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Research Article

Long-Term Auditory Follow-Up of Preterm Infants after Neonatal Hearing Screening

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Abstract

Background

Since introduction of neonatal Automated Auditory Brainstem Response (AABR) hearing screening in Neonatal Intensive Care Unit (NICU) graduates, Hearing Loss (HL) is established during the first few months of age. The diagnostic Auditory Brainstem Response (ABR) is used as the gold standard in establishing HL after birth. Aim of this study was to investigate the predictive value of better ear ABR findings at three months Post Term Age (PTA) in preterm infants with bilateral Sensori Neural (SNHL) or Conductive Hearing Loss (CHL). In Preterms with bilateral Auditory Neuropathy Spectrum Disorder (ANSD) the predictive value of Visual Reinforcement Audiometry (VRA) was investigated.

Methods

Outcome data of graduates of a level III NICU, who didn't pass AABR neonatal hearing screening between 2004-2016 were analyzed retrospectively. At follow-up type and hearing level of graduates with bilateral HL was established. Hearing level was investigated at the age of two years using VRA and at four and eight years of age using play-audiometry. The Two One-Sided Tests equivalence procedure for paired means was applied with the magnitude of the region of similarity equal to 10dB.

Results

In all 32 cases ABR at three months PTA correctly predicted the final type of HL. In 8 SNHL children initial ABR was equivalent with the four and eight year's play-audiometry ($p<0.05$). In eight SNHL and 15 ANSD children,VRA levels didn't reflect significantly play-audiometry levels. Almost all cases (89%, N=8/9) with non-syndromic CHL recovered properly.

Conclusion

ABR of the better ear at three months PTA in preterm reliably seems to predict all types of HL in later childhood as well as the hearing level in children with SNHL at follow-up. In case of ANSD the VRA was not predictive for the severity of HL at follow-up. Further research is necessary to substantiate these findings in preterm infants.

Keywords: Auditory brainstem response; Follow-up; Hearing Loss; Preterm Infants

Abbreviations

SNHL - Sensori Neural Hearing Loss
CHL - Conductive Hearing Loss
ANSD - Auditory Neuropathy Spectrum Disorder
PTA - Post Term Age
TOST - Two One-Sided Tests
AABR - Automated Auditory Brainstem Response
ABR - Auditory Brainstem Response
NICU - Neonatal Intensive Care Unit
HL - Hearing Loss
VRA - Visual Reinforcement Audiometry
IVH - Intra Ventricular Hemorrhage
NEC - Necrotising Entero Colitis

Introduction

When Hearing Loss (HL) is diagnosed in the neonatal period it is essential that interventions are started as early as possible. This enables early habilitation, including guidance of parents and fitting of hearing aids, cochlear implants or bone-conduction devices at an early age. This can help the child with normal speech and language acquisitionwhich leads to improved school achievement, self-esteem and psychosocial adaption [1,2].

A two-step Automated Auditory Brainstem Response (AABR) neonatal hearing screening program was gradually introduced in all Neonatal Intensive Care Units (NICU) in the Netherlands between 1998 and 2001 as a first step towards nation-wide neonatal hearing screening [3]. After repetitive referral, audiological diagnostic tests were performed at a Speech and Hearing center to establish neonatal HL as soon as possible,with in three months Post Term Age (PTA). This correction for gestational age is extremely relevant, especially in NICU graduates with an extremely low gestational age. Besides the fact that the stage of the ontogenetic development is related to the duration of pregnancy it is reported in literature that the ongoing process of myelination of the auditory pathway may be delayed or deviant in infants who are born prematurely [4-6]. Therefore, we want to investigate the predictive value of the initial diagnostic ABR findings in the better ear at three months PTA versus the Visual Reinforcement Audiometry (VRA) results at two years and the play-audiometry results at four and eight years of age, with regard to the type and severity of bilateral HL.

