

**BITHERMAL CALORIC STIMULATION TEST IN
PATIENTS WITH POSSIBLE AND DEFINITE
MENIERE'S DISEASE**

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BITHERMAL CALORIC STIMULATION TEST IN PATIENTS WITH POSSIBLE AND DEFINITE MENIERE'S DISEASE.**RATREE LIKHITAMNUAY 4336253 RACD/M****M.Sc.(COMMUNICATION DISORDERS)****THESIS ADVISORS : CHANCHAI JARIENGPRASERT, M.D., M.Sc., M.A.,
CHEAMCHIT THAWIL, M.A., MONTIP TIENSUWAN, Ph.D.****ABSTRACT**

Meniere's disease (MD) is a disorder of the inner ear associated with the presence of endolymphatic hydrops. At present there is no single test that makes the diagnosis of MD. Caloric test has been proven as useful in lateralizing the side of a vestibular lesion and in identifying disorders of the labyrinth and the vestibular nerve. The reports were not found in generally available collective literature studying the correlation between bithermal caloric stimulation test parameters and patients with possible, and definite MD. The purposes of this study were to study the caloric responses in patients with possible and definite MD, to compare the caloric responses between patients with possible and definite MD, and to study the relationship among caloric parameters and duration of disease in patients with possible and definite MD.

In bithermal caloric test, each ear would be irrigated with water 125 cc.at 30°C and 44°C in all patients. Possible MD group consisted of 5 males and 25 females, definite MD group consisted of 14 males and 16 females. The mean ages, duration of disease, pure tone average (PTA) of right ears, PTA of left ears were 44.33 years, 4.40 years, 17.06 and 17.24 dBHL, respectively for possible MD group and 45.30 years, 5.19 years, 39.58 and 40.94 dBHL, respectively for definite MD group. Patients reported the functional level (at the level of 1, 2 and 3), tinnitus, aural fullness problems were 93.34%, 43.33% and 13.33% respectively for possible MD group and 93.33%, 93.33% and 53.33%, respectively for definite MD groups. The results for possible and definite MD group indicated that the means canal paresis (CP) and directional preponderance (DP) value showed no significant difference between right and left values. The maximum slow phase velocity (Vmax) showed no significant difference between the right and the left ears, the right and the left beats. The Vmax of irrigation revealed that the warm irrigation was significantly weaker response than the cool irrigation ($p < 0.001$). When comparing the results between both groups, the mean CP and DP values of patients with definite MD group were significantly higher than those in possible MD group ($p < 0.05$). No significant difference of mean Vmax for warm and cool water responses between both groups. No relationship between caloric findings and duration of disease in both groups.

From the Vmax result, marked accentuation of the response to cold water irrigation was found in both groups. The reasons might be due to patients with MD having had a change of the central nervous system mechanism or the influence of pressure effects. The study of total CP and total DP indicators found that possible MD could represent a low functional impairment of the vestibular organ. This finding showed that patients with definite MD group might have more vestibular disturbance than possible MD group.

From this study, the comparison intergroups should be interpreted by using direct Vmax combination with CP or DP indicators to make the diagnosis instead of the comparison by using the direct Vmax of warm or cool irrigation alone; bithermal caloric testing should be used as a test battery in clinical evaluations of definite MD and should be first conducted by warm water irrigation in order to reduce patients' reaction to the test because of MD patients marked accentuation of the response to cold water irrigation.

**KEY WORDS : MENIERE'S DISEASE / BITHERMAL CALORIC STIMULATION TEST
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การตรวจกาลอริกในผู้ป่วยโรคมึเนียร์ (BITHERMAL CALORIC STIMULATION TEST IN PATIENTS WITH POSSIBLE AND DEFINITE MENIERE'S DISEASE)

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วท.ม. (ความผิดปกติของการสื่อความหมาย)

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บทคัดย่อ

โรคมึเนียร์เกิดจากความผิดปกติของความดันน้ำในหูชั้นใน ปัจจุบันยังไม่สามารถใช้การทดสอบใดเพียงอย่างเดียวในการวินิจฉัยได้ การทดสอบกาลอริกได้รับการพิสูจน์แล้วว่ามีความประโยชน์ในการบอกถึงหูข้างที่มีพยาธิสภาพของระบบการทรงตัวและบ่งชี้ถึงความผิดปกติของหูและประสาทการทรงตัวได้ ไม่พบว่ามีรายงานใดที่ศึกษาเกี่ยวกับตัวแปรของการทดสอบกาลอริกในผู้ป่วยมีเนียร์กลุ่ม possible และกลุ่ม definite วัตถุประสงค์ของการศึกษานี้เพื่อศึกษาการตอบสนองของการทดสอบกาลอริกในผู้ป่วยมีเนียร์กลุ่ม possible และกลุ่ม definite, เพื่อเปรียบเทียบการตอบสนองของการทดสอบกาลอริกระหว่างผู้ป่วยทั้งสองกลุ่มและศึกษาความสัมพันธ์ระหว่างผลของการทดสอบกาลอริกกับระยะเวลาของการเป็นโรคในผู้ป่วยทั้งสองกลุ่ม

การทดสอบกาลอริกทดสอบโดยใช้ น้ำ 125 ลูกบาศก์เซนติเมตรที่อุณหภูมิ 30 และ 44 องศาเซลเซียส ทดสอบทั้งสองกลุ่ม ๆ ละ 30 คนในกลุ่ม possible ประกอบด้วยเพศชาย 5 คน หญิง 25 คน, กลุ่ม definite ประกอบด้วยเพศชาย 14 คน หญิง 16 คน อายุเฉลี่ย, ระยะเวลาของการเป็นโรคเฉลี่ย, ค่า pure tone average (PTA) ของหูขวาและ PTA ของหูซ้าย คือ 44.33 ปี, 4.40 ปี, 17.06 และ 17.24 dBHL, ตามลำดับ และ 45.30 ปี, 5.19 ปี, 39.58 และ 40.94 dBHL, ตามลำดับ ระดับความสามารถในชีวิตประจำวัน (ที่ระดับ 1, 2 และ 3), ปัญหาเสียงดังในหู และปัญหาความรู้สึกแน่นอื้อในหู พบว่ามีร้อยละ 93.34, 43.33 และ 13.33 ตามลำดับสำหรับกลุ่ม possible, และร้อยละ 93.33, 93.33 และ 53.33 ตามลำดับสำหรับกลุ่ม definite ผลการศึกษาในกลุ่มทั้งสอง ได้ผลเช่นเดียวกันคือ ค่าเฉลี่ยของ CP และ DP ไม่แตกต่างกันระหว่างหูซ้ายและขวา beat ซ้ายและขวา ตามลำดับ ค่าเฉลี่ยของ Vmax ในหูที่มีปัญหาไม่แตกต่างกันระหว่างหูซ้ายกับหูขวา, beat ซ้ายกับขวา ในขณะที่ค่าเฉลี่ยของ Vmax ระหว่างน้ำอุ่นและน้ำเย็นพบมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติที่ระดับ 0.001 ผลการเปรียบเทียบระหว่างกลุ่มทั้งสอง พบมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติของค่าเฉลี่ย CP และ DP ระหว่างข้างซ้ายกับขวาที่ระดับ 0.05 ในทางกลับกันค่าเฉลี่ยของ Vmax ทั้งน้ำเย็นและน้ำอุ่นไม่แตกต่างกันระหว่างสองกลุ่ม เมื่อศึกษาความสัมพันธ์ระหว่างผลของการทดสอบกาลอริกและระยะเวลาของการเป็นโรคในผู้ป่วยทั้งสองกลุ่มพบว่าไม่มีความสัมพันธ์กัน

จากผลการศึกษาค่า Vmax พบว่าอาจมีอิทธิพลของความดันหรืออาจมีความเปลี่ยนแปลงของกลไกของระบบประสาทส่วนกลางที่ทำให้ผู้ป่วยทั้งสองกลุ่มมีการตอบสนองต่อน้ำเย็นมากกว่าน้ำอุ่น การศึกษาค่า CP รวมและ DP รวมพบว่ากลุ่ม possible มีความบกพร่องของหน้าที่การทำงานของอวัยวะในการทรงตัวเล็กน้อย อาจเกิดจากปัญหาประสาทการทรงตัวในกลุ่ม definite มีมากกว่ากลุ่ม possible จากการศึกษา การเปรียบเทียบระหว่างกลุ่มควรใช้การเปรียบเทียบค่าตรงของ Vmax ร่วมกับการเปรียบเทียบร้อยละของความแตกต่างระหว่างหู (CP) หรือระหว่าง beat (DP) มาช่วยในการวินิจฉัยแทนการเปรียบเทียบโดยใช้ค่าตรงของ Vmax ของน้ำอุ่นหรือของน้ำเย็นเพียงอย่างเดียวอย่างหนึ่งเท่านั้น, การทดสอบกาลอริกควรนำมาใช้เป็นการตรวจประจักษ์ร่วมกับการทดสอบอื่นเพื่อประเมินความผิดปกติในผู้ป่วยกลุ่ม definite และควรเริ่มการตรวจด้วยวิธีการตรวจด้วยน้ำอุ่นก่อน เพื่อลดปฏิกิริยาของผู้ป่วยต่อการตรวจเนื่องจากผู้ป่วยมีการตอบสนองต่อน้ำเย็นมากกว่าน้ำอุ่น

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LIST OF ABBREVIATIONS

MD	Meniere's disease
ENG	Electronystagmography
CP	Canal paresis
UW	Unilateral weakness
DP	Directional preponderance
V _{max}	Maximum slow phase velocity
RW	Peak slow-phase eye speed of the response following the right ear-warm temperature irrigation.
LW	Peak slow-phase eye speed of the response following the left ear-warm temperature irrigation.
RC	Peak response for the right ear-cool temperature irrigation.
LC	Peak response for the left ear-cool temperature irrigation
FI	Fixation Index
FFS	Failure of fixation suppression
PTA	Pure tone average
dB	Decibel
Hz	Hertz (cycle per second)
kHz	Kilohertz
EcochG	Electrocochleography
SP	Summating potential
AP	Action potential
MR	Magnetic Resonance
ml	Milliliter
VOR	Vestibulo-ocular reflex
CNS	Central nervous system

CHAPTER I

INTRODUCTION

1.1 Statement of problem

Meniere's disease (idiopathic endolymphatic hydrops) is a common peripheral vestibular disorder (1). It is a disorder of the inner ear associated with a complex symptom consisting of spontaneous, episodic attacks of vertigo; sensorineural hearing loss that usually fluctuates; tinnitus; and often a sensation of aural fullness (2). The presence of endolymphatic hydrops, or increase volume of endolymph in a closed fluid system, damages and distorts the cochlear duct and sensory nerve endings (hair cells) by a transient increase in pressure, resulting in the audiovestibular symptoms (3). The presence of a low-frequency sensorineural hearing loss, recruitment, and a loss of vestibular function provide evidence to support the diagnosis (4).

At present there is no single test that supports the diagnosis of Meniere's disease. Moreover, diagnosis is made most importantly by a complete history, including a detailed description of the pattern of disease presentation, and then supported by quantitative testing (2). Caloric test has been proved to be useful in lateralizing the side of a vestibular lesion and in identifying disorders of the labyrinth and the vestibular nerve. The bithermal caloric stimulation test is specifically a test of the horizontal semicircular canal by irrigating each external auditory canal twice, once with water (or air) that is above body temperature and once with water (or air) that is below body temperature. Each irrigation affects the vestibular receptors of the irrigated ear and provokes a nystagmus response. The responses provoked by right ear irrigation are compared with those provoked by left ear irrigation to determine whether there are any differences in sensitivities of the left and right vestibular mechanisms (5,6). So that caloric test is valuable in diagnosing peripheral vestibular disorders especially Meniere's disease (7).

