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ORIGINAL PAPER

A. Marita Valkama · Kyösti T. Laitakari · E. Uolevi Tolonen
Mirja R.H. Väyrynen · Leena K. Vainionpää · Maila E. Koivisto

Prediction of permanent hearing loss in high-risk preterm infants at term age

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Abstract The aim of this series was to assess hearing screenings; auditory brainstem responses (ABR), transient evoked otoacoustic emissions (TEOAE) and free field auditory responses (FF) for the prediction of permanent bilateral hearing loss in high-risk preterm infants at term post-conceptional age. A total of 51 preterm infants (gestational age < 34 weeks, birth weight < 1500 g) underwent examinations at term and hearing, speech and neurological development were followed up until a corrected age of 18 months. Significant hearing defects were verified by broader ABR examinations under sedation and by clinical ward observation including responsiveness to sounds and enhancement of hearing using an amplification device. Seven bilateral fails in ABR were found, together with nine bilateral fails in TEOAE and four fails in FF screening at term age. Six preterm infants were later confirmed to have a significant permanent bilateral hearing loss, four of whom had also cerebral palsy. Bilateral failure in ABR screening predicted hearing loss with a sensitivity of 100% and a specificity of 98%, TEOAE with a sensitivity of 50% and a specificity of 84% and in the FF examination at the levels of 50% and 98%, respectively.

Conclusion Transient evoked otoacoustic emissions alone seem not to be so applicable to the neonatal screening of hearing in high-risk preterm infants as shown earlier in full-term infants, possibly because a hearing defect may be due to retrocochlear damage. Consequently, auditory brainstem response screening seems to be more suitable for very low birth weight preterm infants.

Key words Auditory brainstem responses · Free field auditory examination · Hearing loss · Premature infant · Transient evoked otoacoustic emission

Abbreviations *ABR* auditory brainstem responses · *BOA* behavioural observation audiometry · *CP* cerebral palsy · *FF* free field auditory examination · *GQ* general development quotient · *HL* hearing level · *SQ* sub-quotient · *TEOAE* transient evoked otoacoustic emissions

Introduction

Preterm infants have functional and developmental disabilities much more often than the general population [7] and it is agreed that the sickest infants in neonatal care run the greatest risk of hearing disabilities [2, 18]. In addition to prematurity, asphyxia, hypoxia, ischaemia, elevated bilirubin concentrations, congenital infections,

A. M. Valkama (✉) · L. K. Vainionpää · M. E. Koivisto
Department of Paediatrics, University of Oulu,
Kajaaninte 52A, 90220 Oulu, Finland
e-mail: marita.valkama@oulu.fi
Tel.: +358-8-3152011; Fax: +358-8-3155559

K. T. Laitakari · M. R. H. Väyrynen
Department of Otorhinolaryngology,
University of Oulu, Oulu, Finland

E. U. Tolonen
Department of Clinical Neurophysiology,
University of Oulu, Oulu, Finland

septicaemia and ototoxic medication have been reported to cause disturbances in hearing [2].

Language development is one of the most important indicators of cognitive abilities in childhood. A delay in linguistic skills may be caused by severe or profound hearing loss and the sooner it becomes possible to intervene in the hearing loss, the better will be the prognosis for language development and academic skills, as well as participation in an enjoyable social life [26].

It has been proved in full-term infants that a simple and quick measurement of otoacoustic emissions, reflex activity of the outer hair cells in the cochlea, is a sensitive screening method for detecting of permanent hearing defect in the neonatal period [1, 14, 23]. In high-risk preterm infants the effectiveness of transient evoked otoacoustic emissions (TEOAE) as a hearing screening at term age has not been systematically confirmed [5, 8, 17, 21]. The measurement of the bioelectric auditory brainstem evoked responses (ABR) represents an objective, non-invasive electrophysiological screening and diagnostic method for detecting disturbances in the auditory pathways at the level of cochlea and brainstem [16, 18, 22, 25]. Our study was designed to establish whether ABRs, TEOAEs or conventionally used free field auditory behavioural responses (FF) would predict reliably permanent bilateral hearing loss in high-risk preterm infants at term post-conceptional age.

