Review

Otolithic organ function in patients with profound sensorineural hearing loss

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Abstract

Profound sensorineural hearing loss (PSHL) is not uncommonly encountered in otology. In clinics, there is a high incidence of otolithic damage in patients with PSHL, but relevant reports are few. Sharing a continuous membranous structure and similar receptor cell ultrastructures, the cochlea and vestibule may be susceptible to the same harmful factors. Disorders of the inner ear may result in a variety of manifestations, including vertigo, spatial disorientation, blurred vision, impaired articulation, and hearing impairment. Considering the diversity of clinical symptoms associated with PSHL with otolithic dysfunction, it may be frequently misdiagnosed, and objective means of testing the function of otolithic organs should be recommended for hearing-impaired patients. Vestibular-evoked myogenic potentials (VEMPs) via air-conducted sound are of great importance for the diagnosis of otolithic function. Hearing devices such as cochlear implants are commonly accepted treatments for PSHL, and early identification and treatment of vestibular disorders may increase the success rate of cochlear implantation. Therefore, it is necessary to increase awareness of otolithic functional states in patients with PSHL.

Contents

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1. Introduction

Profound sensorineural hearing loss (PSHL) is a specific form of sensorineural hearing loss (SNHL) caused by congenital or acquired lesions of the cochlea, auditory nerve and auditory center. The average air conduction audibility frequencies are 500, 1000, 2000and 4000 Hz, in which 0–25 dB represents normal hearing, 26–40 dB mild damage, 41–60 dB moderate loss; 61–80 dB severe damage, and more than 80 dB indicates profound hearing loss (Syka, 2002). PSHL is not uncommonly encountered in otology (Xu et al., 2016). The main features of PSHL are that it is most often associated with congenital hearing loss and infectious diseases. Congenital hearing loss is often bilateral and articulation is commonly impaired, as hearing loss often develops rapidly (Ozel et al., 2012). In addition to hearing loss, symptoms associated with the vestibular system may appear occasionally, such as nausea and vertigo. In children with PSHL, the incidence of otolithic damage is very high (Xu et al., 2015). It has been reported that the maximum possibility of discovering vestibular malfunction in children with hearing impairment is approximately 70% (Angeli, 2003), but this issue has not received sufficient attention from physicians. On account of the close physical connection between the cochlear and vestibular systems – for example, the cochlea and the saccule share the same membranous labyrinth (Sazgar et al., 2006) – they are frequently affected by the same factors. That said, the pathophysiology and causes of many conditions of the cochlear and vestibular systems remain to be fully determined.

Routine vestibular function tests such as Romberg's test, rotatory test and positional nystagmus test do not evaluate the function of otolithic organs. For this reason, it remains impossible to evaluate the degree of damage to the vestibular system definitively via these routine vestibular tests. In some situations, PSHL may potentially be accompanied by dysfunction of otolithic organs, which can be detected via vestibular-evoked myogenic potential (VEMP) responses (Xu et al., 2016). VEMP test, an electrophysiological examination, therefore deserves more attention. The main VEMP indexes include amplitude, latency and threshold. It can detect disorders of otolithic organs and the integrity of their pathways accurately, and is an easy and simple test of vestibular functions in clinical practice (Patko et al., 2003; Murofushi, 2016; Kim et al., 2015). PSHL with vestibular problems may affect individuals throughout their whole life, and may occur in infants as well as elderly individuals. Physicians should ensure that they are sufficiently knowledgeable in this area, in order that they may provide optimal treatment to this group of patients. Currently available hearing devices such as cochlear implants and hearing aids have facilitated great progress in hearing restoration. When physicians encounter PSHL, attention should be paid to otolithic functions during both diagnosis and treatment. VEMPs as a well-established test are particularly suited to the detection of latent otolithic dysfunction in patients.

