

# Endolymphatic hydrops in idiopathic intracranial hypertension: prevalence and clinical outcome after lumbar puncture. Preliminary data

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**Abstract** Idiopathic intracranial hypertension is characterized by raised intracranial pressure (ICP) without any underlying pathology, presenting with (IIH) or without papilledema (IIHWOP). Headache, often on daily basis, is the most frequent symptom. Among audiovestibular symptoms, tinnitus and dizziness are commonly reported, while vertigo and hearing impairment are infrequent reports. Endolymphatic hydrops (ELH) is the typical histopathologic feature of Ménière disease, a condition featured by episodes of vertigo, dizziness, fluctuating hearing loss, tinnitus, and aural fullness. Evidences suggest that ICP is transmitted to inner ear. The aim of this study is to investigate the prevalence of ELH symptoms in IIH/IIHWOP and the relationship between the raised ICP and ELH. The prevalence of chronic headache and of ELH symptoms was investigated in a consecutive series of IIH/IIHWOP patients, and a standard audiometry with hearing threshold measurement (pure-tone average—PTA) was performed. Differences in chronic headache and ELH symptoms prevalence and changes of PTA threshold were calculated after ICP normalization by lumbar puncture (LP). Thirty-one patients (17 with IIH and 14 with IIHWOP) were included. Before LP, chronic headache was present in 93.5%. The percentages of patients reporting tinnitus, dizziness, vertigo, and aural fullness were 67.7,

77.4, 22.6, and 61.3%, respectively. Headache frequency as well as ELH symptoms and PTA significantly improved after LP. The improvement of PTA and of ELH symptoms observed after LP in this series of IIH/IIHWOP patients indicates that a raised ICP, a condition known to be involved in the progression and refractoriness of migraine pain, has also a role in ELH. We propose that intracranial hypertension may represent the shared pathogenetic step explaining the large epidemiological comorbidity between migraine and vestibular symptoms, at present conceptualized as “vestibular migraine.”

**Keywords** Raised intracranial pressure · Idiopathic intracranial hypertension · Endolymphatic hydrops · Vestibular migraine · Ménière disease

## Introduction

Idiopathic intracranial hypertension (IIH) is characterized by raised intracranial pressure (ICP) without any underlying pathology. Headache, mainly on a daily basis, is the most frequent symptom. The typical sign of papilledema may be absent (IIHWOP), complicating the diagnostic work-up as the clinical presentation of IIHWOP may be indistinguishable from primary forms of chronic headache [1–3].

In addition to headache, patients with IIH/IIHWOP may be affected by visual symptoms, back and/or radicular pain and audiovestibular symptoms. Among the latter, tinnitus and dizziness are reported by up to half of the patients [4]; vertigo and hearing impairment, mainly on low frequencies, are uncommon complaints [5].

The pathophysiology of audiovestibular symptoms in IIH remains poorly understood. Tinnitus may be provoked

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by flow turbulence across sinus stenosis, a common finding in IIH patients with pathogenetic relevance [6, 7], which improves after ICP normalization [5, 8]. Little is known about hearing loss in IIH patients. A reversible hearing threshold elevation has been documented in raised ICP attributed to brain tumors or hydrocephalus [9]. Transmission of ICP changes to the inner ear fluids has been demonstrated in both humans [10, 11] and animal models [12, 13]. Preclinical evidence showed that the inner ear fluid pressure (both in the endolymph and perilymph) increases proportionally to the ICP increase, inducing the alteration of cochlear auditory system [13].

Endolymphatic hydrops (ELH) is the anatomopathologic correlate of inner ear pressure increase and may result from several conditions [14]. Ménière disease (MD) is considered the “idiopathic syndrome of ELH” [15] and its typical presentation includes vertigo, dizziness, tinnitus, hearing fluctuation and aural fullness.

### Aim of the study

To further elucidate the relationship between the raised ICP and ELH, we evaluated the prevalence of typical ELH symptoms in patients affected by IIH/IIHWOP before and after ICP normalization by lumbar puncture (LP).

### Patients and methods

Consecutive patients diagnosed with IIH/IIHWOP according to recent diagnostic criteria [16] were included in this study. All the patients signed an informed consent. The study has been performed in accordance with the Declaration of Helsinki and latest revisions.

All patients underwent an uncontrasted magnetic resonance (MR) of the brain with venography (MRV) and an ophthalmological evaluation to assess the presence/absence of papilledema. Data regarding the characteristics and frequencies of headache and of possible ELH-related audiovestibular symptoms occurring during the month preceding LP were collected. Each ELH symptom was considered as “present” if it was reported at least once. Each patient performed a standard audiometry within the week before LP, and a second test was performed after LP (within 1 week or at the resolution of post LP headache). A pure-tone average (PTA) threshold at each of the 0.125, 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz was calculated for each ear separately, and the PTA values of both ears of each patient were used for subsequent analyses. We used the PTA in dB as a continuous variable. Low-frequency PTA (125, 250, and 500 Hz) and high-frequency PTA (2, 3, 4, 6, and 8 kHz) were also calculated. LP was performed in the

recumbent lateral position; ICP was measured as opening pressure (OP) and every 2 ml of cerebrospinal fluid (CSF) withdrawal up to about 100 mm H<sub>2</sub>O.

At a follow-up visit one month after LP, chronic headache and each ELH symptom (tinnitus, dizziness, aural fullness, and vertigo) were considered “improved” if their frequency was reduced at least by 50%. Changes in symptoms frequency was evaluated as percentage change: (new percentage – old percentage)/old percentage. Differences in symptoms frequency were evaluated by McNemar test on paired proportions. Significance level was set at 0.05. The differences in PTA between pooled ears before and after LP were assessed using the Wilcoxon test with significance level at 0.05. Analyses were performed using the software SPSS version 22.

### Results

Thirty-one patients (29 women and 2 men; mean age  $35.2 \pm 11.0$ ) were included (17 with IIH and 14 with IIHWOP). Chronic headache with migraine feature was present in 29 out of 31 patients (93.5%). Significant sinus stenosis was found in 30 patients (96.7%). This was unilateral in 21 (67.7%) and bilateral in 9 (29%). The percentage of patients referring tinnitus was 67.7%, dizziness was present in 77.4%, aural fullness was referred by 61.3% of the patients, and episodes of vertigo observed in 22.6% of the cases.

Mean OP was  $287 \pm 47.4$  mmH<sub>2</sub>O ( $302 \pm 55.9$  mmH<sub>2</sub>O in IIH and  $267 \pm 22.9$  mmH<sub>2</sub>O in IIHWOP). A mean of 27.0 ml of CSF was subtracted (range 16–36).

At 1 month after LP, a chronic pattern of headache (>15 days per month) was encountered in only 6 out of 31 patients (19.4%) with a percentage reduction of 79.2% compared with baseline ( $p < 0.01$ ). The prevalence of each ELH symptom after LP significantly reduced ( $p < 0.05$ ): [tinnitus 16.1% (76.2% reduction); dizziness 12.9% (83.3% reduction); aural fullness 9.7% (84.2% reduction); and vertigo 0% (100% reduction)].

The median of PTA at baseline was 16.9 dB (interquartile range 10.6) and it significantly reduced to 14.1 (interquartile range 11.7) after ICP normalization ( $p < 0.05$ ). A difference in low-frequency PTA ( $p < 0.05$ ) was found after LP, while no difference in high-frequency PTA was observed.

### Discussion

As expected, almost all the patients of this series carried significant intracranial sinus stenosis, confirming its role as a neuroradiological marker of raised ICP [16, 17]. We

found a high prevalence of vestibular symptoms in our series of IIH/IIHWOP patients. Besides tinnitus, dizziness and vertigo, which have already been associated to the condition [4, 5], aural fullness also is commonly complained by these patients. To the best of our knowledge, this association has not been previously reported. Thus, the cluster of vestibular symptoms occurring in IIH/IIHWOP fully overlap with typical ELH clinical presentation [15]. This observation may be of relevance in IIHWOP diagnosis, a neglected condition often overlooked or misdiagnosed as a primary chronic headache [1–3]. We documented a dramatic reduction of both chronic headache and ELH symptoms soon after the LP as well as the improvement of PTA. These findings strongly support a role for the raised ICP in ELH mechanisms, possibly mediated by direct pressure transmission to the inner ear fluids [13].

Vertigo, dizziness, and migraine are commonly comorbid conditions. The identification of migraine-associated vertigo or dizziness led in the past decades to the definition of Vestibular Migraine (VM) [18], experimental diagnostic criteria of which have been included in the appendix of the ICHD 3beta version [19]. Mechanisms underlying this association still need to be clarified. A recent study revealed the presence of ELH in VM patients by locally enhanced inner ear MR [20], suggesting that vestibular symptoms in VM are caused by a derangement of inner fluids pressures.

Sinus stenosis is a very common finding in chronic headache patients [1, 21, 22], and a raised ICP may be causatively involved in pain mechanisms in these patients [1]. Our findings suggest the causative role of raised ICP also in ELH, allowing us to hypothesize that an overlooked IIH/IIHWOP may represent the shared pathogenetic step explaining the large epidemiological comorbidity between migraine and vestibular symptoms, at present conceptualized as “vestibular migraine.”

## Conclusions

Vestibular symptoms in IIH/IIHWOP also include aural fullness, therefore mimicking the typical ELH syndrome, and revert after ICP normalization. This finding supports the hypothesis that an overlooked IIHWOP may represent the shared pathogenetic step explaining the association between migraine and vestibular symptoms in VM. Further studies assessing the prevalence of sinus stenosis and of other neuroradiological signs of intracranial hypertension in VM patients are needed.

## Compliance with ethical standards

**Conflict of interest** The authors certify that there is no actual or potential conflict of interest in relation to this article.

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