

Newborn Hearing Screening with Combined Otoacoustic Emissions and Auditory Brainstem Responses

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Abstract

Accurate assessment of neonatal hearing screening performance is impossible without knowledge of the true status of hearing, a prohibitive requirement that necessitates a complete diagnostic evaluation on all babies screened. The purpose of this study was to circumvent this limitation by integrating two types of screening measures obtained near simultaneously on every baby. Peripheral auditory function was defined by otoacoustic emission results. A complete diagnostic evaluation was performed on every baby who received a "Refer" outcome for auditory brainstem response screening. The integrated results for auditory brainstem response screening in an unselected group of 300 newborns estimated sensitivity at 100%, specificity at 99.7%, overall referral rate at 2.0%, and a positive predictive value of 83.3%. Conductive loss associated with amniotic fluid in the middle ear can persist several weeks after birth; conductive loss can produce a "Refer" outcome for auditory brainstem response screening; and auditory neuropathy can be detected with screening measures. Prevalence results were consistent with the published literature. The implications of this study are that otoacoustic emissions and auditory brainstem measures provide much more information than either alone and that both are needed for a comprehensive hearing screening program.

Key Words: Auditory brainstem response, distortion-product otoacoustic emission, neonate, sensitivity, specificity, universal hearing screening

Abbreviations: ABR = auditory brainstem responses; OAE = otoacoustic emissions; PPV = positive predictive value; NIH = National Institutes of Health

Sumario

La evaluación precisa del desempeño en el tamizaje auditivo neonatal es imposible sin conocer el verdadero estado de la audición, un requisito prohibitivo que exige una evaluación diagnóstica completa de todos los bebés evaluados. El propósito de este estudio fue superar esta limitación integrando dos tipos de medidas obtenidas casi simultáneamente en cada bebé. La función auditiva periférica fue definida por los resultados de las emisiones otoacústicas. Se realizó una evaluación diagnóstica completa en cada bebé que obtuvo un resultado de "refer" en el tamizaje por respuestas auditivas de tallo cerebral. Los resultados integrados para el tamizaje por respuestas auditivas de tallo cerebral, en un grupo no seleccionado de 300 recién nacidos, estimaron una sensibilidad de 100%, una especificidad de 99.7%, una tasa global de referencia de 2.0%, y un valor predictivo positivo de 83.3%. Una pérdida conductiva asociada con líquido amniótico en el oído medio puede persistir semanas después del nacimiento; una pérdida conductiva puede generar como resultado un "refer" para tamizaje por respuestas auditivas de tallo cerebral; una neuropatía auditiva puede ser detectada con medidas de tamizaje. Los resultados de prevalencia fueron consistentes con los publica-

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dos en la literatura. Las implicaciones de este estudio establecen que las emisiones otoacústicas y las medidas de potenciales auditivos del tallo cerebral aportan juntas más información que cada prueba por separado, y que ambas se necesitan en un programa integral de tamizaje auditivo.

Palabras Clave: Respuestas auditivas del tallo cerebral, emisiones otoacústicas por productos de distorsión, neonatos, sensibilidad, especificidad, tamizaje auditivo universal

Abreviaturas: ABR = Respuestas auditivas del tallo cerebral; OAE = emisiones otoacústicas; PPV = valor predictivo positivo; NIH = Institutos Nacionales de Salud

For over a quarter of a century, accumulated clinical experience with millions of babies has supported the value of auditory brainstem responses (ABR) in newborn hearing screening (Hecox and Galambos, 1974; Schulman-Galambos and Galambos, 1975). Initially, hearing screening was limited to babies meeting selected criteria placing them at risk for hearing loss (AAP, 1982; Mauk et al, 1991). The development of automated ABR technology was a major factor contributing to the emergence of universal newborn hearing screening (Hall et al, 1987; Stewart et al, 2000). Similarly, beginning with the earliest published reports over 20 years ago, transient evoked otoacoustic emissions (OAE) (Bray and Kemp, 1987; Johnsen et al, 1988; Vohr et al, 1998; Norton, Gorga, Widen, Vohr et al, 2000), and then distortion product OAEs (Lafreniere et al, 1991; Bonfils et al, 1992; Smurzynski et al, 1993; Gorga et al, 2000; Hall, 2000), have assumed an important role in newborn hearing screening. Subsequently, several papers also described the combined use of ABRs and OAEs in newborn hearing screening (Norton et al, 2000; Stewart et al, 2000; Gorga et al, 2001), although not always with automated devices. A variety of automated OAE devices are now available commercially. Despite recommendations for a two-step or two-stage screening approach (Norton, Gorga, Widen, Folsom et al, 2000; Gorga et al, 2001), there are among the dozens of studies documenting the usefulness of ABR or OAE techniques in newborn hearing screening no published papers describing the application of both technologies, in combination, and with a single, automated commercially available device.