For the study in Meniere's disease, some investigators found that caloric test is the most reliable for determining the involved ear (8,9). A significant caloric response reduction was found in 48% to 74% of patients with Meniere's disease. Complete loss of vestibular function, as elicited by the caloric test, was reported in 6% to 11% of Meniere's disease patients (2).

Enander and Stahle (10) studied in 343 patients with Meniere's disease and the caloric responses were compared with the hearing loss as measured by pure tone audiometry. The results indicated that there was a relationship between hearing loss and caloric response. The greater of the pure tone threshold increases, the tendency of the caloric response reduces. This observation has since been supported by Brix & Ehrenberger, and Stahle (1,11). They have found relatively strong correlations between hearing loss and vestibular response.

Stahle and Bergman (12) studied the incidence of bilateral Meniere's disease cases. The result showed that the incidence of bilaterality increased with increasing duration of disease. In contrast the numbers of case with reduced excitability were not correlated with increased duration of the disease. And the directional preponderance seems to have no definite correlation to the disease side. This result which differs from previous report (13).

Enander and Stahle, and Thomas & Harrison found that the duration of disease appeared to have little effect on distribution of patients with different types of audiograms (14,15).

Stahle and Bergman (12) found that both hearing loss and reduction of caloric excitability increase with the duration of symptom. Caloric hypofunction was more frequently found in the poorer hearing ears than in the better ears. Hyperfunction was recorded in the better hearing ear in one patient. According to the previous study, there was a correlation between caloric hypofunction and hearing loss in Meniere's disease (10).

Dobie et al. (16) studied in 206 patients with Meniere's disease, the result showed that there was absolutely no correlation between electronystagmography (ENG) and audiometric findings. This suggests that Meniere's disease may progress independently in the auditory and vestibular portions of the labyrinth. They

mentioned that abnormalities were statistically unrelated to all other parameters : age, duration, sex, glycerol test results and audiologic measures.

Karlsen et al. (17) conducted the study in 75 hearing loss patients ranging, age from 18 to 87 years, the results showed that hearing loss and sex were not related to degree of caloric responsiveness in bithermal calorics. However, in warm water caloric, age had significant effects on the speed of the slow component, response duration, frequency and amplitude of nystagmus. These parameters decreased when the age of subjects increased. In cool water calorics, only response duration decreased with increasing age. On the other hand, Bruner and Norris showed no age-related changes in caloric response unilateral weakness (18).

Several studies that investigated vestibular function in Meniere's disease show different results due to different techniques or criteria in setting the normal limits. The reports were not found in generally available collective literature studying the correlation between bithermal caloric stimulation test parameters and patients with possible Meniere's disease, and definite Meniere's disease. Therefore, in this research intends to study the caloric parameters in possible and definite Meniere's disease. The result of this study might be used as a guideline in using caloric stimulation test for routine audiological evaluation or assessment of prognosis and the choice of therapy in patients with Meniere's disease.

1.2 Purpose of this study

This study aimed to

- 1.study the canal paresis value, the directional preponderance value and the maximum slow phase velocity in patients with possible Meniere's disease
- 2.study the canal paresis value, the directional preponderance value and the maximum slow phase velocity in patients with definite Meniere's disease
- 3.compare the canal paresis value, the directional preponderance value and the maximum slow phase velocity between patients with possible and definite Meniere's disease

4.study the relationship among the canal paresis value, directional preponderance value, maximum slow phase velocity and duration of disease in patients with possible Meniere's disease

5.study the relationship among the canal paresis value, directional preponderance value, maximum slow phase velocity and duration of disease in patients with definite Meniere's disease

1.3 Research questions of this study

This study intended to answer these following questions as follows.

1.How were the canal paresis value, the directional preponderance value and the maximum slow phase velocity in patients with possible Meniere's disease ?

2.How were the canal paresis value, the directional preponderance value and the maximum slow phase velocity in patients with definite Meniere's disease ?

3.Were there any differences among the canal paresis value, the directional preponderance value and the maximum slow phase velocity between patients with possible and definite Meniere's disease ?

4.Did the correlation exist among the canal paresis value, directional preponderance value, maximum slow phase velocity and duration of disease in patients with possible Meniere's disease ?

5.Did the correlation exist among the canal paresis value, directional preponderance value, maximum slow phase velocity and duration of disease in patients with definite Meniere's disease ?

1.4 Expected outcome of this study

1. The result of this study might be used as a guideline in application of caloric stimulation test for routine evaluation in patients with Meniere's disease.

2. The result of this study might be used for assessment of prognosis and the choice of therapy.

CHAPTER II

LITERATURE REVIEW

This chapter presented some information of Meniere's disease. The caloric test and the caloric response in Meniere's disease were reviewed.

2.1 Meniere's disease (MD)

Prosper Meniere is widely credited with the first description of endolymphatic hydrops. Meniere's discovery was made possible through a combination of technical and scientific advances, a supportive scientific environment, and a keen intellect able to put the pieces of puzzle together (19). Prosper Meniere described the pathological picture of disease in 1861, now bearing his name, and claimed that its cause had to be found in labyrinth. The finding of endolymphatic hydrops was confirmed by Lindsay (1947), Egmond et al (1956), Williams (1965) (20).

The lack of clear definitions and uniformity in MD has led to misunderstanding and confusion. The amount of proven scientific knowledge is quite small, and many questions remain unanswered. This has resulted in widely varying views within the specialty regarding the nature of this disease, its pathophysiology and its precise diagnosis and treatment (21).

2.1.1 Incidence

The actual incidence of MD is unknown. Some figures and estimates were reported in world literature. In Sweden, the study examining hospital discharge and outpatient data on population of over two million, the incidence of MD was found to be 46 per 100,000 (22). Estimates of the prevalence of MD are even more difficult to obtain than incidence figures. In view of its nature as a non-lethal, non communicable disease, inadequate public health records exist in most countries. Based on the Swedish study, however, conservative

estimated and data indicated that MD was at least four times more common than clinical otosclerosis (23). Clinically, MD is responsible for 10 % of visit to a dizziness unit at Sunnybrook Health Science center, University of Toronto (24). In Finland at the end of 1996, the prevalence of at least 43 per 100,000 and average annual incidence of 4.3 per 100,000 (25).

a) Racial variation

There was no racial difference in the distribution of the MD has been established (9,26). The incidences in Caucasians and Blacks are the same, and the incidence of the frequency of associated symptom such as nausea is the same for American whites as for Japanese patients (26).

b) Gender preponderance

Gender preponderance in MD has been described by a number of investigators. In Sweden, Stahle, Stahle and Arenberg (22) found a female preponderance in a ratio of 3:2. In Japan, Watanabe (27) made a review of several earlier statistical reports. In the period 1934-1960, male preponderance in a ratio of 3:2. In the period 1975-1976, female preponderance in a ratio of bilateral MD was 3:2. In Britain, there is no difference in the gender (15). Balkany, Pillsbury and Arenberg (28,29) did not report gender preponderance, nor did Paparella (30).

c) Age at onset

Age at onset of symptoms varies. MD in children under the age of 10 years is rare, with the youngest case children aged 4 years have been reported. The disease begins in most patients before the age of 60 years (15,22,31) the peak incidence is in those aged 50-60 years (32).

d) Frequency of bilateral MD

Frequency of bilateral MD also is unclear. The reported incidence of bilateral affliction varies widely, from less than 10% to almost 80% (15,28,33-36). There are several reasons for this, one being a lack of consensus as to what criteria constitute the entity (28). A second reason for the lack of consensus as to incidence of bilateral disease results from the progressive nature of the disease and the stage at which patients are diagnosed (2). A third reason is attributable to differing periods of follow up observation (37).

In the largest study, the British's survey of 610 patients with MD followed for at least 5 years found that the incidence of bilateral disease was 31.8 % (15). Rosenberg (38) found that 72 % of patients who developed bilateral MD did so within 5 years of diagnosis in first ear. Interestingly they found that the incidence of bilateral MD was 17 % in medically treated patients and significantly lower at 5.9 % in surgically treated patients. The most likely reason for this was that most patients had had MD for at least 5 years prior to surgery. During this time, approximately 75 percent of patients would have developed bilateral MD and would not be candidates for surgery. However, patients undergoing vestibular neurectomy had no involvement of the opposite ear is a mystery (38). In a large population study by Kitahara (39) in Japan, bilaterality of disease was noted in 9.1 % of patients in their first year of symptoms. This percentage increased steadily to 41.5 % after 20 years of disease (39). Subclinical MD may exist in the second ear along before the development of overt symptoms (40). Greven and Oosterveld (31) found 10 % of 292 patients had developed classical MD in the second ear, but that 73 % of the patients in this group had signs of hearing disturbance in the second ear, such as sensorineural hearing loss, recruitment, or tinnitus.

e) Familial occurrence

Familial occurrence of MD has been reported in 10 % to 20 % of patients in one review (30). In the Swedish study, 14 % of 91 patients studied were noted to have familial distribution of the disease. It was concluded that genetic inheritance played a role, but the mode of transmission was variable (41).

2.1.2 Clinical features and natural history

MD (endolymphatic hydrops) classically is episodic in nature and presents with a triad of symptoms : sensorineural hearing loss, vertiginous episodes, and tinnitus (35), any symptom may precede the others, however, by months or years (42). Neurologic symptoms or signs are absent in MD. Patients may complain of some blurring of vision because of eye drift during nystagmus, but there are no abnormalities of visual acuity, field, or motility (37).

a) Hearing loss

Hearing loss in MD is sensorineural and characterized by loudness recruitment, decreased speech discrimination scores, acoustic distortion, and loudness intolerance ;

hearing is fluctuating ; and progressive and has variable pattern (42). The majority of cases are unilateral. Barber (43) describes two common patterns of sensorineural hearing loss. One group has low frequency loss at 250 and 500 Hz with thresholds rising to normal by 1000 Hz. The other group has an inverted V configuration of their audiometric curve with low-frequency loss maximal at 250 Hz, rising to normal or near normal by 2000 Hz and descending again at 4000 and 8000 Hz (14,32). According to Enander and Stahle (14), fluctuation or variability of hearing is a characteristic of approximately half of patients with Meniere's syndrome, especially those with a low-frequency hearing loss, and is particularly frequent during the early years of the illness. It is not rare, however, even when the disease is advanced, hearing thresholds generally decline throughout the course of the illness. It is not known whether the rate of progression of baseline hearing loss is greatest during periods of frequent fluctuation or whether the baseline hearing drops during intervals when fluctuation is absent or infrequent (37).

Devaiah et al. (44) studied closer examination of audiometric measures in their study revealed more differences in the patients with possible and definite MD. Where they noted relative hearing stabilization in patients with possible disease, they found that there was improvement in those with definite disease. The patients with definite disease showed the greatest improvement (compared with similar changes seen in patients with possible disease) when examining the threshold at 0.5 kHz. No significant differences in discrimination scores were seen in their study.

b) Vertiginous episodes

Vertiginous episodes may be immediately preceded by a sensation of fullness or pressure in the ear, increased hearing loss, increased tinnitus, or an alteration in the quality of these symptoms. The onset of vertigo is frequently sudden, reaching maximum intensity within a few minutes, usually lasting for an hour or more. The severity, duration, and frequency of attack vary greatly in different patients and in the same patient (42). Oosterveld (32) studied in 457 Meniere's disease cases the results showed that the duration of vertiginous episode was two to four hours in 38 %, thirty minutes or less 10 %, and longer than six hours in 17 %.

