Int. Adv. Otol. 2010; 6:(2) 188-194

ORIGINAL ARTICLE

Hearing and Dizziness in Patients with Definite Meniere's Disease after the Long Term Use of Diuretics

Seung Won Chung, Chang Hyun Cho, Gyu Cheol Han

The Department of Otorhinolaryngology-Head and Neck Surgery, Gachon University of Medicine & Science, Graduate School of Medicine, Incheon, South Korea

Objective: We attempted to identify the effects of diuretics administered for over a year to patients with Meniere's disease.

Materials and Methods: Retrospective reviews about 27 patients with Meniere's disease. Diuretics were maintained for more than a year with sodium restriction.

Results: The patients were allocated based on follow-up duration to; a 2-year (n=27), a 4-year (n=15), a 6-year (n=10), and an 8-year (n=6). Pure tone audiogram thresholds were available for 6 months before treatment and for 2, 4, 6, and 8 years. Dizziness was analyzed at all time points using dizziness handicap inventory. Hearing improved in 33.3% of 2-year group, 26.7% of 4-year group, 20% of 6-year group, and in 16.7% of the 8-year group. Initial hearing was preserved in 59.3%, 63.3%, 50%, and 16.7% in each group. Hearing was preserved or improved in 70~92 % of 2, 4, and 6-year groups, but 4 patients (66.7%) showed aggravation in 8-year group. The differences of total, functional, emotional and physical DHI scores were statistically almost significant.

Conclusion: Long term treatment with diuretics was effective in controlling dizziness. Diuretic therapy for over 1 year showed hearing preservation or improvement in about 85% of subjects at 2~6 years.

Submitted : 04 March 2010 *Accepted : 06 April 2010*

Introduction

Meniere's disease is a disorder characterized by hearing loss, tinnitus, and disabling vertigo. New guidelines for the diagnosis and evaluation of therapy in Meniere's disease were introduced by the American Academy of Otolaryngology-Head and Neck Surgery (AAOHNS) committee on Hearing and Equilibrium in 1995.[1] The use of salt restriction and diuretics in Meniere's disease was presented by Furstenberg et al., and currently accepted regimens are derivatives from these original observations.[2,3] Until now, diuretics (thiazide or acetozolami de) have been used to try and reduce the severity and frequency of episodic vertigo, but information is lacking on the effect of diuretics on vertigo, hearing loss, tinnitus, or aural fullness in Ménière's disease. Furthermore, Meniere's disease is known to show a natural course involving a decrease in vertigo episodes and hearing aggravation to about 50 dB, and thus, it is difficult to determine the effects attributable to diuretics.[4] We recommend patients to take diuretics for more than 1 year, and hearing and dizziness symptom severities were evaluated before treatment and at each follow up visit. The objective of this study was to determine the effects of long-term diuretic treatment on hearing and dizziness.

Materials and Methods

Patient Selection

A retrospective chart review was performed of patients with dizziness, a hearing disturbance, or ear fullness registered from January 1995 to July 2009. According to the criteria of the 1995 AAOHNS Committee on Hearing and Equilibrium, 168 patients with a definitive diagnosis of Meniere's disease were initially screened for this study, and 30 patients followed during more than 24 months were selected. The exclusion criteria applied were; a previous otologic disease history, incomplete symptom documentation, a previous history of diuretic use in other hospital due to Meniere's disease, irregular use of prescribed medicines, inadequate follow-up data and the history of endolymphatic sac surgery or intratympanic gentamicin injection. Finally, 27 patients were included in the study. This study was approved by the institutional review board of the Gachon Graduate School of Medicine.

