



Original Article

Evaluation of the Effects of Chronic Kidney Disease and Hemodialysis on the Inner Ear Using Multifrequency Tympanometry

Akihiro Tamae , Kazuyuki Ishizu , Takamasa Yoshida , Kazuhiko Kubo , Nozomu Matsumoto , Tetsuro Yasui , Kosuke Masutani , Kazuhiko Tsuruya , Takashi Nakagawa

Department of Otorhinolaryngology, Hamanomachi Hospital, Fukuoka, Japan (AT)

ISHIZU Otorhinolaryngology Clinic, Fukuoka, Japan (KI)

Department of Otorhinolaryngology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan (TY, NM, TY, TN)

Department of Otorhinolaryngology, Chidoriyashi General Hospital, Fukuoka, Japan (KK)

Kidney Care Unit, Kyushu University Hospital, Fukuoka, Japan (KM)

Department of Integrated Therapy for Chronic Kidney Disease, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan (KT)

ORCID IDs of the authors: A.T. 0000-0002-2204-6160; K.I. 0000-0001-5024-5047; T.Y. 0000-0002-2946-9481; K.K. 0000-0002-6447-9028; N.M. 0000-0003-0799-6704; T.Y. 0000-0002-8061-1607; K.M. 0000-0001-9190-4600; K.T. 0000-0002-8390-2928; T.N. 0000-0002-3198-639X.

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OBJECTIVES: To evaluate the effects of chronic kidney disease (CKD) and hemodialysis (HD) on the inner ear using the G width (the width between the bimodal peaks of the conductance (G) tympanogram at 2,000 Hz), which reflects the inner ear pressure and/or the existence of endolymphatic hydrops.

MATERIALS and METHODS: We selected five patients (10 ears) from the patients with CKD who were hospitalized for creation of arteriovenous fistula prior to initiation of HD (non-HD group), and we selected seven patients (14 ears) from the patients with CKD who were undergoing HD (the HD group). As a control group, we selected 80 healthy individuals (160 ears); these were mainly the medical staff of the hospital. We measured the G width of the control group and that of patients with CKD using multifrequency tympanometry.

RESULTS: The mean G widths of the HD (measured just before an HD session), non-HD, and control groups were 210.7, 128.4, and 97.0 daPa, respectively. The G width of the HD group was significantly greater than that of the control and non-HD groups ($p < 0.01$ and $p < 0.01$, respectively; Tukey–Kramer test after one-way analysis of variance). The non-HD group also had a greater G width than the control, but it was not significant ($p = 0.20$; Tukey–Kramer). No significant changes were observed in the G widths of the HD group, just before and after a single HD session ($p = 0.423$; paired t-test).

CONCLUSION: The greater G width observed in hemodialyzed CKD patients suggests either an increased inner ear pressure or the existence of endolymphatic hydrops in these patients, which is probably related to their otologic symptoms.

KEYWORDS: Multifrequency tympanometry (MFT), inner ear, hearing loss, chronic kidney disease, hemodialysis

INTRODUCTION

It is well known that otologic symptoms, including dizziness, tinnitus, and hearing loss, are often observed in patients with chronic kidney disease (CKD), especially those who are undergoing hemodialysis (HD)^[1-6]. Since CKD and HD affect the homeostasis of bodily fluids and electrolytes, their symptoms may be similar to endolymphatic hydrops, which is an imbalance of fluid volume or pressure between the perilymph and the endolymph in the inner ear. However, the pathophysiology of the inner ear remains unknown.

Multifrequency tympanometry (MFT) is a method for the measurement of acoustic impedance of the ear at multiple frequencies from 200 to 2,000 Hz. It provides tympanograms of admittance (Y), susceptance (B), and conductance (G) at each frequency. It also estimates the resonance frequency (RF) of the ear. Previously, Darrouzet et al.^[7,8] demonstrated using chinchilla experiments that

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Corresponding Address: Akihiro Tamae E-mail: akihirotamae@yahoo.co.jp

