Brain-stem auditory evoked potentials in at-risk infants and follow up assessment in Sri Lanka

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Abstract

Background: The effect of various risk factors on hearing impairment (HI) in infants has not been studied extensively in Sri Lanka until now.

***Objectives*:** To determine the influence of perinatal risk factors on the brainstem auditory evoked potentials (BAEP) in infants in Sri Lanka and to assess the follow up BAEP waveforms of infants with elevated hearing thresholds after 6 months.

Method: We recorded BAEP waveforms of 100 eligible at-risk infants using auditory click stimuli. Prematurity, prolonged neonatal intensive care unit (NICU) stay >5 days, very low birth weight (VLBW), hyperbilirubinaemia, ototoxic medications, mechanical ventilation, meningitis and sepsis were the perinatal risk factors considered. Risk factors of HI were determined using multiple logistic regression modeling. We did a follow up assessment after 6 months in 26 infants with elevated hearing thresholds and compared the data of the two assessments.

Results: Prematurity (odds ratio: 3.08, 95% CI: 1.05-9.04, p=0.04) and prolonged NICU stay (odds ratio: 3.67, 95% CI: 1.00-13.49, p=0.05) were the significant risk factors for developing HI as indexed by increased BAEP threshold levels. Seventeen out of 26 infants attended the follow up study and five improved.

Conclusions: Prematurity and prolonged NICU stay were the statistically significant risk factors for developing HI as indexed by increased BAEP threshold levels.

(Key words: BAEP, Hearing impairment, Prolonged neonatal intensive care unit stay, Prematurity)

Background

Hearing impairment (HI) in children is a complex condition with many medical and social consequences. If not detected early, it can impair speech and language acquisition, social and emotional development of a child. According to the Joint Committee on Infant Hearing (JCIH), the risk indicators associated with hearing loss in childhood include neonatal intensive care unit (NICU) stay of more than 5 days, mechanical ventilation or extra-corporeal membranous oxygenation, ototoxic medications, hyperbilirubinaemia that requires exchange transfusion, in-utero infections, cranio-facial anomalies, culture-positive postnatal infections, caregiver concern, head trauma, family history, neurodegenerative disorders and chemotherapy[1]. Prematurity (<37 gestational weeks) and very low birth weight (VLBW) (<1.5 kg) are also known associations of HI[2,3]. It is also recommended to screen infants with early hyperbilirubinaemia requiring treatment or hyperbilirubinaemia at any day of life requiring either intensive phototherapy or exchange transfusion[4].

Brainstem auditory evoked potential (BAEP) testing is a non-invasive electrophysiological technique that assesses the functional integrity of the subcortical auditory pathways. It is the mainstay of investigating HI in high-risk infants, and is used to confirm the diagnosis in universal hearing screening[5]. In settings where universal hearing screening is not possible, WHO recommends screening of targeted populations with risk factors[6]. Sri Lanka is a low middle-income country where electrophysiological testing facilities are limited. This precludes screening all infants, making it necessary to identify at-risk infant groups. An extensive study in this regard has not been carried out in Sri Lanka until now. Therefore, the results of this study would be beneficial when

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implementing guidelines for hearing screening programmes in resource limited settings like Sri Lanka in the future. It is well documented that most of the congenital defects and developmental delay conditions are highly associated with hearing defects in children. But the risk of the other factors for hearing defects is still not well established. Therefore, it is beneficial to evaluate such risk factors for occurring hearing defects. Also congenital disorders due to genetic factors which are responsible for nearly 40% of childhood hearing loss cannot be prevented[7]. World Health Organization (WHO) estimates that about 60% of hearing loss is due to preventable causes which include the risk factors which we have considered[7]. Therefore it would be more beneficial to find out the association between more modifiable risk factors rather than factors which cannot be easily modified. Therefore we have considered the infants with perinatal risk factors without congenital disorders and developmental delay in our study.

Timing and number of follow up assessments for children with risk factors should be customized and individualized depending on the risk factors[1]. Hence, early and more frequent assessments may be indicated for children with some risk factors. However, even if an abnormality is detected in the early part of infancy, BAEP latencies can improve within the first year of life. Many studies have shown the importance of administration of follow-up hearing tests as the hearing thresholds of infants with sensorineural hearing loss can improve during the first year of life[8-10].

