FAST PTCs AND THRESHOLD EQUALIZING NOISE (TEN) TEST IN INDIVIDUALS WITH MENIERE'S DISEASE

Srishti Rawat

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ALL INDIA INSTITUTE OF SPEECH AND HEARING,

MANASANGOTHRI, MYSORE – 570006

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CERTIFICATE

This is to certify that this dissertation entitled **"Fast PTCs and Threshold Equalizing Noise (TEN) test in individuals with Meniere's disease"** is the bonafide work submitted in part fulfillment for the Degree of Master of Science (Audiology) of the student with Registration No. : 11AUD026. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Prof. S.R. Savithri

Director

Mysore

May, 2013

All India Institute of Speech and Hearing,

Manasagangothri, Mysore-570 006

CERTIFICATE

This is to certify that the dissertation entitled **"Fast PTCs and Threshold Equalizing Noise (TEN) test in individuals with Meniere's disease"** has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier in any other University for the award of any Diploma or Degree.

Dr. Sandeep M.

Guide

Lecturer in Audiology

Department of Audiology

All India Institute of Speech and Hearing

Manasagangothri, Mysore - 570 006.

Mysore

May, 2013

DECLARATION

This is to certify that this Master's dissertation entitled **"Fast PTCs and Threshold Equalizing Noise (TEN) test in individuals with Meniere's disease"** is the result of my own study under the guidance of Dr. Sandeep M., Lecturer in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted in any other University for the award of any Diploma or Degree.

Mysore

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Chapter 1

INTRODUCTION

Meniere's disease is an idiopathic condition which leads to inner ear disorder, characterized by episodic vertigo, fluctuating hearing loss, aural fullness and tinnitus (Sajjadi & Paparella, 2008). Hearing loss is one of the major symptoms, usually reported in one ear, typically at low-frequencies (Ophiem & Flottorop, 1995).

Stahle, & Arenberg (1973) reported a prevalence of 46 cases per 1, 00, 000 population. From 1975 to 1990, several studies from Japan, which were carried out for a Research Committee on Meniere's Disease and a Committee on Peripheral Vestibular Disorders, showed a prevalence of 17 cases per 100 000 population. Kotimaki (2003) investigated 5 million people from Finnish population during 1992 - 1996 with the AAO-HNS criteria and indicated a prevalence and incidence of 43 per 100 000 and 4.3 per 1, 00,000 population, respectively.

Endolymphatic hydrops is suggested to be the mechanism causing Meniere's disease, with support from histological studies (Hallpike & Cairns, 1938; Horner, 1991). Endolymphatic hydrops refers to bulging of the cochlea at the scala media boundaries due to endolymph build up (Hall, 2007). This excess fluid accumulation inside the scala media tends to bulge basilar membrane where it is most flaccid. Excess pressure of endolymph thus becomes most evident at the apex of the cochlea, and mostly shall affect the low-frequency hair cells.

Ge, Shea, and Orchik (1999) reported that low frequency hearing loss can occur in all stages of Meniere's disease. However, Enander, and Stahle (1967) found that hearing loss only in initial stages of Meniere's disease is restricted to low frequencies, while in later stages it becomes flat. Based on the degree of hearing loss,

AAO-HNS (1995) proposed four stages of Meniere's disease; stage 1 to stage 4. The degree was estimated by taking the arithmetic mean of pure tone thresholds at 500, 1000, 2000 and 3000 Hz, wherein stage 1 depicts hearing loss of ≤25dB while stage 4 depicts an average of more than 70dB, in worst audiogram during an interval of six months before the treatment.

Literature reports heterogeneity in terms of the causative factors of Meniere's disease. Causative factors of endolymphatic hydrops may include obstruction of endolymphatic flow, endolymph malabsorption, vasodilation, allergy, autoimmunity and viral infection. It has been suggested that endolymph comes primarily from the stria vascularis with small contributions from the planum semilunatum and is absorbed in the endolymphatic duct and sac. The evidence suggests a slow process of longitudinal flow and a fast process of radial flow occur concurrently (Paparella, 1991). Gibson and Arenberg (1997) reported that because of endolymphatic sac obstruction, hormones such as saccin are secreted to enhance production of endolymph and overcome the obstruction. As a result of excess of endolymph behind the obstruction, the blockage might be relieved and the sudden escape across the sac leads to vertigo.

Histologic studies of human ears have shown ruptures of membranous labyrinth secondary to Meniere's disease (Schuknecht, 1984), resulting in mixing of inner (endolymph) and outer (perilymph) fluids which in turn damages hair cells and leads to hearing loss (Rutka, 2010). Thornton and Farrell (1991) found that pressure increase in the scala media alters the stiffness of the basilar membrane and hence increases the speed of the travelling wave. They therefore proposed that basilar membrane travelling wave velocity can be used to detect endolymphatic hydrops.

Nadol and Thornton (1987) performed a morphometric analysis on hair cells, spiral ganglion cells, dendritic fibers in the osseous spiral lamina, afferent and efferent endings, and afferent synaptic contacts in an individual with documented unilateral Meniere's disease. They found damaged outer and inner hair cells, including disruption of the cuticular bodies and basal-ward dislocation of some outer hair cells. Also, there were significantly less number of afferent nerve endings and afferent synapses at the base of hair cells in the ear with Meniere's disease as compared to the contralateral ear.

The damage of OHCs and IHCs can be psychoacoustically determined using psychophysical tuning curves (PTC) and threshold equalizing noise (TEN) test. PTCs show broader tuning curve for OHC damage and shift in the peak frequency indicates off frequency listening due to IHC damage. Although clinically very useful, the traditional method for determining PTCs was a lengthy and time consuming procedure (Moore, 2004). This lead to advent of fast PTCs. Sęk, Alcantara, Moore, Kluk and Wicher (2004) introduced a fast method for determining PTCs, using a band of noise that sweeps in centre frequency and a Bekesy method to adjust the masker level required for threshold. They reported that the PTCs shapes were similar for the fast and traditional methods, for both normally hearing and hearing-impaired individuals.

TEN (HL) test, on the other hand, is an established test for assessing IHC dysfunction and takes lesser time than conventional PTCs. However, precise identification of edge frequency is not possible due to the large mid octave steps utilized in the TEN (HL) test.

1.1 Justification for the Study

Studies have shown that there is a reduction in the number of afferent nerve endings and afferent synapses at the base of both inner hair cells (IHCs) and outer hair cells in the ears with Meniere's disease (Nadol & Thornton, 1987). Consequently, predominant low frequency hearing loss has been reported in these individuals. However, there is a dearth of documentation of IHC functioning in Meniere's disease. The low frequency hearing loss seen in individuals with Meniere's disease may involve IHC dysfunction.

Fluctuating nature is a trademark of Meniere's disease. The understanding of IHC functioning in the individuals would help us infer about reversibility of hearing loss and thus, guide in counseling the clients. Further, the understanding may also be useful in hearing aid gain prescription, thus aiding rehabilitation process. Hence, the present study was taken up.

1.2 Objectives of the study

Following were the two specific objectives of the study:

1. To investigate presence of Inner hair cells dysfunction, if any, in MD using fast PTCs and TEN test.
2. To measure the extent of correlation between fast PTCs and TEN test in MD patients.

1.3. Hypothesis

The present study tests the a null hypothesis that there is no significant effect of Meniere's disease on the results of Threshold equalizing noise test and Fast psychophysical tuning curves.

Chapter 2

REVIEW OF LITERATURE

The purpose of present study was to assess functioning of inner hair cells in individuals with Meniere's disease (MD) using Threshold Equalizing Noise (TEN) and fast Psychophysical tuning curves (PTCs). The following sections provide a brief review on the etiology, clinical manifestation, histopathology, diagnosis and psychoacoustic characteristics of MD. For the clarity of presentation, the contents are organized under the following subheadings:

1. Etiology and symptoms
2. Effect of MD on outer hair cells
3. Tools for diagnosis of MD
4. Psychoacoustical characteristics of MD

2.1 **Etiology and Symptoms**

MD can be considered idiopathic with no acceptable justification of its cause. It can arise from genetic factors, infection, trauma, inflammatory, and immunologic dysfunction, and vasculopathy (Paparella & Sajjadi, 1999).

Patients with MD have symptoms of both peripheral vestibular as well as auditory disorders. Rauch (2010) reported high variability in the symptoms of MD. These symptoms were shown to occur in clusters or sporadically. Typically, symptoms occurring due to cochlear involvement include hearing loss, tinnitus, vertigo and a feeling of fullness. These symptoms may be present continuously or may be episodic in nature.