Subjects and methods

The subjects were a cohort of 48 consecutive surviving preterm infants and three pilot ones born between November 1 1993 and October 31 1995 of <34 weeks gestational age with a birth weight below 1500 g including three co-born siblings with birth weights of 1645 g, 1650 g and 1800 g admitted to the neonatal intensive care unit at the Paediatric Clinic of Oulu University Hospital (Table 1). For the sake of comparison of the screening methods, 52 full-term healthy newborn infants with no known risk of hearing defects were picked out at random for hearing examinations from a normal well-baby ward at the Obstetric Clinic of Oulu University Hospital (Table 1).

This research was approved by the local University Ethics Committee and informed parental consent was obtained in all cases.

Audiological screening at term age

All the audiological examinations were arranged without premedication after feeding to minimise restlessness during the procedures. Examinations were carried out at term post-conceptional age in the preterm infants and after 3 days of age in the full-term infants during the primary hospital stay.

Auditory brainstem responses

All 51 preterm and 21 randomly selected full-term infants underwent ABR examinations with a Disa 1500 system (Disa, Denmark). Rarefaction clicks of 100 μs duration were delivered separately to both ears through earphones. The stimulus rate was 10 Hz (alternating with 7 and 15 Hz), the intensity 75 dB normal hearing level (HL) with contralateral masking (−40 dB) and the time base 20 ms. The low and high bandpasses were set at 20 and 3000 Hz respectively. Vertex responses to stimulation of each ear were recorded with cup electrodes and referenced to both the ipsilateral and the contralateral mastoid. Reproducible waveform responses to 2000 clicks or more were averaged at least twice. Clear, reproducible responses representing at least waves of type V at the test level were taken as a pass and their absence as a fail [11, 25]. An infant failed the test if both of the ears failed and passed if at least one ear passed.

Transient evoked otoacoustic emissions

Bilateral TEOAEs were carried out on 44 preterm and 52 full-term infants because this method was available since the beginning of 1994. TEOAEs were measured with an ILO88 measuring system (Otodynamics Ltd, Southampton, UK) with guidelines for probe design, signal processing and technical procedures as described elsewhere [24]. The results were analysed by an audiologist without knowing the origin of the infants and their clinical data, and interpreted as pass if emissions were found at 3 dB signal to noise ratio in at least one of the 1–2, 2–3 or 3–4 kHz frequency bands reflecting cochlear function under 30–40 dB HL [3, 24]. A recording was graded as a fail if no emissions were seen and a bilateral fail resulted a fail in the screening.

Free field auditory examination

All preterm and full-term infants underwent FF examination. The lowest reaction level was assessed from arousal and startle or auropalpebral reflexes in an infant's behaviour elicited by sounds in 1/2-octave frequency bands around 1, 2 and 4 kHz at intensities 60 to 100 dB normal HL through loudspeakers placed on the sides of the

Table 1 Clinical characteristics and neonatal morbidity in 51 preterm and 52 full-term infants

Characteristics and risks	Preterm infants (n = 51)	Full-term infants (n = 52)
Mean birth weight (g) (SD)	1153 (289)	3728 (504)
Mean gestational age (weeks) (SD)	29.3 (2.2)	40.0 (1.0)
Male/Female (n)	27/24	25/27
Mean Apgar score at 5 min (SD)	7 (1.7)	9 (0.4)
Respiratory distress syndrome (n %)	45 (88)	
Mean duration of ventilator treatment (days) (range)	7 (0–65)	
Median duration of oxygen therapy (days) (range)	29 (0–630)	
Family history of deafness (n %)	2 (4)	
Abnormality in cranial ultrasound (n %)		
Haemorrhage grade I–II	10 (20)	
Haemorrhage grade III–IV	4 (8)	
Periventricular leukomalacia	4 (8)	

infant's head and at ear level in free field behavioural observation audiometry (BOA). Clear repeated reactions to test sounds at any frequency band below 100 dB HL were considered a pass [19].

Audiological and developmental follow-up

All except one of the preterm infants were re-evaluated by means of at least one audiological examination consisting of TEOAE or FF or both. The examination was planned to be carried out at a corrected age of 6 months. In addition, all preterm infants with bilateral failures in the hearing screenings (ABR and TEOAE/FF) at term age were further evaluated in the Hearing Centre and on the audiophonological ward by repeated audiological methods (TEOAE/FF and ABR under sedation).