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the G width (the width between the bimodal peaks of the G tympanogram at 2,000 Hz) increased when the inner ear pressure was increased (Figure 1). Komune^[9] also reported in his study that involved guinea pigs that the G width is correlated with the inner ear pressure. Furthermore, Franco-Vidal et al.^[10] reported that the G width of healthy human subjects increases when the head is lowered. In this position, the intracranial pressure increases transiently. It is presumed that the inner ear pressure increases transiently because the inner ear is interconnected with the cerebrospinal fluid space via the cochlear and vestibular aqueducts. Therefore, this finding is consistent with those of the aforementioned animal experiments. On the other hand, during a clinical study, Franco-Vidal et al.^[11] reported that the G width is greater in patients with Meniere's disease, an idiopathic endolymphatic hydrops. Sugawara et al.^[12] and Ishizu et al.^[13] also reported the usefulness of MFT in the diagnosis of Meniere's disease. Additionally, Kato et al.^[14] demonstrated using contrast magnetic resonance imaging (MRI) that the G width was greater in patients who were diagnosed with endolymphatic hydrops. Thus, it has become a consensus that the G width reflects the inner ear pressure and/or the existence of endolymphatic hydrops, although this is not conclusive.

In this study, we attempted to evaluate the condition of the inner ear using MFT in patients with CKD with/without HD, based on the G width.

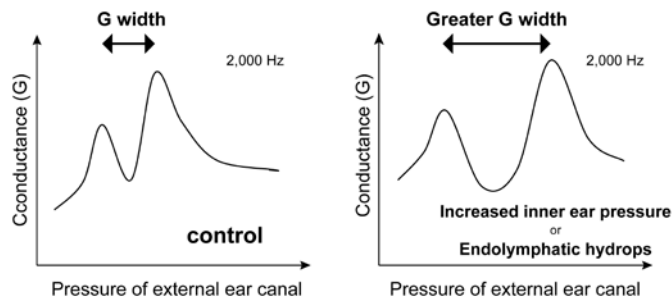


Figure 1. Conductance (G) tympanogram at 2,000 Hz. The G width (the width between the bimodal peaks of the conductance (G) tympanogram at 2,000 Hz) increases in patients with endolymphatic hydrops.

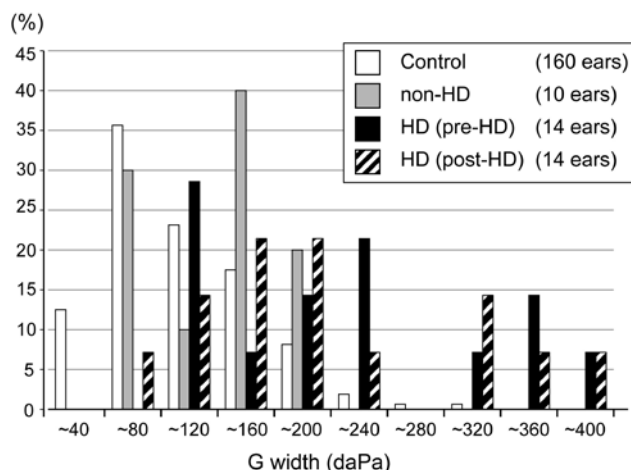


Figure 2. Distribution of the G width (see also Table 1). The G width is defined as the width between the bimodal peaks of the conductance (G) tympanogram at 2,000 Hz. The control, non-HD, and HD groups consist of normal subjects, non-hemodialyzed CKD patients, and hemodialyzed CKD patients, respectively. Those in the HD group were examined twice, just before and after a single HD session (pre-HD and post-HD, respectively). HD: hemodialysis; CKD: chronic kidney disease

MATERIALS and METHODS

We selected five patients who were not initiated on HD, without a history of ear diseases, and with normal tympanic findings (10 ears, 60-77 years old, mean age 70.0 years). These patients were hospitalized at the Kyushu University Hospital for creation of vascular access for HD (the non-HD group). We also selected seven patients without a history of ear disease and normal tympanic findings who were undergoing HD at the Kyushu University Hospital (14 ears, 18-83 years old, mean age 54.0 years) (the HD group). As the control group, we selected 80 healthy individuals without a history of ear disease, most of them being the medical staff of the hospital (160 ears, 22-76 years old, mean age 40.8 years).

We used the Grason-Stadler Tymptstar (Grason-Stadler, Eden Prairie, USA) for evaluating MFT. We calibrated the machine daily before performing the measurements. Since Fukuoka City is located at the sea level, the pressure reading obtained was not adjusted. We measured the G width of the control group and patients with CKD using MFT.