Hearing loss in those with MD is highly variable and often occurs unilaterally. However, in some cases, it is reported to be bilateral also It is frequently fluctuating by nature (Thorp & James, 2005, Arts, Kileny, & Telian, 1997; Levine, Margolis, & Daly, 1998). Vrabec, Simon, and Coker (2007) reported that in early stages of MD, sensorineural hearing loss fluctuates with the loss usually beginning from low frequencies and becomes stable at a moderate to severe SNHL after 8 to 10 years post onset. During the early stages of the disease, hearing sensitivity is typically found to be poorer at low frequencies than at frequencies above approximately 1 kHz. With the advancement of disease, however, other frequencies may also become affected and the hearing loss becomes permanent.

Meyerhoff, Paparella, and Gudbrandsson (1981) attempted to categorize the clinically determined cases of MD according to the pattern of hearing loss, but no single pattern appeared to be diagnostic. They found that 40% of the subjects had flat sensorineural hearing loss and 31% had a peaked pattern. Ries, Rickert, and Schlauch (1999) compared the audiogram configuration on three different patient groups: persons with unilateral MD, persons with unilateral acoustic tumor and persons from the general clinical population. In these results they found that 27% of individuals with unilateral MD showed peaked audiograms in one ear and flat audiometric configuration in the other. Also, results for general clinical population also showed peaked audiometric configurations in 9% of the cases while 12.5% of ears of persons with acoustic tumors also exhibited similar pattern. Therefore, it was concluded that individuals with MD had a higher incidence of peaked audiometric configuration but this pattern cannot be diagnostic of MD.

Although numerous theories have been proposed to account for these patterns, the causative cochlear mechanisms are not yet understood clearly. The theory which is most accepted, is that the pressure increases inside inner ear due to endolymph accumulation. Kimura (1967) induced this condition in experimental animals by closing the endolymphatic duct, thus causing endolymphatic hydrops and found patterns of hearing loss similar to that in humans.

Recruitment is also found to be often associated with hearing loss due to MD. People with hearing loss due to MD usually perceive loud sounds as extremely loud and even painful. This is thought to result from damage to the hair cells in the cochlea (McNeill, McMahon, Newall & Kalantzis, 2008).

Another major characteristic feature of MD is ***Tinnitus*** that is usually reported to be fluctuating and is usually low frequency in nature (McFadden, 1982). Vernon, Johnson and Schleuning (1980) studied characteristics of tinnitus in MD using four tests in terms of pitch, loudness, maskability, and residual inhibition and found that typically, the tinnitus in MD is a low pitched noise. However, in long term MD, tinnitus is often higher in pitch and tonal in quality. The loudness match occurs at very low sensation levels and masking as a relief procedure usually requires low levels of noise and produces residual inhibition, which is usually of longer than average duration.

Further, MD is characterized by episodes of rotatory dizziness and the duration of acute vertigo ranging from 20 minutes to 2 hours. However, rarely the attack may last for several hours or even more (Vassilou, Vlastarakos, Maragoudakis, Candiloros, & Nikolopoulos, 2011).

2.2 Effect of MD on Outer Hair Cells

MD causes an increase in endolymphatic pressure that causes damage to Reissner membrane, which separates perilymph from endolymph leading to destruction of sensory elements. This may cause hearing loss and/or tinnitus (McCall, Ishiyama, Lopez, Bhuta,Vetter & Ishiyama, 2009).

One test that is available for evaluating integrity of outer hair cells is otoacoustic emissions. Transient evoked otoacoustic emissions (TEOAEs), elicited by clicks or tone bursts, are used routinely for clinical purposes. Harris and Probst (1992) studied TEOAEs using 1-kHz tone bursts and clicks in both ears of patients with unilateral MD. Results revealed that OAEs could be measured in most of the Meniere's ears despite the presence of average hearing losses exceeding 30dB HL. Similarly, Bartoli, Galizia, Salonna, and Quarante (1992) recorded TEOAEs in MD and found TEOAEs to be present in 38.4% of 20 Meniere's ears with thresholds larger than 37.5dB HL.

A possible explanation of the variable findings in OAEs lies in different locations of the predominant lesion caused by MD. In a certain fraction of patients suffering from MD, the outer hair cells may be severely damaged, leading to the absence or strong reduction of OAEs. However, in a considerable number of patients the predominant damage may be located elsewhere. Studies indicate that endolymphatic hydrops can cause damage to the stereocilia on the outer hair cells (Horner, Guillaume, & Cazals, 1988). It has been found that stereocilia may be slightly displaced from their rootlets, or subtle changes can occur in the tip-links that connect the stereocilia leading to abnormal OAEs. On the other hand, in some cases more centrally located lesions can be present: at the afferent nerve fiber endings and

synapses at the base of both inner and outer hair cells (Nadol & Thornton, 1987), or at the body of the inner hair cells.

Perez, Espinosa, Fernandez, and Tapia (1999) studied distortion-product OAEs in 65 patients diagnosed as having MD and found that there was a significant a reduction in amplitude and increment in threshold of the DPOAE in the diseased ear. Similar results were found by Kleine, Mateijsen, Wit, and Albers (2002) who studied CEOAEs and DPOAEs in 100 patients with MD and found that incidence of the emissions in affected ears (56%) was lower than in unaffected ears (85%). Also, it was reported that the mean amplitude in affected ears was also significantly lower than in normal-hearing ears.

Cianfrone, Ralli, Fabbricatore, Altissimi, and Nola (2000) measured Distortion product OAEs in 70 patients affected by MD and found that more than 60% of the ears with MD emitted DPOAEs despite the presence of an average hearing threshold level above 40dB HL. Also, in 58 out of 70, DPOAEs were also measured post-glycerol administration and it was found that three-quarters of cases showed a significant enhancement in DPOAE amplitude while one-quarter of patients, who initially did not express DPOAEs, eventually did after intake of the osmotic agent, while no decreased DPOAEs were observed.

Kusuki et al. (1998) investigated changes in DPOAEs associated with hearing improvement in ears with MD. Four parameters were studied; DPOAE amplitudes for a moderate (L1:L2 - 65:55dB SPL) and a high (L1:L2 - 74:64dB SPL) primary level; maximum level of DPOAE amplitudes in the growth function (maximum DP level); and DPOAE detection threshold (DP threshold). Significant correlations were found between all four parameters and hearing threshold, except for

the 65:55-DP amplitude at 1 kHz. Each parameter appeared to reflect the hearing threshold to some extent. Therefore, TEOAE and DPOAE measurement can be a useful examination of OHC functioning in MD.

2.3 Tools for Diagnosis of MD.

2.3.1 Electrocochleography

ECochG is a measurement of stimulus related electrical potentials, which includes the cochlear microphonics (CM), summating potentials (SP) and compound action potentials (AP) of the auditory nerve. It is thought to reflect changes in the anatomic position of the hair cells. This bias in the position of the hair cell is what is expected to occur in active MD (Levine et al., 1998). Therefore, ECochG is widely used in differential diagnosis of MD (David, DeBonis, & Donohue, 2008).

Asai, Mori and Matsunanga(1985) evaluated the change in summating potential and action potential during fluctuation of hearing in 8 individuals with MD by using extratympanic ECochG. The relationship of SP and AP parameters to hearing thresholds was examined. Results of the study revealed that SP amplitude in Meniere ear is independent of degree of hearing loss at each frequency whereas, AP amplitude decrease and SP/AP amplitude ratio increases with increase in hearing loss at higher frequencies. A clinical study supporting the SP/AP amplitude ratio increased in MD was conducted by Aso et al. (1991). ECochG was done on 168 ears with definite MD. The results were compared with recordings from 29 normal ears and 444 ears with other types of sensorineural hearing loss. It was shown that the SP/AP amplitude ratio is much more useful indication than SP amplitude alone for detecting endolymphatic hydrops. A mean values of SP/AP amplitude ratio being near 0.25. From 0.30 to 0.40 of SP/AP amplitude ratio was considered adequate as the upper

limit. Following intravenous administration of glycerol, a significant decrease in SP/AP amplitude ratio was found in 21 Meniere's ears. A postoperative decrease of 10% or more in SP/AP amplitude ratio was observed in 5 individuals. Ten individuals followed up for 2 years or more after surgery did not show a statistically significant change of SP/AP amplitude ratio and pure tone threshold.