Objectives

1. To determine the perinatal risk factors for developing hearing defects, as indexed by BAEP, in infants referred to a tertiary care hospital in Sri Lanka.
2. To assess the follow up BAEP waveforms in infants with initially elevated hearing thresholds 6 months after initial assessment, to determine any improvement or deterioration.

Method

Study design, setting and participants

This was a cross sectional descriptive study with a follow up component of infants who had elevated hearing thresholds at the initial assessment. This study was carried out at the Neurophysiology Department, Teaching Hospital Peradeniya, a tertiary care hospital in Sri Lanka. The Neurophysiology Department receives referrals from paediatric units in the country with a provisional diagnosis of risk factors for developing hearing defects. Data were collected from November 2009 to February 2013 including the follow up component. We tested 100 infants. Mean age was 3.4 ± 2.2 months (range: 0.5-12 months). Sixty-one infants were ≤3 months of age at the initial assessment.

The sample for the study group was drawn from infants referred to the Neurophysiology Unit, for assessment of hearing. Sample size calculation was done using Epinfo version 6, Nov 1993, Statcalc programme. Given the population size taken was 7000 (number of babies born at Teaching hospital, Peradeniya per year referring to the data of monthly perinatal meetings conducted at the hospital), expected frequency 15%, worst acceptable frequency 8% and a confidence interval of 95%, the expected sample size was 99, which we rounded up to 100.

Clinically suspected septicaemia and/or meningitis, hyperbilirubinaemia which needed exchange transfusion or phototherapy, prematurity (<37 weeks of gestation), VLBW (<1.5 kg), exposure to ototoxic medications like gentamycin and loop diuretics, prolonged NICU stay (>5 days) and exposure to mechanical ventilation were the risk factors that we considered.

In this study the infants with only acquired risk factors present at birth or soon after birth were included. Those with congenital anomalies, syndromes and having any features of developmental delay or regression were excluded. Of the 100 infants that we assessed initially, 26 with elevated hearing thresholds underwent a follow up assessment after 6 months.

Procedure

Background information: Before the BAEP test, risk factors were noted down as per provisional diagnosis of the referring paediatrician. Demographic data were collected from the parent or guardian of the infant using an interviewer-administered structured data sheet. All the investigation findings and treatment details were also recorded using the clinical records.

Assessment of hearing using BAEPs: After the above interview, infants were subjected to neurophysiological assessment of hearing using BAEP. Medtronic evoked potential machine (Denmark) was used to produce auditory stimuli and to record and average the BAEP waveforms. As per guidelines of American Clinical Neurophysiology Society, we used click stimuli for our study[11]. The machine is being calibrated annually according to the standards by obtaining the BAEP tracings in an infant or a person who has "normal" hearing to verify the calibration. Initially the infants were sedated with the chloral hydrate

administered at the paediatric ward, Teaching Hospital, Peradeniya. Background noise and distractions were minimized. Recording technique conformed to the International Federation of Clinical Neurophysiology (IFCN) guidelines[12].

BAEPs were recorded using an electrode montage of M1/M2-Cz-Fz for the testing of left ear and right ears, conforming to the international 10-20 electrode placement system[13]. Active electrode was placed over the right (M2) or left (M1) mastoid processes. The reference electrode was placed on the vertex (Cz). The ground electrode was placed on the forehead (Fz). Electrode impedance was maintained below 5kΩ. Data were acquired with a sensitivity of 0.5μ/division. Low frequency filter of 100Hz and high frequency filter of 3 kHz were used. The sweep duration was 20 msec. Auditory click stimuli were administered at a frequency of 11/sec to each infant through a standard noise cancelling headphone. The data was acquired at a sampling rate of 20 kHz. Average waveforms were obtained 90 dB to 30 dB at 10dB decrements. Each ear was tested separately. In our study, intensity scale based on hearing level was used. This scale refers to the intensity in decibels compared to the threshold of hearing in a group of normal subjects tested in a quiet environment[12]. The averaged waveforms were derived from 1000 individual epochs. Wave I, III and V peaks were marked on the averaged waveforms and the absolute latency of each component was measured.

