**Delayed Diagnosis of Childhood Deafness: The Value of False Negatives in the Programme for Early Detection of Neonatal Hearing Loss**

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**KEYWORDS**

Hearing loss; Otoacoustic; False negatives; Screening

**Abstract**

*Introduction:* Despite its importance, the existence of false negatives (patients who are told they hear well, but they have some degree of hearing loss) is rarely evaluated in programmes for early detection of hearing loss. The aim of this study is to determine the variables that can lead to a delayed diagnosis, especially the existence of false negatives and the lack of registration of risk factors.

*Methods:* A retrospective study of prevalence has been carried out, in which the medical records of children diagnosed with sensorineural hearing loss born within 2005 and 2012 in the health centres of study have been analysed.

*Results:* Of the 32 children with sensorineural hearing loss, 16 passed the OAE, 12 did not pass the OAE, and in four they were not carried out. Of the children who passed the OAE, 57% have severe hearing loss. 66% of children with hearing loss presented a risk factor for hearing loss at birth, being the most frequent family history of hearing loss, but only 7% of those with family history of hearing loss were included in the risk group.

*Conclusions:* The results of the study indicate that the late diagnosis of hearing loss is related to the presence of false negatives to the OAE and the non-registration of risk factors.

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PALABRAS CLAVE
Hipoacusia; Otoemisiones; Falsos negativos; Cribado

Retraso en el diagnóstico de sordera infantil: el valor de los falsos negativos en el Programa de Detección Precoz de Hipoacusias Neonatales

Resumen
Introducción: A pesar de su importancia, la existencia de falsos negativos (pacientes a los que se les dice que oyen bien, pero en realidad son hipoacúsicos) no suele ser evaluada en los programas de detección precoz de hipoacusia. El objetivo de este estudio es determinar las variables que pueden a llevar a un retraso diagnóstico, en especial la existencia de falsos negativos así como la falta de registro de factores de riesgo.

Métodos: Se ha realizado un estudio observacional retrospectivo de prevalencia, analizando las historias clínicas de los pacientes con hipoacusia neurosensorial nacidos entre 2005 y 2012 en las áreas de salud del estudio.

Resultados: De 32 niños con hipoacusia neurosensorial, 16 pasaron las OEA, 12 no pasaron las OEA y a 4 no se les realizaron. De los pacientes con hipoacusia pero que pasaron las OEA, el 57% tiene una hipoacusia severa y/o profunda. El 66% de los niños con hipoacusia presentaban algún factor de riesgo de hipoacusia, siendo los antecedentes familiares de hipoacusia el más frecuente, pero solo el 7% de los que tenían antecedentes familiares fueron incluidos en el grupo de riesgo. La tasa de pacientes falsos negativos en el estudio es muy elevada.

Conclusiones: Los resultados del estudio indican que el diagnóstico tardío de las hipoacusias infantiles en las áreas estudiadas está relacionado con la presencia de falsos negativos a las OEA y con la falta de registro de los factores de riesgo.

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Introduction

Hearing loss in children has implications for their emotional, academic and social development, as well as their capacity for acquiring language and speech. The debilitating potential of this disease is largely mitigated if it is diagnosed early and the appropriate treatment and rehabilitation is started promptly.1

Newborns with risk factors have an increased incidence of hearing loss, between 10 and 20 times higher than those with no risk factors. Similarly, between 50% and 75% of children with bilateral hearing loss equal to or above 40 dBHL have one or more risk factors.1 Up to 80% of hearing loss in the paediatric population already presents at birth or in the neonatal phase and around 95% occurs in children born to families with normal hearing.

Hearing loss screening was officially implemented in our community in 2004 and from then on every hospital with a mother and baby unit, whether public or private, has screened all newborns.

