Prognosticating hearing outcome in patients with idiopathic sudden sensorineural hearing loss by means of otoacoustic emissions and auditory brainstem response

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Abstract
This is an analytic-descriptive study, parallel with a randomized, controlled trial performed at Amir’Alam Hospital, a tertiary referral center, with the aim of evaluating the correlation between otoacoustic emission (OAE) and auditory brainstem response (ABR) findings with hearing outcome after treatment of idiopathic sudden sensorineural hearing loss (SSNHL). Sixty patients with idiopathic SSNHL who presented to the emergency services and otology clinics between 2012 and 2014, and whose symptoms had begun <10 days previously, enrolled in this study. Before commencing treatment, distortion-product OAE (DP-OAE) and ABR were performed for all patients. They also underwent magnetic resonance imaging ± gadolinium. Therapeutic intervention was done in a parallel randomized, controlled trial, and responders to the medical therapy were selected for our final analysis. There was no significant correlation between the OAE record and responsiveness to treatment, but there was a correlation between ABR presence and the probability of responsiveness in patients with profound hearing loss who responded to medical therapy and had at least wave V ABR. In conclusion, in patients with profound hearing loss, studying the waves of ABR could be a factor in predicting hearing loss resolution after treatment.

Introduction
Sudden sensorineural hearing loss (SSNHL) is a true emergency in otolaryngology, which is idiopathic in 88% of cases. Its annual incidence varies from 5 to 20 per 100,000 persons. It is defined as sensorineural hearing loss of 30 dB or more at three consecutive frequencies over 3 days or less.

The exact etiology is still unknown. However, some theories point to viral infection, vascular obstruction, abnormalities in the inner membrane of the cochlea, and autoimmune factors. Basically, treatment should be tailored to the etiology. Since the etiology is unknown in idiopathic cases, treatment is based on experimental protocols.

Blood supply of the inner ear is provided by the labyrinthine artery, which is a terminal artery that supplies both cochlea and vestibule. Hence, a vascular origin of this condition is emphasized.

The treatment of SSNHL is controversial. According to existent evidence, the accepted protocol is as follows: oral prednisolone (60 mg daily), which is tapered off in 2 weeks in conjunction with 1-week treatment with an antiviral agent such as acyclovir. If this treatment fails, intratympanic injection with dexamethasone or methylprednisolone as salvage therapy is done.

Localizing the lesion site in SSNHL will help in the selection of an appropriate treatment protocol. Oto-
The treatment protocol can be developed. The location of the lesion is determined, the more appropriate response. It is also possible that the more exactly the tests are done to find out the role of these tests in predicting treatment and their relationship with clinical improvement to OAE changes and ABR waves in patients with SSNHL.

The lesion site in idiopathic SSNHL. We decided to study the pattern of the ABR wave can be helpful in locating the lesion site in idiopathic SSNHL. We decided to study OAE changes and ABR waves in patients with SSNHL and their relationship with clinical improvement to find out the role of these tests in predicting treatment response. It is also possible that the more exactly the location of the lesion is determined, the more appropriate the treatment protocol can be developed.

Patients and methods

The study protocol was approved by the ethical committee of Tehran University of Medical Sciences and is in conformity with the ethical guidelines of the 1975 Declaration of Helsinki.

In this analytic-descriptive study, adult patients who were admitted to the emergency department and otology clinics of Amir’Alam Hospital between 2012 and 2014 with the diagnosis of SSNHL whose symptoms had started within <10 days of admission were eligible to enter the study. All patients underwent tuning fork examination and complete audiometry evaluation.

Of 112 patients enrolled in a parallel randomized, controlled trial performed by the same research team (registration number: IRCT201202159039N1), a subset of 60 patients were chosen for whom the diagnosis was confirmed using audiometry test results.

Exclusion criteria included treatment at another center; contraindication for magnetic resonance imaging (MRI); history of previous SSNHL; an explicit etiology during physical examination, such as neurologic deficits, indicating a cerebrovascular accident; history and laboratory tests indicating syphilis, or common rheumatologic diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, and Sjögren syndrome); hypothyroidism; admission more than 10 days after symptom onset; and uncontrolled severe diabetes mellitus.

At the beginning, after giving informed consent, all patients completed a questionnaire regarding demographic variables, when symptoms began, concomitant symptoms such as tinnitus and vertigo, and background conditions such as diabetes, familial history of SSNHL, and trauma. Additionally, in the randomized, controlled study, laboratory tests including antineutrophil cytoplasmic antibody, venereal disease research laboratory test, antinuclear antibodies, thyroid function test, fasting blood sugar, complete blood count, triglycerides, erythrocyte sedimentation rate, and rheumatoid factor were ordered for all patients.

