

The Potential Significance of Reversed Stapes Reflex in Clinical Practice in Idiopathic Intracranial Hypertension

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Abstract

Background: Stapes reflex test is a method of evaluating the involuntary muscle contraction of the stapedius muscle in response to a high-intensity sound stimulus. The formation of this reflex involves the intact function of the 7th nerve, brain stem, 8th nerve, and middle ear. Due to ease of administration and information yielded, the stapedial reflex is considered one of the most powerful differential diagnostic audiological procedures. Numerous studies have remarked on the fluid communication between the intracochlear and intracranial spaces through the cochlear aqueduct. Currently, the potential significance of a noninvasive audiological technique in the discrimination of raised intracranial pressure constitutes a crucial topic of interest. **Methods:** We have performed the pre-LP and post-LP detailed otorhinolaryngological investigations, including the detailed inspection, audiometric testing, tympanometry, and stapedial reflex in a total of four consecutive patients with IIH. Results: We found that the stapedial reflex was bilateral absent initially in two of the patients. However, the second stapedial reflex investigations after LP showed reversal of the reflex responses in both of the patients. **Conclusions:** We suggest some hypotheses and propose some clinical applications. Future studies focusing on the potential utility of this reflex in the monitorization of IIH may provide crucial perspectives.

Keywords: Audiological tests, idiopathic intracranial hypertension, monitorization, stapedial reflex

INTRODUCTION

The stapedial reflex reflects the contraction of the stapedial muscle in the middle ear, which is elicited by high-level sounds, especially those of low frequency. The function of this reflex is to protect the inner ear from overstimulation from loud sounds, including both sounds in the external world and self-generated vocalizations.^[1] Numerous studies have remarked on the fluid communication between the intracochlear and intracranial spaces through the cochlear aqueduct, and many authors have investigated the potential use of the stapedial reflex arc as a noninvasive test in discrimination increased intracranial pressure.^[2-6] However, its significance in the clinical practice of idiopathic intracranial hypertension (IIH) is unclear.^[2,4,7,8]

Idiopathic intracranial hypertension (IIH) is a syndrome characterized by increased intracranial pressure (ICP) without any focal signs of neurological dysfunction except for cranial nerve palsies.^[9] Although the etiology of the disorder is not well understood, disturbed cerebrospinal fluid (CSF) dynamics are assumed to be the basic mechanism. The current diagnostic criteria include the presence of symptoms and signs of generalized intracranial hypertension or papilledema, CSF opening pressure greater than 250 mm H₂O, normal CSF composition, no structural lesion in MRI, and excluding other causes of intracranial hypertension.^[9] Ophthalmological evaluations, including fundus examination, visual acuity testing, visual field testing, and optical coherence tomography, constitute crucial methods for the monitoring of the disease.^[10] However, we know that these are indirect measurements and do not always enlighten the severity of the disease. Moreover, there is no clear correlation between the

resolution of the ophthalmological findings and the severity of the disease in terms of temporal course such that the resolution of the ophthalmological findings occurs after an interval of the recovery of the ICP. Therefore, it is difficult to evaluate the degree of the response to treatments in some critical scenarios. As such, the lumbar puncture (LP) investigation may be required to make critical treatment decisions in some circumstances. Furthermore, in addition to the optimal monitoring method of these patients, there are controversies regarding the diagnosis of this entity and the determination of the prognosis.

Taken together, we believe that introducing a noninvasive and practical paraclinical marker may help critically in clinical decision-making. Therefore, we aimed to present the data of our preliminary case study investigating the clinical significance of the stapedial reflex in our small group of patients with IIH.

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METHOD

We performed detailed otorhinolaryngological investigations in an IIH patient with pulsatile tinnitus and found that acoustic reflex was bilateral negative at admission which was reversed by LP drainage and appropriate medical treatments (Case 1). Upon our observation, we performed the pre-LP and post-LP detailed otorhinolaryngological investigations, including the detailed inspection, audiometric testing, tympanometry, and stapedial reflex in a total of four consecutive patients with IIH (within 2-months' interval) who consented to participate in this research and who had normal audiometric testing results. The diagnosis of IIH was made according to the revised Friedman diagnostic criteria.^[11] None of the patients had comorbidities such as conductive hearing loss, sensorineural hearing loss, middle ear effusion, tympanic membrane perforation, or facial nerve palsy that might affect the acoustic reflex response (among the seven IIH patients included within this time interval, two patients did not agree to participate in the study and one subject was excluded by the reason of a previous medical history of middle ear effusion due to chronic otitis media and associated conductive hearing loss). During the acoustic reflex investigation, the dynamic changes occurring from the contraction of stapedius were measured at stimuli frequencies of 500, 1000, 2000, and 4000 Hz at a sound pressure level of 80 dB. Due to technical problems related to the machine (MADSEN Zodiac Type 1096), the reflexes were measured only ipsilaterally.

