Definition Menière Groningen
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Chapter 10

Non-invasive perilymphatic pressure measurement
In patients with Menière’s disease

Introduction

In animal experiments, measurement of the hydrostatic pressure in the endolymphatic and perilymphatic compartments of normal ears and ears with endolymphatic hydrops is performed using small micropipettes and pressure transducers [1,2,3]. However, these direct invasive measurement techniques are not suitable for human inner ears. The MMS-10 Tympanic Displacement Analyser (Marchbanks Measurement Systems Ltd, United Kingdom) provides a non-invasive measurement system for analysis of inner ear pressure in humans. This instrument is based on the principle that displacement of the tympanic membrane, induced by the stapedial reflex, depends on the resting position of the stapes footplate. The resting position alters with different perilymphatic pressure levels. Displacement of the tympanic membrane can be evaluated as small volume variations in the external auditory canal [4,5].

The Tympanic Displacement Analyser has proved to be useful in studies of intracranial pressure changes. The cerebro-spinal fluid compartment is connected to the perilymphatic spaces through the cochlear aqueduct [6]. Pressure variations of the cerebrospinal fluid are reflected in the perilymphatic pressure [7]. Using the Tympanic Displacement Analyser, hydrocephalic patients with a ventricular shunt and patients with spina bifida were compared with normal subjects [8,9,10]. Other applications are described in studies of otological disorders such as Menière's disease [11,12]. Menière's disease is defined as the well known triad of periodic hearing loss, vertigo and tinnitus. Since Hallpike and Cairns [13] and also Yamakawa [14] described hydrops of the endolymphatic system in the inner ear of patients with Menière's disease, endolymphatic hydrops is generally accepted as the histopathological lesion in this condition [13,14]. Endolymphatic hydrops represents swelling of the endolymphatic space of the inner ear, leading to distension and bulging of Reissner's membrane into the scala vestibuli. In 1965, Kimura and Schuknecht reported endolymphatic hydrops in guinea pigs after surgical obliteration of the endolymphatic duct and sac. From this it is suggested that in Menière's disease there is impaired absorption of endolymph in the endolymphatic sac [15]. Other experiments have demonstrated endolymphatic hydrops as a result of excessive production of endolymph after pharmacological stimulation of Na/K-ATPase in the inner ear [16,17]. Recently, a new dynamic two-phase concept in Menière's disease has been proposed which is based on decreased absorption in the endolymphatic sac in combination with a periodic overproduction of endolymph by hormonal stimulation of Na/K-ATPase in the inner ear [18]. Distension and bulging of Reissner's membrane towards the perilymphatic space, as seen in endolymphatic hydrops, can occur only when a mechanical force from the endolymphatic to the perilymphatic compartment is in action. In fluid compartments the acting force on a surface is proportional to the hydrostatic pressure. In a closed fluid compartment, such as the endolymphatic and perilymphatic spaces, the hydrostatic pressure depends on the fluid volume and the compliance of the walls. In normal ears, the highly compliable Reissner's membrane immediately equalizes pressure differences between endolymph and perilymph by movement towards the compartment with the lower pressure. In longstanding endolymphatic hydrops, the compliance of Reissner's membrane decreases with increasing distension. Additional
increase of endolymphatic volume is no longer fully compensated by further distension of Reissner's membrane. In this condition, endolymphatic-perilymphatic pressure gradients are found. In experimental endolymphatic hydrops after surgical obliteration of the endolymphatic sac, periodic pressure gradients between the endolymphatic and perilymphatic spaces occur, which contribute to the deterioration of the auditory thresholds [2].

By means of the MMS-10 Tympanic Displacement Analyser it becomes feasible for the first time to measure the inner ear pressure in patients with Menière's disease. In this study the perilymphatic pressure was measured in 70 patients with Menière's disease and compared with the perilymphatic pressure in 50 young normal hearing subjects. Perilymphatic pressure measurement was performed at the beginning of a four day hospital stay. In order to detect possible perilymphatic pressure variations in Menière's disease, this measurement was repeated for a subgroup of 25 patients.