All the preterm infants were followed up neurologically and developmentally by using the Griffiths' development scales [9]. A general development quotient (GQ) and a separate sub-quotient (SQ) for the hearing and speech development sub-scale was calculated at the corrected age of 6 and 18 months. GQ and SQ value over 80 represents normal development. The hearing ability of the full-term control infants was followed by conventional methods (distraction test and speech and language development) at the Family Health Care Centres. In addition, hospital records and a questionnaire administered at the age of 2–3 years were used to verify the hearing and speech development.

Definition of hearing ability

Diagnosis of permanent hearing loss was based on 1) absence of responses in a 60–105 dB HL ABR examination under sedation, 2) failing behavioural responses to sounds during observation period on an audiophonological ward and 3) ability of amplification device trials to enhance reactivity to sounds. Hearing was considered to be normal when speech development was normal after passed hearing tests. In preterm infants with severe cerebral palsy (CP) and without normal speech ability, hearing was considered to be normal or at least not severely affected when an infant passed hearing tests repeatedly and responded to sounds.

Statistics

The data were processed using the Statistical Package for the Social Sciences (SPSS version 7.5). A χ^2 test or Fisher's Exact Test at low frequencies was used for prediction purposes. Sensitivity, specificity and significance ($P < 0.050$) were calculated.

Results

Audiological screenings at term age

Out of all 51 preterm infants in our series, 7 had bilateral and 3 unilateral fails in ABR. All tested 21 full-term infants passed the test. Of the 44 preterm infants, 9 had bilateral and 9 unilateral fails in TEOAE. Only 2 out of the 52 full-term infants failed TEOAE in one ear. Four preterm infants failed FF and all full-term infants passed (Fig. 1).

Audiological and developmental follow-up

Six preterm infants (12%) were confirmed to have a significant (60–105 dB) bilateral hearing loss (see definition) and four of whom had also CP (Table 2). One infant without CP died at the corrected age of 9 months before any hearing appliance could be used. Daily use of hearing instruments in another preterm infant without CP was manageable at 5 months of corrected age and in the four infants with CP at 6, 12, 34 and 39 months. Two infants with moderate/severe CP had a long delay (12 and 39 months) because of difficulties in confirmation of amplification device enhancement ability in otherwise disabled infants. They both had had grade IV intracranial haemorrhage and another also cystic periventricular leukomalacia on neonatal cranial ultrasound. One infant with mild CP had moved away and missed the amplification service until the age of 34 months (Table 2).

Audiological re-evaluation examinations at the corrected age of 6 months were delayed up to a mean age of 9.9 (4.2) months because of infection and middle ear effusion problems in 34 (67%) of the 51 preterm infants. Examinations were performed in a symptom-free period after the treatment. A total of 17 (33%) preterm infants had tympanostomy tubes inserted in both ears for glue ear, and 6 of them had also undergone adenoidectomy. All six preterm infants with hearing loss had suffered from otitis media and all but one of them had been given ventilation tubes. No further infants with permanent significant hearing loss were found during follow-up to a corrected age of 18 months. None of the full-term control infants had hearing loss. Of the full-term infants, 20 (38%) had suffered from otitis media, and 4 (8%) had undergone adenoidectomy and insertion of tympanostomy tubes during the corresponding time period.

Of all 51 preterm infants, 6 had SQ values for hearing and speech less than 80 on the Griffiths' development scales at a corrected age of 6 months. Four of the six infants had hearing loss (Table 2) and the remaining two without significant hearing loss had CP. At a corrected age of 18 months, 4 of 49 preterm infants had SQ values for hearing and speech less than 80, three of whom had hearing loss and one had severe dystonic CP with oral difficulties. One infant with a score value of 84 was wearing amplification devices during the test (Table 2). Data of two infants with hearing loss were missing due to the fact that one had died of severe chronic lung disease before the latter assessment and the other was living elsewhere at that age. All six preterm infants with hearing loss received a mean SQ (SD) value for hearing and speech in comparison to GQ (SD) value of 59(27)/69(15) on the Griffiths' development scales at a corrected age of 6 months, and four of these infants received mean (SD) values of 54(28)/60(34) at a corrected age of 18 months; for the remaining 45 infants without hearing loss values were 112(18)/107(15) and 109(17)/107(16), respectively.