We obtained informed consent from all patients, and the study was conducted in accordance with the Declaration of Helsinki. All procedures in this study were approved by the research committee of the Department of Otorhinolaryngology in Kyushu University.

Statistical Analysis

Statistical analysis was done using Microsoft Excel 2016 (Microsoft Japan Co., Ltd, Tokyo, Japan). Further, statistical analysis was performed using JMP 13 (SAS Institute Japan Inc., Tokyo, Japan). To evaluate the significance of differences in means, we used a one-way analysis of variance (ANOVA) followed by the Tukey-Kramer post-hoc or paired t-test, with significance set at $p < 0.05$.

RESULTS

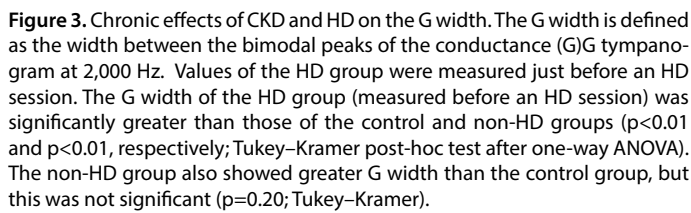
The mean value of the G width of the control group was 97.0 daPa (160 ears; range 20-305 daPa, standard deviation [SD]=52.0 daPa), that of the non-HD group was 128.5 daPa (10 ears; range 75-200 daPa, SD=45.0 daPa), while that of the HD group measured just before an HD session was 210.7 daPa (14 ears, range 90-390 daPa, SD=100.0 daPa). On the other hand, their mean G width was 200.7 daPa (14 ears, range 75-390 daPa, SD=95.0 daPa) when measured just after an HD session (Table 1, Figure 2).

Table 1. Statistics for G width in each group (see also Figure 2)

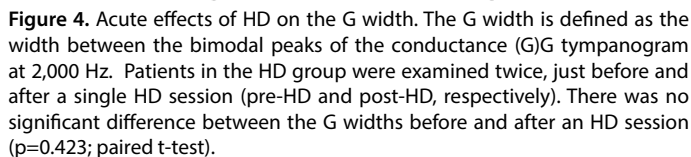
	Number (ears)	G width Range (daPa)	G width Mean \pm SD (daPa)
control	160	20-305	97.0 \pm 52.0
non-HD	10	75-200	128.3 \pm 45.0
HD (pre-HD)	14	90-390	210.7 \pm 100.0
HD (post-HD)	14	75-390	200.7 \pm 95.0

The G width is defined as the width between the bimodal peaks of the conductance (G) tympanogram at 2,000 Hz. The control, non-HD, and HD groups consist of normal subjects, non-hemodialyzed CKD patients, and hemodialyzed CKD patients, respectively. Those in the HD group were examined twice, just before and after a single HD session (pre-HD and post-HD, respectively).

HD: hemodialysis; CKD: chronic kidney disease; SD: standard deviation



Multifrequency tympanometry (MFT) assesses several parameters of the ear, including the RF as well as Y, B, and G tympanograms at each frequency, and is usually used to detect the middle ear disorders. Previous reports from animal experiments and clinical studies demonstrated the usefulness of MFT for the evaluation of the condition of the inner ear ^[7-14] (see Introduction), in cases where the outer and middle ears of patients were normal. Among the parameters obtained from MFT, the authors used the G width, RF, and Y width (the width between the bimodal peaks of the Y tympanogram at 2,000 Hz, similar to the G width). According to these reports, the G width seems to be more effective in the diagnosis of Meniere's disease. Meniere's disease is an idiopathic endolymphatic hydrops, which is an imbalance of fluid pressure and/or volume between the perilymph and endolymph. It is presumed that the perilymph and endolymph in the inner ear have similar pressures, even during endolymphatic hydrops ^[15-17]. This is because of the high compliance of the Reissner's and basilar membranes separating the two compartments. An endolymphatic hydrops is not the same as increased inner ear pressure. However, the greater G width observed in Meniere's disease, similar to experimentally induced high inner ear pressure ^[7, 8, 10-12, 14], suggests that the inner ear pressure is increased in at least some of these patients. The G width might be useful for evaluating the inner ear pressure or the existence of endolymphatic hydrops, although this remains to be validated clinically, experimentally, and theoretically.



