Otolith and balance function evolution related to cochlear implantation in hearing loss with inner ear malformations

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Abstract

Objectives: In recent years, with the incidence of bilateral cochlear implantation (CI) increasing, understanding the impact of CI on otolith function is of greater necessity. This study aims to investigate the development of gross motor and otolith function in patients with inner ear malformations (IEMs) by vestibular evoked myogenic potentials (VEMP). **Materials and Methods:** A total of 78 patients with sensorineural hearing loss (SNHL) (age 5.7±4.1 years) were divided into two groups based on the presence (IEM group, n=39) or absence (control group, n=39) of IEMs. VEMP was conducted before and 1–3 months after CI, and gross motor development assessed. **Results:** The mean ages of head control and independent walking were delayed in the IEM group compared with control group (p=0.02). The preoperative cVEMP and oVEMP response rates were higher in the control groups (60% and 86.95%) than in the IEM group (57.69% and 74.35%) (p<0.05). Additionally, abnormal cVEMP was associated with delayed acquisition of independent walking (p=0.017). Saccular and utricular functions after CI were lost by 40% and 31.75%, respectively, in group of patients present preoperatively VEMPs waveform (n=25). **Conclusions:** Balance development is more reduced in patients with SNHL and IEMs than in patients without IEMs. The otolith-vestibular nerve conduction pathway can be affected by CI and lead to otolith function impairment. As such, evaluating the otolith and balance functions before CI is necessary and should be considered in clinical practice.

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ABSTRACT

Objectives: In recent years, with the incidence of bilateral cochlear implantation (CI) increasing, understanding the impact of CI on otolith function is of greater necessity. This study aims to investigate the development of gross motor and otolith function in patients with inner ear malformations (IEMs) by vestibular evoked myogenic potentials (VEMP).

Materials and Methods: A total of 78 patients with sensorineural hearing loss (SNHL) (age 5.7±4.1 years) were divided into two groups based on the presence (IEM group, n=39) or absence (control group, n=39) of IEMs. VEMP was conducted before and 1–3 months after CI, and gross motor development assessed.

Results: The mean ages of head control and independent walking were delayed in the IEM group compared with control group (p =0.02). The preoperative cVEMP and oVEMP response rates were higher in the control groups (60% and 86.95%) than in the IEM group (57.69% and 74.35%) (p <0.05). Additionally, abnormal cVEMP was associated with delayed acquisition of independent walking (p =0.017). Saccular and utricular functions after CI were lost by 40% and 31.75%, respectively, in group of patients present preoperatively VEMPs waveform (n=25).

Conclusions: Balance development is more reduced in patients with SNHL and IEMs than in patients without IEMs. The otolith-vestibular nerve conduction pathway can be affected by CI and lead to otolith

function impairment. As such, evaluating the otolith and balance functions before CI is necessary and should be considered in clinical practice.

Keywords: Otolith function, Cochlear implantation, Inner ear malformation, Pediatric, Balance function

Key Points

There is limited studies on otolith function in patients with IEMs before and after cochlear implants (CI).

We conducted a prospective study of otolith function with IEMs using vestibular evoked myogenic potentials (VEMP).

We included 78 children (41 females and 37 males) who underwent CI, all patients were divided into two groups based on the presence (IEM group) or absence of IEMs (control group)

The IEM group had a lower response rate of cVEMP (X^2 =4.768, p =0.003) and oVEMP (X^2 =4.408, p =0.003) compared to the control group. The abnormal cVEMP and oVEMP rate after surgery was increased in the control group ($p< 0.001$) but decreased in the IEM group.

Evaluating the otolith and balance functions before CI is necessary and should be considered in clinical practice.

INTRODUCTION

Cochlear implantation (CI) is an important treatment for severe or profound sensorineural hearing loss (SNHL), and pediatric candidates with inner ear malformations (IEMs) can obtain long-term positive auditory and speech outcomes with CI. Some children with SNHL may also present congenital vestibular dysfunction because of the anatomical and embryological relationship between the cochlea and vestibule. The prevalence of vestibular dysfunction in children with SNHL ranges from 20% to 85%. Moreover, a recent review confirms that electrode insertion can induce various vestibular damages in 50%–85% of patients, and in the pediatric population, this figure is approximately 18–85%[1]. Children with vestibular dysfunction and SNHL generally present with profound hearing loss, and their gross motor functions, such as head control or independent walking, are usually delayed[2, 3]. Cochlear and vestibular dysfunctions can exist alone or coexist, but patients with IEMs are also susceptible to semicircular canal and saccular dysfunctions[4]. Jin et al.[5] performed the vestibular evoked myogenic potential (VEMP) test on seven patients with different degrees of IEMs, of which only two patients elicited VEMP on the malformed side. Notably, studies on vestibular function in patients with IEMs are limited.

