CLINICAL RESEARCH

AGE INFLUENCE IN OTOACOUSTIC EMISSIONS FOR HEARING LOSS SCREENING IN INFANTS

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ABSTRACT

Objective: To determine the most favorable age for detection of otoacoustic emissions in newborns and for repeated testing. Methods: Observational, retrospective, descriptive study in 2,567 newborns. Results: The incidence of any degree of hearing loss was 7 per thousand newborns. It was proportionately higher in the group that did not have otologic risk factors. The distribution of otoacoustic emissions by age groups followed a significant linear trend in the first month of life. The time lapse to obtain a positive result on the second otoacoustic emission test was 6 days from the first one. Conclusions: Otoacoustic emission screening should be performed in all newborns as late as possible after birth (from the first 48 hours after birth), but before hospital discharge for the test to be effective and efficient. A repeat, test if required, must be performed at least six days after failing the first one.

INTRODUCTION

Currently, nobody disputes the validity of Evoked Otoacoustic Emissions (EOEs) as a method of selection in the premature detection of infantile hypoacusis1-4 combined with Evoked Auditory Potentials of the Cerebral Trunk (EAPCT) for the diagnostic confirmation.5,6 If EOE are absent it indicates a suspicion of hypoacusis greater than 30 dBs of transmissive origin and/or from the cochlear, recommending repetition before a month of age. If the absence persists, a study of EAPCT must be carried out, which determines the level of loss (in acute: 2-4 Hz) and situates it throughout the system up to the cerebral trunk. This allows us a premature diagnosis (from 3-6 months) a fundamental mainstay of the necessary early stimulation of children with hearing loss7,8.

However, one of the main problems that affect the development of this type of programme is the time at which the test should be carried out. There is a general consensus that it must be done before the end of maternity. Nevertheless, and due to the current tendency to allow premature hospital discharge, the age at which the test has been carried out has been going down gradually, the number of false positives has been increasing and the recommended fundamentals for the selection to be effective have been put at risk. Studies are rare (normally with a limited number of cases) that establish at what age this test is best carried out on the newborn.

The objective of the present paper is to study and understand the characteristics of the detection of EOEs in newborns and to demonstrate the influence of age on the efficiency of the test.

MATERIALS AND METHODS

For the execution of this observational, retrospective and descriptive study, the Otoacoustic emissions in all live newborns during the period June 1999 to June 2001 inclusive, with the previous informed consent of their parents or guardians, were assessed. The information was collected on a data base that included: details of the particulars of the newborn, age, factors of otological risk, date and result of the first EOE test and of any necessary repetition, as well as the results of the EAPCT if this took place.

All the newborns were tested by means of EOE (Echocheck®) before the end of maternity (normal birth 2 days, Caesarean 5 days). If it was not possible in this period for strategic reasons (holidays, weekends), the patient made another appointment to undergo the test during the first week of life. If no EOEs were detected, the test was repeated before the end of one month. If a suspicion of retrocochlear hypoacusis did not appear in this second test, we continued on to a diagnostic study by means of EAPCT. As there are families of late hearing loss onset and retrocochlears that the EOEs do not detect, all the children of high risk1,4, independent of the result of the Otoacoustic emissions test, were summoned for a follow up consultation by means of conductual tests.

The place chosen for the registration of the Otoacoustic emissions was the newborn’s own room although they were not required to be sleeping or under sedation. The system used for carrying out the test was the Echocheck® (Otodynamics Ltd, Hatfield, Herts AL10 8BB, UK) of which scientific evidence of its validity already existed6.

The results according to the internal validation of the apparatus were classified in two categories: “NORMAL” (Otoacoustic emission was detected); and “NOT NORMAL” (total or partial Otoacoustic emission was missing) A child was considered to have passed the test when the NORMAL result was obtained from both ears. When either or both ears showed NOT NORMAL results, the test was repeated. If, after this repetition, the result remained unchanged, EAPCT was carried out for diagnostic confirmation.

The classification of the grade of hypoacusis in each ear according to the result of the EAPCT was: mild (V wave at 40 dBs HL), moderate (V wave at 60), severe (V wave at 80) and profound (absence of waves).