Patients and methods

Seventy patients suffering from Meniere's disease were extensively investigated according to a diagnostic protocol during a four day stay in the Department of Otorhinolaryngology of the University Hospital Groningen. The diagnosis of Menière's disease was defined by simultaneous fulfilment of three criteria: cochlear hearing loss, tinnitus and periodic attacks of vertigo (at least two in the past). Of these 70 patients (38 men, 32 women, mean age: 50 years, range: 19-77 years) 44 suffered from unilateral and 26 from bilateral Menière's disease. In total 96 ears were affected.

The diagnostic protocol consisted of routine ENT examination, audiovestibular tests, routine laboratory investigations, measurement of blood pressure, electrocochleography (ECoG), oto-acoustic emission examination and magnetic resonance imaging (MRI) of the temporal bones and the cerebellopontine angle.

The perilymphatic pressure of all 70 patients was measured non-invasively by means of the MMS-10 Tympanic Displacement Analyser at the beginning of the stay in hospital with the patient in a sitting position. A second perilymphatic measurement was done for a subgroup of 25 patients at the end of their stay in the hospital. This subgroup consisted of 25 patients (13 men, 12 women), 22 suffered from unilateral and three from bilateral Menière's disease. In total 28 ears were affected. Prior to the tests, the middle ear pressure and the stapedial reflex threshold at 1000 Hz were determined by a conventional impedance measurement instrument: the GSI 33 middle ear analyser. Test stimuli of 1000 Hz with an intensity of 10, 20 and 25 dB above stapedial reflex threshold were used for the Tympanic displacement tests. No stimuli louder than 115 dB (HL) were used. Stimulus duration was 500 milliseconds, measurement duration 1,5 seconds and the inter-stimulus interval was 7 seconds. In all cases the measurement parameters Vi and Vm were determined. Vi is defined as the maximum inward displacement in nanolitres of the tympanic membrane. Vm is the mean displacement in nanolitres from the time at which Vi is reached until the acoustic stimulus offset.

The results of the perilymphatic pressure measurement of patients with Menière's disease were compared with values for a group of 50 young normal hearing subjects.
(30 men, 20 women, mean age: 25.4 years, range 20-34 years. These subjects had no otological complaints. The measurement results were analysed using the SPSS 9.0 program and the Student's T-test.

Results

For Vi and for Vm no significant differences were found between the affected and unaffected ears in the same patient. The measurement parameters of Vi and Vm of affected ears of Menière patients did not differ significantly from the control group of 50 normal hearing subjects (100 ears) measured under the same conditions (p > 0.01). The average values for this control group was -167 nl for Vi (standard deviation 149 nl) and 33 nl (standard deviation 212 nl) for Vm (table 1). The inter-individual variation in our control group was large.

Table 1. Vi and Vm (in nanolitres) in 70 patients with menière’s disease and in 50 subjects with normal hearing. Vi represents the maximum inward displacement of the tympanic membrane, Vm represents the mean displacement from the time at which Vi is reached until the acoustic stimulus offset.

<table>
<thead>
<tr>
<th></th>
<th>Menière patients, affected ears (n=96)</th>
<th>Normal ears (n=100)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Vi</td>
<td>Vm</td>
</tr>
<tr>
<td>Mean</td>
<td>-127</td>
<td>28</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>169</td>
<td>251</td>
</tr>
<tr>
<td>Minimum</td>
<td>-900</td>
<td>-894</td>
</tr>
<tr>
<td>Maximum</td>
<td>0</td>
<td>755</td>
</tr>
<tr>
<td>Range</td>
<td>900</td>
<td>1649</td>
</tr>
</tbody>
</table>

Table 2. Vi and Vm (in nanolitres) in 28 affected ear on admission and at end of hospital stay.