Vestibular damage after CI is more severe if it is presented before 1 year of age, because during this time, infants have not yet developed their walking and balance abilities[6]. Hence, vestibular function should be evaluated before CI, and surgeons must avoid inducing vestibular injury during surgery.

Currently, VEMP is the most commonly used vestibular function test in children, which can reflect the neurophysiological function of the otolith organ and vestibular nerve[7, 8]. VEMP test includes cervical VEMP (cVEMP) and ocular VEMP (oVEMP)[9].

Considering that the number of SNHL children undergoing CI has increased, especially bilateral surgery[10], there is an urgent need to evaluate the effects of CI on the vestibular system. This study used VEMPs to investigate gross motor and vestibular function changes after CI in pediatric patients, especially in patients with IEMs.

MATERIALS AND METHODS

Patients

This study included 78 children (41 females and 37 males) who underwent CI at the Department of Otorhinolaryngology Head and Neck Surgery at Beijing Tongren Hospital between January 2021 and February 2022. The children's mean age at implantation was 5.7±4.1 years (range, 0.7–17.8 years). All participants met the dignosis criterion for bilateral profound or severe hearing loss and met the CI implanted criterion.

In order to eliminate residual hearing or impact of crossover from the normal ear ,single-sided deafness was excluded here. Besides, patients aged >18 years, with cognitive and psychological impairments, and unable to participate in follow-up examinations were excluded from this study.

The type and degree of IEMs were classified according to the work of Sennaroglu et al. in 2017[11]. The IEM group classification is listed in Table 1. All patients were divided into two groups based on the presence (IEM group) or absence of IEMs (control group). Each group had 39 patients.

Before surgery, inner ear computed tomography (CT) and magnetic resonance imaging (MRI) scans, audiological assessments (including standard pure tone audiometry, auditory brainstem response evaluation, auditory steady-state response assessment, distortion product otoacoustic emission, cochlear microphonics evaluation), and cVEMP test, were performed. Electronic ear endoscope or tympanograms performs prior to VEMP testing to ensure there was no middle ear fluid or an ongoing hemotympanum. The O-VEMP was performed on patients who were able to cooperate. This study was approved by the Institutional Review Board of Beijing Tongren Hospital.

Gross motor development

We interviewed the children's parents regarding the age at which patients started to acquire gross motor abilities, including head control and independent sitting, crawling, and walking. If the age of acquiring head control was >4 months and the age of independent walking was >12 months, the development of gross motor function was considered to be delayed[12].

Vestibular evoked myogenic potential (VEMP) test

Patients underwent cVEMP and oVEMP tests 1 week prior to CI and then again 1–3 months after. The electromyography signal from the stimulated side was amplified using the Neuro-audio Auditory evoked potentiometer system (version 2010, Neurosoft Ltd., Ivanov, Russia) in a soundproof examination room. The cVEMP test was performed with the electromyogram auto-correction mode. The children were tested in a natural awake state. Older children with the ability to cooperate were asked to obtain a sitting position, and younger children were placed in a 30° forward head tilt position with their parents holding them. The sound was emitted through a calibrated earphone, with an air-conducted 500 Hz short pure tone (tone burst) and a stimulation intensity of 105 dB nHL. The active electrode was placed in the middle of the sternocleidomastoid muscle (SCM), the reference electrode was placed above the sternoclavicular joint, and a ground electrode was placed on the midline of the forehead. The inter-electrode resistance should be <5 kΩ. The head of the children was turned to the opposite side during the cVEMP test. The SCM force in the test ear was maintained between 30 and 70 μV. The signal was recorded ipsilaterally by monitoring electromyography.

oVEMP testing was performed in the sitting position. An active electrode was placed 0.5 cm below the lower lid of each eye in line with the pupil, a reference electrode was placed below the active electrode, and a ground electrode was placed on the midline of the forehead. The inter-electrode resistance was also <5 kΩ. Each child was instructed to gaze upward, focus on one specific place, and avoid blinking. The stimulation sound was similar to that of the cVEMP and administered bilaterally. The signal was recorded on the opposite side. If the test ear had CI, the test was performed with the CI device turned off.