Ethical issues: The study design and protocols complied with the code of ethics of the World Medical Association Declaration of Helsinki. The ethical clearance for the study was obtained from the Committee on Research and Ethical Review, Faculty of Medicine, University of Peradeniya, Sri Lanka (2009/EC/54 dated 06.08.2009). Informed written consent was obtained from the parents or guardians of the infants included in the study.

Data analysis: The BAEP threshold was determined for each ear separately. HI in the study group of infants was determined based on the BAEP threshold. The threshold was considered to be the intensity at which the last peak or trough was barely seen. As in the documented literature[12], the wave V was the very last deflection to disappear in the majority of the subjects. Based on the BAEP thresholds observed, HIs were classified into mild (31–40 dB), moderate (41-60 dB), moderately severe (61-70 dB), severe (71-90 dB) and profound (≥91dB) impairment[14]. This was based on the quantitative definitions of HI established by the American National Standards Institute (ANSI). The follow up assessment was done after 6 months from the initial testing in infants who had elevated hearing thresholds.

Significant risk factors for presence of any degree of HI were determined using a multiple logistic regression (MLR) analysis. Some potential risk factors recorded in this study highly correlated with each other. Accordingly, high co-occurrence was observed between 1) meningitis and septicaemia, 2) VLBW and prematurity and 3) mechanical ventilation and NICU stay. Therefore, we eliminated meningitis, VLBW and mechanical ventilation from the MLR model. Prematurity, septicaemia, prolonged NICU stay, exposure to ototoxic medications and hyperbilirubinemia were included as potential risk factors in the final MLR model[15].

For all analyses, level of significance was taken as $p < 0.05$. The data were analysed using Statistical Package for Social Sciences (SPSS) for Windows Version 22.0 and Stata statistical package version 9.1.

Results

In our test group, there were 65 male and 35 female infants. Age of the infants ranged from 0.5-12 months with a median age of 3 months. There were 65 patients with prolonged NICU stay, 13 with VLBW, 61 with meningitis, 58 with ototoxicity, 26 with prematurity, 35 with septicaemia and 20 with exposure to mechanical ventilation. The median gestational age in the prematurity group was 33 ± IQR 2 weeks and 39 ± IQR 2 weeks in the full-term group. Of the total sample, 26 had HI as indexed by the elevated BAEP thresholds. From among the hearing-impaired group (n=26), 13 had moderately severe, 5 had severe, 3 had moderate, 4 had mild and only 1 had profound HI.

Table 1 summarizes the results of the multiple logistic regression (MLR) model of different risk factors. The overall model was significant ($p= 0.01$, pseudo $R^2=0.125$). Prolonged NICU stay and prematurity emerged as highly significant risk factors for HI. The odds of HI in premature infants were 3 times than full term infants (odds ratio: 3.08, 95% CI: 1.05-9.04, p=0.04). The odds of HI in infants with prolonged NICU stay was 3.7 times that of the infants who had not been in the NICU (odds ratio: 3.67, 95% CI: 1.00-13.49, p=0.05). Septicaemia, hyperbilirubinaemia and ototoxic drugs did not appear as significant risk factors in this model.

Table1: ***Multiple logistic regression model for risk factors of hearing impairment***

Risk factor	Odds ratio (95% confidence interval)	p value
Prematurity	3.08 (1.05- 9.04)	0.04
Prolonged NICU stay	3.67 (1.00- 13.49)	0.05
Septicaemia	0.57 (0.19- 1.69)	0.31
Hyperbilirubinaemia	1.35 (0.45- 4.03)	0.59
Ototoxic drugs	0.41 (0.14-1.23)	0.11

NICU: Neonatal intensive care unit

Of the 26 infants who had elevated hearing thresholds in the first assessment, 17 (65.4%) attended follow up. Among them, 5 (29.4%) showed improvement in threshold. Of the five, four had complete improvement up to 30dB. All four of them had either moderately severe or moderate HI. The other one with severe HI in the first assessment had improved to moderately severe category in the follow up evaluation.