<table>
<thead>
<tr>
<th></th>
<th>Vi</th>
<th>Vm</th>
<th>Vi</th>
<th>Vm</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>On admission</td>
<td>At end of admission</td>
<td>On admission</td>
<td>At end of admission</td>
</tr>
<tr>
<td>Mean</td>
<td>-174</td>
<td>-164</td>
<td>-19</td>
<td>16</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>182</td>
<td>162</td>
<td>214</td>
<td>617</td>
</tr>
<tr>
<td>Minimum</td>
<td>-808</td>
<td>-718</td>
<td>-414</td>
<td>-323</td>
</tr>
<tr>
<td>Maximum</td>
<td>-15</td>
<td>-8</td>
<td>602</td>
<td>556</td>
</tr>
<tr>
<td>Range</td>
<td>793</td>
<td>710</td>
<td>1016</td>
<td>879</td>
</tr>
</tbody>
</table>
The parameters $V_i$ and $V_m$ showed large inter-individual differences in the affected ears as well as in the unaffected ears (table 2). For the affected ears as well as the non-affected ears the $V_i$ and $V_m$ of patients with Menière's disease did not change significantly during their stay in the hospital. Nevertheless, the correlation of the test-retest results within one subject and one ear was high [19]. The individual $V_i$ results of the 28 affected ears of the subgroup ($n=25$) are shown in figure 1. Although the measurement results showed large variations over all patients, for each patient the correlation between the measurement at the beginning and at the end of the hospital stay was high ($r = 0.8$). No significant correlation could be found between perilymphatic pressure measurement results and hearing thresholds, blood pressure, gender and age. There was no difference between uni- and bilaterally affected patients.

![Figure 1](image_url)

**Figure 1.** Individual measurements results of 28 affected ears of the subgroup of Menière patients ($n=25$). The X-axis represents 28 ears and the Y-axis the maximum inward displacement ($=V_i$) in nl at the beginning of the hospital stay (○) and at the end of the hospital stay (●).

**Discussion**

In animal experiments inner ear pressure has been extensively measured by means of (micro)pipettes and pressure transducers [1,2,3]. However, these invasive methods can not be used in humans. The MMS-10 Tympanic Displacement Analyser is the only commercially available device to measure the human inner ear pressure non-invasively. In this study perilymphatic pressure in patients with Menière's disease was compared with controls.

On average the difference between the perilymphatic pressure in patients with Menière's disease and in young normal hearing subjects was not significant. There was no difference between uni- and bilaterally affected patients. However significant differences between uni- and bilateral disease were noticed on 3DFT-CISS Magnetic
Resonance Imaging of the temporal bone and the cerebellopontine angle in the same patient group [19].

Our results showed large inter-individual variations of the parameters Vi and Vm. This fact is in concordance with series of normal hearing subjects in our Ménière population found by Rosingh et al. [20]. It is also according to the literature concerning patients with other otological, neurological and neurosurgical disorders [7,8,9,10,11,12,20,21].

No significant differences were found between the perilymphatic pressure measurements at the beginning and the end of 4 day period. The differences found between the beginning and the end of the stay can therefore be considered as a result of differences between test and retest measurements, as also found in normal hearing subjects measured in the morning and late in the afternoon [21].

Endolymphatic hydrops is considered to be the histopathological correlate of Ménière's disease. Increased endolymphatic hydrostatic pressure causes the distension and bulging of Reissner's membrane [2]. In normal guinea pig ears the endolymphatic pressure is always equal to the perilymphatic pressure [2,22]. Simultaneous invasive measurement in guinea pigs demonstrates a rigid coupling between the hydrostatic pressure of both inner ear compartments [2].

Also, in the early stages of experimental endolymphatic hydrops, no endolymphatic-perilymphatic pressure gradients are observed and the perilymphatic pressure can be considered representative for the endolymphatic pressure. However, when Reissner's membrane loses its high compliance, as seen in longstanding endolymphatic hydrops, further endolymph volume increase causes an endolymphatic-perilymphatic pressure gradient.

In animal experiments, auditory thresholds are not affected by simultaneous increases of both endolymphatic and perilymphatic pressure [2]. Endolymphatic-perilymphatic pressure gradients may cause the so-called leaky membranes, subsequent ruptures of Reissner's membrane and saccular membranes and contribute to the deterioration of the auditory thresholds [2]. In our series of patients with longstanding Ménière's disease, patients presumably had periodic endolymphatic perilymphatic pressure gradients in the past, which had contributed to their hearing impairment. Inner ear dysfunction such as sensorineural hearing loss, has also been described as a result of cerebrospinal fluid changes [23,24]. The cerebrospinal fluid compartment communicates with the perilymphatic space through the cochlear aqueduct [6]. The pathophysiology of hearing impairment has been attributed to changes in perilymphatic pressure caused by transmission of cerebrospinal fluid pressure through the cochlear aqueduct. In these patients short, periodic endolymphatic perilymphatic pressure gradients may occur, resulting in reversible or irreversible hearing impairment.

References


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