The recommendations of the Comisión para la Detección Precoz de la Sordera (Committee for the Early Detection of Deafness), are detailed in Table 1.2 Based on these recommendations, the objectives of the Programa de Detección Precoz de las Hipoacusias Neonatales en la Comunidad Autónoma (Programme for the Early Detection of Neonatal Hearing Loss in Autonomous Communities) are2:

1. To detect hearing disorders in all newborns in the Region of Murcia in the first month of life.
2. To diagnose any hearing disorder before three months of life.
3. To establish treatment for all children who have been diagnosed with hearing loss before six months of life.

Detecting patients with risk factors is essential in the programme, because there is a greater prevalence of hearing loss in these patients. They should be easy to register and the main risk factors are well known. The fact that a patient has a hearing loss risk factor makes it necessary to use another test in addition to otoacoustic emissions.

Furthermore, the existence of false negatives (patients that pass otoacoustic emission tests but in fact have hearing loss) in the screening programme might result in a significant delay in diagnosis, due to a false sense of security that the patient has passed the first test successfully.

Numerous assessments have been made of the programmes for the early detection of hearing loss in the different autonomous regions of Spain. In the great majority, the main indicators analysed are coverage, false positives and follow-up in the different phases of the screening programme until diagnosis and in the treatment and rehabilitation stages.3-9 However, we have found no study that analyses the rate of false negatives in the Spanish programme, although one mentions their possible existence,10 confirming that half the diagnostic centres acknowledge that they have encountered late cases of hearing loss that had achieved a “PASS” in the initial hearing screening.

We found one article that precisely studies a series of cases of children with sensorineural hearing loss despite having passed the hearing screening test. The study undertaken in Pennsylvania (U.S.A.)11 analysed the clinical histories of 923 children with sensorineural hearing loss diagnosed between 2001 and 2011, amongst whom 78 (8.5%) had passed
the screening but were diagnosed with hearing loss subsequently. The study’s conclusions mention the real possibility of there being false negatives in early screening for newborn hearing loss, and the false sense of security given to both the family and healthcare staff when the newborns pass the screening, overlooking other signs of hearing loss and delaying diagnosis.

We start from the hypothesis that a great many delays in diagnosis and treatment of these patients are due to false negatives and a failure to detect risk factors. The objective of this study is to demonstrate this.

Method

A retrospective, descriptive, observational study of prevalence was undertaken.

In order to obtain our study population, we reviewed the clinical histories of all the children with sensorineural or mixed hearing loss, from moderate to profound in at least one ear, born in the study’s health areas between 2005 and 2012.

Three main sources were used to locate the study population:

1. A search was carried out in the database of the Programa de Detección Precoz de las Hipoacusias Neonatales, identifying all children that had passed the diagnostic phase. This search found 13 children, of whom 3 were excluded because in the end they did not have hearing loss.
2. The BAEPs results were checked. This list provided 18 children with pathological BAEPs and suspected sensorineural hearing loss.
3. The clinical histories were reviewed of all the children who attended the Association of Parents of Children with Hearing Disabilities diagnosed with sensorineural hearing loss. This review provided a total of 25 children, of which 16 were regularly followed-up in the Association. In order to collect these 16 children’s data their families were interviewed after giving their informed consent.

Once the data on all the children had been gathered, they were triangulated, because there were matching and insufficient data in the different series. Eventually a total of 32 candidates for the study was achieved.

From the information gathered, the frequencies of the basic variables and statistics were gathered as the mean and the mode. The Chi-square test was used to study the main qualitative variables or Fisher’s exact test for a statistical significance of P<.05.

The study was undertaken in compliance with current legislation. Acceptance of the project was requested from the Ethical Committee for Clinical Research of the areas studied and was granted. The study subjects who were interview signed informed written consent, which forms part of the study, in compliance with the principle of patient autonomy.

Results

The clinical histories of 32 patients with moderate, moderate-profound and profound sensorineural hearing loss, of whom 21 (66%) were boys and 11 (34%) were girls.

Ninety-four percent of these children were born to parents with normal hearing. Only 2 of them were the children of deaf parents.