Prediction of permanent hearing loss

All six preterm infants with verified permanent bilateral hearing loss recorded bilateral failures in the initial ABR examination, so the method predicted hearing loss with

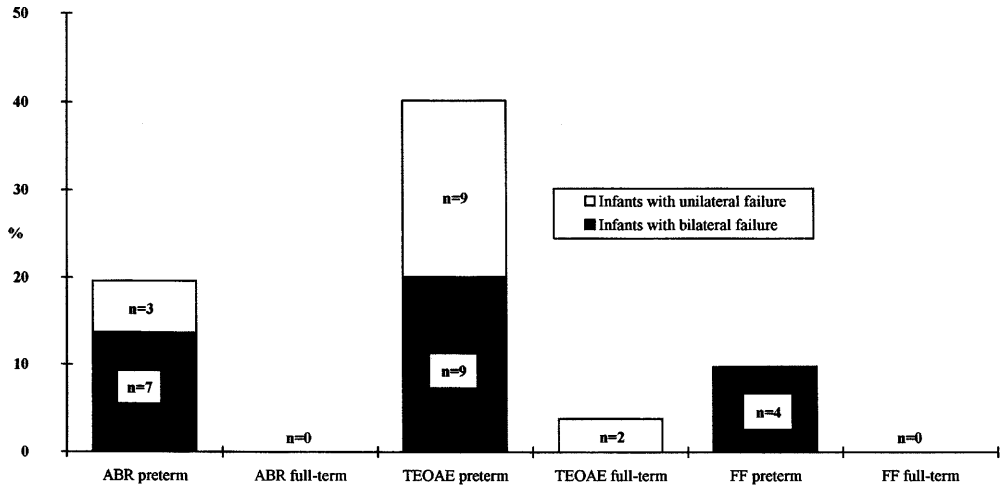

Fig. 1 Failure percentages for the preterm and full-term infants in ABR, TEOAE and FF examinations at term post-conceptional age

Table 2 Results of ABR, TEOAE and FF examinations at term age, brain imaging by cranial ultrasound, ratio of the SQ to GQ on the Griffiths' development scales at corrected ages of 6 and 18 months and neuromotor outcome in preterm infants with a hearing defect confirmed in follow-up

Preterm infants		Hearing screening at term age			Brain imaging	Scores on Griffiths' scales and outcome		
Case and sex	Birth weight (g)	ABR	TEOAE	FF	Ultrasound	SQ/GQ 6 months	SQ/GQ 18 months	Neuromotor outcome
1 Female	870	Bilateral fail	Bilateral fail	Pass	Normal	70/77	Not tested	Normal up to death
2 Female	740	Bilateral fail	Bilateral fail	Fail	Bilateral grade I hemorrhage	49/77	84/99[a]	Normal
3 Male	885	Bilateral fail	Bilateral fail	Fail	Slight dilatation of lateral ventricles	22/48	28/25[a]	Severe spastic tetraplegia
4 Male	1065	Bilateral fail	Pass right Fail left	Pass	Left grade IV haemorrhage	87/73	73/77[a]	Moderate right spastic hemiplegia
5 Female	1085	Bilateral fail	Bilateral pass	Fail	Left grade IV haemorrhage, right cystic periventricular leukomalacia	36/53	32/40	Severe spastic tetraplegia
6 Male	1120	Bilateral fail	Pass right, Fail left	Pass	Bilateral grade I hemorrhage	88/85	Not tested	Mild spastic diplegia

[a] Infant wearing hearing aids during the test

a sensitivity of 100% and a specificity of 98% ($P = 0.000$). Three of the six preterm infants with bilateral permanent hearing loss failed initially in TEOAE screening. Bilateral failure in TEOAE screening with a sensitivity being 50% and a specificity 84% did not predict severe hearing loss well ($P = 0.089$). Three preterm infants with hearing loss failed in FF, so the sensitivity was 50% and specificity 98% ($P = 0.004$).