Devaiah et al. (44) found that patients with possible MD also achieve better control of vertigo than patients with definite MD, as seen by comparing disease class. These

findings supported the idea that patients with possible MD have early MD but have not yet developed complete symptomatology to classify them as having definite MD.

c) Tinnitus

Tinnitus associated with MD has two characters. Initially it is nonpulsatile and low pitched or roaring (45). This type is associated with the aural pressure that precedes acute attacks of vertigo and fluctuating hearing. Later in the illness, when baseline hearing was dropped, there was a continuous humming, buzzing, or ringing tinnitus. The tinnitus may be developed a high-pitched component (36), continuous tinnitus associated with advanced hearing loss may be the chief complaint of many patients, especially those with bilateral MD (43).

d) The natural history of MD

The natural history of MD is highly variable. The most common sequence is for unilateral hearing loss and tinnitus to occur first, followed at some future time by episodic vertigo (20,46). Thomas and Harrison (15) observed vertigo as the presenting symptom in 50 % of 610 cases. In these same series, the second symptom of triad arose within 1 year in 45.5 % of cases, within 2 years in 75 %, and within 5 years in 97.4 % of cases.

2.1.3 Etiology of MD

The cause of MD has remained obscure in spite of the considerable advances in a knowledge of the finer structure of the areas concerned with the production, resorption and the chemical composition of the labyrinthine fluids under normal and pathological conditions (47). Recent research has incriminated various hypo-metabolic state and hyper-metabolic state as well as allergy and personality type in the causation of the disease. Many modern otologists believe that metabolic factors can produce endolymphatic hydrops and that, when all of these entities have been discovered, MD will cease to exist (21).

a) Genetic

There have been several reports of familial MD. Brown (48) in 1941 reported on five families having two members with Meniere's syndrome, in 1949 she reported on three siblings (children of first cousins) and two identical twins bearing the syndrome (49). Bernstein (50) reported on seven families having two or more members afflicted by the symptoms. These reports showed association between Meniere's syndrome and migraine

headaches. Although there were no detailed pedigree studies in order to clarify the mode of genetic transmission. Oliveira and Braga (51) investigated a family with a father, three daughters, and one son afflicted with typical MD and paroxysmal headaches, a pedigree which suggested an autosomal dominant transmission of the disease in some familial cases.

Paparella (30) and Birgeron et al. (41) studied a familial tendency in MD. They found a familial tendency that was 14-20 % of patients with MD, and resulted in the search for a locus of genetic aberration to explain the disorder. Koyama et al. (52) believed that Human Leucocyte Antigens (HLA) influence the T lymphocyte repertoire. Their data imply that individuals who have neither Cw4 nor DR2, in particular DRB1*1602, are better equipped to resist MD than those who are positive. These data taken together suggested that DR2, in particular DRB1*1602, and Cw4 related genetic factors might be involved in the susceptibility to the etiologic or pathogenic mechanisms underlying MD.

b) Traumatic

Trauma could in some way lead to biochemical dysfunction of cells producing endolymph or more likely cells involved in absorption of endolymph. Trauma causing a shock to membranous labyrinth may results in displaced epithelia of the sensory end organs and other cellular elements including the otoconia of the saccule or utricle. Trauma may simply cause the release of debris into the endolymph which could then obstruct the endolymphatic duct and sac resulting in endolymphatic hydrops and thus, Meniere's syndrome. It may be that the pathogenesis (endolymph absorption dysfunction) of trauma in causing Meniere's syndrome is similar to the pathogenesis of idiopathic MD (53).

c) Viral infection

Schuknecht (54) believed that the damage to the endolymphatic sac and duct by viral infection has been proposed as an etiological mechanism in MD. Neurotropic viruses have been considered the most likely offenders. Viruses have been implicated as etiological agents in a number of clinical conditions related to the temporal bone. These include Bell's palsy and some disorders of vestibular dysfunction, and suspicion exists that they may play a role across the spectrum of idiopathic disorders of inner ear function (55). Bergstrom et al. (56) have investigated the antibody reactivity to human herpes viruses in sera from patients with MD. They found a higher antibody reactivity to herpes simplex virus type 1 polypeptides (HSV-1) in patients with MD, as well as discovering herpes simplex viral DNA in endolymphatic sac tissue of two patients.

d) Allergy

Several clinical reports suggested allergy as a causative or associated factor in the etiology of MD or endolymphatic hydrops (57,58). In the study of 93 patients with MD by Derebery and Valenzuela (59), 81 % had a childhood history of allergy, and the majority of their patients (87 %) related a history of a systemic disorder suggesting allergy at the time of assessment. Both food and inhalant allergy were implicated. Relief of Meniere's symptoms occurred in 62 % patients treated with immuno therapy. Pulec (60) reported that the presence of allergy was the most common association with MD in a study of 120 patients, 14 % of patients were found to have allergic cause and responded to allergic treatment alone.

e) Anatomy

The role of the endolymphatic duct and sac in the etiology of MD is increasable interested. A small vestibular aqueduct has been proposed as a cause of disorder, and some imaging studies of the temporal bones of patients with MD supported this hypothesis (site in 21). Antunez et al. (61) and Bagger-Sjoberg et al. (62) investigated the endolymphatic duct and sac by using the computer-aided and graphic reconstruction techniques. The results showed that the volume determinations indicated that the pars canalicularis in the intermediate portion may be significantly smaller and less active in MD patients than in normal subjects. Suchato et al. (63) performed MR imaging in patients with MD. The vestibulocochlear structures can be shown clearly on MR images when using a surface coil and heavy T2 weighting techniques. The results showed a dilated sacculus and basal turn of cochlea (Saturn ring sign).

f) Autoimmunity

A growing body of evidence suggested that some cases of Meniere's patients may be mediated by immune mechanisms (64). The endolymphatic sac has been shown to contain immunoglobulins and lymphocytes, and is thought to be capable of generating a humoral or cellular immune response (65). Results from Dornhoffer's (64) study suggested that immune complex deposition in the subepithelial vasculature of the endolymphatic sac of patients with MD. Suzuki and Kitahara (66) measured the immunologic abnormality in MD by using the erythrocyte sedimentation rate (ESR) and C-reactive protein levels (CRP); serum immunoglobulin levels; complement level; and autoantibody levels. These results showed that severe immunological abnormalities were present in 16 % of the bilateral cases

and 2 % of the unilateral cases. Most of immune parameters in the severe immunological abnormalities group, however, significantly higher than those in the control group. Derebery et al. (67) finding of elevated circulating immune complexes in 96 % of patients with MD. Antibodies directed against type II collagen have found in the serum of patients with MD.

g) Psychosomatic and personality features

Although a number of authors have evoked a psychosomatic etiology of MD, few works have dealt specifically with these patients. Psychological factors occurring in MD have been described by Eagger et al. (68). There was a significant correlation between the presence of vestibular symptoms and psychiatric morbidity that psychiatric morbidity has been shown to increase along with an increase in vestibular symptoms. Martin et al. (69) studied in 48 patients with MD. The results clearly showed that patients with MD presented a psychopathological profile which significantly differed to that of a reference population, particularly in terms of level of anxiety, depressive tendency and phobia. Hinchcliffe (70) studied, the emotion as a precipitating factor in MD. The results showed that emotional factors were relatable to the onset of symptoms in 63% of patients with MD. The personality profile in MD patients compared with a control population were also showed an increased prevalence of psychosomatic type personality profiles in people with MD. It was therefore generally assumed that the psychological disturbances were secondary to the organic disorder (71). Stephens (72) evaluated the personality of patients with MD. The most notable finding was an elevated obsessiveness score. Berrios et al. (73) studied the psychiatric morbidity in subjects with inner ear disease. As a group, they were found to have higher psychiatric morbidity on the general health questionnaire than either normal subjects or subjects affected by other forms of physical disease.

2.1.4 Quantitative testing for diagnosis MD

The differentiation of MD from other condition causing the symptoms of tinnitus, vestibular problems, and hearing loss often is a difficult diagnosis without considerable expenditure of professional and financial resources (74). At present there is no single test that makes the diagnosis of MD. However, diagnosis is made most importantly by a complete history, including a detailed description of the pattern of disease presentation that

the clinical were selected according to the criteria proposed by AAO-HNS Committee on Hearing and Equilibrium, and then supported by quantitative testing (2).

a) Dehydrating agents

There have also been reports of dehydration techniques, for example, with glycerol, with furosemide, comparing furosemide with glycerol and comparing urea with glycerol (75). The goal is to reduce the volume abnormalities in the inner ear and to produce the measurable change in response, i.e., reduction in summating potential negativity as record by electrocochleography (75-79). The oral glycerol administration test has been used since 1966 throughout the world as a method of detecting endolymphatic hydrops (77). Klockhoff (78) reported a 60% sensitivity in patients with MD. He suggested that a glycerol test can be very helpful in order to catch or confirm the diagnosis of MD. Two methods of administering : the first method was glycerol 500 ml. involved a 2 hours intravenous infusion of 500 ml. of 10 % glycerol in saline with 5 % fructose added as an anti-haemolysis agent and the method of 200 ml. consisted of the intravenous infusion of 200 ml. of 10 % solution over a period of 30 minute, both methods appeared to give similar rates of positive diagnosis for MD (76).

In the study of Ito et al using the furosemide VOR test, the results showed a positive rate of about 50 % when used alone. However, 80-90 % of the patients with unilateral classical MD could be detected by using the furosemide VOR test in combination with glycerol dehydration test or electrocochleography (79). While this information proves useful in some circumstances, most clinicians do not routinely use dehydration test because of unpleasant side effects of the test as well as the availability of other diagnostic studies (76).

b) Electrocochleography

Electrocochleography (ECochG) continues to be an important tool in the objective diagnosis, assessment, and monitoring of MD (80). ECochG use computerized signal averaging techniques to record the electrical signals from the cochlea and the auditory nerve in response to an auditory signal (76). There is clinical evidence that the summating potential (SP) recorded by ECochG is often abnormal in MD (81,82). Generally, it has been reported that a large SP/AP amplitude ratio indicates the presence of endolymphatic hydrops (82,83).

Dauman et al. (84) studied transtympanic ECoG in patients with MD. They found that mean SP amplitude in MD group was larger than sensorineural hearing impaired group and normal subjects group for 1, 2 and 8 kHz. The low frequency (1 or 2 kHz.) SP decreased in 59 % of MD patients during a glycerol dehydration test. The use of ECoG with monitoring of SP thus improves the sensitivity of glycerol test for detection of endolymphatic hydrops. Rodtong (85) found that both SP and AP absolute latencies in definite MD group were significantly longer than that in normal group. And both SP/AP amplitude and area ratio in definite MD group were significantly higher than that in normal group. The sensitivity of the SP/AP amplitude ratio or area ratio yielded the same results (63 %). When combination both of them the sensitivity were increased from 63 % to 67 %.

c) Caloric test

The caloric tests have been recognized as the most beneficial in vestibular diagnosis (86). Stimulation in the caloric test is a nonphysiologic procedure used for inducing endolymph flow in the semicircular canals by creating a temperature gradient from the lateral to medial part of the canal. The standard procedure stimulates only one labyrinth at a time, and the test results can be compared only within the same patient (one ear compared with the other) (89).