Definition of parameters

We defined a reproducible middle-latency biphasic wave as the effective wave type. The waveforms with missing amplitude and unreproduced waves were rejected. P1 and N1 were the first positive and negative peaks, respectively. The P1 and N1 latencies (the interval between 0 ms and the corresponding maximal peak) were calculated by the interval between P1 and N1, and the rectified amplitude (the vertical distance between the P1 and N1 peaks) was recorded. The results were reviewed before and 1–3 months after CI. No significant change in VEMP was defined as no change; disappeared VEMP was defined as clear waveform before CI but waveform disappeared after the implantation.

Statistical analyses

Data were analyzed using IBM SPSS Statistics software version 26.0 (Armonk, New York, USA). Categorical variables (response rates) were compared by Fisher's exact test; Pearson's correlation analysis was performed to analyze the correlation of VEMP parameters between the IEM and control groups. Continuous variables (VEMP parameters) were evaluated by Student's T-test. A significance level of 0.05 was applied to all analyses.

RESULTS

Demographic analysis

Of the 78 patients included in this study, 5 and 73 underwent bilateral and unilateral CI, respectively. The children's average implantation age was 5.7±4.1 years (range, 0.7–17.8 years). The mean age of the IEM group and control group was 5.54±4.31 years and 5.92±3.96 years. The difference in age was not statistically significant between the two groups. All the patients underwent full CI insertion, without any complications.

Gross motor development

Fig. 1 shows the comparison of the mean gross motor development timing between the IEM and control groups. The mean ages of head control and independent walking in the IEM group were 3.73±0.86 months and 15.39±4.5 months, respectively. The independent-samples T-test showed that the balance development of children with IEMs was delayed when compared to the control group (p =0.02).

Additionally, two children in the IEM group presented with vertigo and slight unsteadiness postoperatively, but all symptoms resolved within 48 h. The impaired otolith function did not correlate with vertigo symptoms (logistic regression analysis, p >0.05).

To estimate the effect of otolith dysfunction on the development of gross motor function, we compared the age of acquiring gross motor skills with the results of both the cVEMP and oVEMP test (Table 2). In terms of acquiring independent walking, children who showed abnormal cVEMP responses were significantly more delayed compared with those who showed normal responses (p =0.017). There were no significant differences in the age of acquiring gross motor abilities between children with abnormal oVEMP and normal response (p >0.05).

All patients and a total of 156 ears were tested for cVEMP, whilst 96 ears from 48 patients underwent oVEMP testing before surgery. The chi-squared test showed significant differences in the response rates of cVEMP (X^2 =4.768, p =0.003) and oVEMP (X^2 =4.408, p =0.003) between the IEM and control groups. There was no statistical difference in each parameter between the two groups by the independent samples t-test (Tables 3 and 4).

Effects of cochlear implantation on VEMPs

VEMP changes before and after surgery were recorded, but only the CI ear was analyzed. The postoperative VEMP test was performed 25–39 days after surgery, and 64 CI ears were retested under the condition of CI-off. 50% of the implanted ear cVEMP waveform and 39.1% of the oVEMP waveforms disappeared after CI, the difference in the lost rate was not statistically significant between the implanted ear cVEMP and oVEMP. Moreover, we compare the p13 and n23 latency ,peak amplitude and corrected amplitude, there was no statistically significant difference in above the parameters before and after surgery. In the group of 25 patients with preoperatively present VEMPs, 40% and 31.75% lost their cVEMP and oVEMP, respectively, after implantation. The variation between cVEMP and oVEMP results before and after surgery of the IEM and control groups are shown in Fig. 2. The independent sample T-test showed that the abnormal cVEMP rate after surgery was increased in the control group (p< 0.001). The abnormal oVEMP rate after surgery of all patients together and the control group significantly increased, but decreased in the IEM group (Fig. 2).

DISCUSSION

With the increasing rate of bilateral CI implementation in children with IEMs, vestibular function development has received significant attention. However, studies on this subject remain limited. Due to the close anatomical and developmental relationship between otolith end-organs and the cochlear, hearing impairment may lead to vestibular disorder[13], but vestibular assessment is not routinely performed[14, 15]. One of the reasons for this is the lack of clinically appropriate and effective assessment methods in the pediatric group and a gold standard test for the assessment of balance and postural control in children[16]. Another reason is that vestibular dysfunction can be compensated by other systems, and notably, abnormality in gait and motor coordination is not observed in children with IEMs[17]. The current study aimed to describe the difference in gross motor development in patients with SNHL, and to investigate the otolith functional modifications after CI between children with and without IEMs.