2. Etiology and clinical manifestations in patients with PSHL

2.1. Etiology

Various causes of PSHL are encountered in otology clinics. The major risk factors for congenital PSHL include consanguinity, maternal rubella, and exposure to intrauterine infections, of which cytomegalovirus (CMV) infection is a significant cause of bilateral PSHL in children (Toumpas et al., 2014). Lack of an adequate vitamin A supply during pregnancy may result in the baby suffering developmental retardation in hearing (Emmett and West, 2014). Compared to congenital risks, the etiological factors of acquired PSHL are many and varied. Of them, bacterial meningitis is common among children (Karanja et al., 2013). A previously reported analysis of 310 adult cases included meningitis (24.4%), mumps (11.0%), unknown inflammatory diseases (16.6%), idiopathic sudden sensorineural hearing loss (ISSNHL; 19.4%), chronic suppurative otitis media (CSOM; 6.0%), trauma (6.1%), ototoxic medications (0.4%), and "no known cause" (16.1%) as causes of acquired PSHL (Ozel et al., 2012).

In addition to the above common factors, PSHL is often accompanied by dysfunction of vestibular organs (Wang et al., 2009). In one report, vestibular and cochlear symptoms occurred simultaneously in more than half of the patients (Gao et al., 2015). Given the similar physiological structures of the cochlear and vestibular organs, it is hypothesized that PSHL may prove to be significantly associated with vestibular disorders, especially in children (Cushing et al., 2008).

2.2. Clinical manifestations

In a recent clinical report on 29 patients with PSHL, neither the medical staff nor the patients themselves were mindful of vestibular dysfunction (Xu et al., 2016). Vestibular function can be normal or low in patients with PSHL. In one study, as the extent of hearing impairment increased, the detection rate reportedly gradually increased, although notably this result was not statistically significant (Gao et al., 2015). The cochlea and vestibule are closely related with regard to both anatomy and histoembryology, and both may be prone to the same risk factors. Notably, dysfunction of otolithic organs can cause a variety of serious problems including imbalance, dizziness, spatial disorientation and blurred vision. All these manifestations can be hidden and thus easily overlooked in patients with PSHL (Zhou et al., 2009).

Some patients with PSHL do not exhibit typical features of vestibular malfunction. For example, sometimes vertigo is not apparent even if the saccule is damaged (Hong et al., 2008). The most common chief complaint in PSHL patients may be "no response to sounds" (Xu et al., 2015), while vestibular dysfunction may also have a negative impact on the physical development in children with PSHL, in the form of delayed acquisition of head control or independent walking, or

impaired gross motor function. When a symptom such as dizziness is present, it is often associated with a poor prognosis (Wang et al., 2009). Moreover, hearing-impaired patients are not capable of hearing voices perfectly, and consequently can progressively lose the ability to communicate with others, such that language function degrades slowly (Dehqan and Scherer, 2011).

3. Function of otolithic organs in patients with PSHL

3.1. Anatomy

The vestibular system has a complicated structure, formed by divisions of the lateral, anterior and posterior semicircular canals, and the otolithic organs (saccule and utricle). The semicircular canals provide sensory input pertaining to angular velocities, and the otolithic organs are sensitive to linear and gravitational acceleration (Ciaravella et al., 2007). The saccule and utricle play an important role in maintaining balance by affecting the muscular tonus and influencing positional sensation. The cochlea and vestibule are functionally and anatomically associated as they share a continuous membranous labyrinth and similar receptor cell ultrastructures, and are supplied by a common arterial vessel known as the labyrinthine artery (Xu et al., 2016; Wang et al., 2016). Therefore, it is reasonable to hypothesize that inner ear diseases may affect both the vestibular system and the cochlea, or in other words, that people with cochlear hearing damage may also have vestibular deficiency (Singh et al., 2012). Therefore, patients with PSHL should have their vestibular organ functions tested, especially those of the otolithic organs.

