In Intracranial pressure as a generator of aural noises: Improved differential diagnosis will facilitate effective treatments

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Marchbanks R.J.
Consultant Scientist Director, Non-invasive Intracranial Assessment Unit (NIPA), Medical Physics Department, Southampton University Hospital, Southampton SO16 6YD

e-mail: Rob@marchbanks.co.uk
Fax: + 44 (0) 1590 670443

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Abstract
Raised cerebral fluid pressure (intracranial hypertension) often results in tinnitus, vertigo and sometimes a hearing loss, which may be irreversible. In cases where the expected headache and papilloedema are absent, patients with intracranial hypertension are likely to be referred to the otolaryngological clinic for investigations of the audiovestibular symptoms, yet these patients are rarely cross-referred to neurology.

A multi-centre study which is supported by 'Defeating Deafness -- the Hearing Research Trust' is currently underway. This study aims to more clearly define the characteristics of the tinnitus, vertigo, aural fullness and hearing loss found with intracranial hypertension. From this work a questionnaires and objective clinical tests such as made by the 'TMD Cerebral and Cochlear Pressure Analyser' will be combined to provide an ‘At Risk Profile’ to facilitate cross-referral of patients with intracranial hypertension to neurology.

Certain aspects of this multi-centre study are discussed. Two case studies highlight inappropriate diagnosis of intracranial hypertension as otological disorders. Low frequency tinnitus of a pulsatile and/or 'whooshing' 'sea-like' nature appears to be the key symptom for diagnosing intracranial hypertension and in many cases may be the only defining symptom. The existence of a cohort of mostly female patients with these symptoms, which are due to undiagnosed intracranial hypertension, has both a cost implication for the health service and is a ‘quality of life’ issue for the individual. Correct diagnosis of intracranial hypertension in the otolaryngological clinic is important to avoid ineffective treatments. It also allows recognised treatments and management regimes to applied which should provide the patient with total relief from audiovestibular symptoms.

Introduction
It is recognised that raised cerebral fluid pressure (intracranial hypertension) often results in aural noises, dizziness and sometimes a hearing loss, which may be irreversible. It is apparent that patients with intracranial hypertension are being missed in virtually all otology clinics, since the few centres which look to identify these patients, find them. Currently in nearly all cases the condition will be wrongly diagnosed as being a ‘Ménière’s like’ or a non-specific inner ear disorder which may include tinnitus as the primary symptom. Yet this condition is treatable if correctly diagnosed, with often a complete remission of the audiological symptoms.
There is a particular interest in the audiovestibular symptomatology of patients with a condition known as Benign Intracranial Hypertension (BIH) also known as pseudotumour cerebri or idiopathic intracranial hypertension [1]. How do we differentiate these patients with this condition from those with an actual otological disease process? How common is this problem and what are the referral patterns? What are the effective diagnosis and treatment regimes? What are the underlying mechanisms for this disorder and in particular the intracranial-labyrinthine interactions?

A multi-centre UK study funded by ‘Defeating Deafness - the Hearing Research Trust’ is beginning to address some of these questions. This collaborative action includes: - the NIPA (Non-invasive Intracranial Pressure Assessment) Unit, Southampton; the Department of Neuro-Otology, National Hospital for Neurology and Neurosurgery, London; the Academic Department of Neurosurgery and the Department of Neuro-Otology, Addenbrooks, Cambridge; the Queens Medical School and Institute of Hearing Research, Nottingham.

These centres will research the exact nature of the symptomatology and utilise a non-surgical method of assessing the cerebral and cochlear fluid pressure on patients with proven intracranial hypertension (the MMS-11 TMD Cerebral and Cochlear Pressure Analyser). The aims are: - (1) to advance our understanding of inner ear physiology by testing the hypothesis that ‘Connectivity between the cerebral and cochlear fluids is associated with specific forms of tinnitus, vertigo and hearing loss’ (2) to provide an ‘At Risk Profile’ to help all major audiology and neuro-otology clinics identify and successful treat patients with this condition.

This paper provides a résumé of the methods being employed in this multi-centre trial and illustrates the importance of this work in terms of two patients who were wrongly diagnosed as having otolaryngological disorders and where later found to have BIH.

The Clinical Study

In the current multi-centre trial, patients with confirmed raised intracranial pressure and in particular with BIH are being cross-referred from neurology/neurosurgery to the audiology and neuro-otology centres of the participating hospitals. A full neurological assessment is made on these patients and BIH is diagnosed on the basis of absent cerebral lesion and tumours, normal ventricle appearance, cerebrospinal fluid (CSF) of normal composition and abnormal high CSF on lumbar puncture. A complete assessment of visual acuity, visual fields and enlarged blind spots is also made and papilloedema is almost always present.