Otoliths are important receptors of the vestibulospinal reflex pathway, which helps to maintain balance and is significantly important for the human body to control the erect head and the spatial orientation of the body[18]. Balance and motor development in early childhood are delayed in patients with IEMs, as observed in children with severe congenital hearing loss[19]. In patients with IEMs, otolith function may be significantly compromised, and these patients often present with impairments in balance control, such as delays in head control and independent walking, because such functions are related to abnormal inner ear structures[20, 21]. Consistent with previous studies[22, 23], we reported that children with IEMs performed worse than those in the control group with regards to gross motor development. The mean ages of head control and independent walking in the IEM group were 3.73±0.86 months and 15.39±4.5 months, respectively. While follow-up research continues,, even when these children were able to walk, their balance ability, such as performance on the single-leg standing test, remained tardive. Moreover, they also had a higher risk of falling during advanced balance activities, such as bicycle riding, than the normal children.

Farideh et al.[24] reported that 68.2% and 14.3% of children with IEMs and SNHL (normal cochlear anatomy), respectively, presented with vestibular dysfunction after CI. Hosseinzadeh et al.[6] used the Bruininks–Oseretsky motor ability test (BOT) and sensory organization test for postures to test the standing/walking stability of four patients with common cavity deformity (CCD) under open and closed eyes conditions. Their results indicated that the balance function of the patients with CCD was more delayed than that of other patients with SNHL. We evaluated the gross motor development preliminarily because in our study, most of the CI candidates had not reached the standard BOT-2 assessment age (>4 years). In our study, the gross motor development of children with IEMs was significantly more delayed compared with that of the control group. Specifically, the mean age of independent walking in the IEM group was 15.39 months. This result is similar to those of previous studies, which indicate that the otolith end-organ plays an essential role in obtaining gross motor abilities before the age of 2 years. If any postoperative balance damage is identified, such as instability after surgery, the solution of early rehabilitation should be recommended for the best and most rapid balance recovery.

The VEMP test is a noninvasive test that can sensitively identify otolith function variation in younger children. Some studies have shown that VEMP plays an important role in evaluating the otolith function and vestibular nerve integrity of patients before and after CI[25, 26]. However, assessment of otolith function in children with SNHL, especially in IEMs, remains limited. In this study, we aimed to analyze the difference in VEMP between children with IEMs and children with SNHL with normal cochlear anatomy.

Previous findings have revealed that the function of the saccular and utricle may receive certain damage by CI, and this damage can last for a long period of time and the cVEMP response rate is more likely influenced by CI than oVEMP, because the saccule is anatomically closer to the cochlea and has a major risk of CI[27]. To determine the real variation of otolith function in relation to CI, we analyzed the VEMP variation only in the ears that had a present response for cVEMP and oVEMP preoperatively. In the present study, 40% of patients lost the cVEMP response and this variation may suggest the risk of injury during CI, specifically during intracochlear port electrode insertion, which may seriously affect the saccular neuroepithelium.

The higher postoperative cVEMP loss rate in our study might be related to the patients' age. The youngest children assessed for waveform were 9 and 12 months old in the normal cochlear group and IEM group, re-

spectively. It was not easy for children to maintain an adequate SCM tone during the whole test process. The second factor is that the electrical stimulation of the CI device can have an effect on VEMP responses[28-30]. However, the VEMP tests in our study were performed in CI-off conditions to prevent the electrical stimulation from having an effect on the responses to evaluate the actual residual otolith function only. Another factor is different surgical techniques. Studies on this matter, that is whether the surgical approach can induce VEMP loss, remain inconclusive. Some studies have indicated that cochleostomy might be more likely traumatic for the otolith end-organ than the round window approach[31]. In this study, the approach used for most patients was the round window approach, except for children with CCD, who underwent the slotted labyrinthotomy approach. The latter can significantly shorten the surgery duration and effectively reduce the rate of postoperative cerebrospinal fluid leakage and vertigo probability[32]. Similarly, Cozma et al.[33] reported normal saccular function in 73.3% of the CI ears using the round window approach and in 68.42% of ears using the cochleostomy approach, which suggests that the round window port electrode insertion is the recommended strategy to avoid saccular impairment. In this study, all children underwent AC-cVEMP tests, and previous studies have revealed that CI can induce peripheral mechanical changes, leading to air–bone gaps, which can lead to absent AC-cVEMP responses without underlying vestibular deficit[34, 35]. Moreover, inaccuracies in measurement methods can also lead to a higher rate of VEMP loss.