Discussion

We tested the hearing levels in 100 infants with clinically suspected risk factors referred to a tertiary-care hospital in Sri Lanka. As indexed by BAEP threshold, 26% had some degree of HI. In a study in India, 27.6% infants had hearing loss[16]. In a study in China 29% high risk infants had HI[17]. However, in developed countries prevalence rate of hearing defects in at-risk infants was 3-7%[18].

We examined the association of perinatal risk factors with occurrence of HI. In the present study, premature infants were 3 times more prone to develop HI than full term infants. Also, infants who were in the NICU were 3.7 times more prone to develop HI than those who were not in the NICU. Thus, if all infants cannot be screened for HI in a resource limited country, at least the ones with prolonged NICU stay and prematurity have to be screened. Many studies show that the children with sensorineural hearing loss who are treated in the NICUs have complex neurologic and other health problems which may have caused the development of hearing defects[19]. It is mentioned that infants in the NICU who are often exposed to continuous loud noise are at increased risk for hearing loss[20].

Prematurity is a well-known risk factor for developing hearing defects[21]. Reported independent risk factors for HI in premature infants are: low gestational age, prolonged mechanical ventilation, hyperbilirubinaemia, hypoglycaemia and prolonged treatment with aminoglycoside antibiotics[22]. But in our study, after adjusting with other risk factors, prematurity became a significant risk factor. It is theorized that multifactorial mechanisms including mitochondrial deoxyribonucleic acid mutations, aminoglycosides and loud noise are known to increase the ototoxicity in extremely preterm neonates[21]. According to the results, one of our recommendations is that it is mandatory to screen all infants who had prolonged NICU stay and prematurity in a resource limited setting.

In our study, meningitis and septicaemia were not significant risk factors. This may be partly because our study sample did not include infants with culture positive meningitis or septicaemia; in the local setting, as soon as the infants are suspected of having meningitis or septicaemia, treatment with antibiotics is started without waiting for the cerebrospinal fluid culture or blood culture results.

In our follow up, we did hearing-assessments in infants who had elevated hearing thresholds in the initial evaluation. The increase in early diagnosis has led to greater opportunities for early intervention. But in a resource limited country, early interventions cannot be done in all the diagnosed children with HI as early as possible. In our sample, out of 17 infants with moderate to profound HI, five improved with time. We can suggest that there is a possible recovery in BAEP threshold in some at-risk infants with time. In the literature also it is evident that the results of follow-up hearing tests performed in infants have shown that hearing acuity easily changes during the first year of life[23]. Thus, it is important to consider the concept of delayed maturation of the auditory pathway in the differential diagnosis of young children with sensorineural hearing loss[8]. Another reason for improvement of the BAEP thresholds would be that those infants were suffering from a conductive type of hearing loss. Once the cause of conductive type of hearing loss has been cured, the thresholds also may have been improved. We realize that, if we have included tympanometry or bone conduction ABR as a combined assessment with BAEP, we could have found out the infants with conductive type of hearing loss and our results would be much more informative. But the fact that 12 out of 17 infants did not improve in hearing at all indicates that it is necessary to consider early interventions.

Nine infants did not participate the follow up stage of the study though the parents / guardians of the infants were adequately informed about the importance of the follow up assessment of hearing of their children. This is a limitation of our study.

As the number of infants in our follow up study is too small, further prospective studies are necessary to elucidate the patterns of recovery over time. Though the risk factors considered in our study are known to cause hearing defects in infants, in a resource limited country like Sri Lanka, it is essential to find out the exact and most important risk factors among all of them. Therefore, the findings of our study would be beneficial when implementing screening guidelines for resource limited settings. In this regard, prematurity and NICU stay for more than 5 days are the risk factors with the largest effect. We consider that it is mandatory to screen premature infants and infants who had prolonged NICU stay more than 5 days using BAEP in a resource limited setting.

Conclusions

Prematurity and prolonged NICU stay were the statistically significant risk factors for developing HI as indexed by increased BAEP threshold levels.

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