3.2. Otolithic organ tests

For a long time, a lack of means to test otolithic organs has meant that most clinicians are relatively unfamiliar with the development of otolithic (saccular and utricular) dysfunction in patients (Young, 2015). As a result, there have been relatively few relevant studies to date. The function of otolithic organs can be evaluated by the VEMP test, which was first reported by Colebatch et al (Colebatch and Halmagyi, 1992) in 1992, and has since been the subject of substantial research. It is now the standard test for otolithic function in people with vestibular impairment. Two types of VEMP tests are currently available: the cervical VEMP (cVEMP) test and the ocular VEMP (oVEMP) test (Curthoys et al., 2011). The cVEMP test can reportedly reflect saccular function and the functioning of the inferior vestibular nerve input pathway, which has strong projections to the sternocleidomastoid muscle but only weak projections to the oculomotor system (Walther and Blodow, 2013). The oVEMP test can reportedly reflect utricular function and the functioning of the superior vestibular nerve input pathways, which have strong projections to the oblique muscle of the lower eyelid (Niu et al., 2016). In the oVEMP test, VEMPs generated by activation of utricular afferents and mediated by a crossed otolith-ocular pathway are analyzed (Niu et al., 2016). A recent theory proposed by Govender et al

(Govender et al., 2015) suggests that saccular components comprise 74% (utricular components = 26%) of air-conducted 500 Hz cVEMPs, and 61% (utricular components = 39%) of bone-conducted 500 Hzc VEMPs resulting from stimulation at the forehead (AFz). Moreover, according to the theory, utricular components comprise 68% (saccular components = 32%) of air-conducted 500 Hz oVEMPs, and 80% (saccular components = 20%) of bone-conducted 500 Hz (AFz) oVEMPs. That said, cVEMP and oVEMP tests in humans yield values that match those ascribed to saccular and utricular components by theory.

The two types of VEMPs play important roles not only in assessing common vestibular diseases such as vestibular migraine, Meniere's disease and vestibular neuritis, but also in detecting new clinical entities (Murofushi, 2016). Additionally, oVEMP and cVEMP tests are easy to perform non-invasively, and the results they yield are highly reliable. Notably, a recent study has shown that cVEMPs can be elicited in newborns at day 5, but that oVEMPs cannot be elicited in the neonatal period (Young, 2015). The cVEMP and oVEMP tests are in dispensable as clinical tools, and awareness regarding them should be increased.

3.3. Dysfunction of otolithic organs in patients with PSHL

The relationship between hearing level and vestibular dysfunction in PSHL patients remains unclear. Recently, based on evaluations of otolithic organ function via cVEMP and oVEMP tests, some researchers have proposed that otolithic organs and their input pathways may be damaged in patients with PSHL (Xu et al., 2015, 2016). The impairment or absence of VEMPs indicates dysfunction of otolithic organs. In a recent investigation, Xu et al (Xu et al., 2016) detected oVEMP responses in 38.9% of ears in patients with PSHL, while the response rate was 100% in healthy subjects. In that same study, 44.4% of ears in patients with PSHL yielded cVEMPs, while the response rate in healthy subjects was 100%.These data demonstrate that patients with PSHL have a high incidence of damage to the otolithic organs. Similarly, Xu et al (Xu et al., 2015) investigated oVEMP and cVEMP results in 43 children with PSHL and 20 healthy children, and found that oVEMPs were induced in 58.1% of ears in children with PSHL, while the response rate in the healthy children was 100%.Similarly, cVEMPs were induced in 61.9% of ears in children with PSHL, while the response rate in the healthy children was 100%.While many children with PSHL may not exhibit symptoms of otolithic organ dysfunction, it is nonetheless important to pay attention to vestibular function. A study reported by Jafari et al (Jafari and Asad, 2011) also showed that vestibular disorder may accompany hearing damage in patients with PSHL. Thus, in both children and adults with PSHL, attention should be paid to otolithic organ function, and cVEMP and oVEMP tests should be performed.

Zuniga et al (Zuniga et al., 2012) reported a strong association between hearing loss and saccular function, suggesting that PSHL patients may exhibits saccular and inferior

vestibular nerve dysfunction. Many studies have verified that patients with diagnosed sensorineural hearing loss may already have saccular disorders. There is a correlation between saccular dysfunction and the extent of hearing loss in children with PSHL, suggesting that saccular dysfunction may be a concomitant indicator of the severity of hearing disorders (Emami and Farahani, 2015). Sazgar et al (Sazgar et al., 2006) showed that patients with SNHL were likely to have sub-clinical disorders of the vestibular system, particularly disorders involving the saccule. Similarly, Zhou et al (Zhou et al., 2009) detected abnormal cVEMPs in 91% of children with PSHL, and also showed that the cVEMP threshold was higher in these children. Thus, evidently, abnormality of saccular function is associated with PSHL. Another study reported that only 26.9% of patients with PSHL exhibited abnormal or absent cVEMP responses, but it also showed that the more severe the hearing loss, the more likely the saccule was to be involved (Hong et al., 2008).

