonstrated that lidocaine perfusion significantly regulates magnesium levels (6).

Especially in cases with severe tinnitus; reductions in quality of life, depression, anxiety, stress, cognitive dysfunctions and insomnia are frequently reported (7). Since tinnitus is only perceived by the patient and also absence of any standard protocol in assessment, tinnitus management depends on self-reported measures and the hearing test results (1,8). 'Tinnitus Handicap Questionnaire' (THI) widely accepted, reliable and effective tool for clinical applications to assess tinnitus on daily life (9).

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Magnesium, misoprostol and lidocaine treatments were frequently applied and assessed for their efficacy on tinnitus up to now (10,11). Although none of the therapeutic approaches eliminated the noise perceived by the patients completely, cognitive behavioral effects of the therapies are shown to improve the quality of life and significantly lessen the perceived noise (12). Thus, multi-disciplinary treatment options with a multi-professional approach are essential in tinnitus management. Therefore, we aimed to contribute to the algorithm of tinnitus treatment by assessing efficacy of oral magnesium in acoustic trauma-related tinnitus, and oral misoprostol in cases with normal hearing results. We also aimed to demonstrate the intravenous lidocaine efficacy in cases that did not benefit from the first line therapy according to the THI results.

MATERIAL and METHODS

This study was performed with the Institutional Review Board protocol approval date 25/05/2013 and number 4 in Karadeniz Technical University Faculty of Medicine, Department of Otorhinolaryngology between January 2011 and January 2012. In this study, 58 patients aged between 18-50 years old with tinnitus complaints were evaluated retrospectively.

Inclusion criteria defined as; existence of tinnitus at least for 6 months duration, absence of air-bone gap in none of the frequencies with pure tone audiometry, and controlled hypertension. Subjects with hearing-aid, history of ear surgery, presence of any pathology which may cause tinnitus (Meniere's disease, chronic otitis, otosclerosis), hearing loss, any neuropsychiatric, metabolic, or systemic disease, pregnancy as well as patients who did not comply with the scheduled therapy were excluded from present study. Additionally participants were enrolled in the study after obtainment of written informed consent. After complete clinical, otorhinolaryngology, and pure tone audiometric examinations 18 patients who did not met inclusion criteria and also did not comply with the therapy were excluded from the study. Remaining 40 patients (30 male and 10 female) with mean pure-tone 25 dB and above were included and evaluated.

Measures

Tinnitus Handicap Inventory (THI): A self-report scale that created by Newman et al. in order to evaluate tinnitus effects in patients. Turkish validity and reliability was performed by Aksoy et al. in 2007.13,14 The scale consists of 25 items and further divided into 3 subscales to assess emotional, catastrophic and functional effects of tinnitus. Each item scale ratings range from 0 (no) to 4 (yes). Participants are evaluated in five levels depending on their scores;

• 0-16 Grade 1 = Slight - Only heard in quiet environments.

• 18–36 Grade 2 = Mild - Easily masked by environmental sounds and easily forgotten with activities.

• 38-56 Grade 3 = Moderate - Noticed in presence of background noise, though daily activities can still be performed.

• 58-76 Grade 4 = Severe - Almost always heard, leads to disturbed sleep patterns and can interfere with daily activities.

• 78–100 Grade 5 = Catastrophic - Always heard, disturbed sleep patterns, difficulty with any activities (13,14).

Audiological Assessment: All audiometric assessments were performed by an audiometry device (Madsen Orbiter Audiometer, 922, Denmark) in accordance with the "Industrial Acoustic Company (IAC)" standards. Pure-tone air- and bone-conduction thresholds were 250-8000 Hz, and 500-4000 Hz respectively. Pure-tone averages (PTA) were calculated for three frequencies; 250 Hz+500 Hz low, 1000-2000 Hz, and 4000-8000 Hz high.

Treatment protocol: Patients were divided into two treatment groups for the first line therapy; magnesium group (n=20) includes patients with acoustic trauma history, or sensorineural hearing loss and misoprostol group (n=20) with no acoustic trauma history and without hearing loss. Magnesium group patients are treated with an oral magnesium 300 mg/day (Magnesium-Diasporal a sachet once a day)(Assos Pharma/Turkey) for one month, while misoprostol group patients are treated with an oral misoprostol 800 µgr/day (Cytotec/Pfizer/USA) (1 tablet 4 times a day) for one month.