Conlon and Gibson (2000) conducted a study to analyze ECochG recordings obtained from ears demonstrating symptoms highly suggestive of MD by using transtympanic recording needle, situated in the round window niche. Analysis was made of the 1 kHz tone burst SP and the SP/AP amplitude ratio response to a 90dB click. Results demonstrated a significant difference in the 1 kHz SP response, and the SP/AP amplitude ratio, between normal hearing ears and Meniere's ears. Sensitivity of the test using tone burst approached 85%. This study also suggested the usefulness of electrocochleography in diagnosing endolymphatic hydrops, and demonstrated higher sensitivity of the 1 kHz SP response, compared with SP/AP amplitude ratio for clicks, in the diagnosis of MD.

Similar findings were also obtained in a study conducted by Al-momani, Ferraro, Gajewski, and Ator (2009) to assess the sensitivity and specificity of the ECochG for suspected MD individuals. They measured both the amplitudes and areas of the SP and AP to clicks (to derive the SP/AP amplitude and area ratios), and the SP amplitudes to 1000 and 2000 Hz tone burst. Results indicated that the most sensitive and specific ECochG parameters include SP amplitude and area, total SP-AP area, and SP/AP area ratio to click stimuli. Sensitivity and specificity values associated with these measures were 92% and 84%, respectively.

A study conducted by Baba, Takasaki, Tanaka, Tsukasaki, Kumagami, and Takahashi (2009) evaluated the utility of the SP/AP area curve ratio in transtympanic ECochG for the diagnosis of MD. One hundred and ninety eight individuals (209 ears) with MD were considered. Result of the study showed that with regard to SP/AP amplitude ratio, 57.1% in definite cases of MD, 39.6% in probable cases of MD and 50.0% in the cases who had transformed from probable MD to definite MD showed abnormally high values. Abnormally high values were observed in 43.9%, 27.7%, and 30.0% in SP/AP area ratio in three groups respectively, indicating that abnormal values were observed more frequently in the amplitude ratio than in the area ratio in all three groups. This study, hence, suggested that SP/AP area ratio may not necessarily have higher sensitivity in the diagnosis of endolymphatic hydrops of MD than SP/AP amplitude ratio in transtympanic ECochG. Therefore, EcochG is considered to be an ideal test for the diagnosis of MD (Levine, Margolis, & Daly, 1998).

2.3.2 Cochlear Hydrops Analyses Masking Procedure (CHAMP)

Cochlear hydrops analysis masking procedure (CHAMP) was introduced as a method to objectively distinguish active MD individuals (Don, Kwong, & Tanaka, 2005). The method consists of measurement of the change of the latency of wave V response in the auditory brainstem response, caused by the addition of high-pass making noise to the click stimulus. A reasonable assumption in cochlear hydrops is the increase in endolymphatic pressure could increase the stiffness of the basilar membrane. This increased stiffness could increase the speed of travelling wave propagation (Tonnodorf, 1957; Flottorp, 1980). Using ABR latencies obtained with high pass masking noise and assuming a normal frequency place map in the cochlea,

Thornton and Ferrell (1991) and, Donaldson and Ruth (1996) calculated abnormally high travelling wave velocities in individuals with MD. Thus, in individuals with MD it is assumed that increased endolymphatic pressure alters basilar membrane's mechanical property which in turn increases the apparent travelling wave velocity (Don et al., 2005).

De Valck, Claes, Wuyts, and Paul (2007) evaluated the diagnostic value of CHAMP in a series of MD and non-MD individuals. They concluded that CHAMP does not differentiate individuals with Meniere's from non- MD. This yields a sensitivity and specificity of 28% and 31% respectively. No significant mean latency difference was seen between Wave V of the MD group (0.43 ms) and the non-MD group (0.65 ms). Don et al. (2007) reviewed the data obtained in the study by De Valck et al. (2007) and found data errors that led to an improper conclusion. All the responses errors were reviewed and suggested that once these errors are corrected, sensitivity and specificity will consistently improve to 100% and 80% respectively.

Singh (2010) studied CHAMP in subjects with suspected and confirmed MD and compared with the findings with Non-MD individuals. The results revealed an overall specificity and sensitivity of CHAMP to be 76.6% and 73.8% respectively, when the latency shift of wave V responses for 0.5 kHz high pass masking noise from click alone were measured. This study also showed that the latency shift of wave V increases with successive decreases in high pass masking noise from 8 kHz to 0.5 kHz. But the shift was minimum in individuals with MD.

Kingma and Wit (2010) studied the benefits of the CHAMP as a diagnostic test in subject with definite unilateral MD. Results revealed that there was a delay in latency in both ears. The mean latency delay of wave V responses for the MD ears

(0.55 ms; standard error, 0.12 ms) was found to be significantly different from that for the unaffected ears (3.36 ms; standard error, 0.43 ms). These authors considered less than 2 ms as cutoff criteria for shift in latency to validate a diagnosis of MD in CHAMP.

Pallavi and Prawin (2010) compared CHAMP and ECochG in cases with MD and stated that CHAMP used in combination with ECochG was found to be beneficial. If agreement is shown between the findings of two tests, then it is possible that the patient has MD. However, in cases of disagreement, patient needs to be closely assessed, and other assessment tests should be used. Both tests were found to be feasible in detecting early stage Meniere disease.

2.3.3 Non-Audiological Tests

A non-audiological test that can be used for MD is *AAO-HNS Criteria*, which is mainly based on the case history. It was established by AAO-HNS CHE in 1972 and has been revised many times to reflect the improvement in the knowledge achieved from the research on MD. They classified the diagnosis of MD into four levels: "*possible*", "*probable*", "*definite*", and "*certain*" (Members of the Committee on Hearing and Equilibrium, 1995).

For an individual to be diagnosed as having "*possible*" MD, they must have all other possible causes of vertigo excluded and have experienced an episode of spontaneous rotational vertigo lasting for 20 minutes or more, often prostrating and accompanied by balance problems which may last for days. Nausea is common and horizontal rotatory nystagmus is always present. The patient must also have no audiometrically established hearing loss or a fluctuating or fixed sensorineural hearing loss with disequilibrium but without definitive episodes.

For "*probable*" MD, the person must show one episode of vertigo, audiometrically established SNHL on at least one occasion, and tinnitus or aural fullness in the affected ear, with all other possible causes of the vertigo excluded.

For "*definite*" MD, the person must have two or more episodes of vertigo that lasts for at least 20 minutes as well as audiometrically established SNHL on at least one occasion, and tinnitus or aural fullness during vertigo episodes in the affected ear, with all other possible causes of the vertigo excluded.

Finally, to have a diagnosis of "*certain*" MD, the individuals must have presented with definite MD and have post-mortem histopathological confirmation.

2.3.4 Glycerol Test

Another tool which is frequently used for MD is **Glycerol test.** A positive glycerol test is considered to be a specific diagnostic sign of MD (Snyder, 1971, 1974). In addition to its diagnostic use, the glycerol test is also said to be valuable for assessing the suitability of individuals for endolymphatic sac operations (Arenberg & Spector, 1977). This is particularly true of glycerol-positive cases, because the disease in such individuals is thought to be in an early phase. Thomsen and Vesterhauge (1979) expressed the view, however, that there is a great impact of psychological factors on the results of the glycerol test, and they warn against selecting individuals for operative treatment solely on the basis of outcomes of glycerol test.

Karjalainen, Karja, and Nuutinen (1984) investigated the correlation of results of the glycerol test to hearing level and caloric reactions in MD. This was used to investigate if the test results depend on the stage of the disease. Results revealed that glycerol test was positive in twenty seven patients and negative in thirty three

patients. Pure tone average (PTA) was found to be 56.7dB (Range 45 to 77dB) in glycerol-positive individuals, and 43.6dB (Range 23 to 75dB) in glycerol negative individuals. Also, it was found that the outcome of the glycerol test in individuals with MD depends on the pre-test threshold levels. If the hearing loss was mild or moderate, the number of negative test results and normal caloric reactions appeared to increase. In this study, the PTA values in the glycerol-negative individuals were 13.1dB better than the PTA values in glycerol-positive individuals. The difference was statistically significant. Threshold values were distinctly better in glycerol negative individuals with normal caloric reactions.

Mori, Asai, and Matsunaga (1985) compared between electrocochleography and glycerol test in the diagnosis of MD. These tests were performed in 51 Meniere's ears. The percentage of cases where these tests were positive was compared and it was found that the positive rate of ECochG and glycerol test was 63 % and 51 %, respectively. The ears with positive result of both tests and of either test were 15/51 ears (29%) and 43/51 ears (84%). respectively. The positive rate of ECochG was higher in ears with a moderate to severe hearing loss at high frequencies, while the positive rate of glycerol test was higher in ears with a moderate to severe hearing loss at low frequencies. This study has demonstrated that ECochG is different in selectivity of detection of the endolymphatic hydrops from glycerol test and that the combination of both tests increases the detection rate of the endolymphatic hydrops in MD.