In the sample, a mean of 4 cases was diagnosed annually. The greatest frequency of cases was in 2007 with 8 cases, and the the fewest cases were in 2009, with only one case.

The 32 cases included 13 with moderate, 10 with severe and 9 with profound hearing loss. With regard to the treatment used, of the 32 children, 26 used hearing devices and 6 and did not (the 5 cases of unilateral loss and one case of moderate loss associated with a syndrome of unknown origin resulting in severe cerebral paralysis who refused a hearing aid). Of the 26 who used hearing devices, 18 used a hearing aid, 2 used a hearing aid and a cochlear implant, 4 used a cochlear implant alone, one used 2 cochlear implants and one used a bone-anchored implant (26% of the children with bilateral hearing loss), compared to the 66% who used hearing aids.

The total coverage of the health areas of the study between 2005 and 2012 was 86.37% (33,593 of 38,895 newborns).

Eighty-seven point five percent of the children (28 out of the 32) underwent OAE at birth and the remaining 4 did not (12.5%). Those who underwent OAE, 12 did not pass the test, i.e., 43%, whereas 16 achieved a normal result (pass), representing 57%.

Of the 12 that did not pass the otoacoustic emissions test 10 underwent BAEPs, 100% obtaining an altered result and therefore entering the diagnostic phase. One of these 10 did not attend the diagnostic appointments, and was subsequently diagnosed with hearing loss at 39 months. The 2 children who did not undergo BAEPs consulted later with suspected hearing loss and were diagnosed at 16 and 23 months respectively. The mean age of diagnosis of the children who did not pass the otoacoustic emission tests was 10 months (with a range of between 2 and 39 months). If we remove the 2 children who did not undergo the screening BAEPs and the child who did not attend the appointments, the mean age of the remaining 9 children was 5 months.

Of the 16 children who achieved a normal result in the OAE, 7 had risk factors for hearing loss, but only one

<table>
<thead>
<tr>
<th>Table 1 CODEPEH Recommendations for an Effective Early Screening Programme.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To study both ears in at least 95% of all live newborns</td>
</tr>
<tr>
<td>2. To detect all cases (or at least 80%) of bilateral hearing deficit above 40 dBHL</td>
</tr>
<tr>
<td>3. Rate of false positives equal or below 3% and 0% rate of false negatives</td>
</tr>
<tr>
<td>4. Remission rate for audiological study and confirmation of diagnosis below 4%</td>
</tr>
<tr>
<td>5. A definitive diagnosis and intervention should be made at no later than six months of age</td>
</tr>
</tbody>
</table>
underwent BAEPs, achieving an altered result and diagnosed with profound hearing loss at 2 months of life; hearing loss of unknown origin as an auditory neuropathy despite positive otoacoustic emissions.

Of the remaining 15 with a normal result, 3 developed early infancy risk factors subsequently (one case of bacterial meningitis, one case of severe nosocomial sepsis and one syndromic hearing loss diagnosed at one year old). BAEPs were performed on the first 2 cases on detecting the risk factors and were diagnosed with hearing loss. The third case consulted 2 years later with suspected hearing loss and was diagnosed at that time.

Of the 12 children with positive OAE (37.5% of the total), 6 had a family history of deafness that was not recorded during screening. None of them developed new hearing loss risk factors, all of them consulted because their families suspected the condition. The mean age at which the children were diagnosed who passed the otoacoustic emissions test and who did not develop early infancy risk factors was 39 months (with a range of 17–69 months). As yet no case with a diagnosis of auditory neuropathy has been confirmed.

Of the 4 children (100% males) who did not undergo otoacoustic emissions testing at birth, one developed a hearing loss risk factor (bacterial meningitis) and hearing loss was diagnosed immediately afterwards, the other three consulted with suspected hearing loss. The mean age of diagnosis amongst the children who underwent otoacoustic emissions testing at birth and who had no infancy risk factors was 61 months (with a range from 52 to 72 months). Two of them had a family history of hearing loss.