RESULTS

We found that in two patients (case 1 and case 2), the acoustic reflex was bilateral negative, which all reversed rapidly following drainage LP. In two other patients, the stapedial reflexes were found to be initially positive. In these patients (a 30-year-old female and a 28-year-old female), the clinical presentations were mild and characterized by headache and mild papilledema; the LP opening pressures were 250 mm H₂O and 260 mm H₂O, respectively. We present the data of these two cases with reversed acoustic reflex after LP in detail.

Case 1

A 32-year-old female patient presented with progressive headache and diplopia, which had emerged over the previous

1-month period. The patient described frontal, bilateral, constant headache that worsened particularly in the morning and in the lying position. In addition, the complaints of blurry vision had started over the last 2 weeks. Medical history revealed that she had applied to the otorhinolaryngology clinic 2 months ago due to sudden hearing loss in her left ear and pulsatile tinnitus where she had received the diagnosis of sudden sensorineural hearing loss. Intratympanic dexamethasone was initiated over the following 4 days which yielded a significant recovery in hearing loss and tinnitus. Body mass index was 37.4 (weight: 90 kg, height: 155 cm). At admission to our clinic, neurological examination revealed severe papilledema (Frisen stage IV). She had blurry vision in all four quadrants and bilateral "blobs" in her visual field. The visual acuity was evaluated as bilateral 4/5. Visual field examination revealed bilateral mild peripheral restriction. Moreover, the patient could not turn her right eye outward, which was compatible with right sixth nerve palsy. Other neurological exams were evaluated as normal. Laboratory investigations, including hemogram, full biochemistry, TSH, vitamin B12, and folic acid, were within normal limits. Cranial MRI revealed signs of increased intracranial pressure, including empty sella, flattening of the posterior globes, optic nerve head protrusion, and tortuosity of the optic nerve [Figure 1]. She had no complaints of hearing loss; however, pulsatile tinnitus persisted at a milder degree. Therefore, the patient was referred to the otorhinolaryngology clinic for a detailed investigation. The inspection of the ears and nose were bilateral normal. The audiometric testing revealed normal findings. Tympanometry yielded normal bilateral barometric pressure in the middle ear; however, the stapedial reflex investigation showed that the reflex was bilateral absent. The lumbar puncture (LP) investigation revealed 640 mm H₂O CSF opening pressure with normal CSF biochemistry results. Further, 30 ml of CSF was drained and the LP closing pressure was evaluated as 80 mm H₂O. Following LP drainage, the headache and double vision completely recovered. The definite diagnosis of IIH was established and the treatments of acetazolamide and topiramate were initiated. The otorhinolaryngology investigations were repeated the following day of LP which revealed that the acoustic reflex was positive on the left side. The acoustic reflex examination performed 4 days after drainer LP revealed bilateral positive

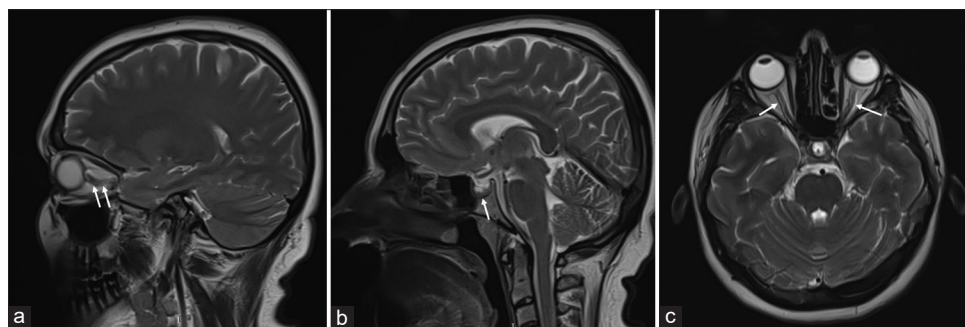


Figure 1: Cranial MRI images showing the pathological signs of increased intracranial pressure: (a) Tortuosity of the optic nerve. (b) Partial empty sella. (c) Optic nerve sheath enlargement (arrows)

acoustic reflex responses [Table 1]. At the final polyclinic visit (6 months after discharge), the patient is symptom-free with normal visual acuity and visual field on treatments of 2 × 250 mg acetazolamide and topiramate 1 × 50 mg.