2.4 Psychoacoustical Characteristics of MD

Changes in hearing sensitivity seen in the patients with MD are often accompanied by alterations in perception of pitch and loudness as well as frequency

selectivity in the affected ear. Webster and Schubert (1954) studied pitch perception in cases with hearing loss attributed to MD and found that in the region where the hearing loss increased rapidly with frequency, the pitch shifted downward between one and two semitones. This may be because of the reason that sound in the affected ear is perceived as distorted due to fluid volume or elasticity changes. In another study, Brannstromm (2009) reported fluctuations in binaural *loudness* and *pitch* matches during consecutive long-term measurements in subjects with MD, which were not seen among normal-hearing participants.

Zwicker and Schorn (1978) studied *frequency selectivity* in PTCs in MD patients and found flat tuning curve indicating almost no frequency resolution remained at low frequencies. Similar results were found by Brainstromm (2009) where, in patients with MD, he found broader and shallower PTCs indicating reduced frequency selectivity especially at low frequencies. These reports indicate damage to OHCs. Thus, although there is a clear understanding of effect of MD on OHCs, its effect on IHCs is not clearly understood. Methods that can be used to study IHC dysfunction are TEN test and fast PTCs, which is a variation of PTCs. However, there are no reports of these two tests in MD. PTCs show broader tuning curve for OHC damage and shift in the peak frequency indicates off frequency listening due to IHC damage. Although clinically very useful, the traditional method for determining PTCs was a lengthy and time consuming procedure (Sek, Alcantara,, Moore, Kluk, Wicher, 2005). This led to introduction of fast PTCs for clinical use. TEN (HL) test, on the other hand, is an established test for assessing IHC dysfunction and takes lesser time than conventional PTCs.

Correlation between these two tests depends largely on the criterion being used for interpretation. Summers, Molis, Walden, Surr, and Cord (2003) found a 56% correlation between PTCs and TEN test using 10% PTC tip shifts and 10dB TEN criteria. On the other hand, Warnaar and Dreschler (2012) who compared 10% and 20% criteria of PTC shift in sensorineural hearing loss cases with TEN test results and recommended use of 20% criterion as there was a better correlation with TEN test results. It was also recommended that in case of any unresolved disagreements, PTC should be given more weightage due to various demerits of TEN test reported in literature. It is found that TEN test measurements may be affected by high presentation levels, producing noise-like perception of pure tones, and is not transparent for OHC activity that may influence results. Further, TEN test may fail to diagnose a dead region when the frequency of the test tone falls only a little inside a dead region (Kluk & Moore, 2005; Moore, 2001; Moore, Huss, Vickers, Glasberg, & Alcantara, 2000) and is affected by factors such as processing inefficiency, central auditory processing deficits etc. (Summers et al., 2003). Therefore, PTC results are more reliable when there are unresolved disagreements. However, neither PTC nor the TEN test can be considered as the 'gold standard' for identification of IHC dysfunction. Thus, the use of both would yield more meaningful conclusions about IHC functioning.

Chapter 3

METHOD

The present study tested a null hypothesis that 'there is no significant effect of Meniere's disease (MD) on the results of Threshold equalizing noise (TEN) test and

Fast psychophysical tuning curves (PTCs)'.To test the hypothesis, TEN test and Fast PTCs were carried out in individuals with MD and results of these tests were analyzed to find the presence or absence of Inner hair cells (IHC) dysfunction. The following method was used in present study.

3.1 Participants

The study involved 9 adults (3 females and 6 males) in the age range of 27 to 59 years. All of them had sensorineural hearing loss consequent to their onset of MD diagnosed by qualified ENT surgeon. The pure tone thresholds were *at least 40dB* at lower frequencies (250, 500, & 1000 Hz) in the affected ear. The symptoms of MD persisted for a minimum of 4-5 months and maximum of 3 years among the 9 participants. There was no indication of middle ear pathology according to immittance findings. Auditory brainstem response and Otoacoustic emissions ruled out the presence of retrocochlear pathology. All participants were categorized as per the AAO-HNS criteria as "definite" MD.

3.2 Instrumentation

A calibrated two channel Maico MA53 audiometer, a personal computer and a Grason- Stadler Incorporated Tympstar (version 2) tympanometer were the equipments used in the study. TEN (HL) and Software for fast psychophysical tuning curves (SWPTC) were used through the computer for administration of TEN test and PTCs. All instruments were calibrated according to ANSI standards.

3.3 Test Environment

All the tests were carried out in acoustically treated audiometric room where the ambient noise levels were within the permissible limits as per calibrated according to ANSI S3.1 (1991).

3.4 Test Procedure

3.4.1 Preliminary Evaluation

Preliminary evaluation was carried out to ensure that the participants fulfilled all the inclusionary criteria. A detailed case history was taken from each participant and presence of triad of MD (hearing loss, tinnitus & vertigo) along with nature and duration of the problem was noted. The individuals who fulfilled the AAO-HNS criteria for "definite" MD, i.e., suffered two or more impulsive episodes of vertigo that lasted for at least 20 minutes, had sensorineural hearing loss, and tinnitus or aural fullness during episodes of vertigo in the affected ear were included. Further, all participants were diagnosed as MD by the ENT surgeon. A written consent was taken from all the participants included in this study.

Pure tone audiograms were obtained using modified Hughson-Westlake method (Carhart & Jerger, 1959). Air conduction thresholds were estimated for 250-8000Hz audiometric frequencies and bone conduction thresholds were estimated between 250 Hz to 4000 Hz. Speech audiometry was administered to measure speech reception threshold (SRT), speech identification score (SIS) and uncomfortable level. Tympanometry was done to rule out middle ear pathology using 226 Hz probe tone. Acoustic reflex thresholds were measured for 500, 1000, 2000 and 4000 Hz. Oto-acoustic emissions and Auditory Brainstem Response (ABR) were used to rule out retrocochlear pathology.

3.4.2 *Experimental Evaluation*

A. Administration of TEN (HL) Test

Unmasked pure tone thresholds were measured for signals from 500 to 4000Hz in 2dB steps with MAICO MA53 audiometer. Patients were instructed to ignore the noise and raise their finger on hearing the tone.

Audiometer was then connected to a computer and two tracks from TEN (HL) CD containing the pure tones and the threshold equalizing noise (TEN) were fed to audiometer, where the tracks were mixed and presented to the same ear. Test frequencies were 0.5, 0.75, 1, 1.5, 2, 3, and 4 kHz. The TEN (HL) level is specified as the level of a one-ERB_N wide band centered at 1 kHz, where ERB_N stands for the equivalent rectangular bandwidth of the auditory filter determined by using young normally hearing subjects at moderate sound levels (Glasberg & Moore, 1990; Moore, 2004). A TEN level of 70dB HL/ERB_N was used (Vinay & Moore, 2007). However, a lower level was used for one participant who was unable to tolerate the loudness of the TEN.

The level of the signal and the TEN were controlled using the attenuators in the audiometer. The signal level was varied in 2dB steps to determine the thresholds (Moore, Glasberg, & Stone, 2004). A 'no response' was recorded when the subject did not indicate hearing the signal at the maximum output level of the audiometer.

B. Fast PTCs

Fast PTC software, SWPTC, installed in computer was used for measuring psychophysical tuning curves (PTCs) using a narrowband noise masker that sweeps in frequency. The software was calibrated before starting the test to ensure the correct

level of signal being transmitted by the computer. The sensitivity of the Senheisser headphones used, i.e., 108.5dB SPL for 0.5 RMS according to manufacturer's specifications, was entered and instrument was calibrated automatically by the software. The software generates a full-scale sine-wave on both channels of the sound card and the RMS voltage was measured manually at the input to the headphones. This voltage was found to be 0.28 VRMS which was entered to get the maximum levels of sine wave and noise band. Maximum levels of sine wave and noise band were found to be 103dB SPL and 91dB SPL respectively.