The risk factors are detailed in Table 2.

Seven cases in total (6 boys and 1 girl) presented no risk factors at birth in infancy, which represents 22% of the total cases (9% of the girls and 29% of the boys). One of them did not undergo OAE at birth, of the remaining 6, 5 had positive otoacoustic emissions and were discharged from the programme without completing the AEPs stage, another child did not pass the otoacoustic emissions test and underwent BAEPs which gave an altered result.

The aetiology of hearing loss is unknown in 56% of cases. The known and presumed aetiologies include: 4 cases of genetic, syndromic hearing loss, 3 genetic, nonsyndromic cases, one case of congenital malformation, 2 cases of perinatal hypoxic episodes and one case of hyperbilirubinemia.

The mean age of the patients at the time of diagnosis is shown in Table 3.

Table 4 shows the errors in implementing the programme, where the high percentage of false negatives is striking.

Discussion

As in most studies, we found more boys than girls with hearing loss. In our case, 66% compared to 34% respectively, these percentages are very similar to those found in studies such as that published in Chile in 2009, in which the percentage of males was 70%.

As national statistics show when they refer to 90%, in this study 96% of children with hearing loss are born to parents with normal hearing.

With regard to moderate hearing loss, the incidence found is also lower than expected (0.95/1000 nv compared to the expected 3/1000 nv). In this case it is possible that there are children with undiagnosed moderate hearing loss, without complete clinical histories or diagnosed in private hospitals and who have not been included in our study.

It is estimated in the white paper on hearing loss that 40% of cases with severe or profound hearing loss would be candidates for cochlear implants. In our population we found a similar percentage, since 36.84% of the cases with severe/profound hearing loss had a cochlear implant (7 out of 19 cases).

In terms of aetiology, it is considered that epidemiologically, at least 50% of profound hearing loss cases in the paediatric population are of genetic origin, 20%–24% are not genetic and 25%–30% are of unknown origin. In our sample we find similar results since 50% of the cases of profound hearing loss were of genetic/hereditary origin, 37% were of

**Table 2** Summary of Hearing Loss Risk Factors Encountered and Recorded.

<table>
<thead>
<tr>
<th>Type of risk factor</th>
<th>Boys</th>
<th>Girls</th>
<th>Total</th>
<th>Relative frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors at birth</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>10</td>
<td>5</td>
<td>15</td>
<td>65%</td>
</tr>
<tr>
<td>Cranial malformations</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9%</td>
</tr>
<tr>
<td>Apgar &lt;4 in 1’ or &lt;6 in 5’</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>9%</td>
</tr>
<tr>
<td>Syndromic hearing loss</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>9%</td>
</tr>
<tr>
<td>Hyperbilirubinaemia</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>8</td>
<td>23</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Infant risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspected hearing loss</td>
<td>15</td>
<td>4</td>
<td>19</td>
<td>73%</td>
</tr>
<tr>
<td>Chronic or recurring otitis</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>12%</td>
</tr>
<tr>
<td>Bacterial meningitis</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>8%</td>
</tr>
<tr>
<td>Ototoxic agents</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td>Syndromic hearing loss</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>6</td>
<td>26</td>
<td>100%</td>
</tr>
</tbody>
</table>
exogenous origin, acquired, and the remaining 13% were of unknown cause.

Of the 32 patients detected, 4 did not undergo OAE. This fact is not acceptable in a universal screening programme and could be explained by the child having been born at a weekend, the OAE equipment being under repair and not replaced, a failure of the patient to attend their appointment after early discharge of the mother, or the patient failing to attend the test. Of the 28 who did undergo the test, 12 did not pass and entered the protocol resulting in a diagnosis of hearing loss in 100%. However, of the 16 that passed, there were 7 with risk factors, who should have undergone BAEPs and only one of them did. Out of another 15 patients, 3 developed risk factors subsequently, but out of the remaining 12, 6 had a family history of hearing loss which was not recorded and they were not followed up, with the consequent delay in diagnosis, therefore it is a fault of the programme that these risk factors were not taken into account.