All patients were evaluated with THI scale before and 1 month after the therapy. Reduction of 10 points or more in THI scores were considered to be significant. Whereas reduction of less than 10 points in THI scores is considered as an inadequate treatment, thus patients were treated with 1.5mg/kg intravenous lidocaine (Jetokain/Adeka/Turkey) (Aritmal 2% 2 ml ampoule) as second line therapy (lidocaine group). Effectiveness of the second line therapy is also evaluated by THI one month after the treatment.

All patients' demographic features, laboratory results, audiological data, internal acoustic channel magnetic resonance imaging, and pre / post-treatment scores of the THI are evaluated and compared between groups.

Statistical analysis

All the data were analyzed with SPSS (Statistical Package for the Social Sciences) software for Windows (v21.0; IBM, Armonk, NY, USA). Individual and aggregate data were summarized using descriptive statistics including mean, standard deviations, medians (min-max), frequency distributions and percentages. Normality of data distribution was verified by Kolmogorov-Smirnov test. Comparison of the variables with normal distribution was made with Student T Test and Paired Sample T Test. The variables which were not normally distributed, the Mann Whitney and Kruskal Wallis tests were conducted to compare between groups. Evaluation of categorical variables was performed by Chi-Square test. P-Values of <0.05 were considered statistically significant.

RESULTS

The 40 patients included in this study were 10 (25%) female, 30 (75%) male, (male/female ratio 3.0) and mean age of total participants were 41.47 (Ranged=21-50). The average duration of tinnitus was 37,73 months (Ranged=12-120). Tinnitus was unilateral in 27 (67.5%) of the patients (10 right-sided, 17 left-sided) and bilateral in 13 (32.5%) patients. Of the patients 50% had history of acoustic trauma, 7.5% diabetes mellitus, and 20% hypertension. All cases (n=40) received first line treatment.

Second line treatment was applied to the total number of 15 patients (2 female, 13 male) who did not benefit from magnesium (8) and misoprostol (7) therapies.

The THI outcomes determined as 5% slight, 35% mild, 30% intermediate, 15% severe, and 15% catastrophic before the treatment; changed to 25% slight, 40% mild, 10% intermediate, 20% severe, and 5% catastrophic after the first line treatment (Table 1). Additionally, no statistically significant difference was observed in lidocaine group after the treatment.

Table 1. THI staging before and after treatment in cases.

	Magnesium Group n (%)		Misoprostol Group n (%)		Lidocaine Groupn (%)		Pre-therapy Total*	Post-therapy Total*
	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy		
Grade 1: Slight	0	5 (%25)	2 (%10)	5 (%25)	2 (%5)	3 (%20)	2 (%5)	10 (%25)
Grade 2: Mild	6 (%30)	5 (%25)	8 (%40)	11 (%55)	14 (%35)	7 (%46.7)	14 (%35)	16 (%40)
Grade 3: Moderate	6 (%30)	1 (%5)	6 (%30)	3 (%15)	12 (%30)	0	12 (%30)	4 (%10)
Grade 4: Severe	4 (%20)	7 (%35)	2 (%10)	1 (%5)	6 (%15)	4 (%26.7	6 (%15)	8 (%20)
Grade 5: Catastrophic	4 (%20)	2 (%10)	2 (%10)	0	6 (%11)	1 (%6.7)	6 (%11)	2 (%5)

* First stage treatment, before-after

The mean score of pre-treatment THI was 53.90±24.5 in magnesium group, and 40.5±20.2 in misoprostol group, whereas it was 45.0±28.2 in magnesium group and 27.6±14.0 in misoprostol group after treatment. Therefore the decreases in the mean scores of post-treatment THI were found statistically significant for both magnesium and misoprostol groups (p-values = 0,001 and 0.007 respectively). The mean score of pre-treatment THI was 41.60±26.6 and it was 39.20±26.9 after treatment in lidocaine group. No statistically significant difference was found between pre - and post treatment scores of the THI in lidocaine group (p = 0.492) (Table 2).