The test is performed with the patient lying on a table with the head anteroflexed 30 degrees, to bring the horizontal canal into the vertical position. A thermal stimulus, usually water, flows into the external ear canal, water temperatures of 30°C and 44°C are used, and approximately 250 ml. of water is delivered over a 30-second period. When cold water is used, the temperature of the water is transmitted to the wall of the horizontal canal, which cools the endolymph and causes the fluid to become more dense as it falls in the vertically positioned canal. This process sets up a fluid motion in the canal that deflects the cupula causes the resting neural discharge to drop relative to opposite ear and thereby creates a neural imbalance that results in nystagmus with the slow phase toward the side of irrigation and the fast phase away from the irrigated side. The opposite occurs when warm water is used: the nystagmus beats toward, rather than away from the irrigated ear (89,90,91). In order to minimize central suppression of the caloric responses, the patient is instructed to perform aloud a concentration task e.g. counting backward from 200 by 3, 4, 7 etc. during each response. The task's difficulty is adjusted to match the patient's ability (92).

Several variables must be carefully controlled in order to obtain accurate nystagmus measurements such as the water temperature, amount of water used for stimulation, head position, alertness of the patient, whether the eyes are opened or closed, as well as certain drugs and alcoholic beverages, the nystagmus may be influenced by these factors (90). For the study in MD, some investigators found that caloric test is the most reliable for determining the involved ear (8,9). A significant caloric response reduction was found in 48% to 74% of patients with MD. Complete loss of vestibular function, as elicited by the caloric test, was reported in 6% to 11% of MD patients (2).

2.2 Caloric investigations in human

The caloric test is one of the most useful clinical methods for evaluating vestibular function. The traditional Fitzgerald and Hallpike (1942) caloric test consists of irrigating each ear with water at 30°C and 44°C is one of the most commonly used techniques (87). The bithermal caloric test is the most widespread used today and still the only direct method of obtaining information about the independent functioning of the left and right vestibular nerves and end-organ (20,88).

The three most common abnormal and clinically important findings of the caloric test are unilateral weakness, bilateral weakness, and failure of fixation suppression (93).

2.2.1 Unilateral weakness (UW) or Canal paresis (CP)

Unilateral weakness (UW) is defined as the amount by which the two responses provoked by right ear irrigations differ in intensity from those provoked by left ear irrigations (6). To quantify the difference in the caloric response strength of the two ears, most examiners use the formula, proposed by Jongkees and Phillipszoon (1964) (see in appendix, Table A-1). The normal limit of ± 20 to 25 % is widely accepted (6). Thepmontar (94) studied in Thai normal persons aged 20-40 years. The reference range (mean \pm 2SD) of CP of caloric test was 0-27 %. Kamphangkaew (95) studied in Thai normal persons aged 40-60 years. The reference range (mean \pm 2SD) of CP of caloric test was 0-26 %. Mean and reference range (mean \pm 2SD) of CP in Thai normal subjects were presented in Table 1 (94,95).

Table 1 Mean and reference range (mean \pm 2SD) of canal paresis (CP) in Thai normal subjects.

Caloric test	Age range (years)	n	Mean	Reference range
CP	20-40	32	-4.31	0-27
	41-60	21	11.76	0-26

Modified (94,95)

From the basic assumption of the caloric test is that both ears receive equal caloric stimuli; therefore, if both ears are normal, they should produce approximately equal caloric responses. If not, the patient is said to have a unilateral weakness, which is evidence of a lesion of the labyrinth or vestibular nerve on the side of the weak response (94). It is therefore a peripheral finding (91,96).

Brask & Falbe-Hansen (97) who studied ENG and caloric test in 20 normal subjects. The mean CP value of responses from left side was higher than that of right side, although they would be expected to be zero or close to zero (97). The phenomenon may be due to the relatively small material such as the statistical error of the mean. Or the fact that the right ear is always irrigated first. This possibly necessitates a psychic inhibition due to fear of the unknown, a factor which is perhaps not present at the subsequent irrigation of the other ear. However, there was no significant difference of the CP between right and left side.

2.2.2 Directional preponderance (DP)

Directional preponderance (DP) is defined as the represents of the difference in intensity between the two right-beating nystagmus responses (provoked by right ear-warm temperature and left ear-cool temperature irrigations) and the two left-beating responses (provoked by left ear-warm temperature and right ear-cool temperature irrigations). Directional preponderance is calculated by the formula in appendix, Table A-2. In most clinics, an inter-ear difference of 30 % or greater is considered abnormal for DP (98). In the studies of Thepmontar (94) and Kamphangkaew (95), they found that the reference range of DP of caloric test in Thai normal subjects aged 20-40 years and 40-60 years was similar and equaled to 0-30% (94,95).

Table 2 Mean and reference range (mean \pm 2SD) of directional preponderance (DP) in Thai normal subjects.

Caloric test	Age range (years)	n	Mean	Reference range
DP	20-40	32	5.95	0-30
	41-60	21	10.52	0-30

Modified (94,95)

Directional preponderance is believed to be toward the side of central lesion and away from the side of a peripheral lesion (86). The DP should reflect an imbalance in the vestibular system that causes the caloric nystagmus to be more pronounced in one direction than in the other, regardless of the ear stimulated (87). A caloric DP can be due to either peripheral or central pathology. It is therefore a nonlocalizing abnormality (91,96).

Vesterhauge and Larsen (99) studied ENG and caloric test in a total of 50 normal subjects. Fifteen subjects were re-examined 24 hours after the first examination. The intention of their procedure was to determine normal limits for patients examined twice and thereby obtain a greater accuracy than is possible with the result of a single examination. The mean DP value of the right beating was higher than the left beating nystagmus for double and single examinations. However, there was no significant difference between the mean values of double and single examinations.

2.2.3 Maximum slow phase velocity (Vmax)

Maximum slow phase velocity or maximum slow-phase eye speed (Vmax) is defined as the average slow phase eye speed during the 10 sec interval in which the response is most intense usually between 55-65 sec after beginning the irrigation, although it must be determined by inspection of the tracing in each case (6).

The velocity of the slow phase is considered to be the most accurate predictor as to the etiology of the disease. In order to have a significant classification, the velocity of the slow phase needs to be at least 8 degrees/second. If the total of the slow phase velocity of all alternate binaural bithermal caloric stimulations is less than 30 degree /second, there is bilateral weakness (86). Mean and SD of Vmax (degree/second) for the warm and cool

irrigations induced caloric response from both ears of Thai normal subjects were presented in Table 3 (94,95).

Table 3 Mean and SD of Vmax (degree/second) for the warm and cool irrigations induced caloric response from both ears of Thai normal subjects.

Age range(years)	n	Vmax	Mean	SD
20-40	32	Warm	57.19	38.87
	32	Cool	40.50	21.03
41-60	21	Warm	27.79	15.58
	21	Cool	23.17	11.22

Modified (94,95)

The slow-phase velocity of nystagmus is one of the most sensitive parameters of vestibular function and is currently the standard for evaluating the caloric test. Vestibular asymmetry appears globally pronounced with Vmax and Vmax may be accepted as a more sensitive indicator of a labyrinthine lesion (87).

Mehra (100) studied in 30 normal subjects. The result showed no significant difference of the Vmax between the right versus the left ears, the right versus the left beats. There was found individual readings which were significantly higher for the warm irrigation (t value of 4.47). These findings were therefore in agreement with Sill et.al (101) and Ford (102) who indicated that there was a significant difference between Vmax results from warm and cool stimulation of normal subject ears ($p < 0.02$).

2.2.4 Visual suppression of caloric nystagmus

In a normal vestibular system or in one with peripheral vestibular disorder, when the caloric-induced nystagmus is intense, opening the eyes should reduce or eliminate the nystagmus by ocular fixation (86). The effectiveness of visual fixation in suppressing caloric nystagmus (fixation index) is calculated and reported as a percentage of the total response. It is calculated by the formula in appendix, Table A-3. If the starting of optic fixation was too early, then, the response was too strong. Therefore, the subjects were unable to suppress the nystagmus or to normal degree resulting in abnormal in fixation

index. If the starting of optic fixation was too late, there would not be enough nystagmus to be calculated (94,95). The fixation index value as 0-70 % is normal (99,103). Mean and reference range (mean \pm 2SD) of FI of caloric test in Thai normal subjects were presented in Table 4 (94,95).

Table 4 Mean and reference range (mean \pm 2SD) of fixation index (FI) of caloric test in Thai normal subjects.

Caloric test	Age range (years)	Mean	Reference range
FI	20-40	0	0
	41-60	0	0

Modified (94,95).

At the peak of the caloric response, normal subjects are able to suppress nystagmus intensity by at least 50 % if they have an intact visual-cerebellar-vestibular pathway (cited in 104). However, in some patients with CNS disorders, nystagmus intensity with eyes open nearly equals, match, or exceeds that with eyes closed (6). In some central lesions, the caloric induced nystagmus does not appear until the eyes are opened. The nystagmus may also significantly increase when the eyes are opened or showed no signs of suppression of the already present induced nystagmus (86). This effect is known as failure of fixation suppression (6). The failure of fixation suppression of caloric-induced nystagmus is an important finding of the caloric test.

The FI is considered abnormal when it is greater than 70 % (103). Although FFS is sign of central nervous system dysfunction, two benign causes of FFS have been demonstrated and must be ruled out: sedation, particularly by barbiturates, and contact lenses, particularly if they are new or uncomfortable. In addition, as with all central ENG abnormalities, peripheral ocular pathology must be ruled out in the patient demonstrating FFS (91). The failure of fixation suppression is a strong indication of CNS (cerebellum/brainstem) disease, although the examiner should ensure that the patient has sufficient visual acuity to perform the test properly (89).

2.2.5 Hyperactive responses

Caloric responses may exceed the upper limit of normal variation, 50 degrees/second slow-phase eye speed for cool irrigations and 80 degrees/second for warm irrigations. Hyperactive responses may occur if the caloric transfer qualities of the stimulated ear are greatly enhanced, such as when tympanic membrane is perforated, atrophic, or retracted (6). Hyperactive caloric responses are encountered in psychogenic patients. If there is a hyperactivity of the subjective responses without a coincident hyperactivity of nystagmus, a neurosis should be suspected. However, hyperexcitability of the vestibular apparatus occurs rarely in peripheral disease, but more frequently in diseases causing irritation of the central vestibular nuclei or their pathways, or release of these from inhibitory centers. Hyperactive caloric responses are a significant finding in some intracranial lesions (105).

2.3 Caloric investigation in clinical subjects

Enander and Stahle (10) studied in 343 patients with MD and the caloric responses were compared with the hearing loss as measured by pure tone audiometry. The results indicated that there was a relationship between hearing loss and caloric response. The greater of the pure tone threshold increases, the tendency of the caloric response reduces. This observation has since been supported by Brix and Ehrenberger, and Stahle (11). They have found relatively strong correlations between hearing loss and vestibular response.

Stahle (11) studied in 356 patients with severely disabled MD, the mean duration of disease was 8 years. Among the 318 unilateral cases, the caloric response was reduced in 188 subjects, exaggerated in 4 subjects and normal in 126 subjects. Directional preponderance was not taken into consideration in their investigation. Moreover, he found that the hearing deteriorated considerably in the early stage of disease, but the hearing level stabilized with time. Reduction of pure tone threshold was accompanied by a progressive decrease in caloric response. He found that both hearing loss and reduction of caloric excitability increase with the duration of diseases (11,12). The explanation may be that during the protracted illness the apparently healthy or better ear has been afflicted by

vestibular impairment even though there is no characteristic hearing loss. This should reduce the discrepancy in caloric response between two labyrinths.