Corresponding address:
Department of Otorhinolaryngology-Head and Neck SurgeryGachon University of Medicine & Science, Graduate School of Medicine
Incheon, South Korea 1198 Guwal-dong, Nam dong-gu, Incheon, Korea 405-760
Phone: +82-32-460-3324; Fax: +82-32-467-9044; E-Mail: han@gilhospital.com

Therapeutic Intervention and Follow Up

Selected patients were treated with a low sodium diet (<1500mg/day) and hydrochlorothiazide (50mg/day, Dichrozid®). The medical treatment was maintained for at least 12 months regardless of vertigo or hearing changes, and was extended for a maximum of 6 months based on considerations of vertigo attack. Endolymphatic sac decompression was performed on 1 patient with intractable dizziness that did not respond to maximal medical treatment, and 2 patients were administered an intratympanic gentamicin injection. These invasive procedures were undertaken after patients had been provided with detailed instruction and sufficient counseling by the senior author. But these three patients were excluded from the study to determine only the effect of medication. To ensure proper data collection, we recommended regular follow up visits at 1~2 month intervals during the initial 2 years and at 3~6 months after 2 years.

Hearing Data Collection

Data collected to determine hearing levels was obtained according to the 1995 AAO-HNS guidelines.[1] Pretreatment hearing threshold was determined from 6 months before treatment. Post treatment hearing thresholds were determined at 18~24 months, 42~48 months, 66~72 months and 90~96 months after medical treatment commencement. Pure-tone average was calculated at thresholds (dB) of 0.5, 1, 2, and 3 KHz. Audiogram results were determined based on the poorest result measured during each of the periods defined as above. In all patients, stage was determined according to the pretreatment PTA (stage 1: ≤25 dB, stage 2: 26~40 dB, stage 3: 41~70 dB, stage 4: ≥70 dB). Changes in decibels between pretreatment and post treatment audiogram thresholds were measured to determine the effect of treatment on hearing. A change of less than 10 dB was regarded as "no change" and changes of more than 10 dB were regarded as "significant change" (improvement or aggravation).[1]

Dizziness Data Collection

In determining changes in impairment and disability, we used the dizziness handicap inventory (DHI) scales (Korean version), which is based on 25 questions rather than the functional classes (A~E) of the AAOHNS 1995 guideline.[5] These questions address 6 physical, 9 emotional, and 10 functional issues (the poorest score possible is 100 and the best score is 0). The statistical reliability of the Korean version DHI has been confirmed by the Korean balance society (Cronbach's alpha value=0.95 for Total DHI, 0.90 for functional DHI, 0.89 for emotional DHI, and 0.83 for physical DHI).[6] We examined pretreatment and the last follow-up DHI scores to determine overall subjective changes in dizziness. In addition, to determine changes in functional, emotional, and physical impairment, we separately calculated the pretreatment and post treatment DHI scores of the 10 questions on functional (40~0), the 6 questions on emotional (24~0), and the 9 questions on physical aspects (36~0).

Statistical Analysis

Wilcoxon's signed ranked test was used to compare DHI scores achieved before treatment and at last follow-up, and the Mann-Whitney U test was used to determine changes in hearing level. Pearson's chi square test was used to explore the correlation between initial disease stage and hearing change. Statistical analysis was performed using a commercially available statistical software package (SPSS Version 12.0; SPSS Inc, Chicago, IL). Statistical significance was accepted at a confidence level of 5%.

Results

Patient demographics and analysis of stage

Mean duration of follow-up was 52.4 months (24~122 months). Mean patient age was 41.1 years (27~68 years) at diagnosis, and the male to female ratio was 13:17. The affected ear ratio was 12:20 (right to left) and both sides were affected in 2 patients. Mean duration of diurectic treatment was 13.2 months (12~18 months). In bilateral cases, stage at initial diagnosis was decided using the hearing result of the poor side. Four patients were included in stage 1, 10 in stage 2, 10 in stage 3, and 3 in stage 4. Twelve patients were followed for more than 2 years from treatment commencement, 5 patients for more than 4 years, 4 patients for more than 6 years, and 6 patients for more than 8 years. We defined the subject number of 2-year group as 27 (12+5+4+6) and so the results of patients with follow up duration of more than 4 years were included in the data of 2-year group. As the same way, the subject number is 15 in 4-year group, 10 in 6-year group, and 6 in 8-year group (Figure 1).