Determining true sensitivity and specificity for any neonatal hearing-screening program is virtually impossible for two

reasons. First, all babies would have to have complete diagnostic evaluations at the time of the screening to fulfill the basic requirements of such determinations. Second, a very large number of babies would have to be screened to have sufficient numbers of hearing-impaired babies because of the rather low incidence of hearing impairment in the general population (<1%). Therefore, to calculate true sensitivity and specificity, and to document accurately the false negative rate, many tens of thousands of babies would have to be screened, and all of them would have to receive complete diagnostic evaluations often done under light sedative. This approach is prohibitive because of the amount of effort required and the financial cost. Sedating so many normal-hearing babies may also be a dubious practice on an ethical basis as well. However, with the use of combined OAE and ABR screening, one type of testing can be used to evaluate or crosscheck the other type of testing. Though this reasoning is circular, combining OAE and ABR technologies offers a viable approach to establishing reasonably accurate sensitivity and specificity values. This approach is a substantial improvement over all previous approaches that have not used an independent hearing measure on all babies. Further, the strategy offers an advantage over the approach taken in the large-scale multicenter, multiyear National Institutes of Health (NIH) study (Norton, Gorga, Widen, Folsom et al, 2000), namely, the two measures can be made essentially concurrently compared to the many months separating the screening measures and the behavioral measures of hearing. This last point should be stressed. In a population with a high incidence of transient conductive problems, comparison of test results separated by even a few minutes may complicate interpretation of the data.

Combined automated OAE and ABR screening offers a variety of other potential advantages. Integrated OAE and ABR technology allows for an individual patient's in-ear calibration of signal levels for ABR, as well as for OAE test signals. Screening efficiency is enhanced by a combined OAE and ABR screening capability that allows immediate application of many different protocols that account for differences in hearing loss prevalence and etiology (Gorga et al, 2001). For example, a protocol may be selected for a well-baby nursery whereby a baby initially is screened rapidly with an automated OAE and then screened with an automated ABR in the case of an OAE "Refer." A different protocol may be selected for a neonatal intensive care nursery with a higher prevalence of hearing loss and fewer restrictions associated with longer hospital stays. For example, a baby initially may be screened with an automated ABR and then immediately screened with an automated OAE in the case of an ABR "Refer."

With the combination of automated OAE and automated ABR technologies, universal newborn hearing screening can yield a refer rate of <2% and a false-positive rate of <2.0% (Stewart et al, 2000; Gorga et al, 2001). Parental anxiety can be minimized by reducing the period between an initial newborn screening in the hospital and the secondary screening scheduled later, or the diagnostic assessment scheduled after hospital discharge. Follow-up rates for infants who do not pass hearing screening are often far below the 95% target set by the American Academy of Pediatrics (Erenberg et al, 1999). With low refer rates, the number of babies that must return for diagnostic audiologic assessment is lower, and therefore, it is likely that fewer hearing-impaired infants will be lost to follow-up. Also, the low refer rates characteristic of combined OAE/ABR screening result in the need for fewer diagnostic follow-up assessments and markedly lower costs associated with the identification of each hearing-impaired child. The combined use of OAEs and ABRs in newborn hearing screening permits, before hospital discharge, the initial differentiation of conductive versus sensory versus neural auditory dysfunction. For example, the combination of an OAE "Refer" with an automated ABR "Pass" suggests a peripheral conductive etiology such as vernix caseosa in

the external ear canal or subtle middle ear dysfunction. This possibility can then be confirmed with other procedures, for example, tympanometry. Immediate differentiation among major types of auditory dysfunction, in turn, can result in quicker and more appropriate management. Finally, the combined application of OAE and ABR in newborn hearing screening leads to early identification of auditory neuropathy in the well-baby population, as well as in the intensive care nursery. A "Pass" outcome for OAE screening, coupled with a "Refer" automated ABR outcome, raises the question of auditory neuropathy and certainly warrants follow-up diagnostic audiometry.