Of all the children (2,588), 5 did not participate in the study. In addition 16 were excluded from the study, 4 of whom, for different reasons had the test carried out on them more than 31 days after their birth and 12 who had a result of NOT NORMAL on their first EOE test and did not turn up for the repetition of the test. Of these last, at least 5 had a factor of risk.

To determine the age of positivisation of the EOEs, all those children that had passed the test, either the first or second, were considered. Those newborns submitted to a study by means
of EAPCT (those in which the EOE test was never normalised because they suffered from some grade of hypoacusis) were excluded.

The following Risk Factors (RF) were considered:
- RF1 Family history of hypoacusis.
- RF2 Gestational infection.
- RF3 Craneofacial malformations.
- RF4 Underweight (<1500 g).
- RF5 Hyperbilirubinemia.
- RF6 Otoxicity in pregnancy.
- RF7 Ototoxicity in the neonate.
- RF8 Hypoxicischaeamic accident.
- RF9 Assisted ventilation.
- RF10 Syndromes associated with hypoacusis.

The children were classified into groups according to age in hours when the first test of Otoacoustic emissions was carried out: - group 1: <24 hours, - group 2: 24-47 hours, -group 3: 48-71 hours, -group 4: 72-95 hours, -group 5: 96-119 hours, -group 6: 120-143 hours, - group 7: 144-215 hours, - group 8 >216 hours.

In order to allow us to study the time passed between the first and second test until it was normalised, the children whose test was not repeated were excluded.

For the statistical study of the data, an analysis by Pearson's \( \chi^2 \) for qualitative data was applied. By means of the McNemar test for matched qualitative data, we evaluated if laterality existed in the response of EOEs. An analysis of the variation with polynomic analysis of lineal tendency was used, to study the relation between quantitative and qualitative variables.

For a comparison of quantitative data we used the Student T test of comparison of averages. Finally it was considered statistically significant when \( P < 0.05 \) with an interval of confidence of 95%.

RESULTS

The coverage of the test from the population of newborns studied was 99.4%. After the analysis of the records obtained was filtered, 2,567 children were finally considered for the study, 53.4% (1,372) male and 46.6% (1,195) female.

Result from the first test of EOEs: The presence of “Normal” Otoacoustic emissions in both ears was 77%. The result was “Not normal” in both ears in 6.9% and unilaterally in 16.1% (Table 1). The average age of fulfilment of the first test of Otoacoustic emissions was 73.9 hours (3.08 days); Min: 3 hours, Max: 744 hours; SD: 109.75 hours.

Result of the second test of EOEs: A second test of EOEs was carried out on 591 newborns (23%) that did not pass the first test. The presence of “Normal” Otoacoustic emissions in both ears was 96% (568) (99.1% of the total). In 11 children (1.8%) the Otoacoustic emissions were negative in unilateral form and in 12 children (2.2%) bilaterally (Table 1). The average age of fulfilment of the second test of Otoacoustic emissions was 206.7 hours (8.6 days); Min: 24 hours, Max: 2352 hours; SD: 235 hours.

Diagnosis of confirmation: 24 children (0.93% of the total) were submitted for diagnosis by EAPCT (23 that showed Otoacoustic emissions “Not normal” after the second test and one child with EOEs with a “Normal” result but with a suspicion of a retrocochlear pathology due to hyperbilirubinemia. Of these 24, three did not attend the diagnostic test, another three gave normal results and 18 were classified as deaf at different grades.

The prevalence of hypoacusis detected was 7.01 per thousand at any grade and 2.3 per 1000 of severe or profound hypoacusis uni or bilateral.