Analysis of audiometric results

At final follow-up visits, in 2-year group, 9 patients (33.3%) showed hearing improvement, 16 (59.3%) no change, and 2 (7.4%) hearing aggravation. In the 4-year group, 4 patients (26.7%) showed improvement, 8 no change, and 3 aggravation. In the 8-year group, 4 of 6 (66.7%) showed hearing aggravation. In the 2-year group, 25 (92.6%) either showed preserved initial hearing or an improvement, but in the 8 year group, hearing level was reduced in 4 (66.7%) (Figure 2). We also compared pretreatment PTA averages with post treatment PTA averages in each group. No prominent change in PTA results was not found in the 2-year (pretreatment 44.85±19.68 dB, post treatment 39.30±21.99 dB), 4-year (pretreatment 44.73±23.34 dB, post treatment 43.67±20.95 dB), or 6-year (pretreatment 40.80±20.47 dB, post treatment 45.40±19.31 dB) group. In the 8-year group, the post treatment PTA average (48.17±19.53 dB) was higher than the pretreatment average (36.67±15.21 dB). However, no significant difference was found for any of the four groups (Figure 3). In the 2-year and 4-year groups, we tried to find a relation between initial stage and hearing after treatment. Stages 1 and 2 were defined as low stage and stages 3 and 4 as high stage. In the low stage group (14 subjects) of 2-year group, initial hearing was improved in 5 patients, preserved in 7 patients and 2 showed aggravation. In the high stage group (13 subjects) of 2-year group, hearing improvement was achieved in 4 patients and hearing was preserved in 9 patients. However, these differences were not significant by Pearson's chi square test in 2-year group. In the low stage group (9 subjects) of 4-year group, initial hearing was improved in 1 patient, preserved in 6 patients and 2 showed aggravation. In the high stage group (6 subjects) of 4-year group, hearing improvement was achieved in 3 patients and hearing was preserved in 2 patients except 1 patient showing hearing aggravation. However, these differences were not significant by Pearson's chi square test in 4-year group (Table 1). We observed a hearing change in 6 patients in the 8 year group. Three patients maintained their initial hearing levels until 6 year after treatment commencement and 1 subject showed preserved initial hearing until 4 years. However, at 8 years, 4 patients showed hearing

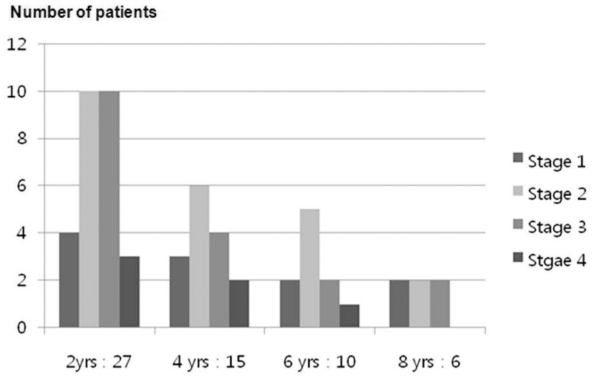

Figure 1. Distributions of patients classified by initial stage and follow up duration.

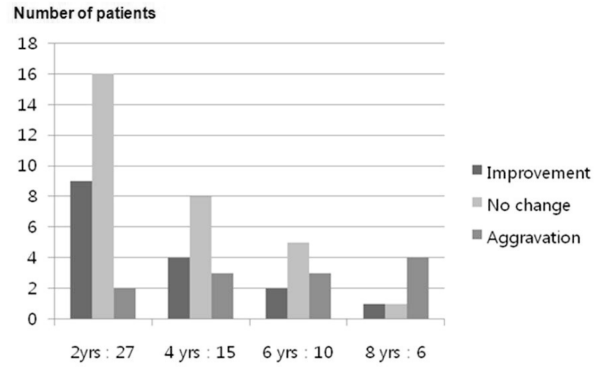

Figure 2. Pretreatment to post treatment changes in hearing in the four groups.