SWPTC software was installed on a PC with a standard sound card. The signals were played out from the PC and presented using Sennheisser HDA200 headphones. The masker was a narrowband noise that continuously swept in frequency. The probe signal was a pulsed pure tone signal fixed in frequency and presented at an intensity of 10dB above the absolute threshold at the probe frequency. Probe frequencies of 250 to 4000 Hz in mid-octave steps were used. The center frequencies of the noise ranged from one octave below the probe frequency to one octave above the probe frequency. Ear to be tested was selected in the software and participant's task was to detect a sinusoidal signal, which pulsed on and off, in the presence of masker whose centre frequency slowly changed, from low to high (Forward sweep). The intensity of the masker was increased at a rate 2dB/s as long as the signal remained audible, after which, intensity was decreased at the rate of 2dB/s. In this way, the software tracked masker level required just to mask the signal using a Bekesy tracking method. The frequency tip of Psychophysical tuning curves was derived from the output curve.

3.5 Response Analysis

3.5.1 TEN Test

Pure tone thresholds without TEN were compared with that of the masked thresholds. The criteria for presence or absence of IHC dysfunctions were as follows (based on Moore, Glasberg & Stone, 2004):

1. If the masked threshold is 10dB or more above the TEN level, and the TEN elevated the absolute threshold by 10dB or more, then an IHC dysfunction was considered to be present.
2. If the masked threshold in presence of TEN is less than 10dB above the TEN level and the masked threshold is greater than the unmasked threshold 10dB or more, then no IHC dysfunction.

3.5.2 Fast PTCs

In this study both 10% and 20% PTC shift criteria were taken to detect IHC dysfunction, i.e, a shift in tip of PTC more than 10% and 20% respectively, of test frequency will be considered as IHC dysfunction.

3.6 Data Analysis

The data obtained from individuals with MD was analyzed to infer the following:

a. Presence of IHC dysfunction in ears with MD.
b. Extent of correlation between fast PTCs and TEN test in MD patients.
c. Prevalence of IHC dysfunction as a function of Audiometric Threshold at the Test Frequency
d. Relationship between IHC dysfunction and Age

e. Relationship between IHC dysfunction and duration of MD

Chapter 4

RESULTS

A total of 10 ears of 9 participants with Meniere's disease were assessed using Threshold equalizing noise (TEN) test and fast psychophysical tuning curves (PTC) and this chapter reports results of these evaluations under the following headings:

4.1. Individual demographic data and basic audiological details of participants.

4.2. Prevalence of IHC dysfunction.

4.3. Prevalence of IHC dysfunction as a function of hearing threshold at the test frequency.

4.4. Relationship between IHC dysfunction and duration of MD.

4.1. Individual Demographic Data and Basic Audiological Details of Participants

Low frequency pure-tone average (LPTA) was derived for all the participants on the basis of three-frequency average (0.25, 5, and 1 kHz) (Battista, 2004**).** Data of each patient are as follows. Table 4.1 gives the case-wise demographic details, duration of MD and the result of pure tone audiometry.

All subjects were in age range of 27 to 59 years with mean age of 41 years. The duration of MD ranged from 4 months to 3years. Low frequency pure tone average (250, 500 and 1000 Hz) revealed hearing loss above 40dB with most of the participants (8/10) having flat hearing loss.

Criterion recommended by Moore, Huss, Vickers, Glasberg, and Alcantara (2000) was used to classify TEN test results as normal or abnormal. Fast PTCs tips were generated using MATLAB. Results of Fast PTCs were compared with both 10% and 20% (Warner & Dreschler, 2012) shift of PTC tip criteria.

Table 4.1: *The case-wise demographic details, duration of MD and the result of pure tone audiometry*

Case	Age(years)	Gender	Duration	Configuration	LPTA
1	28	Male	4-5months	Rising	41.33
2	59	Male	1 year	Flat	50.66
3	56	Male	3 years	Flat	63.33
4	32	Female	1-1.5 y	Flat	62.66
5	48	Male	1year	Rising	56.00
6	38	Female	1.5 years	Flat	46.66
7	56	Male	2 years	Flat	54.6
8	27	Female	10 months	Flat	48.00
9	27	Female	10 months	Flat	50.00
10	42	Male	3 years	Flat	47.33
***LPTA-** average of pure tone thresholds at 250, 500 and 1000Hz.					

4.2 Prevalence of Inner Hair Cell Dysfunction

Prevalence, in this context, refers to proportion of the group found to have inner hair cell dysfunction. Out of ten subjects, three were found to have no inner hair cell dysfunction at any frequency in any of the tests. In rest of the seven participants, there was an indication of inner hair cell dysfunction on PTCs using 10% shift criterion at one or more frequencies. The number of participants with inner hair cell dysfunction decreased to five when 20% shift criterion was used. On the other hand, in TEN test, only three participants showed inner hair cell dysfunction at one or more

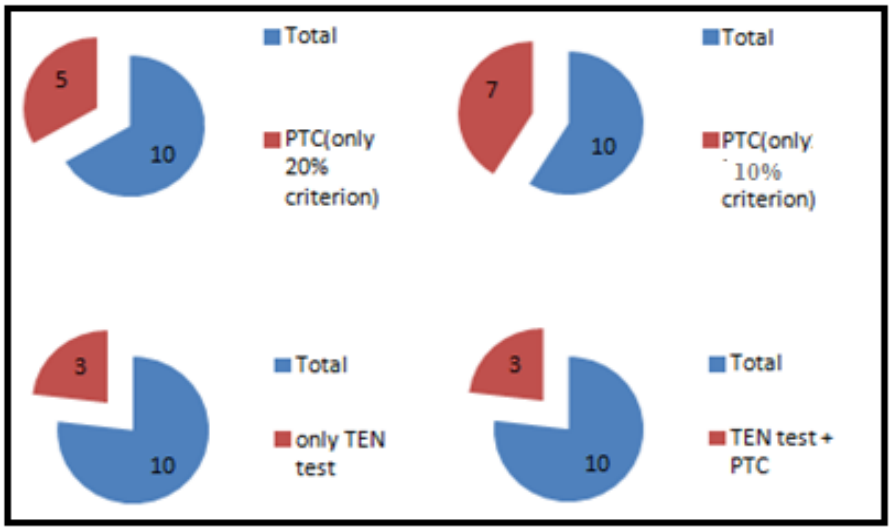

Figure 4.1: *Pie chart depicting the number of participants detected as IHC dysfunction based on both TEN test and PTCs, PTC (20%), PTC (10%) and TEN (HL) tests.*

frequencies, while in others IHC functioning was found to be normal. Figure 4.1 shows **t**he number of participants detected as IHC dysfunction based on both TEN test and PTCs, PTC (20%), PTC (10%) and TEN (HL) test.

4.3 Prevalence of Inner Hair Cell Dysfunction as a Function of Hearing Threshold at the Test Frequency

Figure 4.2 shows the pure tone audiogram of each individual in the ears with MD. The frequencies showing IHC dysfunction marked 'O' (PTC using 20% criterion), '□' (PTC using 10% criterion) and 'Δ' (TEN test). Most participants having inner hair cell dysfunction had their audiometric thresholds above 50dB HL at the test frequency. No IHC dysfunction was found at any audiometric frequency when the hearing loss was 40dB or less, except in Case 1 on fast PTCs using 10% criterion indicated presence of IHC dysfunction. All the participants with LPTA of more than 60dB were found to have inner hair cell dysfunction at least at one test