Once diagnosed as BIH, these patients undergo an audiological assessment and a detailed questionnaire is administered by the researching clinician to assess the nature and severity of any tinnitus, dizziness, head and aural fullness, hearing deficits, visual obscurations, headache and the patient's general feeling of wellbeing.

A non-invasive measurement of the cochlear pressure is made using the 'MMS-10/11 TMD Cerebral and Cochlear Pressure Analyser' which is also used to quantify the level of cardiovascular noise being emitted from the external ear canal [2,3,4]. Cerebral to cochlear fluid connectivity is also assessed by inducing a change in intracranial pressure by moving the patient from a sitting upright to supine position [5,6]. A corresponding change in cochlear pressure is assumed to represent a patent fluid pathway between the cerebral and cochlear fluids. The relationship between the change in pressure with posture and the existence of tinnitus and cardiovascular activity in a particular ear will be
investigated to see if a patent cerebral-cochlear fluid pathway is a prerequisite for having low frequency tinnitus, and possibly stimulation of the cochlea directly by cerebral pressure waves.

The aim is to test up to 48 patients with BIH, with each of the 4 centres contributing about 12 patients. In addition, the symptom questionnaire devised for the BIH patients has also been answered by an age and gender matched control group of 60 normal female subjects. These subjects have undergone a full TMD cerebral/cochlear pressure, hearing and tympanometric assessment.

Early results

To date 60 normal female controls and 10 BIH subjects with proven intracranial hypertension have been tested at Southampton. It is not possible to draw definite conclusions at the current time, nevertheless, the findings to date are in general agreement with the earlier Southampton study which included 34 BIH patients [7]. In this earlier study an open fluid connection between the cerebral and cochlear (perilymphatic) fluids could be demonstrated using the ‘TMD Cerebral and Cochlear Fluid Pressure Analyser’ in 29 patients. Of these patients 16 (55%) complained of tinnitus which was unilateral in 6 (21%) cases and it was bilateral in 10 (34%) cases. As in the current series, if tinnitus exists it is principally of a low frequency nature with pulsatile characteristics in some instances.

Comparing these findings with the normative data, none of the 60 normal females questioned reported daily headaches, low frequency or pulsatile tinnitus as found in most, but not all of the BIH patients.

Case Studies

The multi-centre study seeks to investigate the premise that patients with intracranial hypertension are being seen for otological conditions, but are not being cross referred to neurology. Of the 10 patients seen in the current series, it is interesting to note that 2 patients were being seen by ENT consultants who were treating the patients for otolaryngological disorders. In both cases, only by chance the patients visited their opticians for a regular check-up, and the opticians fortunately identified papilloedema and immediately referred them to our Wessex Neurological Centre where BIH was confirmed.

Case 1

The first case is an slightly over-weight 18 year old female who had been studying for her A levels when one morning she woke up with a 'whooshing' tinnitus in her left ear (November 1997). This was described as being like 'a fast train' noise which was incidental with her heart beat. She noticed that the tinnitus stopped when turning her head, but became worse with physical activities such as squash. The 'whooshing' tinnitus was always present and frequently interfered with daily activities and sleep. She did not have any balance problems, no sensations of pressure or fullness, and no significant headaches.

The patient's GP referred her to an ENT consultant so that the pulsatile tinnitus could be investigated further (15/01/98). The ENT consultant found no clinical abnormalities and the audiogram was normal. The CT scan was normal and it was decided to undertake a neurological vascular examination.
About 8 months after the start of the condition the patient visited her optician for a regular check-up and he found bilateral papilloedema (25/06/98). She was immediately referred to our Wessex Neurological Centre where the TMD technique was used to provide a non-invasive assessment of the intracranial pressure and to assess patency of the cerebral-cochlear fluid pathways (26/06/98). There appeared to be a cerebral-cochlear connection in the left ear where the tinnitus was present but not the right ear which was without tinnitus. A lumbar puncture gave an excessive opening pressure of 46 cm of saline. The CSF composition, cell count, glucose and protein were all normal and BIH was diagnosed. Interestingly she commented that the tinnitus was no longer present 2 to 3 weeks after the lumbar puncture.