Stahle and Bergman (12) studied 300 MD patients, their results showed abnormal CP in 153 subjects of the total 258 patients with unilateral MD. A stronger response from the affected side was recorded in 22 patients. A combination of reduced response and DP was recorded in 158 subjects, 82 subjects of whom also showed reduced excitability on one side. Directional preponderance alone was noted in 76 patients. Directional preponderance from 158 subjects with unilateral disease, the DP in 42% was directed toward the affected ear, and in 58% was away from the affected ear. The direction of preponderance seemed to have no definite correlation to the diseased ear. In addition, they found that both hearing loss and reduction of caloric excitability increase with the duration of symptom. This result is approximately the same as those reported by Stahle (11). Caloric hypofunction was more frequently found in the poorer hearing ears than in the better ears. Hyperfunction was recorded in the better hearing ear in one patient. According to previous study there was a correlation between caloric hypofunction and hearing loss in MD (10).

Hulshof and Baarsma (13) conducted a study in 151 patients with unilateral MD in the interval between vertigo attacks. All of their patients had undergone the vestibular tests during a week of clinical observation. The result was revealed that the excitability was reduced unilaterally by more than 20% in 111 subjects. In 9 subjects a non-responsive labyrinth was found. In their study, 46 subjects showed a DP more than 20%, 18 of them was directed away from the affected ear and 28 was directed toward the affected ear. A combined lesion was found in 39 subjects. In addition, there was a correlation between the duration of disease and the extent of caloric response reduction. The result revealed that caloric response reduction increased with increasing duration. The number of patients with abnormalities in caloric test also increased with the duration of complaints.

Fraysse et al.(106) studied in 17 patients with MD, from their observations, a correlation was found between the degree of endolymphatic hydrops and the response to caloric tests. In patients whose the membranes of the saccule and utricle were normal or slightly dilated, the results showed no effect to caloric response. In patients whose the saccule against the footplate, the caloric test results showed no response.

Karlsen et al. (17) studied in 75 hearing loss patients ranging in age from 18 to 87 years, the results showed that hearing loss and sex are not related to degree of caloric responsiveness in bithermal calorics. However, in warm water caloric, age had significant effects on the speed of the slow component, response duration, frequency and amplitude of nystagmus ($p < 0.05$). These parameters decreased when the age of subjects increased. In cool water calorics, only response duration decreased with increasing age.

Dobie et al. (16) conducted the study in 206 MD patients with the mean duration of disease was 5.9 years. They studied in patients with various severity. The results were revealed abnormal CP in 49% and abnormal DP in 36%. There was absolutely no correlation between caloric responses and audiometric findings. This suggests that MD may progress independently in the auditory and vestibular portions of the labyrinth. They mentioned that abnormalities were statistically unrelated to all other parameters : age, duration, sex, glycerol test results and audiologic measures.

Cawthorne et al.(107) studied 9 MD patients, the caloric test was performed both before and after labyrinthectomy of the affected ears. The results of MD ears showed a marked accentuation of the response to cold water irrigation in six of nine ears. This result was the similar to the post-operative results of unaffected ears. While the pre-operative results of unaffected ears showed a marked accentuation of the response to hot water irrigation in eight ears. Their discussion may be directed to the possible nature of central processes which must be for the upset of the normal caloric responses effected by destruction of the opposite deemed responsible labyrinth and for its later restoration. They postulated this variation of the unaffected ears was due to changes of the central nervous system mechanism (107). Therefore, this variation of MD ears might be due to the lateral semicircular canal sensitivity was changed of by central nervous system mechanism (107).

CHAPTER III

MATERIALS AND METHODS

In this chapter, the criteria for two groups of patients were presented. Instruments, procedure and data collection were described. Data analysis and procedures of statistics were specified.

3.1 Subjects

Meniere's disease patients from otolaryngologic clinic of Ramathibodi hospital were served as subjects.

All patients must have normal outer ears and tympanic membrane by otoscopic examination, ages ranged between 20-60 years. MD was diagnosed according to the criteria established by the Committee on Hearing and Equilibrium (108), see Appendix Table A-4. The subjects were separated into 2 groups: group 1, possible MD, consisted of 30 patients : and group 2, definite MD, consisted of 30 patients.

Patients' permission should be allowed and inform consent should be signed before starting the data collection.

The exclusion criteria were:

- 1) history of ear disease : chronic otitis, otosclerosis, head trauma
- 2) history of ear surgery that might affect a caloric response
- 3) presence of eye movement disorders, severe visual deficit or amblyopia

3.2 Research Instruments

The instruments used in this study were:

- 1) otoscope

- 2) audiometer-GSI 16
- 3) the computerized electronystagmography , model Nicolet Nystar™ Plus version 4.33 (with monitor), with two channels recording
- 4) the curve light bar with diameter of the light diodes of 3 mm.

3.3 Procedure

History of illness and personal data were obtained after MD patients were completely examined by otoneurologist. The audiologic and otoscopic examinations were performed at the Speech and Hearing Clinic, Department of Otolaryngology in Ramathibodi hospital. Before starting the caloric stimulation test, the patients were fulfilled following conditions:

- 1) no medications (antihistamine, tranquilizers, and sedative) for 24-48 hours (94,95)
- 2) no alcohol for 48 hours (94)
- 3) no foods and drinks for 4 hours (95,109,110)

All patients were received audiological evaluation in the sound treated room as follows: pure tone audiometry including pure tone air conduction (0.25, 0.5, 1, 2, 3, 4, and 8 kHz) and pure tone bone conduction (0.5, 1, 2, and 4 kHz), speech audiometry including speech reception threshold and speech discrimination score.

Bithermal caloric stimulation test

Before beginning the test, patient was instructed that each ear would be irrigated twice with water 125 cc at 30°C and 44°C for 30 seconds (1,94,95,111). The caloric test was performed in the dark room. After a careful skin preparation, the surface electrodes were placed on outer canthus of right and left eyes, above and below the left eyebrow and the general electrode placed on the forehead (112,113). Then the patient was requested to sit on the chair that tilted downward from the vertical plane at an angle about 60 degrees (6,94,95,113). A horizontal light bar was place approximately 91 cm. in front of the patient. When the patient was ready for the first irrigation, calibration the recording system should be done at the beginning of the test by asking the patient to look straight ahead in front of the light bar and follow the target without moving the head.

The caloric test was first conducted by applying irrigation to the patient ear with greater hearing loss, nystagmus response and vertigo usually appeared near the end of the

irrigation. During the test, he/she should close his/her eyes and perform mathematical or mental tasks such as answering the questions, saying the name of persons etc., to counteract with central voluntary inhibition of the nystagmus. After the response has begun to decline approximately 90-100 seconds after the beginning of the irrigation (6), then patient was asked to open his/her eyes and fixate on a spot on the horizontal light bar for 10 seconds. Then, patient was asked to close his/her eyes again. The patient continued the mental tasks again until completing each test in 240 seconds as measured from the start of irrigation.

The next irrigation of other ear should be postponed at least 5-10 minutes for the labyrinth to reach body temperature again. The percent of caloric response was calculated and printed out by the computer automatically. The calculation of Vmax for right and left ears, right and left beats, warm and cool irrigations were not taken the Vmax of the unaffected ears into the consideration. Also, PTA of the unaffected ears were not taken into the consideration. The PTA of air conduction threshold was calculated from the threshold at 0.5, 1, and 2 kHz.

3.4 Data analysis

The SPSS program for windows was conducted in analysis of the caloric data:

- 1). Mean and standard deviation were applied the CP, the DP and the Vmax of the caloric test for both groups.
- 2). T-test were conducted to determine the differences of the normal distribution parameters (CP, DP and Vmax) in patients with possible and definite MD, and in both groups, respectively.
- 3). Mann-Whitney U test were conducted to determine the differences of the abnormal distribution parameters (CP, DP and Vmax) in patients with possible and definite MD, and in both groups, respectively.
- 4). Pearson's correlation coefficient was performed in analyzing the relationship between CP, DP, Vmax and duration of disease in both groups.
- 5). Percentage represented patients who had abnormal CP and DP in possible and definite MD groups.

CHAPTER IV

RESULTS

This chapter presented results of caloric test finding in patients with possible and definite MD.

The experiment was conducted on sixty patients with MD, divided into two groups. The first group, possible MD, consisted of 5 males and 25 females whose age ranged between 20-60 years, mean age was 44.33 years (SD=9.24). The mean duration of disease was 4.40 years (SD=5.42). During the last six months, the occurrence of vertigo was ranged from 0 to 30 times per month. From Table 5, 93.34% of the subjects reported the functional level of 1, 2 and 3.

From the results of clinical and audiological examinations, they were found that the disease was bilateral in 4 subjects, right unilateral in 13 subjects and left unilateral in 13 subjects. From Table 6, 43.33 % and 13.33% of the subjects complained of the tinnitus and aural fullness problems, respectively. From Table 7, the mean pure tone average (PTA) of air conduction threshold at 0.5, 1, and 2 kHz of right ear was 17.06 dBHL (SD=7.16) and left ear was 17.24 dBHL (SD=5.60). There was no significant difference of the means PTA between right and left ears. The raw data of caloric tests in patients with possible MD was presented in appendix, Table A-6.

The second group, definite MD, consisted of thirty patients, which consisted of 14 males and 16 females whose age ranged between 20-60 years, the mean age was 45.30 years with SD of 7.35 years. The mean duration of disease was 5.19 years (SD=3.65). During the last six months, the occurrence of vertigo was ranged from 0 to 30 times per month. From Table 5, 93.33% of the subjects reported the functional level of 1, 2 and 3.

From the results of clinical and audiological examinations, they were found that the disease was bilateral in 7 subjects, right unilateral in 12 subjects and left unilateral in 11 subjects. From Table 6, 93.33 % and 53.33% of the subjects complained of the tinnitus and aural fullness problems, respectively. From Table 7, the mean pure tone average (PTA) of

air conduction threshold at 0.5, 1, and 2 kHz of right ear was 39.58 dBHL (SD=17.59), and left ears was 40.94 dBHL (SD=18.45). There was no significant difference of the means PTA between right and left ears. The raw data of caloric tests in patients with definite MD was presented in appendix, Table A-7.

Table 5 The frequency of patients with possible and definite MD in each functional level.

Functional level	Possible MD	Definite MD
1	5 (16.67%)	8 (26.67%)
2	12 (40%)	10 (33.33%)
3	11 (36.67%)	10 (33.33%)
4	2 (6.67%)	1 (3.33%)
5	0 (0%)	1 (3.33%)
6	0 (0%)	0 (0%)

Details of the functional level were presented in appendix, Table A-5.

Table 6 Side of tinnitus' ears and aural fullness' ears of patients with possible and definite MD.

Side	Possible MD		Definite MD	
	Tinnitus	Aural fullness	Tinnitus	Aural fullness
Right ear	8 (26.67%)	1 (3.33%)	13 (43.33%)	7 (23.33%)
Left ear	4 (13.33%)	2 (6.67%)	10 (33.33%)	6 (20%)
Both ears	1 (3.33%)	1 (3.33%)	5 (16.67%)	3 (10%)
None	17 (56.67%)	26 (86.67%)	2 (6.67%)	14 (46.67%)

Table 7 Comparison of the means PTA of affected ears between right and left ears of patients with possible and definite MD by using t-test.