Many universal neonatal hearing screening programs use only the ABR as an indicator of the status of the baby's hearing. Though all screening ABR devices automatically determine the presence or absence of the ABR, measurement procedures differ substantially across devices and are not standardized. One automatic ABR screening device determines the presence of an ABR by matching the measurement to a template representing a normal response. An increasing number of other ABR screening devices determine the presence of the response by ascertaining if the measured variance ratio, an ABR signal-to-noise ratio, exceeds a criterion.

The most common ABR variance ratio is based on the magnitude of the response in the averaged ABR waveform (the signal) divided by the magnitude of the noise. In babies who have an ABR, the measured response is larger than the noise, and the signal-to-noise ratio is a value greater than 1.0. In babies who do not have an ABR, the measured response is approximately the same as the noise, and the signal-to-noise ratio is approximately 1.0. Originally this signal-to-noise ratio was labeled F_{sp} (Don et al, 1984) because the response was evaluated with the F statistic using the variance of the value at a single point in the ABR waveform to measure the magnitude of the noise. Though the signal-to-noise ratio values in all modern devices are based on multiple points for calculating the noise variance rather than a single point, the older F_{sp} label is still commonly used and also will be used in this paper. The effectiveness of F_{sp} values for neonatal hearing screening in combination with the use of concurrent OAE measures in assessing

screening performance is the focus of this paper.

The magnitude of an ABR is quite stable in an individual for stimuli at a fixed level. Conversely, the magnitude of the noise varies greatly depending on patient-related factors (unrelated brain activity, muscle movements, etc.), environmental factors (stray electrical activity from lights, other electronic equipment, etc.), and most importantly, measurement parameters. Signal averaging reduces the noise allowing the ABR to be detected. In general, the more the response is averaged, the more the noise is lowered, which in turn increases the F_{sp} value.

In the large NIH-sponsored multicenter study of over 7,000 newborns (Norton, Gorga, Widen, Folsom et al, 2000), the authors specifically used F_{sp} as the parameter for ABR measures. Further, they demonstrated that a criterion F_{sp} value of 3.1 effectively separates normal-hearing babies ("Pass") from those who require a full diagnostic evaluation ("Refer").

Desktop systems that employ a personal computer and various related amplifiers and components generally have sufficient capability to both adequately measure and store ABRs and perform the complex data processing necessary to calculate F_{sp} values. However, desktop devices are not optimized for screening because of their complexity, their size, and the fact that they require an AC outlet, an arrangement that usually results in transporting the babies to the device. Even those systems that use a battery-operated laptop computer are not optimized for screening because the AC line is still required for the other components. On the other hand, a self-contained battery-operated, handheld device is better suited for neonatal screening because it allows the measurements to easily be made wherever the baby is located, including the mother's room.

PURPOSE

The purpose of the present study was to estimate sensitivity and specificity values using ABR measures alone and when combined with OAE measures obtained nearly simultaneously in a well-baby population. A secondary purpose was to determine if a recommended criterion F_{sp} value (3.1) was valid for ABR measures. The intent was to determine the validity of a new

hearing screening approach and to evaluate the recommendations from a large NIH study.

METHOD

Subjects

A series of 300 neonates in a well-baby nursery were measured using convenience sampling. There were no exclusion criteria. Both OAEs and ABRs were measured concurrently in both ears 13 to 42 hours after birth. The number of females (161) was slightly more than the number of males (139). Institutional Review Board approval was obtained for this study.

Screening Instrumentation and Procedures

A self-contained battery-operated handheld hearing screener (Audioscreener, developed by Everest Biomedical Instruments and licensed to Grason-Stadler Instruments) was used for all screening OAE and ABR measures. This device is about the size of a paperback book with a single probe and three electrode wires. The same probe is used for both OAE and ABR measures and allows the two types of measures to be obtained within seconds of each other.

Distortion product OAEs at $2f_1-f_2$ were evoked with two tones (f_1 and f_2) at each of four f_2 frequencies (2000, 3000, 4000, and 5000 Hz), with an f_1 level (L_1) set at 65 dB SPL and an f_2 level (L_2) set at 55 dB SPL ($L_2 - L_1 = -10$ dB) as measured in the external ear canal. Signals were presented, and DPOAEs detected, with a probe assembly that contained a microphone and two miniature loudspeakers. For each subject, a complete probe fit was determined and signal levels were verified and adjusted with real ear measures immediately before data collection. Signal calibration tolerance was within ± 2 dB. The f_2/f_1 ratio was 1.2. DP amplitudes (L_{dp}), and noise floor levels (L_{nf}) were calculated for each test frequency. A "Pass" outcome for DPOAE screening was defined as a minimum signal-to-noise level difference ($L_{dp} - L_{nf}$) of 6 dB, and minimum L_{dp} values of -7 dB SPL for 2000 Hz, -8 dB SPL for 3000 Hz, -5 dB SPL for 4000 Hz, and -7 dB SPL for 5000 Hz (Gorga et al, 1997) at a minimum of three of the four test frequency regions.