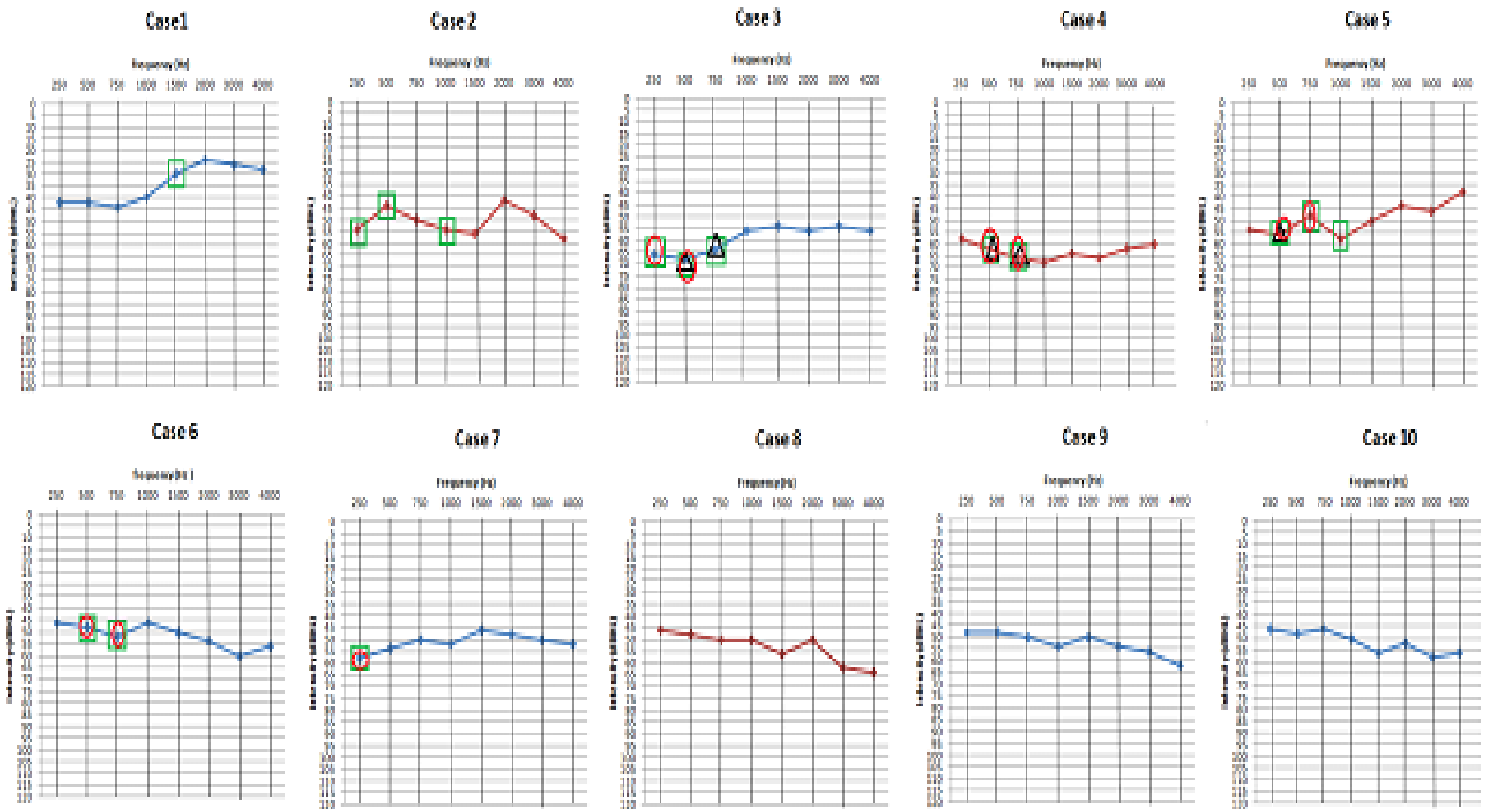

Figure 4.2 The results of the PTC and TEN test plotted on the individual audiogram. Unfilled Red circles depict IHC dysfunction in PTC using a 20% criterion; Green squares indicate IHC dysfunction in PTCs using a 10% criterion; The black triangles indicate IHC dysfunction in TEN test

frequency. The dysfunction was more likely at lower frequencies than higher frequencies.

4.3 Relationship between Inner Hair Cell Dysfunction and Age

To see the effect of age, participants had to be divided into two groups of equal number. For this, a scatter plot of the age was derived and a cut off age that divides the group into two with equal number in both was found. This cut off age was 40 years. First group constituted of younger participants, aging 20 to 40 years and the second group included older participants aging above 40 years.

Table 4.2 gives the number of participants in the younger and older group, detected as having IHC dysfunction according to TEN test and PTCs. From the table it can be noted that number of individuals detected as having IHC dysfunction were more in older group compared to younger group.

Table 4.2: *Number of participants identified as having IHC dysfunction in TEN test, PTC (10% and PTC 20%) in the two age groups*

TEST	No. of Participants with IHC dysfunction	
	Young group	Older group
TEN test	1	2
PTC (20%)	2	3
PTC(10%)	3	4

Frequency-wise analysis of IHC dysfunction, in each group was also carried out. Table 4.3 gives the number of frequencies in each group according to TEN test, and PTCs detected as having IHC dysfunction. Results for individual frequencies indicated that prevalence of inner hair cell dysfunction was more in older group in all

the three tests and more number of participants had inner hair cell dysfunction at low frequencies (250, 500 and 750 Hz) than higher frequencies.

Table 4.3: *Number of participants identified as having IHC dysfunction at test frequency in TEN test, PTC (10%) and PTC (20%) in younger and older group*

Group	Test	Frequency (Hz)								Total
		250	500	750	1000	1500	2000	3000	4000	
Older	TEN	-	2	1	-	-	-	-	-	**3**
	PTC(20%)	1	3	2	1	-	-	-	-	**7**
	PTC(10%)	1	4	3	1	1	-	1	-	**11**
	Total	**2**	**9**	**6**	**2**	**1**	**-**	**1**	**-**	**21**
Younger	TEN	1	-	1	-	-	-	1	-	**3**
	PTC(20%)	1	-	1	1	-	-	-	-	**3**
	PTC(10%)	1	1	1	1	1	-	-	-	**5**
	Total	**3**	**1**	**3**	**2**	**1**	**-**	**1**	**-**	**11**

4.4 Relationship between Inner Hair Cell Dysfunction and Duration of MD

To verify the relationship between IHC dysfunction and duration of MD, the participants were divided into two groups on the basis of duration of MD, such that both groups had equal number of participants. A method similar to that used in age groups was used to derive the cut-off duration of 1 year. Group 1 had 5 participants with duration of MD from 6 months to 1 year while 5 participants from group 2 had MD for more than 1 year.

Table 4.4 gives the number of participants detected as having IHC dysfunction in two groups divided based on age of onset. It can be seen from the table that total

number of participants in group 2 having IHC dysfunction was more than group1. This was true for both TEN test and PTC (10 and 20%).

Table 4.4*: Number of participants identified in TEN test, PTC (10%) and PTC (20%) in different durations of MD*

TEST	No. of Participants with IHC dysfunction	
	Group 1	Group 2
TEN test	1	2
PTC (20%)	1	4
PTC (10%)	3	4
Group 1: 4months- 1year; Group : >1year		

Table 4.5: *Number of participants identified as having IHC dysfunction at test frequency in TEN test, PTC (10%) and PTC (20%) in both groups*.

Group	Test	Frequency (Hz)								Total
		250	500	750	1000	1500	2000	3000	4000	
Group 1	TEN	-	1	-	-	-	-	-	-	**1**
	PTC(20%)	-	1	1	1	-	-	1	-	**4**
	PTC(10%)	1	2	1	2	-	-	-	-	**6**
	Total	**1**	**4**	**2**	**3**	**-**	**-**	**1**	**-**	**11**
Gruop2	TEN	-	1	2	-	-	-	-	-	**3**
	PTC(20%)	2	2	2	-	-	-	-	-	**6**
	PTC(10%)	2	3	3	-	-	-	1	-	**9**
	Total	**4**	**6**	**7**	**-**	**-**	**-**	**1**	**-**	**18**
Group 1: 4months- 1year; Group : >1year										

Frequency-wise analysis of IHC dysfunction, in each group was carried out. Table 4.5 gives the number of frequencies in each group according to TEN test, and PTCs. Results for individual frequencies indicated that prevalence of inner hair cell dysfunction was more in group 2 in all the three tests and more number of participants had inner hair cell dysfunction at low frequencies (250, 500 and 750 Hz) than higher frequencies.

4.5 Correlation between Results of TEN Test and PTCs

The agreement between PTC and the TEN test results was evaluated separately using 10% and 20% criteria. Table 4.6 and 4.7 depicts the agreement of TEN test and PTCs with 20% and with 10% criteria respectively. The agreement between TEN test and PTCs based on the presence or absence of inner hair cell dysfunction across tested frequencies was found to be 93% using 20% tip-shift criterion for PTCs.

Using 20% criterion, PTC and TEN test diagnoses were in 100% agreement in seven ears (Case 1, 2, 4,7,8,9 & 10). In rest of the three ears, for one ear (case 6), agreement was found to be 71.4% while for two ears (case 3 and 5) it was found to be 85%.

On the other hand, the agreement between PTC and the TEN test results based on the presence or absence of inner hair cell dysfunction across tested frequencies was found to be 84% using 10% tip-shift criterion. With this criterion, PTC and TEN test diagnoses were in 100% agreement in 3 ears (Case 8, 9 and 10). In rest of the seven ears, four ears (case 2, 4, 5 and 6) showed agreement to be 71.4% while for the other three participants (case 1,3 and 7), it was found to be 85%.

Table 4.6*: Correlation between PTC (using 20% criterion) and TEN test. First symbol depicts result of PTCs and second symbol stands for TEN test result. "+" and "-" signs depict presence and absence of inner hair cell dysfunction respectively*

	Test frequency (kHz)								Comparison		
Subject	Ear	0.5	0.75	1	1.5	2	3	4	Agree	Disagree	Agreement (%)
1	L	- -	- -	- -	- -	- -	- -	- -	7	0	100
2	R	- -	- -	- -	- -	- -	- -	- -	7	0	100
3	L	+ +	- +	- -	- -	- -	+ -	- -	5	2	71.4
4	R	- -	+ +	+ +	- -	- -	- -	- -	7	0	100
5	R	+ +	+ -	- -	- -	- -	- -	- -	6	1	85
6	L	+ -	+ -	- -	- -	- -	- -	- -	5	2	71.4
7	L	- -	- -	- -	- -	- -	- -	- -	7	0	100
8	R	- -	- -	- -	- -	- -	- -	- -	7	0	100
9	L	- -	- -	- -	- -	- -	- -	- -	7	0	100
10	L	- -	- -	- -	- -	- -	- -	- -	7	0	100
Total									65	5	93

Table 7: *Correlation between PTC (using 10% criterion) and TEN test. First symbol depicts result of PTCs and second symbol stands for TEN test result. "+" and "-" signs depict presence and absence of inner hair cell dysfunction respectively*

	Test frequency [KHz]								Comparison		
Subject	Ear	0.5	0.75	1	1.5	2	3	4	Agree	Disagree	Agreement (%)
1	L	- -	- -	- -	+ -	- -	- -	- -	6	1	85
2	R	+ -	- -	+ -	- -	- -	- -	- -	5	2	71.4
3	L	+ +	+ +	- -	- -	- -	- +	- -	6	1	85
4	R	- -	+ +	+ +	- -	- -	- -	- -	5	2	71.4
5	R	++	+ -	- -	+ -	- -	- -	- -	5	2	71.4
6	L	+ -	+ -	- -	- -	- -	- -	- -	5	2	71.4
7	L	+ -	- -	- -	- -	- -	- -	- -	6	1	85
8	R	- -	- -	- -	- -	- -	- -	- -	7	0	100
9	L	- -	- -	- -	- -	- -	- -	- -	7	0	100
10	L	- -	- -	- -	- -	- -	- -	- -	7	0	100
Total									59	11	84

Therefore, degree of correspondence between TEN test and PTCs using 20% tip-shift criterion is found to be better than correspondence between TEN test and PTCs using 10% tip-shift criterion.

Chapter 5

DISCUSSION

The purpose of the present study was to detect presence of inner hair cell dysfunction in individuals with Meniere's disease. Several interesting results were found in the present study which would be discussed under the following headings.

5.1 Characteristics of participants

5.2 IHC functioning in MD

5.3 Comparison between Psychophysical Tuning Curves

5.4 Subject related factors that affect IHC function in MD

5.1. Characteristics of the Participants

The participants of this study had typical features of MD in terms of demographic, otological and audiological results. Watanabe (1983) reported age of onset of MD to be 41 to 42 years. Similar to his report, although only of 10 individuals, the mean age in the present study was 41.3 years.

All the participants had two or more impulsive episodes of vertigo that lasted for at least 20 minutes in duration as well as sensorineural hearing loss, and tinnitus along with aural fullness during episodes of vertigo in the affected ear. Therefore, all participants fell in range of "*definite*" MD according to AAO-HNS criteria (1972). Most of the participants exhibited sensorineural hearing loss of flat or rising configuration which again is typical of MD. Configuration of hearing loss was flat in most participants, while in some cases it was rising. Enander and Stahle (1967) found that hearing loss in initial stages of MD is affecting only in the low frequencies, leading to rising configuration of audiograms, while in later stages it becomes flat. Therefore, one can infer that most cases in the present study belonged to advanced

stage of MD as they had flat hearing loss configurations. One possible explanation for the flat hearing loss is that, in endolymphatic hydrops which is suggested to be the mechanism underlying MD, (Hallpike & Cairns, 1938; Horner, 1991) there is a heavy accumulation of the endolymph (Hall, 2007). This excess build-up of endolymph inside the scala media tends to distend the membrane where it is most flaccid. Excess pressure of endolymph thus becomes most evident at the apex of the cochlea which is most flaccid, and hence, affects the low-frequency hair cells. As the disease advances, endolymphatic pressure increases, which in turn, causes a rupture in the Reissner membrane leading to mixing of perilymph and endolymph that causes mechanical disturbance in organ of corti and damage to inner and outer hair cells (Li & Egan, 2011). Hearing loss, at this stage becomes flat and irreversible (Halpin, 1994).

Average degree of hearing loss in all the participants was more than 40dB at low frequencies (250, 500 & 1000 Hz). This was one of the important inclusionary criteria as in earlier studies, it was reported that sensorineural hearing loss of 40 to 50dB at low frequencies is often associated with low-frequency IHC dysfunction (Terkildsen, 1980; Thornton & Abbas, 1980; Moore, 2001). Since, aim of the present study was to investigate the possibility of IHC dysfunction in MD, a minimum criterion of low frequency pure tone average of 40dB was used.

5.2. IHC Functioning in MD

Tools available to assess IHC dysfunction include TEN test and PTCs. Although clinically very useful, the traditional method for determining PTCs was a lengthy and time consuming procedure. This demerit led to the advent of fast PTCs, which along with TEN was utilized to detect presence of IHC dysfunction in this study.

The results indicated presence of IHC dysfunction in most participants. These results show experimental evidence for the assumption made by Halpin, Hasso and Thornton (1994). Halpin assumed that IHC dysfunction may be present in MD at advanced stages, when the hearing loss becomes irreversible. This might be due to rupture of the Reissner membrane leading to permanent damage to OHCs and IHCs.

IHCs are transducers of the cochlea which convert the vibration patterns on the basilar membrane into action potentials in the auditory nerve. When the IHCs are non-functioning over a certain region of the cochlea, transduction in that region gets affected (Moore, 2001). Basilar membrane vibration, in such cases, is not detected through the neurons directly innervating that region but through neurons with different characteristic frequency. This is called "off-frequency listening"(Johnson-Davies & Patterson, 1979; Patterson & Smith, 1980; O'Loughlin & Moore, 1981). The presence or absence, and extent of inner hair cell damage can be important in clinical practice for prescription of gain, counselling the client, for deciding on the appropriate form of amplification and for assessing cochlear implant candidacy. For patients with IHC dysfunction, it has been recommended that amplification should not be given at frequencies corresponding to IHC dysfunction as it may cause distortion of the signal. Also, in cases with extensive IHC dysfunction, cochlear implant may be more appropriate rehabilitation option (Baer, Moore, & Kluk, 2002; Moore, 2004; Vickers, Moore, & Baer, 2001).

Criterion recommended by Moore, Glasberg and Stone (2000) was used to classify TEN test results as normal or abnormal, i.e, if the masked threshold is 10dB or more above the TEN level, and the TEN elevated the absolute threshold by 10dB or more, then an IHC dysfunction was considered to be present. Results of TEN test

were compared with both 10% and 20% shift of PTC tip criteria. Moore, Huss, Vickers, Glasberg and Alcantara (2000) stated that a shift of PTC tip by more than 10% of the probe frequency is indicative of IHC dysfunction while Warnaar and Dreschler (2012) found a higher agreement between fast PTCs and TEN test when a PTC shift of 20% was considered. Further, even in normal hearing individuals PTC shift is found to be as high as 20% (Carney & Nelson, 1982). Therefore, in the present study correlation was assessed using both criteria.

IHC dysfunction is found to be correlated with degree of hearing loss. Most participants having IHC dysfunction had their audiometric thresholds above 50dB HL at the test frequency. These results are in agreement with previous studies in suggesting that, for a large number of listeners with moderate to severe hearing loss, cochlear damage may involve IHC dysfunction (Vickers et al., 2001; Summers et al, 2003; Moore, 2001). There was no evidence of IHC dysfunction at any audiometric frequency where hearing loss was 40dB or less, except in Case 1 where fast PTCs using 10% criterion indicated presence of IHC dysfunction. This probably is because of the reason that even in individuals with normal IHC function, PTC tips can vary within 20% of the test frequency (Carney & Nelson, 1982). In such cases, using 10% criterion may cause false alarm.

Degree of correspondence between TEN test and PTCs using 20% tip-shift criterion was found to be better than correspondence between TEN test and PTCs using 10% tip-shift criterion. These results were consistent with the data obtained by Warnaar and Dreschler (2012) that compared 10% and 20% criteria of PTC shift in sensorineural hearing loss cases with TEN test results and recommended use of 20% criterion as there was a better correlation with TEN test results.