The patient was managed on oral diuretics, Frusemide (40 mg per day), for 4 weeks and then a repeat lumbar puncture showed that the CSF pressure was still raised at 38 cm saline. At this time 10ml of CSF was withdrawn which brought the pressure down to 26 cm saline. The papilloedema still was present (14/08/98). A course of steroid (30mg per day Prednisolone) was taken for 1 week and then Frusemide was continued. Ten weeks later there was no papilloedema and the fundi were normal (20/10/98). The opening lumbar puncture pressure was lower, but still abnormally high at 29.5 cm. These findings were repeated after a further 10 weeks following a continuing course of Frusemide (40mg alternative days).

The diuretic was discontinued and when she was reviewed this year her optic disks were normal (12/05/99). At this time TMD assessment of intracranial pressure was used so as to avoid further lumbar puncture, and this indicated there had been a significant reduction in CSF pressure although this pressure may still be greater than normal. The tinnitus was no longer continuous and only occurred 3 to 4 times per month. The character of the tinnitus had changed from the ‘train-like’ whooshing tinnitus to an occasional less intrusive muffled ‘whooshing’. On the basis that the optic disks were normal, the patient has now been discharged and will be review by her GP at regular intervals.

Case 2

This patient is a 35 year old female civil servant who was first referred by her GP to an ENT consultant because of a sensation of aural pressure in both ears, a low frequency fluctuating hearing loss, vertigo and tinnitus which was described as a 'buzzing' (6/01/97). The vertigo was episodic, objective and rotary. Vertigo attacks occurred every few weeks and these could sometimes last all day. The vertigo was accompanied by the tinnitus. The patient felt nauseous during these attacks and vomited on a number of occasions.

The patient was reviewed later in 1997 by the ENT consultant who found that a mild low frequency hearing loss had developed over a period of 11 months since the last audiogram as shown in figure 1. The other symptoms remained largely unchanged and the patient complained that she found the blockage of her ears extremely irritating (14/11/97). Neither Beconase® nor topical steroids improved the condition that was considered to be related to nasal obstruction. The consultant considered the condition to be due to persistent Eustachian tube function with nasal obstruction. ENT surgery was undertaken in terms of trimming of turbinates to clear the nose and septoplasty.

Following this surgery the symptoms continued but were less severe. However, 16 months later the patient was admitted into hospital due to a sudden onset of headache and nausea (16/03/98). The dizziness was now occurring regularly, particularly in the morning. There did not appear to be papilloedema and the CT scan was normal. Following investigation the patient was discharged and was prescribed Serc®, 16 mg per day for 1 month.
In February 1999 the patient visited her optician who found papilledema and immediately referred her to the Wessex Neurological Centre (9/02/99). At this time she reported headaches with visual disturbances, vomiting and diarrhoea. These attacks lasted up to 1 hour and were sometimes accompanied by ‘bright flashing lights’. Over the past 12 months the rotary vertigo had become less severe and now only lasted about 10 minutes, however, she now had periods when she became unsteady on her feet and had a more general feeling of dizziness. This was described ‘as feeling drunk’ and she frequently ‘bumped into things’. Absent acoustic stapedial reflexes precluded TMD assessment.

Over the past 3 months she had noticed a change in her vision in terms of transient blindness which lasted a few seconds and sometimes blurring which lasted a few minutes. She also commented that her night vision had deteriorated and had a feeling of ‘bruising’ behind her eyes. On investigation bilateral papilledema and field defects were found. Lumbar puncture found a raised CSF pressure of 28 cm saline. The diagnosis of BIH was therefore made (10/02/99). The condition is not responding to medication (Acetazolamide) and a lumbar-peritoneal shunt with possibly optic nerve fenestration is being considered.

Discussion and conclusion

It is evident that the otolaryngological symptoms associated with intracranial hypertension can include tinnitus, dizziness, vertigo, a hearing loss which may fluctuate, and a sensation of aural fullness. Depending on the combination and exact nature of these symptoms, intracranial hypertension may be misdiagnosed as Ménière’s disorder, non-specific labyrinthine disorders, Eustachian tube dysfunction and even nasal obstruction. Correct differential diagnosis depends on identifying the underlying signs and symptoms of intracranial hypertension, however, this is seldom possible, even by those experienced in neurology, without reverting to lumbar puncture. The situation is even more complex since we know that most cases intracranial hypertension will occur without the expected pressure-specific headache and papilloedema will either not be present or will go undetected. This may leave the otolaryngological symptoms as the main reason for referrals from the GP to the specialist consultant.