Case 2

A 32-year-old female patient presented with progressive headache and blurry vision which had occurred and progressed over the last 6 months. Her medical history was unremarkable; however, she had gained 10 kg over the last 6 months. Her BMI was 32.9. Neurological examination revealed papilledema (Frisen stage II). Cranial MRI revealed signs of increased intracranial pressure, including empty sella and tortuosity of the optic nerve. The audiometric testing revealed normal findings. Tympanometry yielded normal bilateral barometric pressure in the middle ear; however, the stapedial reflex investigation showed that the reflex was bilateral absent. The lumbar puncture (LP) investigation revealed 340 mm H₂O cerebrospinal fluid (CSF) opening pressure with normal CSF biochemistry results. Further, 20 cc of CSF was drained and the LP closing pressure was evaluated as 90 mm H₂O. The second

investigation showed that the acoustic reflex was bilateral positive [Table 2]. At the final polyclinic visit (three months after discharge), the patient is symptom-free on treatments of 1 × 250 mg acetazolamide and topiramate 1 × 50 mg.

DISCUSSION

In our preliminary study, we found that the stapedial reflex was initially negative in our two patients with IIH; however, the reflex was reversed rapidly following LP. We think that our findings are original and should be evaluated meticulously. Studies focusing on neuro-otologic symptoms and evaluations are rare in the literature.^[2-6] Tinnitus, vertigo, and hearing loss were the most common manifestations reported to be in association with IIH.^[4,8] However, they are rarely the initial manifestation of IIH, and no clear association between these symptoms and the disease course has been clarified to highlight these signs as utilizable in clinical practice. The studies investigating the function of the stapedial reflex arc in IIH are extremely rare.^[2,4,7] In a study by Ozer *et al.*,^[2] 28 patients with IIH were evaluated in terms of the presence of neuro-otologic symptoms. In all these patients, audiological and electrophysiological studies were also performed. The authors found that a significant number of patients suffered from tinnitus; sensorineural hearing loss was also common in this patient group. In conclusion, they drew attention to the importance of the otolaryngology evaluation as neuro-otologic symptoms were prevalent in these patients and many patients had audiological abnormalities despite not presenting a related symptom. They discussed the mechanisms of the stretching or compression of the cochlear nerve and brain stem as a possible mechanism for hearing loss because of the increased intracranial hypertension.^[2,8] Moreover, the authors also found that stapedial reflexes were present in all the ears of the groups. However, they formed the study group from patients on follow-up rather than the subjects at presentation without the intervention of treatment for IIH. Therefore, we cannot know whether the stapedial reflex was absent at presentation before the invasive and medical treatments. In another case-control study,^[4] audio-vestibular evaluations were performed in 20 IIH subjects and it was found that three patients (15%) in the study group had no reflexes while all the healthy subjects had positive stapedial reflex responses. This was not statistically significant ($P > 0.05$); however, the limitation of this study was also that the inclusion time of the patients was not mentioned in detail. Therefore, we do not know if they were in the active phase of the disease or the symptoms were under control by treatments during the acoustic reflex investigations. We found that two of our four cases (50%) had positive stapedial reflex responses before the LP drainage that decreases the value of the absence of this reflex as a diagnostic sign for IIH. However, the strength of our report is that we performed the investigations before and after drainer LP which enabled us to observe the influence of treatment effect.

The mechanisms underlying the absence of stapedial reflex in our two IIH subjects and its reversal by treatment can be explained by some hypotheses. The first explanation may

Table 1: The results at presentation before lumbar puncture drainage

Right Reflex threshold (ipsilateral stimulations)				
Stimulus	0,5 kHz	1 kHz	2 kHz	4 kHz
	*	*	*	*
Left Reflex threshold (ipsilateral stimulations)				
Stimulus	0,5 kHz	1 kHz	2 kHz	4 kHz
	*	*	*	*
The results of the stapes reflex investigations after lumbar puncture drainage				
Right Reflex threshold (ipsilateral stimulations)				
	Sitimus	Sitimus	Sitimus	Sitimus
	90	90	85	90
Left Reflex threshold (ipsilateral stimulations)				
	Stimulus	Stimulus	Stimulus	Stimulus
	90	85	85	85