4. Treatment

Cochlear implantation (CI) is one of the most widely utilized and reliable treatment options for patients with PSHL. The aims of CI are to restore hearing and improve the quality of life of patients with severe deafness. Vestibular dysfunction has a negative impact on the physical development of children with PSHL (Yawn et al., 2015). CI can augment hearing, thereby improving the understanding of speech and environmental sounds. After implantation, children with PSHL can acquire spoken language, communicate with others and attend school. However, not every patient with PSHL can undergo successful CI, which requires integrated vestibulocochlear nerves. Specifically, if the site of the patient's lesion is not outside the central auditory processing stream, CI may not work (Roche and Hansen, 2015). While cochlear implants may improve hearing in patients with PSHL, many patients still use hearing aids instead. Hearing aids are small eletroacoustic devices that can amplify and modulate sound (Ching et al., 2015). Apart from cochlear implants and hearing aids, gene therapy is a new biological treatment modality for PSHL, aimed at preventing hair cell death, and regulating hair cell differentiation (Wang et al., 2015). Many patients with PSHL have genetic mutations, and to date, in many of these cases, there are no biological treatments available (Askew et al., 2015). We believe that in the future, gene therapy will become a useful strategy for treating patients with PSHL.

These kinds of therapies, particularly CI, can improve hearing in patients with PSHL (Yu et al., 2015), but they are not effective treatments for dysfunction of otolithic organs. There are several therapies for otolithic disorders, such as vestibular rehabilitation training and a number of medications. Vestibular rehabilitation training is generally the first recommended treatment. Under the guidance of a physician, patients undergo various kinds of rehabilitation exercises in order to improve balance and maintain stable vision, as well as the interaction between the visual and somato-sensory systems

and the vestibular organs at the brainstem level (Murray et al., 2010). This physiotherapy has a profound therapeutic effect on PSHL patients with vestibular dysfunction and is suitable for the elderly. Conventional pharmacological treatments may help alleviate symptoms, but have less curative effects than vestibular rehabilitation training. Some of these drugs such as anticholinergics may have undesired side effects. In brief, dysfunction of otolithic organs should be diagnosed correctly in patients with PSHL, and it is necessary to provide appropriate treatment.

5. Prognosis

Not all cochlear implants survive for long periods, and surgical replacement is a common source of complications (Eskander et al., 2011). The effect of treatment for PSHL can be influenced by many factors, including the function of otolithic organs. A study by Wolter et al (Wolter et al., 2015) suggested that children who experienced CI failure had more balance problems than those in whom CI was successful. It also revealed that early identification and treatment of disorders of otolithic organs might increase the success rate of CI and prevent impeded language acquisition. In another study, Parietti-Winkler et al (Parietti-Winkler et al., 2015) showed that vestibular evaluations were important in the follow-up of CI, and that vestibular function should be taken into account in the decision-making process prior to CI.

On one hand, lesions of otolithic organs can increase the risk of CI failure, and on the other hand, CI can damage otolithic organs. According to the literature, impairments of the vestibule can be found in many patients after CI (Robard et al., 2015). Thus, alterations of the inner ear associated with CI can cause vestibular disorders. Reduced vestibular system function is also reported frequently after CI. Fina et al (Fina et al., 2003) reported that 39% of patients who underwent CI experienced symptoms of vertigo after the surgery. Given that an increasing number of patients with PSHL may undergo CI in the future, the function of otolithic organs should be tested not only before CI, but also after the surgery.

6. Conclusion

From the present review, it is hard to determine the causality between PSHL and vestibular dysfunction, and relevant research on the relationship between them is lacking. Clinical manifestations in patients with PSHL are variable, and impairment of vestibular function can be concealed by hearing loss and thus overlooked. Given these considerations, VEMP testing should be used as an objective procedure to evaluate potentially hidden dysfunction of the otolithic organs during diagnosis and treatment.

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