**ARTICLE INFO**

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**ABSTRACT**

Background: In the group of objective audiological tests, the most important are tests of auditory brainstem evoked potentials. Objective: To test the configuration, degree of hearing loss and the response characteristics of auditory brainstem evoked potentials in children with hearing loss occurred due to infectious disease. Method: designed as case control study. Statistical significance of differences between calculated parameters in healthy children and children with sensorineural hearing loss was determined. Results: Infectious agents have led to the emergence of various forms of sensorineural hearing loss. We found deviations from the normal values of absolute and interwaves latencies in some children in our group, both among those with hearing loss and among those with normal hearing. Conclusion: We found that in the group of children who had the disease or purulent meningitis born with rubella virus and cytomegalovirus, a retrocochlear damage in children with cochlear and the children without him.

**1. Introduction**

The projection of the central auditory pathways is more complex than the projections of other sensory systems. Central conduction of information carried by auditory nerve begins in the cochlear nucleus (CN), the first mandatory synapse for all nerve fibers. Three pathways of fibers project information from CN to the higher centers of the brainstem. [1,2]

Definition

From audiology aspect, deafness implies the absence of auditory function. Hearing impairment (HI) means the limit of hearing ability. For normal hearing anatomical integrity and functional compliance of all parts of the auditory system: the outer, middle and inner ear, the cochlear nerve and central auditory pathways is necessary.[2]

Hearing impairment risk factors are those pathological conditions which have a significantly higher incidence of HI in the general population. [3] Any child with a HI has to be ethiologically evaluated, that means multidisciplinary examination which is trying to determine cause of impairment. It is important for planning the treatment, habilitation, for medical follow up, planning family etc. According to the origin, all HI in children can be divided into genetic (hereditary) an acquired.[4]

Meningitis as a etiology factor of hearing loss

Bacterial meningitis in 75% of cases in a period before vaccines begin to use, became the single most important cause of acquired sensorineural hearing loss [5]. Between 5% and 30% of BM will develop clinical deafnes, especially infections caused by Streptococcus pneumoniae.

The most frequent causes of bacterial meningitis are Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis, Escherichia coli, Lysteria monocytogenes, Mycobacterium tuberculosis.[5]

Congenital infections as causes of sensorineural HI Cytomegalovirus (CMV) infection is wide spread throughout the world. The prevalence of congenital infection varies from 0,4 to 7,4 %. Up to 10 % of the children with congenital CMV infection showed systemic and neurological symptoms at birth and 61% of these children develop sensorinural HL.[6]

Congenital rubella (KR) is most common due to primary infection during pregnancy, or less frequently due to reinfection or vaccination. The classic triad of KR include congenital heart...
disease, vision problems, and sensorineural HI prior to the development of vaccines against rubella, 0.1% and 0.4% of children born with KR, but since the usage of vaccine, it has become rare. Hearing loss is the most common manifestation and affects 68% to 93% of children with KR. [7]

Patoanatomy substratum of postmeningal hearing loss is purulent labyrinthitis (cochlear sepsis) in almost cases, which was confirmed by numerous experimental works and pathological retrospective studies. [6]

Diagnosis

The diagnosis of sensorineural HI is based on subjective and objective methods for testing hearing. There are two basic approaches to make an accurate and reliable assessment of hearing: behavioral (subjective) and physiological (objective).

In the group of objective, electrophysiological tests, the most important are test of auditory brainstem evoked potentials (AEPMS). For those children who were exposed to the risk factors for HI it is obvious to do these objective tests.

The measurement of otoacoustic emissions is an objective, noninvasive, rapid, reproducible and precise. [8] Neurootological AEPMS measurements include determination of absolute wave latencies (AWL) and amplitudes, interwaves latencies (IWL) and the amplitude ratio. In general, AWL measure the time that passes from the beginning of the stimulus to the highest synchronous activity in a set of generators of the measured components. The most widely used IWL are I-V, III-I and V-III, reflecting the transmission along the auditory pathways between the cochlea and lower colliculus. Functionally intact auditory pathway is typically symmetrical, with equal time of transmission of response to stimulation from the left and right ear. Therefore, a significant interaural difference in the respective measurements of the left and right ear may indicate unilateral functional abnormality. [8] Abnormal extension between the components of the early waves (e.g. I to III) indicates a lesion of the posterior fossa including the VIII nerve and/or the lower brain stem, while prolonged III-V latency suggests intra-axial auditory brainstem dysfunction. [9]