The two cases presented in this paper are good examples of the above. Both were initially referred by their GPs to an ENT consultant to investigate a ‘whooshing’ tinnitus in the first case and in the second case a combinations of tinnitus, dizziness and sensations of aural pressure. With the first patient, one of the key symptoms of intracranial hypertension, headache, was not present and with the second patient, headache was initially not considered to be significant and at a later stage was considered to be nothing more than migraine. Although headaches are the most common symptom found with intracranial hypertension they are not infrequently absent, mild or non-specific. Also headaches often accompany vertiginous episodes or tinnitus. Rassekh and Harker (1992) report that 22% of Ménière’s patients suffer from migraine and this increases to 81% for those with so-called vestibular Ménière’s [8].

Visual problems and papilledema are further important pointers to underlying intracranial hypertension. However, in one of the few otolaryngological clinics where BIH is regularly diagnosed, Sismanis found that only 4/20 (20%) of patients reported actual visual problems [9]. It is also recognised that the absence of papilledema may not be taken to indicate the absence of raised intracranial pressure [10]. Furthermore, papilledema is unlikely to be seen in cases where abnormal pressure is episodic in nature. It is reported that clinically significant changes in the fundus which are recognisable as papilledema
are only apparent in a minority of patients (5-10%) with raised intracranial pressure, and then only after a prolonged period of several days or even weeks [10].

The actual prevalence of undiagnosed intracranial hypertension existing in the GP practice or the otolaryngological clinic is as yet unknown. The generally accepted low incidence of 1 case of BIH per 100,000 population per year cited by Wall and George cannot be taken as representative of undiagnosed intracranial hypertension which is likely to be significantly more common in certain groups of the population for a number of reasons [11]. Firstly, the condition mostly affects women within the age range of 14 to 45 and there will be a cohort of women patients in which the condition is never correctly diagnosed. Secondly, the diagnosis of BIH largely depends on a referral for papilleodema. However, as described above, for each patient with papilleodema there could be 10 or more patients with intracranial hypertension without papilleodema. Added to this, unless the visual condition is progressive, detection of papilleodema may be a perchance event dependent on a visit to a vigilant optician -- of the first 10 BIH patients seen in the latest series half have been referred to neurology from opticians. Self referral by the patient is also highly unlikely, because papilleodema normal goes unnoticed unless a significant visual deficit has developed.

Correct diagnosis of intracranial hypertension in the otolaryngological clinic is important as recognized treatments and management strategies should provide the patient with total relief from audiovestibular symptoms [1,9]. Treatments include dietary management in terms of weight loss if appropriate and restricted salt intake. Medication includes diuretics such as Diamox often in combination with a short 1 week course of a steroid. Surgical treatments have been used for treating the audiovestibular symptomatology and include cerebrospinal fluid drainage by either repeated lumbar puncture or lumbar-peritoneal shunts [12]. As our understanding of intracranial/inner fluid interactions improves we are beginning to see the advent of new surgical treatments such as the posterior fossa cochlear aqueduct occlusion procedure which appears to relieve certain forms of tinnitus and vertigo [13].

The current multi-centre study aims to more clearly define the characteristics of the tinnitus, vertigo, aural fullness and hearing loss found with intracranial hypertension, figure 2. From this a strategy will be developed whereby questionnaires and objective clinical measurements such as the TMD technique can provide an ‘At Risk Profile’ to help identify patients with intracranial hypertension and to allow cross-referral to neurology. If available, the TMD technique is valuable for reducing the need for lumbar puncture by providing a non-invasive alternative for assessing changes in intracranial pressure with symptoms and treatment, figure 3. Since patients with treated intracranial hypertension remain ‘at risk’ of further occurrences, then the TMD technique is also proving valuable for providing pressure assessments with long term patient reviews.