Table 2. Comparison of the mean THI scores between groups before and after treatment

Groups	THI Before Therapy Mean±SD	THI After Therapy Mean±SD	P-value
Magnesium	53.90±24.5	45.0 ±28.2	0.001*
Misoprostol	40.50±20.2	27.60±14.0	0.007*
Lidocaine	41.60±26.6	39.20±26.9	0.492

* = p<0.05 statistically significant

Table 3. Comparison of PTA values among groups before and after treatment

Groups	Right			Left		
	Pre-therapy (Mean±SD)	Post-therapy (Mean±SD)	P-value	Pre-therapy (Mean±SD)	Post-therapy (Mean±SD)	P-value
Magnesium						
PTA 1	15.16±6.25	15.66±6.7	0.366	16.5±7.13	16.5±6.44	0.850
PTA 2	19.41±8.52	18.16±8.34	0.234	20.21±8.12	19.78±8.31	0.342
PTA 3	40.83±15.9	40.66±15.5	0.974	42.0±16.6	42.66±17.2	0.285
Misoprostol						
PTA 1	10.66±4.78	13.33±5.51	**0.007***	9.33±4.53	11.0±4.06	0.063
PTA 2	12.0±3.65	11.16±3.67	**0.012***	13.2±3.60	12.9±3.80	**0.020***
PTA 3	21.33±4.63	20.33±3.88	0.063	21.33±3.80	20.33±5.39	0.105
Lidocaine						
PTA 1	13.3±6.2	14.2±7.06	0.234	14.0±7.0	14.4±6.8	0.680
PTA 2	16.5±7.49	15.11±6.91	0.290	16.9±8.1	15.9±7.9	0.310
PTA 3	33.1±16.2	32.2±15.3	0.480	33.3±15.0	35.11±16.4	**0.023***

* = p<0.05 statistically significant.
** = PTA1:250+500Hz/2, PTA2: 1000Hz+2000Hz/2 , PTA3:4000Hz+8000Hz/2

According to the evaluation of the efficiency of the treatment based on THI scores before and after treatment, differences in THI scores of 12 patients out of 20 (60%) in magnesium group, and 14 patients out of 20 (70%) in misoprostol group were 10 points and higher. Therefore efficiency of the treatment demonstrated to be statistically significant in magnesium and misoprostol groups (p-values = 0,001 and 0.007 respectively).

According to the evaluation of audiologic examination results in magnesium, misoprostol and lidocaine groups before and after treatment; no statistically significant difference was established between the mean values of PTA1 ,PTA2, PTA3 measured in left and right ear before treatment and mean values of PTA1, PTA2, PTA3 measured in left and right ear after the treatment (p<0,005) (Table 3).

DISCUSSION

Tinnitus is rapidly becoming a global problem due to increasing prevalence in recent years. Additionally, systemic meta-analyzes have highlighted that older age and male gender are more commonly associated with tinnitus (15). According to the data derived from National Health Interview Survey records for 75.764 participants in a cross sectional analysis conducted by Bhatt et al., tinnitus reported more prevalent in male gender with the mean age of 53.1 years (16). Tinnitus is frequently reported in studies with low incidence aged < 18 years, and its' prevalence gradually increasing with age. Finally the incidence rate peaks in the 6th decade (1,3). In accordance with these data, mean age of our sample group, which ranged between ages 18-50 years, was found 41.47 years and the male/female ratio was 3.0.

It was noted that approximately half of the individuals with tinnitus had none of the published risk factors specified in studies up to now (4). Furthermore it is also reported that no etiologic factors identified except hearing loss in 42.6% of the patients with tinnitus. Axelsson and Ringdahl reported in a study consisting of 3600 individuals that tinnitus is more frequently observed in cases with hearing loss compared to cases with normal hearing (17). Patients with more than 25 dB hearing loss are not included in this study not to influence ethiological evaluation. Moreover 50% of the patients in the study had acoustic trauma history, 7.5% diabetes mellitus, and 20% had hypertension history.

Typically clinicians depend on self-report measures for managing the appropriate treatment options for tinnitus. Hence, scales should be qualified to evaluate a wide range of factors such as mood disorders, tinnitus severity, sleeping problems, concentration problems, and treatment efficacy (8). Langguth et al. in a study with 72 tinnitus cases, reported the THI values as 18,1% slight , 23% mild, 30,1% moderate, 23,6% severe and 4.2% catastrophic (18). Lim et al. documented THI values of 327 cases as 31% mild, 18% moderate and 19%. The THI results in a study by Karabulut et al. are noted as 13% slight, 42% moderate and 45% (19). In our study THI values were 5% slight, 35% mild, 30% moderate, 15% severe, and 15% catastrophic before treatment. Whereas after first line treatment these values were documented as 25% slight, 40% mild, 10% moderate, 20% severe, and 5% catastrophic.