Table 1. The relationship between initial stage and hearing change in the 2 year and 4 year group.

4 yr group	Improvement	No change	Aggravation	Total
Stage 1,2	1 (11.1%)	6 (66.7%)	2 (22.2%)	9
Stage 3,4	3 (50%)	2 (33.3%)	1 (16.7%)	6
	4 (26.7%)	8 (53.3%)	3 (20%)	15
Pearson's chi square (p value: 0.312)				

2 yr group	Improvement	No change	Aggravation	
Stage 1,2	5 (35.7%)	7 (50%)	2 (14.3%)	14
Stage 3,4	4 (30.8%)	9 (69.2%)	0 (0%)	13
	9 (33.3%)	16 (59.3%)	2 (7.4%)	27
Pearson's chi square (p value: 0.241)				

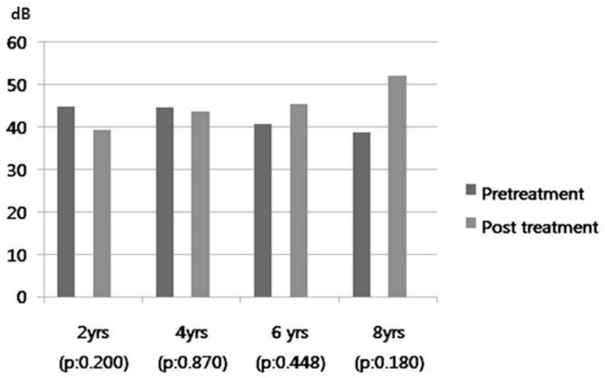

Figure 3. Pretreatment to post treatment changes in average hearing threshold in the four follow-up groups.

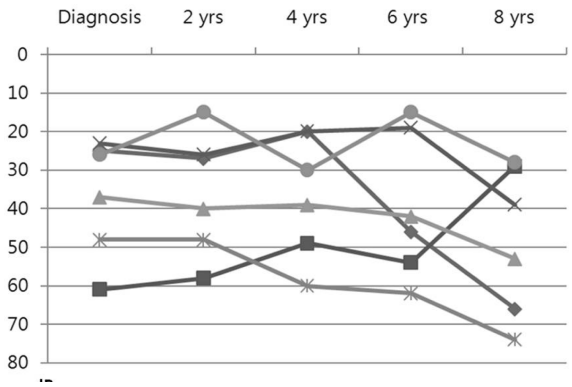

Figure 4. Progression of hearing level in the 6 patients from the 8 year group.

aggravation and 2 patients hearing improvement or preservation (Figure 4).

Analysis of dizziness scores

Pretreatment and post treatment DHI scores were determined in the 4 follow-up groups (score: 0~100). Mean total DHI scores improved versus pre-treatment scores in all four groups, and there were statistically significant differences in all four groups (p=0.000~0.042). Functional DHI scores were also compared (score:0~40), and all four groups showed improvement, which was significant in four groups (p=0.000~0.042). In terms of emotional and physical DHI scores, post treatment scores were lower than pretreatment scores in four groups, and this improvements were significant in three groups except 8-year group (Table 2).

Discussion

As early as 1934, Furstenberg demonstrated a relationship between the retention of sodium and the symptoms of Meniere's disease, and thus, recommended that sodium intake should be substantially reduced.[2] Of the several diuretics used to

Table 2. DHI scores between pretreatment and post treatment period.