Table 2: The results at presentation before lumbar puncture drainage

Right Reflex threshold (ipsilateral stimulations)				
Stimulus	0,5 kHz	1 kHz	2 kHz	4 kHz
	*	*	*	*
Left Reflex threshold (ipsilateral stimulations)				
Stimulus	0,5 kHz	1 kHz	2 kHz	4 kHz
	*	*	*	*
The results of the stapes reflex investigations after lumbar puncture drainage				
Right Reflex threshold (ipsilateral stimulations)				
	Sitimus	Sitimus	Sitimus	Sitimus
	95	95	95	100
Left Reflex threshold (ipsilateral stimulations)				
	Stimulus	Stimulus	Stimulus	Stimulus
	95	95	95	100

be related to the direct effect of increased ICP leading to mechanical disturbance in the endpoint of the reflex, stapedius muscle. Increased ICP may lead to increased pressure of perilymph through the cochlear aqueduct.^[12] Similarly, hypothesized as an explanation for hearing loss in IIH,^[12] the tension of the basilar membrane is increased and the mobility of the stapes footplate is hindered, resulting in the absence of stapedial reflex. Another mechanism may be associated with the increased subarachnoid pressure-related damage to the cranial nerves responsible for the execution of this reflex. The sixth nerve palsy is the most common cranial neuropathy seen in IIH. In addition, more rarely, other cranial neuropathies, including 7th, 3rd, and 4th nerve palsies, may also be involved in the clinical presentation. Although the mechanisms underlying these neuropathies are not exactly clear, the prominent hypothesis suggested is the mechanical effect of the increased ICP. According to this view, the increased ICP exerts traction forces on the extra-axial cranial nerves and the resolution of these neuropathies by appropriate treatment of IIH also supports this hypothesis. In IIH, the dominance of sixth nerve palsy among other neuropathies is classically explained via its specific feature of being the longest coursed cranial nerve making it the most susceptible neuropathy to high ICP. However, the stapedial reflex requires the intact function of both the 7th and 8th cranial nerves and involves a strictly long nerve course theoretically making this function highly vulnerable to increased ICP. However, in the absence of detailed audiological investigations, the malfunction of this reflex cannot be detected clinically, which might lead to the underdiagnosis of this clinical manifestation in IIH.

The clinical significance of the stapedial reflex has also been investigated in neurological conditions other than IIH that might lead to increased ICP.^[3,7] In a crucial study on 58 subjects with diagnoses of hydrocephalus, tumor, and other neurological conditions,^[3] the authors found that changes in the ICP can affect the hydrostatic pressure of the cochlea and influence the peripheral auditory system. Based on the results of their study,^[3] they suggested that tympanic membrane displacement (which is accepted to be mediated mainly by stapedius muscle^[13]) during stapedial contraction may provide a useful noninvasive method for the assessment of perilymphatic pressure. However, in another study on a large number of patients,^[7] tympanic membrane displacement (TMD) measurements were not found to provide reliable data regarding the ICP in patients with hydrocephalus.

Taken together, there is no consistency regarding the utility of the stapedial reflex in discriminating the increased ICP from normal subjects. However, combining the literature data with the results of our study, we suggest that the stapedial reflex may be one of the clinical manifestations of IIH (e.g., sixth nerve palsy) that might reflect the disturbed CSF balance in IIH. Therefore, we hypothesize that the absence of the stapedial reflex may be a finding supporting the diagnosis of IIH. However, the more important point may be that the serial investigation of the stapedial reflex may constitute a

critical monitoring method in IIH subjects with initial negative reflex. The limitation of our report was that due to technical problems, the contralateral stapes reflex could not be studied, which prevented us from understanding the localization of the pathophysiology of the reversible disturbance clearly. Therefore, we plan to conduct a prospective study on a large number of patients including both ipsilateral and contralateral examinations. The clarification of the significance of this reflex in future prospective studies of large case series may provide critical contributions to clinical practice. Involving the detailed study of this reflex, including contralateral measurements, may reveal the underlying pathophysiology more clearly.

Ethical approval

Ethical approval has been obtained from the local ethics committee of the Yozgat City Hospital.

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Conflicts of interest

There are no conflicts of interest.

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