In our study, the rate of VEMP response was significantly different between the two groups, but there were no significant differences in changes within various P1-N1 parameters (Tables 2–4). It is possible that patients with IEMs in this study had a more severe degree of deformity and that they presented little difference in waveforms after CI. Additionally, because the test is performed in young children who do not have typical amplitudes, the differences between the two groups are subtle. Currently, there is no consensus protocol for the quantitative assessment of the P1-N1 parameters wave complex in children. However, the type of change in VEMPs can indicate severity of IEMs affecting the utricle and saccule. Xu et al.[30] reported that cVEMP disappearance occurred more frequently on the CI-implanted ear and that waveform parameter showed abnormal changes, such as decreased amplitude, forward movement of P1 and N1, and shortened interpeak latency at 1 month after CI, suggesting that cVEMP waveforms can reflect the degree of damage to the saccule caused by CI.

The present study consisted of 11 children with CCD, all of which showed no VEMP response before surgery on either cVEMP or oVEMP. In contrast, most patients with IEMs presented with concomitant symptoms with cochleovestibular nerve deficiency and abnormal development of vestibular sensory cells. Hence, patients with IEMs are more likely to have abnormal VEMP response rate and waveform than those without IEMs. In 2006, Jin et al.[28] tested 12 patients with IEMs using VEMP and found that saccule function was more likely damaged after CI, as reflected in the absence of cVEMP waveform in short pure tone stimulation. Our results are consistent with those of previous studies. In the current study, the otolith function in the IEM group was significantly more compromised than that of the control group, which suggests that the VEMPs of IEMs might be more susceptible to influence by CI.

Vestibular sensory cells of the semicircular canals and otolith organs or primary vestibular afferent neurons are possibly present in patients with IEMs to maintain a basic balance function, particularly CCD. These patients do not have difficulty in general activities that require dynamic balance and mobility[36]. In an embryological study, in the human fetal developmental stage, the vestibular system develops earlier than the cochlear system[37][38]. Children with hearing loss who are at high risk for vestibular dysfunction can develop a new sensory distribution process in which visual and somatosensory information becomes essential for postural control when vestibular input is impaired[3, 39]. The above can explain why VEMP can still be present in patients with severe IEMs and how they can acquire balance function at 3–4 years of age. In the present study, one patient with CCD presented with cVEMP waveform 6 months after CI. Considering the small sample size, long-term changes in cVEMP parameters should be analyzed through follow-up.

Additionally, six patients with large vestibular aqueduct syndrome (LVAs) presented with normal VEMP waveform before surgery and normal performance of balance function. These results are similar to those of preceding studies. Patients with LVAs often complain of subjective symptoms of balance disorders, such as

dizziness and unsteady walking, but may have normal waveform on VEMP tests[40, 41]. Due to the small differences between the different types of malformations and the small sample size, there were no statistical differences between different types of malformations.

This study also observed that, IEM group has two children presented with vertigo and slight unsteadiness. all symptoms resolved within 48 h. We analyzed that this may be due to otolith function. In these patients, the balloon and utricle are not fully developed, with strong plasticity, and the otoconia injury has a strong compensatory mechanism and central system adaptability. Another reason is that the operation is gentle, which greatly avoids damage to the vestibular system. Therefore, it is still necessary to understand the otolith function of postoperative patients. Long-term follow-up is needed to determine whether such patients are at risk for vestibular decline along with age growth.

Our study has some limitations. First, recall bias exsist due to the retrospective methodology of determining gross motor delays. Second,the mean follow-up time was 1–3 months after CI. Patients develop or compensate their vestibular function from the visual and central nervous systems rapidly during the age of 1–5 years, which would affect the results of the VEMP tests. Moreover, the otolith function test method was primarily performed; thus, a further vestibular function test battery is required.

CONCLUSIONS

The functional balance performance and otolith function of children with IEMs are more delayed than those of children with SNHL with normal cochlear anatomy. The otolith-vestibular nerve conduction pathway may be affected in CI, which may lead to otolith function impairment. It is necessary to adequately evaluate the children's vestibular and balance functions before CI. Additionally, VEMPs, which are noninvasive and rapid tests, can be used to reflect the status and degree of otolith functional involvement in young children with SNHL.

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