	Pretreatment DHI score		Post treatment DHI score	Pretreatment functional DHI score		Post treatment functional DHI score
2yrs group (n=27)	52.00 ± 12.14	*p = 0.000**	18.27 ± 8.29	29.00 ± 9.54	*p = 0.000**	6.55 ± 4.46
4yrs group (n=15)	52.36 ± 10.58	*p = 0.005**	18.91 ± 7.06	29.09 ± 9.73	*p = 0.005**	6.73 ± 2.24
6yrs group (n=10)	55.43 ± 7.28	*p = 0.018**	18.57 ± 7.98	31.14 ± 9.37	*p = 0.018**	6.29 ± 2.43
8yrs group (n=6)	51.20 ± 6.41	p = 0.042*	12.80 ± 3.63	24.00 ± 7.61	p = 0.042*	3.60 ± 2.19

	Pretreatment emotional DHI score		Post treatment emotional DHI score	Pretreatment physical DHI score		Post treatment physical DHI score
2yrs group (n=27)	13.09 ± 3.58	*p = 0.000**	6.55 ± 3.16	10.6 ± 3.42	*p = 0.000**	5.18 ± 2.67
4yrs group (n=15)	12.91 ± 3.94	*p = 0.016**	6.91 ± 3.27	10.36 ± 3.44	*p = 0.005**	5.27 ± 2.87
6yrs group (n=10)	13.14 ± 4.45	*p = 0.046**	6.29 ± 2.93	11.14 ± 3.80	*p = 0.027**	6.00 ± 3.27
8yrs group (n=6)	16.00 ± 3.65	*p = 0.066**	5.00 ± 1.15	12.00 ± 4.32	*p = 0.066**	4.50 ± 1.91

Wilcoxon signed ranked test (significant of a difference, p < 0.05)

treat Meniere's disease, hydrochlorothiazide is most commonly used as the primary medication[7], but some complications have been reported, such as, hypokalemia, hypotension, hyperglycemia, hyperlipoproteinemia, and skin rashes, and thus, close observation is required with regular blood tests. However, no guidelines have been issued regarding diuretic treatment period or dosage, although most authors accept that medication is required for about 3 months.[7] In the present study, we recommended low dosage diuretic for a minimum of 1 year and we continued the medication for a maximum of 6 months depending on considerations of changes in dizziness. Throughout the follow up period and regular blood studies, no abnormal clinical symptoms or blood study results were encountered that suggested the discontinuance of long term diuretic therapy.

Earlier studies have considered the control of vertigo to be the primary treatment goal. However, over time, the preservation of hearing becomes increasingly important, and vestibular and cochlear manifestations of the disease have been recognized as important endpoints of therapy. Diuretics are used to try and reduce the severity and frequency of vertigo episodes, and the short term effects of diuretic therapy have been reported by several authors,[8-11] but little evidence supports this treatment. The effects of medical management are difficult to evaluate, and no definitive evidence is available about the effects of diuretics until now. The Cochrane database study reported that insufficient evidence is available regarding the effects of diuretics on vertigo, hearing loss, tinnitus, or aural fullness in clearly defined Ménière's disease.[12] However, it is difficult to select a control group and to observe changes in symptoms over 2 years, and it is also difficult to access the specific effects of diuretics, because Meniere's disease has a natural course of fluctuating hearing and dizziness. In the present study, after long-term diuretic therapy, about 85% of patients in the 2, 4, and 6-year groups achieved hearing preservation or improvement. Furthermore, the post treatment values of average PTA were preserved in the 2, 4 and 6-year groups compared to pretreatment values (39.30 dB, 43.67 dB and 45.40 dB versus 44.85 dB, 44.73 dB and 40.80 dB, respectively). However, in the 8-year group, although all 6 patients showed preserved initial hearing levels at 4 and 6 years, 4 patients (66.7%) showed distinct hearing aggravation. The above could be reminiscent of natural disease progression, which shows a hearing decline to near 50 dB at 10 years after disease onset (Stahle et al.). We are tempted to suggest that the administration of diuretics for a year provides a safe and effective means of preserving initial hearing levels for 8 years, but further study of clinical measures and the effectiveness of diuretics is required in an appreciably larger number of subjects.