Although a variety of treatment options are administered for a safe, effective and permanent treatment of tinnitus, currently no FDA or European Medicines Agency (EMA) approved any drug for tinnitus therapy. Success rates of tinnitus treatment methods including placebo applications vary between 30%-80% (15,20). Nevertheless magnesium is known to prevent hairy cell damage by increasing blood flow in cochlea and reducing free radicals in patients with noise induced hearing loss or tinnitus. Furthermore recent studies demonstrated that magnesium treatment is effective in idiopathic hearing loss and acoustic trauma related tinnitus (21, 22). Uluyol et al. compared 76 bilateral and severe tinnitus cases with 86 healthy control individuals and reported significantly lower level of serum magnesium in the case group (2.3±0.4 m/dL'ye vs. 1.8±0.2, p=0.03) (23). Similarly, Cevette et al. stated a statistically significant improvement in THI scores (p=0.03) after daily doses of 532 mg oral magnesium treatment in 26 tinnitus cases (24). Supportively in our study, decrease in mean values of THI was significantly lower after the treatment in magnesium group. Additionally, THI ratios which were specified as 0% slight, 30% mild, 30% moderate, 20% severe and 20% catastrophic before treatment were observed to change as 25% slight, 25% mild, 5% moderate, 35% severe and 10% catastrophic. Therefore, it is concluded that magnesium treatment can be effective on cases with acoustic trauma related tinnitus.

It was shown that prostaglandin acts as a neuromodulator for afferent cochlear transmission, and synthesis by the cochlea (25). Briner et al. compared prostaglandin analogue misoprostol with placebo in 24 cases with severe tinnitus; and researchers reported an improvement rate of 33% in the misoprostol group, in contrast with the 0% improvement with the placebo group (26). Similarly, Yılmaz et al. documented a 46% improvement rate in misoprostol group whereas it was 14% for the placebo group in a study including total number of 42 tinnitus cases with diabetes and/or hypertension (27). In another study by Yılmaz et al. which included 40 tinnitus patients with no comorbidities, improvement ratio for misoprostol group was reported as 64%, and it was 33% for the placebo group; researchers stated that efficacy of misoprostol was significantly higher than placebo (p<0.05) (28). In accordance with these data in present study, the mean scores of post-treatment THI was significantly lower than pre-treatment THI scores in misoprostol group. Additionally, THI ratios which were specified as 10% slight, 40% mild, 30% moderate, 10% severe, and 10% catastrophic before treatment were observed to change as 25% slight,55% mild,15% moderate, 5% severe and 0% catastrophic. Thus, it is concluded that misoprostol treatment can be effective on cases with normal hearing tinnitus.

Lidocaine provides a short-term relief for 70% of the tinnitus patients as a voltage-gated sodium channel blocker. Besides lidocaine has poor bioavailability with serious side effects (particularly on high doses in liver), and it is short-term beneficial for only administered intravenously (15). Kallio et al. compared ropivacaine with 1.5 mg/kg IV lidocaine application and reported improvement in only a few of the cases for both agents in a study consisting of 19 tinnitus cases. Researchers define the effects of these drugs on tinnitus as weak, short-lasting, and random (29). In this study, no statistically significant difference found according to the mean values of THI after treatment in lidocaine group. As it is seen in published data related to lidocaine, effect of IV lidocaine on idiopathic subjective tinnitus patients is controversial. Furthermore, THI evaluation was performed one month after the treatment in present study. Considering on short-term effectiveness of lidocaine, our data is interpreted as consistent with the existing data.

CONCLUSION

In conclusion, we demonstrated that magnesium treatment is effective on tinnitus cases with acoustic trauma and misoprostol is effective on normal hearing tinnitus group, whereas intravenous lidocaine treatment was not found to be effective in tinnitus. In this respect further researches should be perform with larger study groups, may contribute to new treatment approaches in tinnitus.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: This study was performed with the Institutional Review Board protocol approval date 25/05/2013 and number 4 in Karadeniz Technical University.

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