Table 1. Result of the Otoacoustic Emission Tests

<table>
<thead>
<tr>
<th>Type of result</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1.026</td>
<td>950</td>
<td>1.976</td>
<td>334</td>
<td>234</td>
<td>568</td>
</tr>
<tr>
<td>Unilateral not normal</td>
<td>236</td>
<td>178</td>
<td>414</td>
<td>5</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Bilateral not normal</td>
<td>110</td>
<td>67</td>
<td>177</td>
<td>7</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>1.372</td>
<td>1.195</td>
<td>2.567</td>
<td>346</td>
<td>245</td>
<td>591</td>
</tr>
</tbody>
</table>

Table 2. Children diagnosed of hypoacusis by PEACT

<table>
<thead>
<tr>
<th>Types of hypoacusis diagnosed</th>
<th>Total</th>
<th>Unilateral</th>
<th>Bilateral</th>
<th>Presence Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Normal</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2 Mild hypoacusis</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3 Moderate hypoacusis</td>
<td>10</td>
<td>3</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>4 Severe hypoacusis</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>5 Profound hypoacusis</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6 Did not attend test</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>7</td>
<td>11</td>
<td>5</td>
</tr>
</tbody>
</table>
Laterality – in general a significant difference was not found in the procurement of Otoacoustic emissions between the right and left ear in the first test ($\chi^2 = 1.18; p = 0.23$), or in the second test ($\chi^2 = 0.30; p = 0.54$).

Carrying out the analysis of laterality by age groups found a greater response from the right ear in relation to the left in the first test ($p = 0.01$) in newborns of 48 hours of age. No differences existed in the rest of the groups.

In the analysis of the laterality by gender, no significant differences were found.

In the case of the EAPCT, analysis could not be carried out due to the small sample.

Results by gender: In relation to the first test of EOEs, there was a significant difference in the rate for passing the test (result of "Normal test") in favour of the females ($p = 0.004$).

Risk factors: the percentage of patients with factors of high otological risk was 7.6%. The average probability of a newborn having any risk factor (RF) was 7.6% (DE 3.2). 197 RF (+) were detected in 164 children, of who 5 were diagnosed as deaf and 159 as normal. In Table 3, the relation between the presence/absence of risk factors and the newborns that were diagnosed with hypoacusis after selection and application of EAPCT was analysed. The exact estimation of the incidence of hypoacusis in children with risk factors in relation to those with none (relative risk) is 5.16 and its interval of confidence of 95% was 14.3 – 1.86.

The more common risk factor is a family history of hypoacusis (3.8%), followed by a gestational infection (1.17%) and ototoxicity during pregnancy (0.8%). Amongst the deaf children, in order of frequency, were a family history of hypoacusis, being underweight at birth and syndromes associated with hypoacusis. No deaf child had other risk factors and 72% of them had none. Significant differences were not found in the distribution of all the RF evaluated by gender.

Of the children with risk factors but with normal EOEs, consistency in any auditory defect has not appeared in any of the successive revisions carried out.

Table 3. Probabilities associated with Risk Factors and diagnosis of hypoacusis

<table>
<thead>
<tr>
<th>Probability</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>of being deaf, having at least one RF</td>
<td>3%</td>
</tr>
<tr>
<td>of being deaf, not having RF</td>
<td>0.5%</td>
</tr>
<tr>
<td>Average probability of having one RF, being deaf</td>
<td>29%</td>
</tr>
<tr>
<td>Average probability of having one RF, not being deaf</td>
<td>7.5%</td>
</tr>
</tbody>
</table>

Presence of Otoacoustic emissions by age group.

Age at the first test: the rate for passing the test (percentage of normal Otoacoustic emissions) varies in a significant way ($p = < 0.001$) being 58.01% for the newborns less than 24 hours when the test was carried out and increasing progressively until a month of age. The distribution of Otoacoustic emissions by groups of age followed a significant lineal tendency, with positive association, with the group of 48 hours of age showing a greater significance. (Table 4 and Figure 1)

The average age of the newborns in which the first test of EOEs was normalised was 66.5 hours (2.7 days) (DE 53.7), the average value being 48 hours. 85.8% of newborns with “Normal” Otoacoustic emissions had a range of normalisation of between one and four days. With respect to gender, differences in the average age at which the test was normalised did not exist.

The age at repetition of the EOEs: the average age of the newborns in which the second test of EOEs was normalised was 193.8 hours (8.07 days) (SD: 207.9). There was no significant difference with respect to gender.