There are several tests for the diagnosis of endolymphatic hydrops, such as the glycerol or furosemide dehydration test, electrocochleography, and contrast MRI. These tests are somewhat invasive, expensive, and time consuming. In addition, glycerol and furosemide tests cannot be performed in CKD or HD patients due to the underlying renal disorders, and contrast MRI cannot be performed due to the risk of renal systemic fibrosis. On the other hand, MFT is a noninvasive and convenient test that can be easily performed in only a few minutes and even in the dialysis room. In this study, MFT was performed successfully in all participants with no side effect. The diagnostic significance of the G width should be validated in future studies, by comparing from the result obtained from other tests, such as electrocochleography and pure-tone audiometry.

It is known that hearing loss is a common symptom in CKD patients with/without HD [1-5]. An abnormality in otoacoustic emission (OAE) or prolonged latency of auditory brainstem response (ABR) have been reported in these patients [2, 6, 18-20] indicating dysfunctions in the inner ear or retrocochlear auditory pathways, respectively. Since fluids, electrolytes, and metabolites are transported via epithelial cells and a dense capillary network in the inner ear similar to those in the kidney, there might be some common causes of disorders in these organs. These causes may include immunological or metabolic abnormalities. It is also possible that otologic disorders result from CKD and/or HD. Uremic toxins, electrolyte abnormalities, vitamin D deficiency, ototoxic drugs for CKD treatment, or HD itself might affect the auditory function. The etiology and pathophysiology of otologic disorders in these patients remain unclear. Gatland et al. recorded pure-tone thresholds in 31 patients just before and after a single HD session, and documented a low-tone hearing loss, which improved significantly in one-third of the patients after an HD session [21]. Since it is known that low-tone sensorineural hearing loss is related to

endolymphatic hydrops, they discussed the possibility of endolymphatic hydrops being induced by fluid imbalance in these patients. This hypothesis is interesting because some HD patients also suffer repeated vertigo or dizziness like patients with Meniere's disease, even though evidence for this is not conclusive. It remains controversial whether hearing loss in these patients is low-tone dominant or whether hearing loss improves after an HD session [2, 4-6, 18, 19].

In this study, the G width of the HD group was significantly greater than those of the control and non-HD groups, possibly representing a chronic change in the inner ear condition of HD patients, such as an increased inner ear pressure or an endolymphatic hydrops. The non-HD group also seemed to show a greater G width than the control group, even though it did not reach significance. The age distribution of the non-HD group, which was largely different from the age distribution of the other groups, might have affected the results. The effect of CKD on the G width should be elucidated through age-matched studies or a comparison of G width among different stages of CKD. There can be several explanations for our results. First, CKD might have affected the inner ear. The effect of CKD might have persisted even after the initiation of HD. Uremic toxins or abnormalities of ionic composition might have been the cause. It was reported that dialysis improved OAE or ABR through the removal of uremic toxins and improvement in the ionic composition [2, 6, 18, 19]. However, the removal of these toxins using HD seemed to be insufficient for normalizing the inner ear condition, because the increased G width did not decrease after a single HD session in this study (Figure 4). Alternatively, HD but not CKD may be ototoxic. Considering that some patients complain of dizziness, tinnitus, or headache following HD sessions, acute and repeated changes in the intracranial pressure or inner ear pressure might be responsible for their symptoms. Further investigation is needed to understand the pathophysiology of otologic disorders in these patients.

CONCLUSION

The G width observed in hemodialyzed CKD patients was significantly greater than that of the control group. It may represent an increased inner ear pressure or the existence of an endolymphatic hydrops in these patients, which is possibly related to their otologic symptoms.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.T., K.I.; Design – A.T., K.I.; Data Collection and Processing – A.T., K.I., T.Y.; Analysis and Interpretation – A.T., K.I., T.Y., K.K., N.M., T.Y., K.M., K.T., T.N.; Writing – A.T., K.I., T.Y., K.K., N.M., T.Y., K.M., K.T., T.N.

Conflict of Interest: The authors have no conflict of interest to declare.

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