Group	Side	Mean	SD	n	t	p
Possible MD	PTA of right ear (dBHL)	17.06	7.16	17 (ears)	-0.08	0.94
	PTA of left ear (dBHL)	17.24	5.60	17 (ears)		
Definite MD	PTA of right ear (dBHL)	39.58	17.59	19 (ears)	-0.23	0.82
	PTA of left ear (dBHL)	40.94	18.45	18 (ears)		

From Table 8 showed the comparison of the clinical data between both groups by using t-test. The means age of possible and definite MD were 44.33 years (SD=9.24) and 45.30 years (SD=7.35), respectively. The means duration of disease of possible and definite MD were 4.40 years (SD=5.42) and 5.19 years (SD=3.65), respectively. The t-test showed no significant differences of the mean age and mean duration of disease between both groups. On the other hand, the means PTA of right ear of possible and definite MD were 17.06 dBHL (SD=7.06) and 39.58 dBHL (SD=17.59), respectively. The means PTA of left ear of possible and definite MD were 17.24 dBHL (SD=5.60) and 40.94 dBHL (SD=18.45), respectively. The t-test comparison showed that the means PTA of right and left ears of possible MD were significantly lower than those of definite MD, respectively ($p<0.001$).

Table 8 Comparison of the clinical data between patients with possible and definite MD by using t-test.

Clinical data	Group	Mean	SD	n	t	p
Age (years)	Possible MD	44.33	9.24	30 (subjects)	-0.45	0.66
	Definite MD	45.30	7.35	30 (subjects)		
Duration of disease (years)	Possible MD	4.40	5.42	30 (subjects)	-1.53	0.13
	Definite MD	5.19	3.65	30 (subjects)		
PTA of right ear (dBHL)	Possible MD	17.06	7.16	17 (ears)	-4.92***	0.00
	Definite MD	39.58	17.59	19 (ears)		
PTA of left ear (dBHL)	Possible MD	17.24	5.60	17 (ears)	-5.08***	0.00
	Definite MD	40.94	18.45	18 (ears)		

***significant at $p<0.001$

4.1 The values of the canal paresis (CP), the directional preponderance (DP) and the maximum slow phase velocity (Vmax) in patients with possible MD

From Table 9, the caloric responses from patients with possible MD showed that right CP and left CP were found in 18 and 12 subjects, respectively. The means of right CP, left CP and total CP value were 16.67 % (SD=13.47), 18.75 % (SD=18.83) and 17.50 % (SD=15.55), respectively. The t-test showed no significant difference of means CP between right and left CPs.

The right DP, left DP and no DP were found in 10,18 and 2 subjects, respectively. The means of right DP, left DP and total DP value were 16.00 % (SD=11.80), 9.67 % (SD=7.82) and 11.13 % (SD=9.86), respectively. The t-test showed no significant difference of means DP between right and left DPs.

Table 9 Mean, SD, number of subjects, t-value and p-value of the canal paresis (CP) and directional preponderance (DP) in patients with possible MD.

Parameter	Side	Mean	SD	n(subjects)	t	p
Canal paresis	Right CP	16.67	13.47	18	0.33	0.74
	Left CP	18.75	18.83	12		
	No CP	-	-	-	-	-
	Total CP	17.50	15.55	30		
Directional preponderance	Right DP	16.00	11.80	10	1.52	0.15
	Left DP	9.67	7.82	18		
	No DP	0	0	2	-	-
	Total DP	11.13	9.86	30		

From Table 10, the means of maximum slow phase velocity (Vmax) of right ear (RW+RC) and left ear (LW+LC) were 19.97 (SD=14.45) and 22.09 (SD=17.45) degrees/second, respectively. The t-test showed no significant difference of means Vmax of ear between right and left ears.

The means Vmax of right beat (LC+RW) and left beat (LW+RC) were 20.76 (SD=18.29) and 21.29 (SD=13.45) degrees/second, respectively. The t-test showed no significant difference of means Vmax of beat between right and left beats.

The means Vmax of warm irrigation (RW+LW) and cool irrigation (RC+LC) were 9.79 (SD=6.90) and 32.26 (SD=14.42) degrees/second, respectively. The t-test comparison showed that the mean Vmax of warm irrigation was significantly weaker responses than that of cool irrigation ($p<0.001$).

Table 10 Comparison of the means maximum slow phase velocity (Vmax) between right and left ears, right and left beats and warm and cool irrigations in patients with possible MD by using t-test.

Parameter	Value	Mean	SD	n (irrigation)	t	p
Vmax of ear	Rt. Ear (RW+RC)	19.97	14.45	34	-0.55	0.59
	Lt. Ear (LW+LC)	22.09	17.45	34		
Vmax of beat	Rt. Beat (LC+RW)	20.76	18.29	34	-0.14	0.89
	Lt. Beat (LW+RC)	21.29	13.45	34		
Vmax of irrigation	Warm (RW+LW)	9.79	6.90	34	-8.20***	0.00
	Cool (RC+LC)	32.26	14.42	34		

***significant at $p<0.001$

4.2 The values of the canal paresis (CP), the directional preponderance (DP) and the maximum slow phase velocity (Vmax) in patients with definite MD

From Table 11, the caloric responses from patients with definite MD showed that right CP, left CP and no CP were found in 15, 14 and 1 subjects, respectively. The means of right CP, left CP and total CP value were 32.13 % (SD=22.52), 30.71 % (SD=25.06) and 30.40 % (SD=23.66), respectively. The t-test showed no significant difference of means CP between right and left CPs.

The right DP, left DP and no DP were found in 17, 12 and 1 subjects, respectively. The means of right DP, left DP and total DP value were 22.67 % (SD=16.92), 24.64 % (SD=26.52) and 22.63 % (SD=20.73), respectively. The t-test showed no significant difference of means DP between right and left DPs.

Table 11 Mean, SD, number of subjects, t-value and p-value of the canal paresis (CP) and directional preponderance (DP) in patients with definite MD.

Parameter	Side	Mean	SD	n(subjects)	t	p
Canal paresis	Right CP	32.13	22.52	15	0.16	0.87
	Left CP	30.71	25.06	14		
	No CP	0	0	1	-	-
	Total CP	30.40	23.66	30		
Directional preponderance	Right DP	22.67	16.92	17	0.22	0.83
	Left DP	24.64	26.52	12		
	No DP	0	0	1	-	-
	Total DP	22.63	20.73	30		

From Table 12, the mean ranks of maximum slow phase velocity (Vmax) of right ear (RW+RC), left ear (LW+LC), right beat (LC+RW) and left beat (LW+RC) were 37.32, 37.69, 36.73 and 38.27 degrees/second, respectively.

Since the Vmax of left ear and Vmax of right beat were not normal distribution data (see Table A-5), therefore a Mann-Whitney U test were conducted to determine whether the difference of mean ranks for Vmax of ear and Vmax of beat between right and left ears, right and left beats, respectively. The Mann-Whitney U test showed no significant difference of mean ranks for Vmax of ear and Vmax of beat between right and left ears, right and left beats, respectively.

Table 12 Comparison of the means maximum slow phase velocity (Vmax) between right and left ears, right and left beats in patients with definite MD by using Mann-Whitney U test.

Parameter	Value	Mean Rank	n (irrigation)	Z	p
Vmax of ear	Rt. Ear (RW+RC)	37.32	38	-0.08	0.94
	Lt. Ear (LW+LC)	37.69	36		
Vmax of beat	Rt. Beat (LC+RW)	36.73	37	-0.31	0.76
	Lt. Beat (LW+RC)	38.27	37		

From Table 13, the means of Vmax of warm irrigation (RW+LW) and cool irrigation (RC+LC) were 9.08 (SD=11.02) and 26.03 (SD=19.79) degrees/second, respectively. The t-test comparison showed that the mean Vmax of warm irrigation was significantly weaker responses than that of cool irrigation ($p<0.001$).

Table 13 Comparison of the means maximum slow phase velocity (Vmax) between warm and cool irrigation in patients with definite MD by using t-test.

Parameter	Value	Mean	SD	n (irrigation)	t	p
Vmax of irrigation	Warm (RW+LW)	9.08	11.02	37	-4.55***	0.00
	Cool (RC+LC)	26.03	19.79	37		

***significant at $p<0.001$

4.3 The comparison of the canal paresis (CP), the directional preponderance (DP) and the maximum slow phase velocity (Vmax) between patients with possible and definite MD

From Table 14, the means of right CP of patients with possible and definite MD were 16.67 (SD=13.47) and 32.13 (SD=22.52), respectively. The t-test comparison showed that the mean right CP of possible MD was significantly lower than that of definite MD ($p<0.05$).

The means of left CP of patients with possible and definite MD were 18.75 (SD=18.83) and 30.71 (SD=25.06), respectively. The t-test showed no significant difference of means left CP between possible and definite MD groups.

The means of total CP of patients with possible and definite MD were 17.50 (SD=15.55) and 30.40 (SD=23.66), respectively. The t-test comparison showed that the mean total CP of possible MD was significantly lower than that of definite MD ($p<0.05$).

Table 14 Comparison of the means canal paresis (CP) between patients with possible and definite MD by using t-test.

Side	Group	Mean	SD	n(subjects)	t	p
Right CP	Possible MD	16.67	13.47	18	-2.44*	0.02
	Definite MD	32.13	22.52	15		
Left CP	Possible MD	18.75	18.83	12	-1.39	0.18
	Definite MD	30.71	25.06	14		
Total CP	Possible MD	17.50	15.55	30	-2.50*	0.02
	Definite MD	30.40	23.66	30		

*significant at $p<0.05$

From Table 15, the results were revealed that the means of right DP of patients with possible and definite MD were 16.00 (SD=11.80) and 22.67 (SD=16.92), respectively. The t-test showed no significant difference of means of right DP between possible and definite MD groups.

The means of left DP of patients with possible and definite MD were 9.67 (SD=7.82) and 24.64 (SD=26.52), respectively. The t-test comparison showed that the mean left DP of possible MD was significantly lower than that of definite MD ($p<0.05$).

The means of total DP of patients with possible and definite MD were 11.93 (SD=9.72) and 23.41 (SD=20.64), respectively. The t-test comparison showed that the mean total DP of possible MD was significantly lower than that of definite MD ($p<0.05$).

Table 15 Comparison of the means directional preponderance (DP) between patients with possible and definite MD by using t-test.

Side	Group	Mean	SD	n(subjects)	t	p
Right DP	Possible MD	16.00	11.80	10	-1.22	0.23
	Definite MD	22.67	16.92	18		
Left DP	Possible MD	9.67	7.82	18	-2.26*	0.03
	Definite MD	24.64	26.52	11		
Total DP	Possible MD	11.13	9.86	30	-2.74*	0.01
	Definite MD	22.63	20.73	30		

*significant at $p<0.05$

From Table 16, the results were revealed that the means Vmax of warm irrigation (RW+LW) of patients with possible and definite MD were 9.79 (SD=6.90) and 9.08 (SD=11.02) degrees/second, respectively. The t-test showed no significant difference of means Vmax of warm irrigation between possible and definite MD groups.

The means Vmax of cool irrigation (RC+LC) of patients with possible and definite MD were 32.26 (SD=14.42) and 26.03 (SD=19.79) degrees/second, respectively. The t-test showed no significant difference of means Vmax of cool irrigation between possible and definite MD groups.

Table 16 Comparison of the means maximum slow phase velocity (Vmax) between patients with possible and definite MD by using t-test.