There are three main causes of false negatives (patients who are thought to be able to hear because they pass the otoacoustic emissions test, and yet have hearing loss): auditory neuropathy is the first, although late onset hearing loss should also be considered and progressive hearing loss which would not present at birth. Most studies accept that this group could represent between 10% and 20% of cases of sensorineural hearing loss in infancy.13,14

In this study, 46% (n=28) of the cases who underwent OAE obtained a non-pathological result (PASS) and no triggering causes were recorded in their clinical histories to explain subsequent hearing loss. The only case that underwent AEPs early, was diagnosed with profound deafness. None of the 13 cases were diagnosed with auditory neuropathy.

Thus, this 46% of false negatives encountered in our study population is very much higher than expected (10%–20%) and that described in the studies we found (0% [13], at 8.5% [10]) false negatives.

According to González de Dios, hearing loss that escapes diagnosis at neonatal screening (FN) might be due to an incorrect interpretation of the test, to late-onset hearing loss, progressive hearing loss or post-natal acquired hearing loss. These possibilities might be minimised by involving primary healthcare professionals in hearing loss detection through health screening.15

In the framework of this study we cannot state whether we are witnessing a greater incidence of late onset and/or acquired neonatal hearing loss, auditory neuropathies which have not been diagnosed as such or incorrect interpretation of the otoacoustic emissions test. This could be the subject of other studies which could analyse this circumstance in depth, which is clearly beyond what would be expected.

The studies we consulted indicate that in circumstances where a universal screening programme is not applied, the mean age at which hearing loss is diagnosed would be around the age of 3 years (36 months), whereas with universal screening severe/profound hearing loss can be identified at a mean age of 9.2 weeks (2.2 months) and moderate hearing loss at a mean age of 12.9 weeks (3.01 months).14

In our study, the mean age of diagnosis is 26.5 months, and is 22.23 for severe/profound hearing loss and 31.33
months for moderate hearing loss. These figures are very close to those found in contexts where universal screening is not applied.

In the population studied, 66% of cases presented a hearing risk factor at birth, which coincides with Moro and Almenar.\(^\text{34}\) Although in our study the real coverage only reached 16% of children identified with a hearing risk factor; the risk factors were recorded subsequently, once hearing loss had been diagnosed. None of the screening programme assessments we consulted in the different autonomous regions\(^\text{5-8}\) evaluated the rate of false negatives, this being a key indicator in establishing the true success of the programmes. Most of these assessments attach great importance to the percentage of false positives, but, without wanting to play down the importance of the impact that a false positive has on the families, we believe that the impact of a false negative is much greater and more serious, because, as has been seen, it results in a great delay in diagnosis and a poorer prognosis for the development of linguistic skills.

Given all of the above, we believe that the assessments of early hearing loss screening programmes should include this indicator as recommended by the Committee for the Early Detection of Deafness,\(^\text{3}\) for which measures will need to be set up to enable the systematic uptake of these children by the screening programme. Bearing in mind that they can be diagnosed in any hospital, clinic or surgery, it should be made compulsory to declare all hearing loss to the child’s birth hospital or the reference unit of the autonomous region.

Conclusions

The results of the study indicate that, in the study population, the late diagnosis of hearing loss is associated with the presence of false negatives from OAE testing and recording hearing loss risk factors. A high percentage of false negatives was detected, poor coverage of the screening programme and under-recording of hearing loss risk factors.

It is evident that the results of the screening programme over the years covered by the study is far from achieving the objectives set with regard to the mean age of diagnosis and consequent inclusion in the treatment and rehabilitation phase, with all the consequences for the future development of these children that this delay implies.

Conflict of Interests

The authors have no conflict of interests to declare.

References