To patients, vertigo is the most important symptom of Meniere's disease, but measures of vertigo are highly subjective. The AAOHNS 1995 guideline recommends that the frequency of definitive attacks over the period 6 months before treatment should be compared with the frequency during the period between 18 and 24 months after treatment commencement, and that level of vertigo control be graded into five classes (classes A to F).[1] In addition, a six-point functional level scale was also introduced to describe changes in functional disability. Counting the frequencies of episodes provides a reasonable indication of vertigo severity in Meniere's disease, but the frequencies of these vertigo attacks are wholly determined by patient's recall. Furthermore, this scale does not take into account attack severity. Moreover, the functional scale utilizes only a simple 6-grade classification system. In the present study, we used the DHI (the dizziness handicap inventory), which provides a straightforward means of quantifying vertigo. Furthermore, the DHI has the advantage of maintaining result reliability after translation into another language.[5,6] In the present study, we compared pretreatment total DHI scores with post treatment total DHI scores and determined changes in the functional, emotional, and physical aspects of the DHI. A significant change in total DHI score was found all four follow-up groups, and prominent changes were also observed in functional scores. Our experiences suggest that the DHI scoring system provides a useful means of measuring changes in dizziness in Meniere's disease.

In definitive Meniere's disease, the AAOHNS 1995 guideline suggests a staging system based on hearing level before treatment, and also suggests that this staging could be used to analyze treatment results. In 2-year group, initial hearing was preserved in 9 in stage 3,4 patients (69.2%) and improved in 4 (30.8%, pretreatment mean value 53 dB, post treatment mean value 22.75 dB) at 2 years after treatment

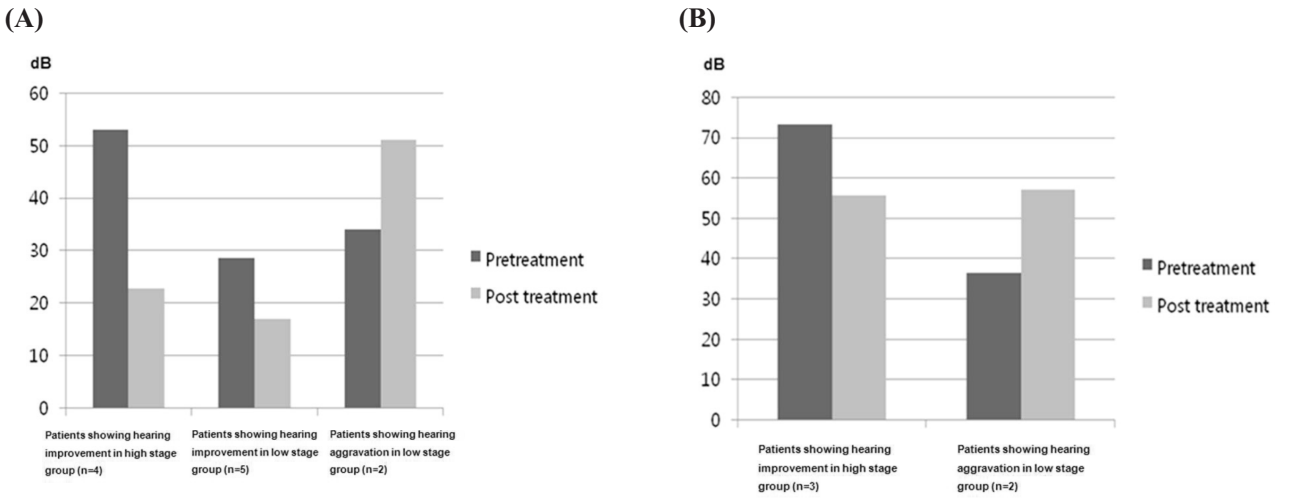

Figure 5. (A) Hearing changes of patients with low or high stage disease in the 2 year group. (B) Hearing changes of patients with low or high stage disease in the 4 year group.