Developmental changes in morphology of the response

There are developmental changes in the morphology of the response, the wave amplitude and latency of waves of AEPMS. Very early in life, only I, III and V waves are evident, and I wave has much larger amplitude than the V wave. Over time the ratio is changing, the V wave becomes the most prominent wave of AEPMS in adults. Mainly changes in latencies provide the most consistent development index of AEPMS. All AEPMS waves decrease in latency during early life. However, the degree of maturation of different wave varies. The first wave has the shortest development period, reaching adult latency values with two - three months. V wave has the longest period of development, reaching adult values at the age of two. III wave matures in period between I and V waves maturation. Interwave latencies (I-III, III-V, I-V) also shows developmental changes. [10] The effect of the age on the responses can be divided into two periods: the period of maturation and adulthood. During maturation, which can be followed up to the age of 2 years, there are significant changes in the components of the amplitude, IWL and AWL. Any team that uses AEPBS measurement should collect their own normative data to compare the test results. [11] (Table 1) Standard recording of AEPMS is ipsilateral.

Objective

To test the configuration, degree of hearing loss and the response characteristics of auditory brainstem evoked potentials in children with hearing loss occurred due to infectious disease. 1) the presence of established responses, or their absence at a certain level of sound intensity at each ear separately 2) length of absolute wave latencies and interwaves latencies.

Method of study

Patients

The study was conducted in the Unit for Audiology and Neurootology, which is part of Department of otorhinolaryngology in Institute for Mother and Child Health Care „Dr Vukan Cupic” (IMD) from 20.01.2000 to 20.12.2013. Design is a case control study.

Total group of 54 patients referred for hearing test caused by infectious diseases after or with which they born were studied. These group includes 21 patients with HI of different forms and degrees, and 33 patients without.

Inclusion criteria in study are follows:

1. Patients who were treated for meningitis and congenital viral infection in the IMD and then sent for hearing test
2. Patients who were admitted to the IMD for further treatment of meningitis started in another hospital and then referred to a hearing test
3. Patients who were admitted to the IMD for further testing because of neurological sequelae after bacterial meningitis and within this test include the hearing.

Patients were not applied with toxic drugs.

We divided the patients into two age groups: up to two and more than two years. The control group consisted of 40 healthy children with normal hearing, also divided into two age groups: up to two and more than two years. First were hospitalized because of performing adenoidectomy, and the older group because of tonsilloadenoidectomy.
Methods – instruments for measuring

In order to confirm the diagnosis and determine which patients will be enrolled in the study the following test are used:

1. a detailed medical history data
2. otorhinolaryngologically review
3. otomicroscopy
4. tympanometry
5. the acoustic reflex recording
6. TEOAE
7. behavioral audiometry
8. tonal liminary audiometry in cases where it is allowed by child's age
9. auditory brain stem evoked potentials in natural sleep or sedation

The AEPMS waves analysis answers were accompanied by the presence of established responses or their absence at a certain level of sound intensity at each ear separately:

The basic condition for AEPMS responses analysis is otological patient status determination. All patients have a normal tympanogram (type A). In this study we used impedance audiometar Danplex tymp 87. Recorded ipsilateral acoustic reflexes at 500,1000,2000 and 4000 Hz at intensity of 70, 80, 90 and 100 db.

In determining the threshold of hearing loss we used methods of subjective and objective audiometry. Tonal liminary audiometry was performed at the Diagnostic Audiometer Interacoustic AD 229 b. Recording transient otoacoustic emissions was performed on the MAICO ERO SCAN device.

Auditory brain stem evoked potential test were recorded on Hortman NEURO OTOMETRY modul. Recording was carried out in a number of cases in a natural sleep. In cases where even after sleep deprivation we were not able to achieve natural sleep, the recording is made in chloral hydrate sedation in the intended dose. In some cases, we used Diazepam. Older children are adequately prepared mentally and the recordings was performed in the presence of one or both parents.

We used ipsilateral stimulation refraction click liminary and supra liminary intesity with automatically set masking of other ear. Before each recording were controlled resistance and of course, only after the acceptable resistance values determination we approached recording.

We used the following parameters of stimulation: stimulus frequency of 24 stimulus per second, 2000 summarizing responses to obtain each curve. We used intesity of 20 db to 110 db.

Results

Evaluation of the etiology sensorineural hearing loss performed on the basis of detailed personal and family history, medical records, treatment history and examination, otorhinolaryngological examination, impedancemetry, determining hearing threshold method of objective and subjective audiometry, virological analysis, radiological examination in suspected existence of any other pathological process unless the lesion cochlea.

Etiological factors have been identified on the basis of reliable data on mother's disease or infection, a clearly positive family history in relation to the HI, based on clear clinical impact of ototoxic drugs occurrence, based on data preterm birth and stay in the Intensive Care Units. In determining the threshold of hearing we used subjective and objective methods of audiometry.

In all patients there was harmony between the results obtained from behavioral and objective audiometry and with the cooperation of patients over four years old we performed a tonal audiometry too.