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Methods

Outcome data from graduates of a single center level III NICU who did not pass AABR neonatal hearing screening between 2004-2016 were retrospectively analyzed. Although the NICU hearing screening program was established in 2001, it is only since 2004 that all the procedures and measurement protocols are standardized and well documented. Auditory retesting was performed at approximately three months PTA in two dedicated referral Audiological Centers (Pento Speech and Hearing Centres Zwolle and Hengelo, the Netherlands). This included an extensive diagnostic ABR, Oto-Acoustic Emissions (OAE) and impedance audiometry, to diagnose the severity and type of HL. During follow-up VRA and play-audiometry were used to investigate possible progression of HL. The quality and timing of this program is guaranteed by the central regulation and registration of data at the Department of Child Health, TNO, Leiden, The Netherlands [7]. For this study, auditory follow-up data were collected from NICU graduates with established bilateral HL at approximately three months PTA. The data included the results of impedance audiometry, OAE, diagnostic ABR, VRA at two years, and play-audiometry at four and eight years of age. Informed consent (oral) was obtained from the parents or legal guardians of all participating patients. This study was approved by the Medical Ethics Committee of the Isala Hospital, Zwolle, The Netherlands (reference number 190508).

Types of hearing loss

For this study, a distinction is made between Conductive Hearing Loss (CHL), Sensori Neural Hearing Loss (SNHL) and Auditory Neuropathy Spectrum Disorder (ANSD).

Diagnostic audiological tests

ABR: Auditory brainstem response audiometry reflects the neuronal activity between the cochlea and the brainstem in response to acoustic stimuli [8]. Interacoustics Eclipse EP15 (Interacoustics A/S, Middelfart, Denmark) was used to measure the ABR responses.

VRA: Visual Reinforcement Audiometry (VRA) is based on the orientation reflex towards a new sound source. It is a subjective auditorytest that requires cooperation of the child and parents. Interacoustics Affinity/AC440 was used (Interacoustics A/S, Middelfart, Denmark) to present the acoustical stimuli.

Play-audiometry: Play-audiometry is an auditory examination of children based on conditioned responses. The child is taught to perform an action only when he or she hears a sound. The test determines the minimal intensity of a warble tone at least at 0.5, 1,2 and 4 kHz at which the child is able to detect the stimulus [9]. The tones were presented through a headphone/insert earphone and a bone-conductor. The bone-conductor was placed on the mastoid bone thus obtaining a pure tone audiogram. Interacoustics Affinity/AC440 (Interacoustics A/S, Middelfart, Denmark) was used to present the acoustical stimuli.

Statistical analysis

For this study, the difference between the better ear ABR level at three months PTA and the betterear at play-audiometry (at four and eight years) or the difference between VRA (at two years) and play-audiometry (at four and eight years) was investigated.

R Version 3.5.1 with library equivalence was used for statistical analysis. The Two One-Sided Tests (TOST) equivalence procedure for paired means was applied with the magnitude of the region of similarity equal to 10dB. The null hypothesis was that the differences in mean dB levels for the different tests were not equal. P-values <0.05 were considered significant.

Within the group of patients with etiologically temporary conductive HL we defined the ABR level to be predictive if at least 75% have normal hearing (<35dB) on the play-audiometry (at four and eight years).

Results

A total of 62 NICU graduates failed neonatal AABR screening of which 59 (N=59/62) bilaterally and three (N=3/62) unilaterally (Figure 1). All three graduates with unilateral AABR failure had no HL at diagnostic testing.

Long term follow-up data were available for 34 (N=34/59) newborns with diagnosed bilateral HL at a PTA of three months. In 14 (N=14/59) no HL was diagnosed and in 11 (N=11/59) the follow-up dataset was in complete due to referral to Speech and Hearing Centers outside the region.

The type and severity of bilateral HL could be diagnosed in 34 NICU graduates: Nine (N=9/34) had CHL, eight (N=8/34) had SNHL, 15 (N=15/34) had ANSD and two (N=2/34) had a combination of ANSD and SNHL.

In this study the last two patients with combined HL were not included in the results, leaving follow-up data of 32 infants for analysis (Table 1).