For each age group we analysed whether the age at fulfilment of the first test influenced the acquisition of a positivisation at repetition (Figure 2). We found a significant difference between the different groups ($p = 0.000$) with a significant lineal tendency ($p < 0.000$) with the higher the age at which normalisation was achieved in the first test of EOEs the higher the age at which the second test was normalised (with the age at which the first test of EOEs was normalised increasing proportionately to the age at which the second test normalised.)

Subsequently the analysis was repeated without the 7 newborns that had an age equal to or greater than 216 hours (9 days) on the fulfilment of the first EOEs in order to avoid a possible slant from the belated positivisation similarly causing a significant difference ($p = 0.03$).

The time period of normalisation of the test of EOEs being of 153.69 (6.40 days) (min 0, max 2.328) (SD: 194.6) was noted in those 562 newborns in which EOEs (Not normals) were not detected in the first test and that had a date of noted repetition. Analysing by age group, a significant lineal tendency was shown ($p = 0.03$) that indicated that when the group was of an
Table 4. Percentage of positive results of EOEs with respect to age group

<table>
<thead>
<tr>
<th>Hours</th>
<th>&lt;6 h</th>
<th>7 to 12</th>
<th>13 to 23</th>
<th>24</th>
<th>48</th>
<th>72</th>
<th>96</th>
<th>120</th>
<th>144 to 198</th>
<th>193 to 384</th>
<th>385</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>4</td>
<td>48</td>
<td>216</td>
<td>260</td>
<td>796</td>
<td>274</td>
<td>98</td>
<td>61</td>
<td>61</td>
<td>87</td>
<td>71</td>
</tr>
<tr>
<td>Not normal</td>
<td>16</td>
<td>38</td>
<td>140</td>
<td>125</td>
<td>195</td>
<td>45</td>
<td>10</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Sum</td>
<td>20</td>
<td>86</td>
<td>356</td>
<td>385</td>
<td>991</td>
<td>319</td>
<td>108</td>
<td>68</td>
<td>65</td>
<td>94</td>
<td>75</td>
</tr>
<tr>
<td>%</td>
<td>20.0</td>
<td>55.8</td>
<td>60.7</td>
<td>67.5</td>
<td>80.3</td>
<td>85.9</td>
<td>90.7</td>
<td>89.7</td>
<td>93.8</td>
<td>92.6</td>
<td>94.7</td>
</tr>
</tbody>
</table>

Figure 1. Presence of Otoacoustic emissions according to age (hours of life)

Validities and Security of the EOE test

We were able to confirm these cases based on previous studies in which it had been demonstrated that the sensitivity of the test of EOE is 100%. The specificity of the first test was 77.49%, the predictive Positive Value (PV+) of 3.05 and the quotient of positive probability (QP+) of 4.44. The evolution of these parameters according to the age of the fulfilment of the test is reflected in Table 5. The specificity of the second test of EOE was 99.88, the predictive Positive Value (PV+) was 85.7 and the quotient of positive probability (QP+) was 84.8. This suggests that if the first test if “Not normal” the probability of being deaf is 3.05% while if the second test shows this, the clinical suspicion rises to 85.7%.

DISCUSSION

The coverage data from the remissions for study and diagnosis achieved amply the minimum criteria recommended for the test to be profitable as a selection one. The number of repetitions of the Otoacoustic emission test may be slightly elevated, 23 with respect to the 14% expected, owing to the acoustic conditions of the test (in the newborn’s own room) and the young age of many of the children. In the same way, the prevalence of hypoacusis (7 per 1000) is similar to that found in previous studies. In spite of the existence of publications in which better results are obtained in the right ear, justified by the fact that placing the probe in this ear is easier, in the present as in prior studies, it could not be demonstrated for the totality of the Otoacoustic emissions carried out. Conclusive results were not obtained when analysing the relation between the laterality of the ear and the gender.

The fact that females had better results (a greater percentage of “Normals”) for the first
with no differences in the repetitions, is probably due to the fact that they show a greater response in decibels having more Spontaneous Otoacoustic emissions at birth.