We analyzed AEPMS responses, curves at different intensities of sound. Table 2.

Here are shown the values of AWL, IWL AEPMS of supraliminal intensities of all the patients who have had an infectious disease. We compared the values of AWL and IWL on the maximum of supraliminal intensity in healthy children with normal hearing and the values of AWL and IWL in children who have had the disease meningitis or were born with congenital infection.

There are two control groups of 20 patients, divided by the age limit of two years. In our group of “sick” patients were 54 patients, therefore, 108 ears were examined, of which 8 patients (16 ears) have a bilaterals profound sensorineural HL and six patients (six ears) have unilateral sensorineural HL, where there are no formed responses with evoked potential, not even under the highest intesity, so AWL and IWL cannot be measured in their curves. This means that there are tested responses in 86 ears of “sick” and 80 ears of “healthy” children.

Given that there are different standards for the length of latency for children up to two years and children over two years, comparison, i.e. testing was done in these two age groups separately, for each ear (left and right) separately. A statistically significant difference (p < 0.05) was determined in the following measurements:

- Between AWL III and AWL V of the control group, and AWL III and AWL V of the children with the impairment on the left ear up to the age of two and older than two years
- Between AWL III and AWL V of the control group and AWL III and AWL V of the children with the impairment on the right ear up to the age of two
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- Between AWL V of the control group and AWL V of the children with the impairment on the right ear older than two years.

- Between the control group and children with the impairment on the left ear up to the age of two and over two, for the values of IWL (I-III).

- Between IWL (I-V) of the control group and IWL (I-V) of the children with the impairment on the left ear older than two years.

- Between IWL (II-V) of the control group and IWL (II-V) of the children with the impairment on the right ear up to the age of two.

- Between IWL (I-V) of the control group and IWL (I-V) of the children with the impairment on the right ear up to the age of two and older than two years.

We became very interested in the results and they made us divide the group of patients with infective disease in two new groups:

1. a group of patients whose values of AWL and IWL were closest to those of the control group.

2. a group of patients whose individual values differed from values in the control group.

Group No 1 children under the age of two consisted of 14 patients (28 ears), and group No 2 also consisted of 14 patients (28 ears).

Group No 1 children over two years consisted of 19 patients (38 ears), and group No 2 consisted of 11 patients (22 ears).

For each characteristic and for each age one-factor ANOVA was performed, which tested whether there was a significant effect of belonging to a particular group (control, group No. 1 and group No. 2) on variation of the measured characteristics. The following results were obtained:

In patients under the age of two, belonging to a particular group had a significant effect on AWL V, IWL (I-III) and IWL (I-V) in the left ear, and AWL III, AWL V, IWL (I-III), IWL (III-V), IWL (I-V) in the right ear.

In children aged over two years, belonging to a particular group had a significant effect on variation in the AWL III, AWL V in the left ear, and the AWL III, AWL V, IWL (I-III), IWL (I-V) in the right ear.

Next, we conducted testing of differences among these groups. Since we made a series of comparisons we had to choose a test that kept the total error of the first kind in the entire series of comparisons at a level of 5%. Test of multiple comparisons was used - Bonferroni test (approximation of Tuckey test) and it showed the following: for AWL V on the left ear in children under the age of two, all three groups differ from each other; while in the characteristics of IWL (I-III) and IWL (I-V) between the control group and the group No. 1 has not been proven statistically significant difference, a group No. 2 is statistically significantly different from the control.

On the right ear of children over two years of age, in all of the characteristics in which effect of group is significant (AWL III, AWL V, IWL (I-III), and the IWL (I-V) no significant difference between the control and the group No 1 was found, but it was found in comparison to the group No 2.

In children older than two years, on left ear no significant difference between the control group and No 1 for values of AWL III, AWL V was found, but there was a significant difference from the group No 2.

In children older than two years, on the right ear no significant difference in the values of AWL V, IWL (I-III), IWL (I-V) between the control group and No 1 was found, but there was a significant difference between the control group and No 2.

In the group No 1 aged up to 2 years was one child with endocochlear sensorineural HL. In group No 1 aged over 2 years were 4 children with sensorineural HL - two with unilateral and two with bilateral SNHI, which means children with endocochlear and retrocochlear sensorineural HL at the same time. In group No 2 children over 2 years there were 5 children with endocochlear and retrocochlear sensorineural HL.