Low frequency tinnitus of a pulsatile and/or 'whooshing' 'sea-like' nature appears to be the key symptom for diagnosing intracranial hypertension and in many cases may be the only defining symptom. This finding concurs with the observations made by other several authors who consider that tinnitus and intracranial pressure generated aural noises may be a better indication of increased intracranial pressure than headache or visual obscurities, and indeed may be the only manifestation of this condition [9,14]. If present, gentle compression of the internal jugular vein will often reduce the intensity of the tinnitus or even cause a complete cessation. Likewise, in cases of unilateral tinnitus, turning the head to the ipsilateral side will often reduce or abolish the tinnitus. In the opinion of Sismanis, idiopathic intracranial hypertension, glomus tumors and carotid atherosclerosis are the most common aetiologies for pulsatile tinnitus seen in the otolaryngological clinic [15].
It is now recognised that the misdiagnosis of intracranial hypertension is not just occurring in otolaryngology. Recent studies show that patients with intracranial hypertension are being referred to headache clinics and the condition is being missed because of one of the key symptoms, papilloedema, is absent. In a recent study conducted at the Houston Headache Clinic all patients with refractory chronic daily headache underwent lumbar puncture even though they did not have papilloedema. Of the 85 patients, 12 (14%) were found to had raised CSF pressure [16]. In a later case-control study, 25 patients with refractory chronic daily headaches were selected on the basis that they had raised CSF pressure without papilloedema. These were compared with 60 patients with similar headaches who had normal CSF pressure. It was concluded that pulsatile tinnitus was the strongest indicator for intracranial hypertension without papilloedema [17].

The existence of a cohort of mostly female patients with undiagnosed intracranial hypertension has both a cost implication for the health service and is a 'quality of life' issue for the individual. It should be remembered that besides the symptoms described above, intracranial hypertension is normally associated with a general feeling of malaise and dulling of memory. These are disabling conditions and are often described by the patient as 'not feeling in this world' or 'feeling in a constant daze'. These symptoms alone may be so severe as to be incapacitating and to make it impossible for the patient to continue with his/her occupation. Failure to diagnose intracranial hypertension, therefore, has significant implications for the quality of life of the patient. If tinnitus is the only well defined symptom, then the apparent degree of incapacitation with this symptom may be perplexing to the clinician and there may be a danger of the patient being labelled as psychosomatic.

The outcome of the current UK multi-centre study should provide a better understanding of the pathophysiology of the audiovestibular symptomatology of intracranial hypertension, and whether this is as a direct consequence of connectivity between the cerebral and cochlear fluids [18,19]. By providing an 'At Risk Profile' to help identify patients with intracranial hypertension, the current 'Defeating Deafness' sponsored study will provide the foundation for future work to establish the prevalence and referral patterns for undiagnosed intracranial hypertension. This in turn should lead to more effective treatment with the likelihood of complete relief from various audiovestibular disorders for certain patients.

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References


Figure 1: Audiogram for a 35 year old patient with intracranial hypertension which shows a mild low frequency hearing loss.
Predominantly female - at least 4 to 1, female/male ratio. The patient may be 20% or more overweight.

Typical age range - 18 to 45 years

Likely to be suffering from a low frequency tinnitus which will be described as 'hum', 'roaring', 'whooshing' or perhaps 'sea like' with sometimes characteristics which are synchronous with the heart beat. About 60% of patients will report tinnitus and of these about 60-70% (36-42% of total) will be of a low frequency type. In cases of unilateral tinnitus, gentle compression of the internal jugular vein will often result in a reduction in the intensity of the tinnitus or even a complete cessation. Likewise turning the head to the ipsilateral side will often reduce the tinnitus.

Most patients will report a mild imbalance or 'unsteadiness on their feet'. About 40% of those with tinnitus will be suffering some form of objective vertigo. This will be described as episodes when the 'room appears to move' and this can last for several minutes and sometimes hours. This is often not fully developed rotary vertigo. The feeling is often associated with nausea, but only infrequently vomiting.

The patient will be suffering from a malaise which will often be associated with a 'deterioration in memory', 'mental slowing' or 'dulling of mind'. The patient will commonly report headaches, however, in most cases these headaches will be mild, sometimes described as a 'dull' headache. The headache may be associated with a pressure or fullness sensations in the head, ears or behind the eyes.

If investigated, papilloedema will only probably be found in less than 10% of cases. Interestingly, although visual deficits are often found, these or visual disturbances frequently go unreported by the patient. If these occur, they may include 'greying' or 'tunnelling' which may occur - as with other symptoms - with change of posture and subsequently last for several minutes.

Low frequency and/or fluctuating hearing losses are also symptoms, but only rarely are significant enough to be noticed by patients.

The most distinguishing associations of intracranial hypertension are probably 'female' and 'low frequency and/or pulsatile tinnitus'. Nevertheless, if this latter symptom alone was taken for a 'clinical screen' for this condition, then we would expect to miss over 50% of the patients.
Figure 3: Clinical Use of the TMD Technique

TMD Intracranial/cochlear Pressure Assessment

Treatment

Intracranial hypertension

Neurological signs & symptoms

Raised perilymphatic pressure

Audiological signs & symptoms

establish effectiveness

establish hypertension

establish associations