At the start of this study, ABR and distortion-product OAE (DP-OAE) values and MRI with and without gadolinium were obtained for all patients.

DP-OAE was measured using the MADSEN Capella computer-based analyzer (Otometrics A/S; Taastrup, Denmark). Two pure tones with a frequency ratio of 1.2 with unequal sound pressure were delivered, and DP-OAE was calculated at two F1-F2 frequencies. F1 was delivered at 65 dB and F2 at 55 dB.

ABR was recorded by a computer-based machine (ICS Chartr; GN Otometrics; Taastrup, Denmark). The stimulator (90 dB) was delivered two times to each ear to ensure its reproducibility. Response to treatment was regarded as a 10-dB improvement in auditory threshold and/or a 15% improvement in word recognition score (WRS).

All intratympanic injections were done by senior residents or residents who had received training for this procedure. It should be emphasized that all patients received acyclovir (400 mg 4 times daily) and omeprazole capsules for 10 days, in addition to steroids. Audiometry was repeated 14 days and 1 month after initiating the study.

After gathering the data, the analyses were done by applying the paired t test, one-way ANOVA (analysis of variance), and Pearson chi-square test.

Results

This analytic-descriptive study was done between 2012 and 2014 (24 months) and involved 60 adult patients with SSNHL. Patients’ mean age was 46 years (range: 22 to 80 years), and there were 41 men (68.3%) and 19 women (31.7%). The highest rate of SSNHL was detected in the fall (61.7%). The right ear was involved in 51.7% of cases and the left ear in 48.3%, with no significant difference. About 61.7% of patients had no contributory medical history. Controlled diabetes mellitus was reported in 8.3% of patients and cardiovascular diseases in 13.3%. A total of 11.7% of the patients had diseases without apparent relationship, such as ulcerative colitis, etc.

The most common associated symptom was tinnitus in 19 patients (31.7%). Eleven patients (18.3%) had vertigo. Nineteen patients (31.7%) had no associated symptoms. Concomitant tinnitus and vertigo, tinnitus and headache and vertigo, tinnitus and headache were reported in 11.7%, 5%, and 7.1% of cases, respectively. Four patients (6.7%) had a family history of SSNHL.

Considering hearing loss categories as mild (20 to 45 dB), moderate (45 to 65 dB), severe (65 to 90 dB), and profound (>90 dB), 45% had profound hearing loss, 20% had severe hearing loss, and 18.3% had moderate and
16.7% had mild hearing loss. After treatment, hearing loss was as follows: mild (56.7%), moderate (21%), severe (11.7%), and profound (10.6%).

There were no significant differences between the three studied groups regarding sex ($p = 0.9$), season ($p = 0.96$), affected side ($p = 0.93$), associated symptoms ($p = 0.95$), history of diseases ($p = 0.13$), family history ($p = 0.34$), severity of hearing loss before receiving treatments ($p = 0.041$), and response rate according to DP-OAE ($p = 0.19$).

DP-OAE waves were only recorded in 26.7% of patients within their first week after admission.

Considering audiologic assessments, WRS changes, and auditory threshold, complete responsiveness was seen in 17 patients (28.3%), partial responsiveness in 28 patients (46.7%), and no response in 15 (25%).

DP-OAE was present before starting treatment in 5 patients who had no response to treatment and 11 patients who responded to treatment. There was no significant relationship between the existence or absence of an OAE record and response to treatment ($p = 0.62$). In examining each group separately, again, no significant relationship was found between the OAE record and response to treatment ($p$ values of 0.61, 1, and 0.27 for intratympanic, systemic, and combination groups, respectively).

When we divided patients into two groups of mild/moderate hearing loss vs. severe/profound hearing loss, there was no significant relationship between OAE and improvement in hearing loss ($p = 0.30$). Also, no significant relationship was detected between patients’ sex and the OAE record ($p = 0.62$) or between sex and response to treatment ($p = 0.75$).

The wave changes observed in ABR are summarized in the table. Regarding the ABR findings, all these abnormalities indicate a sensory lesion. In only 1 patient with profound hearing loss, the abnormal ABR was in the form of a prolonged V wave, which suggests a retrocochlear lesion. However, a retrocochlear lesion was excluded in this patient by MRI with gadolinium.

MRI was performed in all patients. No lesion was observed in any of them. In only one patient, there was a small periventricular ischemic change; he was a 62-year-old man with a history of hypertension.