Discussion

RK Kapoor researched AEPMS responses in 50 children with bacterial meningitis and in 50 healthy children of the same age. Abnormal AEPMS was found in 32 (64%) patients with BM. These abnormalities included presence of prolonged latencies (56.2%), unilateral absence of responses (25%), absence of response on both sides (25%) and the prolonged interwave intervals (25%). Monitoring could be done in 23 patients of 46 survivors. All patients with prolonged latency recovered, or became normal. In all patients with absent responses, abnormalities persist.[11]

K. B. Singh has conducted research on infants younger than 3 months who have had meningitis and babies who have had septicemia. He found that the AWL V and IWL (I-III) and (I-III) of babies who survived meningitis significantly prolonged compared with the same measurements in infants with septicemia.[12]

Kulahli examined AEPBS in 116 children aged from a few days up to 7 years of age who have had the disease BM. 26% have occurred in the first six months, 55% between six months and two years, and 19% after two years. Neurological complications occurred in 30% of cases of meningitis and represented 85% of all
found complications. In 29% of patients AEPMS was abnormal, of which 47% were temporary, 32% endocochlear and 21% retrocochlear damage. [13]

We compared the values of AWL and IWL in supraliminal intensities in healthy children with normal hearing and the values of AWL and IWL in children who have had the disease meningitis or were born with congenital infection, regardless of whether they had sensorineural HL as sequels or not.

The difference is present in terms of extension of aforementioned AWL and IWL, indicating slow conduction along the retrocochlear structures of auditory pathway.

These findings suggest the existence of endocochlear hearing loss in 21 patients caused by infectious agents (CMV, rubella and causative agents of bacterial meningitis), and the existence of retrocochlear damage both in a group of patients with endocochlear impairment and in a group of patients who did not have cochlear damage.

In the group of children without retrocochlear damage under the age of 2, there was one child with endocochlear HL. In this group of children over two years were four children with HL - two with unilateral and two with bilateral SNHL, which means children with endocochlear and retrocochlear HL two at the same time.

In this group of children over two years there were five children with endocochlear and retrocochlear HL.

Conclusion

In accordance with the purpose of research that examined the characteristics of AEPMS response in children with sensorineural hearing impairment caused by infectious agents, following results were obtained:

Table 1. Normative values for our laboratory while applying click intensity of 70 dB established for children younger than two years:

<table>
<thead>
<tr>
<th></th>
<th>AWL left</th>
<th>mean value</th>
<th>right</th>
<th>interaural difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>2.07 ± 0.09</td>
<td>2.07 ± 0.09</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>4.17 ± 0.11</td>
<td>4.17 ± 0.11</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>6.12 ± 0.12</td>
<td>6.12 ± 0.12</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>AWL left</th>
<th>mean value</th>
<th>right</th>
<th>interaural difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-III</td>
<td>2.10 ± 0.09</td>
<td>2.11 ± 0.13</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>III-V</td>
<td>1.95 ± 0.09</td>
<td>1.93 ± 0.12</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>I-V</td>
<td>4.05 ± 0.10</td>
<td>4.05 ± 0.14</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Showing the mean values of AWL and IWL with SD AEPMS of responses at maximum supraliminal intensity in all three groups of patients

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATL I</td>
<td>ATL III</td>
<td>ATL V</td>
<td>ATL I</td>
</tr>
<tr>
<td>Right ear</td>
<td>2.05</td>
<td>4.17</td>
<td>6.11</td>
</tr>
<tr>
<td>ear</td>
<td>0.10</td>
<td>0.11</td>
<td>0.15</td>
</tr>
<tr>
<td>Left</td>
<td>2.07</td>
<td>4.16</td>
<td>6.11</td>
</tr>
<tr>
<td>ear</td>
<td>0.10</td>
<td>0.11</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Normative values for our laboratory while applying click intensity of 70 dB established for children older than two years:

<table>
<thead>
<tr>
<th></th>
<th>AWL left</th>
<th>mean value</th>
<th>right</th>
<th>interaural difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.98 ± 0.09</td>
<td>1.95 ± 0.06</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>4.06 ± 0.12</td>
<td>4.04 ± 0.12</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>5.97 ± 0.11</td>
<td>5.95 ± 0.10</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>AWL left</th>
<th>mean value</th>
<th>right</th>
<th>interaural difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-III</td>
<td>2.08 ± 0.12</td>
<td>2.10 ± 0.12</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>III-V</td>
<td>1.92 ± 0.12</td>
<td>1.90 ± 0.10</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>I-V</td>
<td>4.00 ± 0.12</td>
<td>4.00 ± 0.09</td>
<td>0.4</td>
<td></td>
</tr>
</tbody>
</table>

4) Patients with isolated retrocochlear damage behaved in all other measurements, both behavioral (subjective) and electrophysiological (objective) as normal hearing children. We conducted control measurements after six months and in those children we have received the same, unchanged responses. We did not carry out control measurements of AEPMS with large number of children, but only the control impedancemetry and audiometry.

We found that in the group of children who had the disease or purulent meningitis born with rubella virus and cytomegalovirus, a retrocochlear damage in children with cochlear and the children without him.

LITERATURE:


