Reliability of the vestibular evoked myogenic potential test in assessing intratympanic gentamicin therapy in Meniere's disease

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Reliability of the vestibular evoked myogenic potential test in assessing intratympanic gentamicin therapy in Meniere’s disease

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Abstract

Conclusions. The results of this preliminary study demonstrate that with regard to determining the efficacy of intratympanic (IT) gentamicin treatment in patients with Meniere’s disease, the reliability of testing for vestibular evoked myogenic potentials (VEMPs) is comparable to that of caloric tests. Compared with caloric tests, VEMP measurements are more comfortable and take less time. The results of VEMP and caloric testing do not correlate with the results of hearing tests.

Objective. To test the reliability of VEMP testing to monitor the results of IT gentamicin therapy in patients with Meniere’s disease.

Subjects and methods. Twelve patients with unilateral Meniere’s disease were evaluated with pure tone audiometry (PTA), bithermal caloric tests, and VEMP tests. Patients with measurable caloric and VEMP results before IT gentamicin treatment were included in the study. IT gentamicin (0.5 ml) at a concentration of 40 mg/ml was administered to the patients. Reinjection was performed 10 days later depending on patients’ complaints. Patients were re-evaluated with short- and long-term VEMP, hearing, and caloric test results.

Results. Caloric responses and VEMPs changed following gentamicin therapy in 9 patients and 12 patients, respectively. Long-term results of caloric and VEMP tests in patients receiving IT gentamicin treatment changed in 7 patients and 10 patients, respectively.

Keywords: Vestibular evoked myogenic potentials, Meniere’s disease, intratympanic gentamicin therapy

Introduction

Vestibular evoked myogenic potentials (VEMPs) are electromyographic responses to loud auditory stimuli recorded in the sternocleidomastoid (SCM) muscle during tonic contractions. Geisler and associates (1958) and Bickford and associates (1964) were the first to record electromyographic potentials in the posterior neck muscles after subjects were exposed to noise [1,2]. These potentials have been shown to be vestibular, originating from the saccule [3–5]. VEMPs have been validated as being demonstrative of the sacculocollic reflex [6]. The caloric test relates to the function of the superior vestibular nerve, whereas VEMPs provide information about inferior vestibular nerve function.

Intratympanic (IT) gentamicin therapy is used for patients with vertigo who are unresponsive to classic medical therapy. Compared with surgery, it is less invasive and popular. Audiologic tests and vestibular tests (including caloric, head-thrust, and head-shaking tests) are used to monitor the results of IT gentamicin therapy.

The most significant adverse effect of this treatment is a loss of hearing. This risk may be averted by using different gentamicin protocols in which patients are monitored with hearing and vestibular tests [7].

The aim of this study was to test the reliability of VEMPs to monitor the results of IT gentamicin therapy in patients with Meniere’s disease.

Subjects and methods

Subjects

Twelve patients with unilateral Meniere’s disease (6 right and 6 left ears; 5 female, 7 male; mean age 48.2 years, range 26–61 years) who had presented to the Department of Otolaryngology at Baskent University in Ankara, Turkey, were enrolled. All the patients in the study group were diagnosed as having...
Meniere’s disease according to criteria from the Committee on Hearing and Equilibrium of the AAO-HNS [8]. All subjects received detailed information about the study and the testing that would be involved. Informed consent was obtained from each individual, and the study protocol was approved by the Baskent University Ethics Committee (March 10, 2004, no. KA03/176).

All patients underwent a detailed history-taking and a battery of tests including a physical examination, neuro-otologic examination, pure tone audiometry (PTA), bithermal caloric test, and measurements of their VEMPs before initial application of gentamicin therapy. The inclusion criteria for the patient group comprised the presence of measurable caloric and VEMP results before the study.

Caloric and VEMP tests were done 10 days after the first gentamicin injection, and worsened VEMP and caloric measurements were accepted as successful treatment. A second injection was given according to the patients’ subjective complaints of vertigo with fullness and/or hearing changes.

All patients in the study group were called for a second evaluation in 2007, which comprised VEMP and caloric testing. The time between the last injection and the call for a second evaluation in 2007 was between 6 and 38 months.

Patients with subjective complaints of vertigo were tested during the follow-up, and a second course of gentamicin therapy was given to these patients.

**VEMP**

Surface EMG activity of the SCM was recorded using a Smart EP device (Intelligent Hearing Systems, Miami, FL, USA). An active electrode was placed on the upper half of the ipsilateral SCM. A reference electrode was placed on the suprasternal notch. The SCM muscle was kept contracted using head rotation. Background electromyographic activity was monitored visually for consistent tonic contraction. The amplifier gain was set to 100,000, and signals and bandpass were filtered at 10 to 3000 Hz. Short tone bursts (100 dB nHL, 500 Hz each, with a 1 ms raise-fall time and a 2 ms plateau time) were delivered monaurally via TDH 49P earphones. The stimulation rate was 5 Hz; the analysis time was 60 ms. A total of 128 responses to stimuli was averaged, and measurements were repeated twice to check test wave reproducibility. Latencies of the peak p13 and n23, interpeak p13-23 interval, and p13-n23 amplitudes were measured.

Normative data of VEMP test results from our previous study were used [9]. The mean latency values for p13 and n23 were 13.7 ± 1.0 and 22.1 ± 1.9 ms, respectively, and the upper limits (mean plus 2 standard deviations) for latency at p13 and n23 were 15.7 and 25.9 ms, respectively.

**Caloric tests**

Caloric irrigations were recorded using the Micro-medical device (Micromedical Technologies Inc., Chatham, IL, USA). Caloric tests were performed using 200 ml tap water irrigating the external ear canal for 30 s. The temperature of the tap water was fixed automatically by the device as warm (44°C) or cold (30°C). Canal paresis was defined as a difference of >20% between maximum slow-phase velocity measurements for each ear, when compared with the sum of slow-phase velocities. If cold water failed to obtain a caloric response, the patient underwent ice water caloric tests (2–4°C, 10 ml) to further confirm the caloric areflexia.

**IT gentamicin application**

Application of IT gentamicin (0.5 ml of 40 mg/ml concentration) was done in patients with refractory disease. Reinjection was performed after 10 days if needed. Patient’s heads were elevated 30°, turned to the other side for 45°, and the patient was asked to hold this position for 30 min.

**Results**

Results of VEMP response tests, caloric response tests, and PTA of the 12 patients are summarized in Table I.

**Short-term results**

VEMP and caloric tests were done following completion of the first round of IT gentamicin treatment. No response to caloric irrigation was detected in eight patients, while canal paresis was reported in four patients after IT gentamicin treatment. A change in test results with respect to baseline was observed in nine patients.

The VEMP test result disappeared in nine patients after treatment. Elongation of latency and a decrease in amplitude were observed in three patients. Change with respect to baseline was observed in nine patients.

The VEMP test result disappeared in nine patients after treatment. Elongation of latency and a decrease in amplitude were observed in three patients. Change with respect to baseline was observed in 12 patients. Nine of 12 patients showed worse caloric responses after treatment, while all of the VEMP results (12 of 12) were worse after treatment (Table II).

**Long-term results**

The average follow-up was 21.8 months (range 6–38 months). A second course of treatment with IT gentamicin because of recurrent vertigo attacks was
administered to four patients. One patient was administered IT gentamicin treatment despite the absence of VEMP and caloric test responses. He had a positive ice water caloric test. No response to caloric irrigation after treatment was reported in six patients, while canal paresis was obtained in five patients after treatment. A normal result to the caloric test was obtained in one patient. A change from baseline was seen in seven patients. VEMP results disappeared in nine patients. Elongation of latency and a decrease in amplitude were observed in one patient. Normal VEMPs were detected in two patients. A change with respect to baseline was reported in 10 patients. Briefly, 5 of 12 caloric test responses did not show any change, while 7 of 12 test responses worsened. Two of 12 VEMP test results did not show any change, while 10 of 12 VEMP data worsened. Eleven of 12 patients had complete remission of vertigo spells after one or two IT gentamicin injections (Table I). Evaluations of the long-term results of caloric and audiometric tests in patients with no VEMP test responses are summarized in Table III. Evaluations of the long-term results of caloric and audiometric tests in patients with normal or elongated VEMP responses are shown in Table IV.

The number of the patients in the study group was small. We preferred to compare the measurable VEMP and caloric test results at the beginning and at the end of this preliminary study. Thus, we preferred not to use statistical analyses but to share our results and observations for this small study group.

**Discussion**

Aminoglycosides are well-known causes of ototoxicity, with different sensitivities of cochlear and vestibular sensory cells. Among members of the aminoglycoside family, gentamicin can selectively destroy human vestibular hair cells and, thus, can severely impair vestibular function. Instillation of gentamicin into the tympanic space has been reported to decrease vertigo in patients with intractable Meniere’s disease, because gentamicin is relatively more vestibulotoxic than cochleotoxic; however, its sacculotoxic nature remains uncertain [10].

The primary route of entry of aminoglycosides into the inner ear is through the round window membrane. Alternative routes into the inner ear include the annular ligament of the oval window, the vasculature, or the lymphatics. After passing
through the round window membrane, drug concentrations in the perilymphatic and endolymphatic spaces increase [7]. Audiologic tests and vestibular tests (including the caloric test, the head-thrust test, and the head-shaking test) are used to monitor the results of IT gentamicin therapy [11]. In recent years, the topic of monitoring the effects of IT gentamicin application has been investigated. Day and associates demonstrated, in their animal studies, that gentamicin application in guinea pigs diminishes VEMPs [10]. De Waele and associates treated 22 patients with IT gentamicin. Using galvanic stimulation, they measured the vestibular function using head impulse, caloric, and VEMP tests. They followed the patients for 2 years and observed no recurrent vertigo attacks in patients who had abnormal VEMP test results [11]. Cohen-Kerem and associates published a meta-analysis of seven publications on IT gentamicin with pretreatment and post-treatment caloric test results. In our report, we emphasize short- and long-term caloric results [12]. Piciotti and associates investigated vestibular functions using VEMP tests, dynamic posturography, and the results of caloric tests in 12 patients receiving IT treatment and suggested the use of VEMP test results along with other test results in monitoring treatment [13].