5.3. *Subject Related Factors Affecting IHC Functioning in MD*

Subject- related factors that were found to affect IHC functioning were age and duration of MD. Total number of participants in older age group having IHC dysfunction was more than younger age group for both TEN test and PTCs. These results were consistent with study by Vinay and Moore (2007) where they indicated a higher prevalence of dead regions in adults with sensorineural hearing loss above the age of 50 years. Therefore, age can be considered as a precipitating factor for IHC dysfunction.

The prevalence of IHC dysfunction in participants with longer duration of MD was more compared to those with lesser duration of MD. This might be attributed to the reason that patients with MD since longer time had higher degree of hearing loss as compared to other group. Further, it was seen that most of the participants, with longer duration of MD, who showed IHC dysfunction, were from older age group.

In contradiction to the above, participant-10, who had MD since 3 years (maximum duration of MD in the study), did not show any evidence of IHC dysfunction. On the other hand, participant-3 who also had Menieres's disease for 3 years had IHC dysfunction at three frequencies. This difference can be attributed the fact that the age of onset of MD in participant-10 was 39 years and in participant 3 was 56 years. Thus, it is plausible to infer that duration of MD affects the cochlear function differently depending on the age of onset. Two possible explanations can be considered in this regard; 1) There could have been a pre-existing hearing loss due to aging which might have been exacerbated by the MD, 2) The cochleae in older individuals are generally more vulnerable to damage. All the participants in the study reported of hearing difficulties only after the onset of MD. This supports the second

explanation suggesting the vulnerability of the aged cochlea to damage in the absence of any pre-existing hearing loss. Therefore, age may be considered an important pre-disposing factor for IHC dysfunction. The duration of MD further precipitates IHC dysfunction depending on the age of onset.

5.4. Comparison between TEN test and PTC

Differences in results of TEN test and PTCs in some patients indicate that either of the two tests is only partially reliable in detecting IHC dysfunction. Studies in literature report that the TEN (HL) test may fail to diagnose a dead region when the frequency of the test tone falls only a little inside a dead region (Kluk & Moore, 2005; Moore, 2001; Moore et al, 2000). Vinay and Moore (2007) recommended to apply TEN test only when the audiometric threshold exceeds 60dB HL at one or more frequencies. Furthermore, TEN test measurements may be affected by high presentation levels, producing noise-like perception of pure tones, and is not transparent for OHC activity that may influence results (Warnaar & Dreschler, 2012). Therefore, PTC results are more reliable when there are unresolved disagreements.

PTCs also are affected by various factors like, beats, criterion used for interpretation etc. (Kluk & Moore, 2005). It has been found that even in individuals with normal IHC functioning, the PTC tips may vary within 20% (Carney & Nelson, 1982) or 10% (Sek et al., 2005) of the test frequency.

Therefore, it is better to use a stringent criterion of 20% tip shift. Due to the above cited reasons, neither PTC nor the TEN test can be considered as the 'gold standard' for identification of IHC dysfunction. Thus, the use of both would yield more meaningful conclusions about IHC functioning. Summers et al. (2003) found a 56% correlation between PTCs and TEN test using 10% PTC tip shifts and 10dB TEN

criterion. They suggested that TEN test is not a reliable tool for identifying IHC dysfunction as it is affected by many other factors like processing efficiency deficits and also deficits in central auditory processing unrelated to IHC functioning. Contrary to the above, Warnaar and Dreschler (2012) showed a good agreement of 80% between PTCs and TEN for a 20% PTC tip shift and 10dB TEN criterion, and 67% with a 10% PTC tip shift and 10dB TEN criterion. The results of the current study showed 13% (20% PTC tip shift – 10dB TEN criterion) and 17% (10% PTC tip shift – 10dB TEN criterion) higher agreement between PTCs and TEN test compared to the results of Warnaar and Dreschler (2012). Hence, the criteria of 20% PTC tip shift and 10dB TEN criterion are suggested in identifying IHC dysfunction.

Vinay and Moore (2007) found that individuals with Auditory Neuropathy showed abnormalities on the TEN test and not in PTCs. They suggested that the PTCs primarily reflect cochlear functioning, whereas, TEN results are also affected by retrocochlear lesions. TEN and PTCs reflect different levels of processing of the sound and when used together, provide a better insight into the cochlear and the IHC functioning in particular.

Three of the participants in the current study indicated IHC dysfunction at 250 Hz on the PTCs. But they were missed on the TEN test as the TEN test does not include the 250 Hz frequency. Thus, the use of the two tests in combination would give more reliable and meaningful information about the IHC functioning over a broad range of frequencies. The use of PTCs, especially in the low frequencies are important in studying IHC functioning in conditions like MD, where the low frequencies are relatively more affected.

5.5. IHC Functioning in MD snd Amplification Strategies

Moore and Kluk (2002) and, Vinay and Moore (2007) showed that patients with IHC dysfunction at low frequencies extracted little or no information from low-frequency components in the speech. Further, it was suggested for patients with low-frequency hearing loss that, amplification of the low frequencies via a hearing aid be provided only when there was no IHC dysfunction at low frequencies as in presence of a low frequency IHC dysfunction, even after adequate amplification of low-frequencies, limited benefit is reported in literature. In addition, components of speech are detected and analyzed via higher frequency channels leading to distortion of high frequencies and cause difficulty in understanding the information obtained from the low frequencies (Shannon, Zeng & Wygonski, 1998). Therefore, amplification should be provided in cases of low frequency IHC dysfunction, as in Meniere's disease, with high caution.

It is stated in literature that MD may cause IHC damage at advanced stages, which is due to Reissner membrane rupture and mixing of endolymph and perilymph leading to destruction of sensory elements (Halpin, 1994; Opheim & Flottorp, 1957). The current study provides evidence for the assumption in the above mentioned studies.

The presence of IHC dysfunction in our study was strongly associated with late age of onset, duration of MD and greater degrees of hearing loss. This suggests that IHC dysfunction is seen in advanced stages of MD in contrast to earlier stages. The presence of IHC dysfunction in advanced stages of MD reflects the severity of damage to the cochlear structures. Thus, it is reasonable to assume that the hearing loss associated with IHC dysfunction is possibly irreversible, however, this needs

experimental validation. More evidence in this regard will guide us in the rehabilitation and counseling of individuals with MD.

Chapter 6

SUMMARY AND CONCLUSIONS

The purpose of the present study was to assess Inner hair cells functioning in Meniere's disease. Fast PTCs and TEN test were used to test the IHC functioning. If IHC dysfunction was detected, the secondary purpose was to test the agreement between TEN test and PTC results.

Ten adults (27-59 years) diagnosed as having MD participated in the study. All of them had sensorineural hearing loss of greater than 40dB at low frequencies. Duration of MD ranged between 4 months and 3 years. With their consent to participate in the study, fast PTCS and TEN (HL) test were administered in the standard testing conditions.

Results showed presence of Inner hair cells dysfunction in individuals with MD. The IHC dysfunction seemed to be related to several factors such as audiometric frequency, degree of hearing loss at low frequencies, age of the individual, and duration of MD. IHC dysfunction was more likely at lower frequencies, older individuals, in greater degree of hearing loss and in those having long-standing MD.

There was a good agreement between PTCs and TEN (HL) test, particularly when 20% criterion was used to interpret PTCs. PTCs detected IHC dysfunction in more number of occasions than TEN test.

The findings suggest IHC dysfunction in advanced and more severe stage of MD. Although the exact physiological mechanism for the IHC damage is not known, one can speculate that it is caused due to rupture of the Reissner membrane. This

would lead to mix-up of the endolymph and perilymph leading to permanent damage of outer hair cells and IHCs.

The findings indicate that one needs to asses for the IHC dysfunction at least in those who have hearing loss of greater than 50dB at lower frequencies. Neither PTCs nor TEN test seems to be a gold standard test for detecting IHC dysfunction. Therefore a combination of TEN (HL) test and, PTCs with 20% criteria is recommended for the clinical testing.

The findings of the present study have important implications. One, it contributes to the existing theoretical knowledge in the areas of MD as well as dead regions. Second, the information derived from this study is clinically useful in the management of individuals with MD. If one is found to be having IHC dysfunctions, the amplification should exclude the frequencies showing IHC dysfunction to minimize the input distortions of the signal. The information is also useful in counseling the individuals about the pathophysiology, prognosis and management strategies.

Future Directions

- Further studies can be conducted on a larger population to validate the agreement between two tools to assess IHC functioning in MD.
- Duration, age effect and effect of configuration on IHC functioning in MD can be considered in further researches.

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