Parameter	Group	Mean	SD	n(ears)	t	p
Vmax of warm irrigation	Possible MD	9.79	6.90	34	0.33	0.74
	Definite MD	9.08	11.02	37		
Vmax of cool irrigation	Possible MD	32.26	14.42	34	1.53	0.13
	Definite MD	26.03	19.79	37		

4.4 Correlation among the canal paresis (CP), the directional preponderance (DP), and the maximum slow phase velocity (Vmax) and duration of disease in patients with possible MD

From Table 17, Pearson's correlation coefficients were computed and tested the relationships among the canal paresis, the directional preponderance, the maximum slow phase velocity and duration of disease in patients with possible MD. The Pearson's correlation coefficients for CP, DP, Vmax of warm and cool irrigation were 0.19, 0.27, -0.05 and -0.13, respectively. The Pearson's correlation coefficients analysis showed nonstatistically significant relationships between the caloric parameters and duration of disease.

Table 17 Pearson's correlation coefficient among canal paresis (CP), directional preponderance (DP), maximum slow phase velocity (Vmax) and duration of disease in patients with possible MD.

Caloric parameters	Pearson's correlation	p
CP and Duration of disease	0.19	0.33
DP and Duration of disease	0.27	0.15
Vmax of warm irrigation and Duration of disease	-0.05	0.86
Vmax of cool irrigation and Duration of disease	-0.13	0.62

4.5 Correlation among the canal paresis (CP), the directional preponderance (DP), and the maximum slow phase velocity (Vmax) and duration of disease in patients with definite MD

From Table 18, Pearson's correlation coefficients were computed and tested the relationships among the canal paresis, the directional preponderance, and the maximum slow phase velocity and duration of disease in patients with definite MD. The Pearson's correlation coefficients for CP, DP, Vmax of warm and cool irrigation were -0.02, 0.15, 0.17 and -0.20, respectively. The Pearson's correlation coefficients analysis showed nonstatistically significant relationships between the caloric parameters and duration of disease.

Table 18 Pearson's correlation coefficient among canal paresis (CP), directional preponderance (DP), maximum slow phase velocity (Vmax) and duration of disease in patients with definite MD.

Caloric parameters	Pearson's correlation	p
CP and Duration of disease	-0.02	0.92
DP and Duration of disease	0.15	0.43
Vmax of warm irrigation and Duration of disease	0.17	0.50
Vmax of cool irrigation and Duration of disease	-0.20	0.42

CHAPTER V

DISCUSSION AND CONCLUSIONS

The purposes of this study were to study the caloric responses in patients with possible and definite MD, to compare the caloric responses between patients with possible and definite MD, and to study the relationship among caloric parameters and duration of disease in patients with possible and definite MD.

5.1 The values of the canal paresis, the directional preponderance and the maximum slow phase velocity in patients with possible and definite MD

From the results in Table 9 and 11, the t-test of the means CP showed no significant difference between right and left CPs, the means DP showed no significant difference between right and left DPs in both groups.

From the results in table 10 and 12, the t-test of the means Vmax and the Mann-Whitney U test of the mean ranks for Vmax showed no significant difference between the right and the left ears, the right and the left beats for both groups.

One reason for no significant difference of the means CP between right and left CPs, the means DP between right and left DPs, the means Vmax between right and left ears and the means Vmax between right and left beats of possible and definite MD groups might be due to the means PTA of subjects in each group was no significant difference between right and left ears (see Table 7). The other reason might be due to the relatively small number of subjects. There was no report comparing the right and left CPs, right and left DPs, Vmax of right and left ears, and Vmax of right and left beats of patients with possible and definite MD, respectively. However, Mehra (100) conducted the study in 30 normal subjects. The result showed no significant difference of the means CP between right and left CPs, the means DP between right and left DPs, the means Vmax between

right and left ears and the means V_{max} between right and left beats. According to data of Vesterhauge and Larsen (99), who studied ENG and caloric test in a total of 50 normal subjects. The means CP and DP values of the right side were higher than the left side. However, there was no significant difference between right and left ear. Furthermore, the normal limits for patients examined twice showed no significant difference between the means values of double and single examinations (99).

From Table 10 and 13, from the results of possible and definite MD groups found that the significant difference was noted between means V_{max} of the warm and the cool irrigations, with the cool irrigation producing stronger responses ($p < 0.001$). There was no report comparing the means V_{max} between warm and cool irrigation in patients with possible and definite MD.

This finding was similar to Cawthorne et al.(107). They studied 9 MD patients, the caloric test was performed both before and after labyrinthectomy of the affected ears. The results of MD ears showed a marked accentuation of the response to cold water irrigation in six of nine ears. This result was the similar to the post-operative results of unaffected ears. While the pre-operative results of unaffected ears showed a marked accentuation of the response to hot water irrigation in eight ears. They postulated this variation of the unaffected ears was due to changes of the central nervous system mechanism (107). Therefore, this variation of MD ears might be due to the lateral semicircular canal sensitivity was changed of by central nervous system mechanism (107).

The second reason for a marked accentuation of the response to cold water irrigation might be due to the influence of pressure effects. In normal caloric response, with warm caloric stimulus, the column of endolymph nearest to the middle ear expands causing the cupula to deviate toward the utricle. A cold stimulus produces the opposite effect on the endolymph column, causing the cupula to deviate away from the utricle (105). In the presence of endolymphatic hydrops, increased volume of endolymph, the pressure in a closed fluid system increased (3). Relatively to the deviation of cupula, in the event of stimulated with hot water which was expanding the volume of endolymph in a closed fluid system, the deviation of cupula might be more difficult to happen than stimulated with cold water which was shrinking the volume of endolymph down. So that the cool irrigation markedly accentuated the caloric response than the warm water in MD.

Regarding the CP and DP values in possible MD group, as compare the CP and DP values to the reference range (mean \pm 2.5 SD) of Thai normative data in Table 1 and 2, respectively (94,95). If the absolute CP and DP value exceeded than the normal range in each age range, they were considered abnormal. The result was found that abnormal caloric response was recorded in only 9 subjects (30%). There were normal DP in 28 subjects (93.33%) and only 2 subjects (6.67%) who showed a directional preponderance, one (3.33%) of them was on the ipsilateral side and the other (3.33%) was on the contralateral side of the affected ears. These finding indicated that possible MD group could represent a low functional impairment of the peripheral vestibular organ.

Regarding the CP and DP value in definite MD group, abnormal CP was recorded in 15 subjects (50%). Similar to previous reports that found abnormal caloric response around 50% (12,16). This finding confirmed that vestibular canal paresis may have occurred in half of MD patients. In other investigations, considerably higher incidences have been reported (13,15). Thomas and Harrison (15) studied in 610 patients with MD and found abnormal CP in 80% of their subjects. The difference of abnormal percentages might be due to different criteria in setting the normal limits. The present study placed the limits for normal difference in CP at as wide as 2.5 SD, for the reason gave above, whereas Thomas and Harrison (15) used limits of 2 SD. Besides, the criteria of normal limits, several factors such as patient selection, the composition of the patient group, the difference in the methods of investigation applied and the difference of time at data collection can also make the divergence of abnormal percentage.

In this study, the definite MD group revealed a directional preponderance in 9 subjects (30%) (13,16,114). Eight of them (26.7%) were on the ipsilateral side and one (3.3%) was on the contralateral side of the affected ear. The directional preponderance occurred more often towards than away from the affected side. According to Hulshof and Baarsma (13), from their result 30% of subjects showed a DP, 11% of subjects was directed away from the affected ear and 19% of subjects was directed toward the affected ear (13). However, Stahle&Bergman (12) studied 300 MD patients, results showed that abnormal DP was recorded in 158 subjects, 82 subjects of whom also showed reduced excitability on one side. DP alone was noted in 76 patients. DP from 158 subjects with unilateral disease, 42% directed toward the affected ear, and 58% was away from the affected ear. They found that the preponderance seemed to have no

definite correlation to the diseased ear (12,16). The reason for the contrast might be due either to unrecognized preexisting vestibular disease of healthy ear, such as old vestibular neuritis, or to intermittent paroxysmal positional vertigo caused by the affected or healthy ear, occasionally difficult to distinguish from history (115).

5.2 The comparison of the canal paresis, the directional preponderance and the maximum slow phase velocity between patients with possible and definite MD

5.2.1 Canal Paresis (CP) and Directional Preponderance (DP)

From Table 14 and 15, the mean total CP and mean total DP of patients with definite MD group were significantly higher than possible MD group ($p < 0.05$). The reason for significant difference might be due to the mean of hearing threshold of the definite MD group was higher than that in the possible MD group, the greater of the pure tone threshold increases, the tendency of the caloric response reduces (1,10,11). Enander and Stahle (10) found the relationship between hearing loss and caloric response. They studied in 343 patients with MD and the caloric responses were compared with the hearing loss as measured by pure tone audiometry. The results showed that the greater of the pure tone threshold increased, the tendency of the caloric response reduced (10). In addition, tinnitus and aural fullness problems in definite MD group were found more than possible MD group (see Table 6).

The present study showed that patients with definite MD group might have more vestibular disturbance than possible MD group. No report was found in collective literature which compared method for these caloric values in possible and definite MD.

5.2.2 Maximum slow phase velocity (Vmax)

From the results in Table 16, the means Vmax of warm and cool water responses were higher in possible MD group than definite MD group. However, the t-test of

means Vmax of warm irrigation showed no significant difference between possible and definite MD groups. The reasons for nonsignificant differences might be due to the Vmax is dependent not only on the relationship between the temperature gradient vector and the gravity vector but also on the blood flow to the skin, length of transmission pathway from the tympanic membrane to the lateral semicircular canal, and the heat conductivity of the temporal bone (103). The important variable was the anatomy of the ears, the patients with wide and straight external ear canals will have stronger response than one who has narrow or tortuous ear canals (6). In order to correct for such intersubjects anatomical variations, a larger sample size may be required to result in a smaller SD. The other reason might be due to the intersubjects and intrasubject variations. The comparison by using the direct Vmax are highly variable (92,116). Hamid and Hinchcliffe (116) studied ten normal subject. They reported intersubjects variability ranged between 15% to 45%, and intrasubject variability was about 25% based on ten separate caloric tests on the same subjects (116).

From this finding implied that the comparison by using the direct Vmax of warm or cool irrigation between patients with possible and definite MD group provided much less diagnostic information than the comparison by using the percentage difference of Vmax (CP or DP) between patients with possible and definite MD group. Therefore, the comparison intergroups should be interpreted by using the direct Vmax combination with CP or DP indicators to make the diagnosis instead of the comparison by using the direct Vmax of warm or cool irrigation alone.

5.3 Correlation among the canal paresis, the directional preponderance, the maximum slow phase velocity and duration of disease in patients with possible and definite MD

From the results in Table 17 and 18, there was no statistical significant correlations between CP, DP, Vmax and duration of disease in both groups. These findings were similar to Dobie et al. (16) who studied in 206 MD patients with the mean duration of disease was 5.9 years. They studied in patients with various severity, the result showed that there was no correlation between caloric responses and audiometric findings. They mentioned that abnormalities were statistically unrelated to other parameters : duration, age, sex, glycerol test results and audiologic measures. They suggested that MD may progress independently in the auditory and vestibular portions of the labyrinth.

On the other hand, Stahle (11) and Hulshof and Baarsma (13) found the correlation between the duration of disease and the extent of caloric response reduction. Their result revealed that caloric response reduction increased with increasing duration. The reason for this contrast might be explained by patients selection. Stahle (11) studied only with severe MD and his patients were nearly all surgical candidates, and may have represented a more highly screened referral population than the present study. On the other hand, most of patients' severity in the present study were mild to moderate (see Table 5). The other reason for the contrast might be due to the time at data collection. Hulshof and Baarsma (13) studied in the interval between vertigo attacks. All of their patients had undergone the vestibular tests during a week of clinical observation. While, this research studied either the interval between vertigo attacks during a week of clinical observation or asymptomatic period. The finding in this research study probably showed that duration of disease did not relate to an abnormal caloric finding in patients with possible and definite MD.