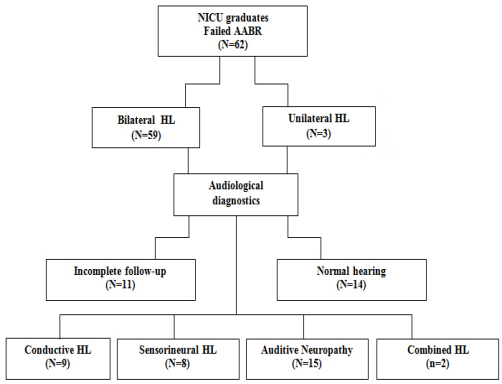

Figure 1: Study enrollment.

Characteristics	NICU graduates N = 32
Gestationalage, mean, weeks	32 (24 - 41)
Birthweight, mean, grams	1912 (665 - 4210)
Gender, male, number (%)	17/32 (53)
Hospitalization NICU, mean, days	29 (1 - 78)
Mechanicalventilation, number (%)	24/32 (75)
Mechanicalventilation, mean, days	9 (1 - 34)
IVH, number (%)	11/32 (34)
NEC, number (%)	1/32 (3)
Sepsis (bloodculture proven), number (%)	5/32 (16)
IVH: Intraventricular Hemorrhage NEC: Necrotizing Enterocolitis.	

Figure 1: Indicates the baseline characteristics supplemented with perinatal risk factors for HL in NICU graduates.

Overall, at follow-up there was no change in type of HL in 32 (100%, N=32/32) NICU graduates. Figures 2, 3 and 4 show the follow up results for each type of HL in box plots.

Sensori Neural hearing loss

In the eight SNHL graduates the observed differences in means between the ABR level at three months PTA and play-audiometry level at four years of age fell within the equivalence bounds of 10dB and was therefore considered practically equivalent, because both one-sided tests were statistically rejected (p=0.036). Similar conclusion could be drawn from the ABR level with the play-audiometry level at eight years of age (p=0.036).

In contrast, the observed differences in means between the VRA level at two years of age in the SNHL group and play-audiometry level at four and eight years of age did not fall within the equivalence bounds of 10dB (resp. p=0.34 and p=0.41) (Figure 2).

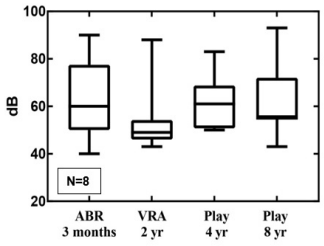

Figure 2: The follow-up results for SNHL in boxplots.

Auditory neuropathy spectrum disorder

The most common diagnosis in our study population was ANSD (N=15/32). In accordance with the definition of ANSD, ABR hearing levels at a PTA of three months could not be set in this patient group. The observed differences in means between the VRA level at two years of age and play-audiometry level at four and eight years of age did not fall within the equivalence bounds of 10dB and was not considered practically equivalent, because both one-sided tests were not statistically rejected (resp. p=0.21 and p=0.93). In eight (53%, N=8/15) children with ANSD VRA hearing levels were better (>10 dB) compared to play-audiometry levels at four and eight years of age (Figure 3).

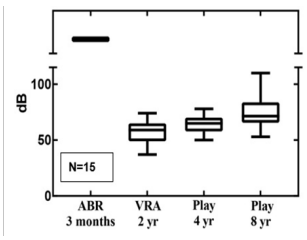

Figure 3: The follow-up results for ANSD in boxplots.

Conductive HL

In almost all cases (89%, N= 8/9) with non-syndromic CHL, the HL recovered below 35dB according to the VRA and play-audiometry at four or eight years of age (Figure 4).

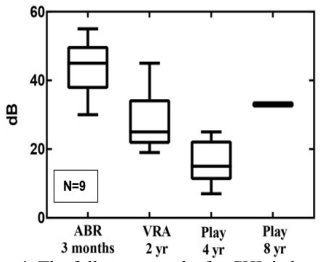

Figure 4: The follow-up results for CHL in boxplots.

Discussion

In this preliminary study the long-term follow-up results at four and eight years of age of NICU graduates after neonatal established HL showed that the initial ABR at the PTA of three months was accurate in predicting the final stage of all types of HL.

In NICU graduates with SNHL the initial ABR and not the VRA was significantly accurate in predicting the severity of HL at four and eight years of age.