It should be noted that the results of the parallel RCT study in three treatment groups will be presented in another article.

### Table. ABR patterns observed in all patients

<table>
<thead>
<tr>
<th>Level of hearing loss</th>
<th>ABR pattern</th>
<th>No. patients</th>
<th>No. patients improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Wave I disappearance</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Latency in appearance of all peaks</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Shortened interval between waves III and V; increased interval between waves I and III</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Normal morphology</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Only wave V appearance</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Latency in appearance of all peaks</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Moderate</td>
<td>Shortened interval between waves III and V; increased interval between waves I and III</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Normal morphology</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Only wave V appearance</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Latency in appearance of all peaks</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Severe</td>
<td>Shortened interval between waves III and V; increased interval between waves I and III</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Peak of wave V was with low amplitude but normal latency</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Shortened interval between waves V and I with normal interpeak latency</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>No wave</td>
<td>19</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Prolonged wave V</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Profound</td>
<td>Increased latency of waves III and V</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Peak of wave V with low amplitude but normal latency</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Shortened interval between waves V and I</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
Discussion
SSNHL is an unpredictable incident. Although some factors such as age, severity of hearing loss, and associated symptoms have been noted as predictive factors, there is limited evidence to support that view.

In some limited studies, the changes seen in OAE response during the process of SSNHL have gained attention, but there is still controversy. Mori et al showed that DP-OAE amplitudes in specific F2 frequencies before treatment are associated with SSNHL resolution. Therefore, they suggested a role of DP-OAE in predicting hearing improvement in such patients.\(^7\)

In another study, it was reported that the function of outer hair cells is partially preserved in mild to moderate hearing loss, but improvement in OAE is not correlated with hearing loss resolution.\(^8\) However, in cases with relatively severe hearing loss, OAE improvement is correlated with hearing improvement. In other words, increased OAE response is associated with hearing improvement in those with an initial pure-tone average (PTA) of >55 dB but not in those with an initial PTA of <55 Db.\(^9\) In another study, it was observed that the presence of a wave in both tests could be a positive predictor of improvement in hearing.\(^10\) In the current study, in all patients with profound hearing loss who responded to treatment, ABR waves (at least a V wave) were seen. However, in those with the absence of any waves, response to treatment was variable. This can indicate that the wave record in those with profound hearing loss can be a favorable predictor in terms of hearing loss resolution. Examining the findings of ABR in the studied sample indicates that sensory abnormality was more likely than the presence of neural or retrocochlear lesions.

Steroids, after undergoing intracellular endocytosis, act either actively or passively in striae and surrounding tissues. Therefore, with higher endocytosis, intracellular efficiency is better. Although there is a concentration difference between the base and the apex of the cochlea, ample medication reaches the apical areas. The presence of medication in the scala media shows its transition to endolymph spaces. Connection between the scala tympani, the organ of Corti, and the spiral ganglion ensures drug diffusion from the round window and rapid exposure to hair and neural cells.\(^11\) Therefore, in the high likelihood of the presence of a lesion inside the cochlea, the intratympanic injection of a steroid could be a safe method in management of SSNHL.

In 2 patients in the current study, with mild hearing loss, no ABR wave was recorded, but both patients showed a positive response to treatment. It is likely that asynchrony of afferent neural fibers contributed to this finding.

This study had some drawbacks. First, some of the data in the current study are included in blinded arms of the parallel randomized, controlled study so cannot be extracted until that study is completed. Second, it would have been more favorable to perform both DP-OAE and ABR before and after the study, but we were unable to obtain post-treatment DP-OAE and ABR results in our series of patients; we were able to moderate hearing loss, indicating that the function of the cochlear outer hair cells was partially preserved.
obtain them only before treatment. Instead, we used post-treatment audiometric responses for evaluating our goals. Finally, while we were seeking an unknown pathophysiologic pathway, it seems that it would be worthwhile to perform VEMP in addition to ABR and DP-OAE. These issues may influence the direction of future studies.

**Conclusion**

Studying patients’ ABR findings suggests that sensory abnormalities are more prominent than retrocochlear parts of the auditory pathway. In the current study, all patients with profound hearing loss who had improvement in hearing, exhibited ABR waves (at least a V wave).

All in all, according to our findings, we advise performing ABR in patients with profound hearing loss to predict the possibility of hearing loss resolution. Also, regarding the possible lesion site as presented in this article, injecting a steroid intratympanically seems to be a logical method of drug delivery in the SSNHL therapeutic protocol.

**References**