Table II. Short-term results of VEMP responses, caloric test responses, and pure tone audiometry of the patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pretreatment caloric</th>
<th>Post-treatment caloric</th>
<th>Pretreatment VEMP</th>
<th>Post-treatment VEMP</th>
<th>Pretreatment VEMP amplitude</th>
<th>Post-treatment VEMP amplitude</th>
<th>Post-treatment SSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43</td>
<td>56</td>
<td>p13:19,3</td>
<td>NR</td>
<td>16,01-17,76</td>
<td>NR</td>
<td>NC (40-48 dB)</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>98</td>
<td>p13:12</td>
<td>NR</td>
<td>34,81-36,4</td>
<td>NR</td>
<td>NC (50-58 dB)</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>95</td>
<td>p13:13,4</td>
<td>NR</td>
<td>35,49-35,56</td>
<td>NR</td>
<td>W (82-93 dB)</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>32</td>
<td>p13:14,87</td>
<td>NR</td>
<td>20,58-22,93</td>
<td>NR</td>
<td>B (75-63 dB)</td>
</tr>
<tr>
<td>5</td>
<td>96</td>
<td>1</td>
<td>p13:13,8</td>
<td>NR</td>
<td>45,15-43,68</td>
<td>NR</td>
<td>W (8-42 dB)</td>
</tr>
<tr>
<td>6</td>
<td>77</td>
<td>45</td>
<td>p13:14,67</td>
<td>NR</td>
<td>40,65-47,61</td>
<td>NR</td>
<td>NC (92-92 dB)</td>
</tr>
<tr>
<td>7</td>
<td>98</td>
<td>45</td>
<td>p13:13,2</td>
<td>NR</td>
<td>15,76-21,67</td>
<td>NR</td>
<td>NC (68-68 dB)</td>
</tr>
<tr>
<td>8</td>
<td>97</td>
<td>97</td>
<td>p13:14</td>
<td>NR</td>
<td>19,66-32,38</td>
<td>NR</td>
<td>W (55-80 dB)</td>
</tr>
<tr>
<td>9</td>
<td>31</td>
<td>95</td>
<td>p13:14,85</td>
<td>EL</td>
<td>20,58-22,93</td>
<td>NR</td>
<td>13,99-14,91 NC (25-33 dB)</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>100</td>
<td>p13:15,73</td>
<td>NR</td>
<td>31,22-19,43</td>
<td>NR</td>
<td>B (68-57 dB)</td>
</tr>
<tr>
<td>11</td>
<td>67</td>
<td>67</td>
<td>p13:12,73</td>
<td>EL</td>
<td>14,74-17,02</td>
<td>10,61-12,42 NC (82-82 dB)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>38</td>
<td>15</td>
<td>p13:15</td>
<td>EL</td>
<td>32,75-29,15</td>
<td>55-15 dB</td>
<td></td>
</tr>
</tbody>
</table>

NR, no response; EL, elongated; W, worse; NC, no change; B, better.

Table III. Long-term caloric and audiometric test evaluations of patients with no responsive vestibular evoked myogenic potentials (VEMP) test.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Post-treatment VEMP</th>
<th>Post-treatment caloric</th>
<th>Post-treatment PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>NR</td>
<td>15</td>
<td>NC (55-51 dB)</td>
</tr>
<tr>
<td>1</td>
<td>NR</td>
<td>50</td>
<td>W (40-67 dB)</td>
</tr>
<tr>
<td>3</td>
<td>NR</td>
<td>60</td>
<td>NC (82-83 dB)</td>
</tr>
<tr>
<td>4</td>
<td>NR</td>
<td>37</td>
<td>B (75-63 dB)</td>
</tr>
<tr>
<td>7</td>
<td>NR</td>
<td>45</td>
<td>NC (68-68 dB)</td>
</tr>
<tr>
<td>2</td>
<td>NR</td>
<td>98</td>
<td>W (50-68 dB)</td>
</tr>
<tr>
<td>5</td>
<td>NR</td>
<td>96</td>
<td>W (8-63 dB)</td>
</tr>
<tr>
<td>6</td>
<td>NR</td>
<td>98</td>
<td>NC (92-92 dB)</td>
</tr>
<tr>
<td>11</td>
<td>NR</td>
<td>96</td>
<td>B (82-76 dB)</td>
</tr>
</tbody>
</table>

NR, no response; W, worse; NC, no change; B, better.
success of IT gentamicin therapy in patients with Meniere’s disease. A more definitive conclusion may be achieved with a larger patient series and statistical analyses.

Acknowledgements

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References