ANSD was set as no response at all above a stimulus level of >90dB while OAE's and/or cochlear microphonics are present. Therefore no level of HL could be established by definition at three months PTA from ABR in children with ANSD. Also in this ANSD groupVRA results showed unequal dB levels with play-audiometry at four and eight years of age. In 53% of these children VRA levels were >10dB better than play-audiometry. This means that hearing levels-established by VRA were not predictive for hearing levels at four and eight years follow-up.

None of the children with CHL had congenital malformations in the auditory pathway. Nearly all cases recovered from a probably temporary CHL. In one case, CHL was mild and persistent without deterioration due to a chronic middle ear infection.

These findings are of importance in the process of parental guiding. In the SNHL group ABR findings at three months PTA supports future hearing type and level findings while in children with ANSD uncertainty about the level of HL is long lasting.

To our best knowledge this is the first study that takes the PTA of the preterm infant at the time of the initial diagnostic ABR into account as a more physiological milestone for the premature new born when investigating long-term follow-up results. Due to the recent introduction of neonatal hearing screening, follow-up studies are limited and mostly refer to a (near) term population of newborns. The follow-up period in these studies ranges from six months to six years of age [5,6,10-15]. This study is unique in its insight into data after a lengthy follow-up period, i.e. four and eight years. These follow-up data were related to the PTA of three months which is in terms of pathophysiology more suitable to very preterm newborns. The diagnostic ABR is used as the gold standard in establishing HL after birth [4]. From literature it is known that in premature infants the ongoing process of myelination of the auditory pathway is delayed or alterated [5,6,16-18]. Eventually the maturational delay catches up at the postconceptional age of 40-42 weeks, which is normally the full-term age of healthy newborns [16-18]. Coenraad, et al., showed a prolonged I-V interval at ABR, combined with normal ABR thresholds,

which declined with an increased postconceptional age referring to a maturational delay in the auditory pathway [4]. The study of Sleifer, et al., confirms these findings with an inverse correlation between gestational age and ABR interpeak latencies I-III, I-V and III-V with gestational age [5]. Jiang, et al., also found that the maturation in central regions of the brainstem is faster compared to the peripheral regions in preterm infants [6]. Other studies also showed that in preterm infants, <28 weeks of gestation, there is an improvement in HL up until the age of 40 weeks post-term, suggestive of maturational problems of the auditory pathway [17]. The study of Vohr, et al., supports this data [18].They observed that even in the absence of brain injury there are alterations in maturation and vulnerability of the brain as a consequence of premature birth leading to structural changes within the brain. For these reasons follow-up data in this study were related to the PTA of three months which seems to be proper in the SNHL (very) preterm newborns.

The play-audiometry results at four and eight years of age reflect the most objective stage of HL in the child. The less severe hearing level thresholds at VRA in comparison with play-audiometry levels in the ANSD group may raise questions.The subjective character of the interpretation of the VRA test might possibly bean explanation for the different results between VRA and play-audiometry hearing levels. Another explanation could be a more progressive character or a more heterogeneous course of ANSD in NICU graduates. Robertson et al. concluded earlier in 2002 that NICU graduates with severe respiratory failure frequently developed late-onset progressive ANSD without a clear explanation for this phenomenon [19]. One can also argue that the more positive results of VRA are partly consequence of the altered or delayed maturation of the brain [5,6]. This study does not support an ongoing deterioration reflected by stable play-audiometry levels between four and eight years of age in children with ANSD. Gardner-Berry, et al., followed twelve infants with ANSD until the age of two years. They found that a reliable VRA was difficult to obtain and resulted in a time delay in further audiological management [15].

Limitation of this study is the limited number of included newborns. We realize there was no sufficient statistical power to detect a lack of difference. Though, the initial results were encouraging for extending this study.

We conclude that the preliminary findings in this study suggests that in NICU graduates ABR of the better ear at three months PTA reliably predicts the type and severity of HL at four and eight years of age in children with SNHL. In the group of children with ANSD VRA levels were lower and not predictive for the severity of HL at four and eight years of age with play-audiometry. These initial results warrant more future research in a larger study group to substantiate reliable predictions with greater precision of the severity of HL in relation to the initial findings at the young age in very preterm NICU graduates to support early intervention and adequately rehabilitation.

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