Conclusions

The results from this study indicate the following.

1.The results for possible and definite MD group showed that the means CP and DP value showed no significant difference between right and left values. The Vmax showed no significant difference between the right and the left ears, the right and the left beats.

2.The Vmax of irrigation revealed that the warm irrigation was significantly weaker response than the cool irrigation. The reasons for significant difference might be due to patients with MD might have changed of the central nervous system mechanism or influenced of pressure effects that marked accentuation of the response to cold water irrigation in both groups.

3.The mean CP and DP value of patients with definite MD group produced a significantly higher than that produced in possible MD group. There was no significant difference of mean Vmax in warm and cool water responses between possible and definite MD group.

4.The study of CP and DP indicators found that possible MD could represent a low functional impairment of the vestibular organ. This finding showed that patients with definite MD group might have more vestibular disturbance than possible MD group.

5.There was no significant difference correlations between CP, DP, Vmax and duration of disease in patients with possible and definite MD.

Recommendations

The following recommendations from this study included :

1. Caloric testing should be used as a test battery in clinical evaluations of definite MD.
2. The comparison intergroups should be interpreted by using the direct Vmax combination with CP or DP indicators to make the diagnosis instead of the comparison by using the direct Vmax of warm or cool irrigation alone.
3. Bithermal caloric testing in patients with Meniere's disease should be first conducted by warm water irrigation.
4. Further study should be focused on the results in patients with MD with various duration of disease.
5. The subjects in further study should be increased in order to make a small standard deviation.

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APPENDIX

APPENDIX

Table A-1 Calculative formula for unilateral weakness

Unilateral weakness

Unilateral weakness (UW) or canal paresis (CP) is defined as the amount by which the two responses provoked by right ear irrigations differ in intensity from those provoked by left ear irrigations (6).

To quantify the difference in the caloric response strength of the two ears, most examiners use the following formula, proposed by Jongkees and Phillipszoon (1964)

$$CP = \frac{(RW + RC) - (LW + LC)}{(RW + RC + LW + LC)} \times 100$$

where: RW is peak slow-phase eye speed of the response following the right ear-warm temperature irrigation.

RC is peak response for the right ear-cool temperature irrigation.

LW is peak response for the left ear-warm temperature irrigation.

LC is peak response for the left ear-cool temperature irrigation (6).

Table A-2 Calculative formula for directional preponderance**Directional preponderance (DP)**

Directional preponderance (DP) is defined as the represents the difference in intensity between the two right-beating nystagmus responses (provoked by right ear-warm temperature and left ear-cool temperature irrigations) and the two left-beating responses (provoked by left ear-warm temperature and right ear-cool temperature irrigations). Directional preponderance is calculated by the following formula:

$$DP = \frac{(RW + LC) - (LW + RC)}{(RW + LC + LW + RC)} \times 100$$

where: the abbreviations are the same as those used in the formula for calculating unilateral weakness (6).

Table A-3 Calculative formula for visual suppression of caloric nystagmus**Visual suppression of caloric nystagmus**

Fixation index (FI) is a measure of the effectiveness of visual fixation in suppressing caloric nystagmus. It is calculated by the following formula:

$$FI = \frac{SPES (EO)}{SPES (EC)} \times 100$$

where: SPES (EO) is the slow-phase eye speed of two or three representative beats occurring while the eyes are open and fixating.

SPES (EC) is the slow-phase eye speed of two or three representative beats occurring just before the eyes are opened (6).

Table A-4 Diagnosis of Meniere's disease (108)**Certain Meniere's disease**

- Definite Meniere's disease, plus histopathologic confirmation

Definite Meniere's disease

- Two or more definitive spontaneous episodes of vertigo 20 minutes or longer
- Audiometrically documented hearing loss on at least one occasion
- Tinnitus or aural fullness in the treated ear
- Other causes excluded

Probable Meniere's disease

- One definitive episode of vertigo
- Audiometrically documented hearing loss on at least one occasion
- Tinnitus or aural fullness in the treated ear
- Other causes excluded

Possible Meniere's disease

- Episodic vertigo of the Meniere type without documented hearing loss or
- Sensorineural hearing loss, fluctuating or fixed, with dysequilibrium but without definitive episodes
- Other causes excluded

Table A-5 The functional level 1-6**Functional level**

Functional level are the overall current state of subjects, not just during attacks (choose the one that best applies)

1. Your dizziness have no effect on their activities at all.

2. When you feel dizzy you have to stop what you are doing for a while, but it soon passes and you can resume activities. You continue to work, drive, and engage in any activities you choose without restriction. You have not changed any plans or activities to accommodate your dizziness.

3. When you are dizzy you have to stop what you are doing for a while, but it does pass and you can resume activities. You continue to work, drive, and engage in most activities you choose, but you have had to change some plans or make some allowance for your dizziness.

4. You are able to work, drive, travel, take care of your family, or engage in most essential activities, but you must exert a great deal of effort to do so. You must constantly make adjustments in your activities and budget your energies. You are barely making it.

5. You are unable to work, drive, or take care of a family. You are unable to do most of the active things that you used to. Even essential activities must be limited.

6. You are unable to do the daily activities. You are disabled.

Modified (108)

Table A-6 Raw data of caloric test in patients with possible Meniere's disease.

Subjects (No.)	Age (years)	Vmax of warm stimulus (degrees/sec)		Vmax of cool stimulus (degrees/sec)		CP (%)	DP (%)	Duration of disease (years)	Functional level	PTA	
		rt.ear	lt.ear	rt.ear	lt.ear					rt.ear	lt.ear
1	26	0	12	21	26	-29	12	8	3	15	10
2	27	6	8	40	42	-4	0	0.83	3	10	13
3	31	7	12	28	29	-8	5	1	3	27	23
4	32	6	12	22	24	-13	6	0.58	1	10	12
5	34	8	3	34	52	-13	-24	2	2	7	8
6	35	6	8	26	25	-2	5	0.67	2	8	13
7	35	4	16	16	12	-17	33	10	2	13	8
8	38	0	11	28	50	-37	-12	1.75	2	15	17
9	38	29	21	132	70	28	21	10	3	12	15
10	39	0	0	17	21	-11	-11	0.17	3	13	12
11	42	8	4	39	48	13	5	0.08	2	23	18
12	43	0	8	8	11	-41	19	2	2	25	27
13	43	26	39	36	80	-31	-17	18	2	20	17
14	43	7	0	17	19	12	-21	1	2	13	15
15	45	0	12	35	37	-17	12	15	1	13	15
16	46	11	13	67	60	3	6	3	3	25	23
17	46	16	20	51	59	-8	-3	1.17	4	17	15
18	47	12	13	35	30	4	7	2.75	2	17	18
19	48	7	6	32	24	13	10	20	4	13	10
20	48	12	9	40	36	7	1	3	2	17	15
21	51	6	6	12	39	-43	-43	6.5	1	18	22
22	51	12	12	47	45	2	2	2.25	2	12	15
23	52	50	22	64	25	42	7	9	2	12	28
24	54	12	13	54	63	-7	-6	3	3	20	25
25	54	13	5	26	12	39	11	0.5	1	18	17
26	55	14	22	40	29	3	18	0.5	3	17	17
27	56	22	20	35	39	-2	-5	5	1	22	20
28	56	4	8	32	34	-8	3	4	3	38	35
29	57	32	7	49	14	59	10	0.08	3	18	18
30	58	16	12	27	40	-9	-18	0.25	3	15	15

CP : The value of + represents the left canal paresis

The value of - represents the right canal paresis

DP : The value of + represents the left directional preponderance

The value of - represents the right directional preponderance

Functional level : Number 1-6 represents the subjects current state of overall function, not just during attack (See appendix Table A-5)

Table A-7 Raw data of caloric test in patients with definite Meniere's disease.

Subjects (No.)	Age (years)	Vmax of warm stimulus (degrees/sec)		Vmax of cool stimulus (degrees/sec)		CP (%)	DP (%)	Duration of disease (years)	Functional level	PTA	
		rt.ear	lt.ear	rt.ear	lt.ear					rt.ear	lt.ear
1	28	0	0	9	24	-45	-45	9	3	50	33
2	33	16	4	36	20	37	5	3	3	8	33
3	36	3	4	28	31	-6	-3	5	1	47	10
4	36	0	5	19	20	-14	9	14	1	68	55
5	37	7	12	0	20	-64	-38	0.42	3	43	10
6	37	4	28	27	36	-35	16	4	1	40	18
7	39	15	18	15	56	-42	-37	5	2	45	13
8	40	6	5	14	48	-49	-52	12	2	45	13
9	41	13	11	42	39	5	1	4	3	62	7
10	42	8	14	21	27	-17	0	2	2	27	32
11	43	25	7	33	40	10	-24	5	1	20	53
12	43	6	11	34	13	25	41	1.75	3	17	53
13	43	9	13	10	33	-42	-29	13	3	62	10
14	45	0	15	7	69	-85	-52	2.67	3	65	22
15	47	12	9	20	20	5	-5	10	2	13	52
16	47	7	8	21	28	-13	-9	3	2	18	28
17	48	0	11	41	42	-13	11	2.42	4	18	10
18	48	4	7	25	15	14	25	6	3	22	13
19	48	22	16	26	9	32	15	10	1	23	43
20	48	4	8	28	40	-20	-10	1	3	45	17
21	49	8	0	17	13	32	-11	1.83	5	10	60
22	50	67	12	60	87	12	-36	5.42	1	10	43
23	51	8	7	21	22	0	-3	2.33	2	13	18
24	52	7	12	38	66	-27	-19	8	2	18	28
25	52	15	11	37	52	-10	-17	1.42	3	22	30
26	53	25	0	24	4	85	-9	3.33	2	22	62
27	55	0	0	46	6	77	77	4	2	17	58
28	55	7	4	21	17	14	2	4	1	22	33
29	56	0	8	62	13	49	69	7	2	18	53
30	57	65	19	80	54	33	-9	5	1	42	18

CP : The value of + represents the left canal paresis

The value of - represents the right canal paresis

DP : The value of + represents the left directional preponderance

The value of - represents the right directional preponderance

Functional level : Number 1-6 represents the subjects current state of overall function, not just during attack (See appendix Table A-5)

Table A-8 Distribution test in patients with possible and definite Meniere's disease.

One-Sample Kolmogorov-Smirnov Test				
Parameters	Possible MD		Definite MD	
	Kolmogorov-Smirnov Z	p	Kolmogorov-Smirnov Z	p
Right CP	0.93	0.36	0.67	0.77
Left CP	0.99	0.28	0.70	0.71
Total CP	1.35	0.51	0.85	0.46
Right DP	0.47	0.98	0.85	0.47
Left DP	0.92	0.37	0.88	0.43
Total DP	1.09	0.19	0.98	0.29
RW	0.49	0.97	1.15	0.15
LW	0.65	0.80	0.42	0.99
RC	0.49	0.97	0.93	0.35
LC	0.82	0.51	1.02	0.25
RW+RC	0.80	0.55	1.00	0.27
LW+LC	0.91	0.39	1.56*	0.02
LC+RW	0.84	0.48	1.38*	0.04
LW+RC	0.84	0.48	0.97	0.31
RW+LW	0.89	0.41	1.25	0.09
RC+LC	0.63	0.83	1.32	0.06

*significant at $p < 0.05$

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