commencement. 5 patient (35.7 %, pretreatment mean value 28.6 dB, post treatment mean value 17 dB) with stage 1, 2 disease achieved a hearing improvement , 7 patients (50 %) achieved hearing preservation, and 2 patients experienced hearing aggravation (14.3%, pretreatment mean value 34 dB, post treatment mean value 51 dB). In 4-year group, initial hearing was preserved in 2 patients in stage 3,4 patients (33.3%) and improved in 3 (50 %, pretreatment mean value 73.3 dB, post treatment mean value 55.7 dB) at 4 years after treatment commencement. 1 patient (11.1 %) with stage 1, 2 disease achieved a hearing improvement, 6 patients (66.7 %) achieved hearing preservation, and 2 patients experienced hearing aggravation (22.2 %, pretreatment mean value 36.5 dB, post treatment mean value 57 dB) (Table 1, Figure 5). Although differences were not significantly different, we believe that patients with a low initial stage are likely to show hearing aggravation after long-term diuretic treatment. Furthermore, the above results suggest that initial stage at diagnosis could be used to classify patients with Meniere's disease. Nevertheless, we consider that the staging system of AAO 1995 guideline is limited in terms of predicting hearing change after medical management.

Some limitations of this study should be borne in mind. The most obvious limitation concerns patient numbers. We were able to follow changes in hearing level but the number of patients followed over the 4-year study period was statistically inadequate. Accordingly, a substantially larger scale study is required to determine the effects of long-term diuretic therapy. The absence of a comparative group is another important limitation. A prospective-controlled study is required of patients that have taken diuretics for different time to confirm that diuretic therapy over 1 year more effectively protects hearing in the long term more so than therapies over 3 or 6 months.

Conclusion

The early treatment of Meniere's disease with diuretics is essential for the preservation of hearing and the control of dizziness. We believe that long-term diuretic therapy is a safe and effective tool for controlling dizziness in Meniere's disease, provided that patients are routinely examined for symptom changes and therapy-induced complications. Furthermore, the present study carefully suggests that the long-term use of diuretics may decrease the natural progression of sensorineural hearing loss in definitive Meniere's disease for ~8 years. Finally, we suggest that DHI scores over a convenient means of quantitatively analyzing dizziness.

References

1. Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Menière's disease. Otolaryngol Head Neck Surg. 1995; 113:181-5.

2. Furstenberg AC, Lashmet FH, Lathrop F. Menière's symptom complex: medical treatment. Ann Otol Rhinol Laryngol. 1992; 101:20-31.

3. Minor LB, Schessel DA, Carey JP. Ménière's disease. Curr Opin Neurol. 2004; 17:9-16.

4. Stahle J, Friberg U, Svedberg A. Long-term progression of Meniére's disease. Acta Otolaryngol Suppl. 1991; 485:78-83.

5. Jacobson GP, Newman CW. The development of the Dizziness Handicap Inventory. Arch Otolaryngol Head Neck Surg. 1990; 116:424-7.

6. GC Han, EJ Lee,.JH Lee, SN Park, HY Lee, et al. The Study of Standardization for a Korean Adaptation of Self-report Measures of Dizziness. Journal of the Korean Balance Society. 2004; 3:307 - 25.

7. Hamed Sajjadi. Medical management of Meniere's disease. Otolaryngol Clin N Am. 2002; 35:581-9.

8. Van Deelen GW, Huizing EH. Use of diuretic(Dyazide) in the treatment of Meniere's disease. A double-blind cross-over placebo-controlled study. ORL J Otorhinolaryngol Relat Spec. 1986; 48:287-92.

9. Klockhoff I, Lindblom U. Meniere's disease and hydrochlorothiazide (Dichlotride): A critical analysis of symptoms and therapeutic effects. Acta Otolaryngol 1967; 63:347-365.

10. Klockhoff I, Lindblom U, Stahle J. Diuretic treatment of Meniere's disease. Long-term results with chlorthalidone. Arch Otolaryngol. 1974; 100:262-5.

11. Grant IL. Welling DB. The treatment of hearing loss in Meniere's disease. Otolaryngologic Clinics of North America 1997; 30:1123-44.

12. Thirlwall AS, Kundu S. Diuretics for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2006; 19;3:CD003599.