Despite the fact that the incidence of hypoacusis is 5.16 times greater in newborns with some RF (+) (value of positive prediction 3%), as the group that lacked them is greater (97% of the total newborns) in complete value the patients with hypoacusis belonged mainly to the group of children without risk. This justifies the carrying out of the detection universally, given that carrying it out only on children with risk factors would prevent the diagnosis of at least 50% of cases of deafness (72.2% of the deaf children in this study)

Nowadays, different hypotheses (none confirmed) that explain the absence of EOEs in some newborns are confused: lack of cochlear maturation, vernix caseosa in the EAC or amniotic liquid in the tympanic box. However, in practice, in the present study it was established that the older the child the better the result obtained in the first test of Otoacoustic emissions would be, showing a gradual improvement in the efficiency of the test up to the first month of age. We found similar tendencies in another two studies (Figure 3) where the rate for passing the first EOEs is compared according to age, although we obtain lower values of normal Otoacoustic emissions until they equalize on the 4th/5th day (above all in the first 24 hours being 67% as opposed to 85% in the Trinidad series).

In the same way, the age group 48-71 hours constituted the average value of the distribution of age of our newborns and best represented the age most advisable for the fulfillment of the first test of Otoacoustic emissions given the asymmetry of the sample distribution. It is therefore recommended that the test be carried out on newborns who are at least 48 hours, given that at this time, the prevalence of disability detected is 9.1%, the specificity is 81.1% and the percentage of false positives is considerably diminished at 18.94% (being 41.48% in those less than 24 hours and 31.68% in the 24 hours age group). It means, therefore, that the first test of EOEs must be carried out within the maternity period with the key objective being that the coverage of the test is profitable, but as late as possible before the hospital discharge in order to pick up the totality of newborns and thus obtain a greater efficiency in the test, whilst achieving the objectives of precision and efficacy.

Although there is great controversy with respect to the most adequate maximum point in time for carrying out the first test, a limited date within the first month does not exist that would yield a better result as it has been clearly shown that an increase in the age at which the test is carried out increases the likelihood of detection of the diagnosed illness, its predictive value + and ultimately its diagnostic efficiency with a diminishment of the number of false positives in the test. In any case, the establishment of this maximum period is of relative interest now that the objective of any protocol should include that no newborn leaves the hospital without undergoing a routine form of test. Equally, ensuring that special attention be paid to a
subsequent capture of those in whom, for different reasons, EOEIs were not detected on discharge from hospital, now that it is important to value the losses, because in more than 40% of them some risk factors exist and subsequent attempts at localisation were unfruitful.

Segui et al (14) assure that the detection of the EOEIs must be repeated should they not be obtained, since they probably return to normal. They do not determine exactly the interval of days necessary, although it is recommended that it be within the first month of life. To clarify this aspect is fundamental to forming a protocol for the fulfilment of the second test in those children with “Not normal” results in the first test, since the number of positivisations of EOEIs in this test justified its repetition prior to the fulfilment of the diagnostic study. In our case, the necessary time that had to pass for the positivisation of the second EOE test was approximately 6 days after carrying out the first test. We see that the age of the children that are positivised (according to the groups of fulfilment of the first test) moves in a wide range from 6-8 days in children less than 24 hours old up to 13 days in children older than 4 days. The increase is progressive in proportion to the age at which the first test was carried out being greater. This tendency maintains itself after assessing the possible distortion of the results by the groups of extreme age (Figure 2).

Therefore we conclude that:

- The use of a protocol of EOEIs and EAPCT combined for the premature detection of infantile hypoacusis is recommended.
- The age at which detection of EOEIs is carried out should be as late as possible before discharge from hospital, although not before the first 48 hours of life, anticipating a better result in females.
- In the case of not detecting EOEIs in the first test, the test should always be repeated, since the number the positivisations justifies it and the number of children that need to be submitted for a diagnostic test is thus reduced.
- A second test being necessary, the repetition of the test should be left until 6 days after the first attempt.
- Universal neonatal selection remains justified for a high number of deaf children, including those that do not have risk factors of hypoacusis.

In future studies, it would be desirable to try to determine why there is a lack of Otoacoustic emissions in some newborns and to establish some relation with the confused hypotheses to date (Vernix in the EAC, liquid in the box, neurological prematurity) in such a way that could help prevent the distress that is caused to the families of children with false positive results.

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REFERENCES