Discussion

The failure rates in our series of the high-risk preterm infants in the ABR, TEOAE and FF examinations at term age were clearly higher than those of the present healthy full-term infants and those reported earlier [1, 18]. An obvious contributing reason for that is that high-risk infants in this series were less than 1500 g and 34 gestational weeks at birth and one third of them had an abnormality on cranial ultrasound. Two of the four preterm infants with hearing loss and CP had severe brain involvement on neonatal cranial ultrasound.

To reduce the percentage of false failures, we examined infants at term age in post-conceptional weeks using a moderate suprathreshold sound level (75 dB normal HL) in ABR screening, as preferred earlier for newborns [12]. Although ABR screening such as we used here includes problems, it is time-consuming and it reflects mainly the detection of frequencies only around 2 kHz, it detected all the significant bilateral hearing defects in the present series with only one false fail. Modern automated ABR screeners should shorten examination time [15, 22], but we had not such equipment in use.

TEOAE screening in preterm infants has been preferred to take place at 35 weeks gestation [8] or around term age because the amplitude and frequency ranges of TEOAEs increase with age [4, 5]. In a universal hearing screening, a bilateral failure rate of around 9% has been reported in preterm and full-term infants when measured shortly after birth or at the age of 3–4 weeks [1]. By comparison with those figures, our series of preterm infants showed a higher failing rate being, however, in agreement with earlier reports in preterm infants below

1500 g [17] and in neonatal intensive care unit populations [6].

The presence of TEOAE in at least one ear has been suggested as a criterion for passing the screening, since one hearing ear allows normal speech and language development [20]. Preterm infants obviously have some disturbing features, e.g. noisy breathing or middle ear effusion or dysfunction, that result in false fails and needs for further or repeated examinations as this and other series show [6, 8, 21]. On the other hand, TEOAE may give false passes in infants with brain damage. Two infants with hearing loss in this series passed a TEOAE test at term age possibly because of retrocochlear injury. Our full-term infants were successfully examined 3 days after birth to avoid any effects of residual fetal fluid or tissue debris in the middle ear and external canal.

Before TEOAE in 1994 we used FF as a primary method of infant auditory screening. BOA tests like FF measure the ability and acuity of perception of environmental sounds or pure tones in the whole auditory pathway and therefore require a response from both the auditory and motor pathways. One of the most important difficulties involved in behavioural reactions to filtered environmental sounds in a free field situation is the considerable inter-subject variability in the ratio of hearing thresholds to reaction thresholds. The threshold of behavioural reaction to pure tones has been found to be higher for preterm than for full-term infants, with a catch up interval of 9 months of age [13]. In addition, the recruitment phenomenon can cause false passes as subjects with sensorineural hearing loss may perceive loud sounds equally well as normal subjects. This series showed that FF is not alone a suitable hearing screening method in preterm infants.

Preterm infants with hearing loss without accompanying CP had lower scores on the Griffiths' hearing and speech sub-scales than on general developmental scales resembling the profile in a deaf child [9]. On the contrary, infants with hearing loss and severe spastic CP had both low SQ and GQ values that did not increase during follow-up because most of the sub-scales demand locomotion ability. Therefore, in view of the high proportion of preterm infants with developmental difficulties, not only a clinical follow-up but also hearing screening methods are needed to detect infants with hearing loss.

In order to exclude speech and language development delay after fluctuating conductive hearing loss associated with secretory otitis media [15], this condition was treated before the follow-up re-evaluation examinations. Many of the preterm infants had infections that included middle ear effusions before the corrected age of 6 months and therefore examinations were delayed. Actually they had already been living extra-uterally for up to 4 months longer than their corrected age indicated. Although we did not find any more severe deficits over the follow-up period, it has been reported that one third of very preterm infants have some bilateral abnormal audiological findings at the age of 5 years [10]. It is very important as early as possible to find a hearing screening method that is both sensitive and specific.

In this series ABR was superior to TEOAE and FF as a hearing screen, possibly because of its ability to detect both cochlear and brainstem lesions. It is significant that four out of the six preterm infants with permanent hearing loss had CP. Their hearing defect may at least partially have been in relation to retrocochlear damage. Our series favours the use of ABR, and possibly automated ABR, in the future.

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