The ABRs were recorded from the scalp using disposable electrodes placed at Fz (noninverting) and the ipsilateral mastoid process (Mi, with the contralateral mastoid process used as ground) in response to click signals (100 μ sec) presented through the same probe assembly that was used for DPOAE measurements. The device was configured to present rarefaction clicks at 35 dB nHL at a rate of 37.1/sec. A unique feature of this device is that the adequacy of the probe fit and the level of the ABR stimulus is verified and adjusted in the actual ear being measured instead of relying on a coupler calibration as is typically done. The level of the real-ear ABR stimulus was determined automatically using the microphone built into the probe, similar to the procedure used for OAE. The ABR was collected with a high-pass filter setting of 100 Hz and a low-pass filter setting of 3000 Hz. Electrode impedance was ≤ 12 kohms, while the maximum electrode impedance mismatch between electrodes was ≤ 5 kohms.

The device stores "Pass" or "Refer" results, OAE levels in dB SPL, Fsp values, and the averaged ABR waveform for each ear in a single record for each baby. These data can then be downloaded through a wireless infrared port and stored in an external software application (Audiotrac) on an external computer and then exported into conventional statistical and other software applications for further, more detailed analyses.

The presence or absence of an ABR was determined with the Fsp statistic described earlier. The Fsp value for each auditory brainstem response was based on a fixed number of 3000 sweeps to allow direct comparison of Fsp values across subjects.

Screening Data Analyses

The OAE results were used to determine if peripheral auditory function was normal. Specifically, an ear that had OAEs that exceeded the "Pass" criteria was assumed to have normal-hearing sensitivity and no significant conductive abnormality. In the analysis of the ABR screening data, OAEs provided an independent indication of peripheral auditory status.

The criterion for an ABR "Pass" outcome was an Fsp value ≥ 3.2 , the closest setting to the recommended value of 3.1 from the large NIH multicenter study. All of the ears that

received an ABR "Pass" result had normal peripheral auditory status as determined by an OAE "Pass" result obtained nearly simultaneously. No further testing was performed on these ears.

Each ear that obtained an ABR Fsp value of less than 3.2 received a "Refer" result regardless of the OAE outcome. All babies who received an ABR "Refer" result in one or both ears received a full diagnostic evaluation on an outpatient basis after the initial screening. These diagnostic evaluations employed auditory threshold searches using a diagnostic ABR desktop system and a full complement of other diagnostic measures, for example, aural immittance measures, diagnostic OAEs, behavioral audiometry, and so forth.

Diagnostic Instrumentation and Procedures

A comprehensive diagnostic evaluation was performed within four to six weeks of the initial hospital referral for every neonate with an ABR "Refer" screening outcome. Prior to the diagnostic audiologic assessment, each infant underwent a medical evaluation by an otolaryngologist. Repeat ABR and OAE screenings first were performed with the screening device at the time of the diagnostic evaluation.

A comprehensive ABR and OAE assessment was conducted within our medical practice or in an audiology clinic under natural sleep or at one of the outpatient surgical centers under light sedation (chloral hydrate or Versed) with anesthesiology support. A full diagnostic ABR was performed with a commercially available auditory evoked response system (Bio-Logic Traveler SE EP system or Bio-Logic Navigator Pro EP System). Air-conduction clicks and tone-burst signals were delivered monaurally at rates of 27.1 to 37.1/sec via insert earphones (ER-3A). Stimulus polarity was either rarefaction or condensation. Clicks were 100 μ sec, and tone-burst signals were centered at 500, 1000, 2000, and/or 4000 Hz with Blackman ramping and duration of two cycles of rise/fall time, and 0 cycle plateau. Stimulus level was referenced to normal-hearing levels for adults (dB nHL). Bone-conduction stimulation was utilized, as appropriate, based on otologic findings or the pattern of air-conduction ABR findings. Diagnostic ABRs were recorded with scalp electrodes located

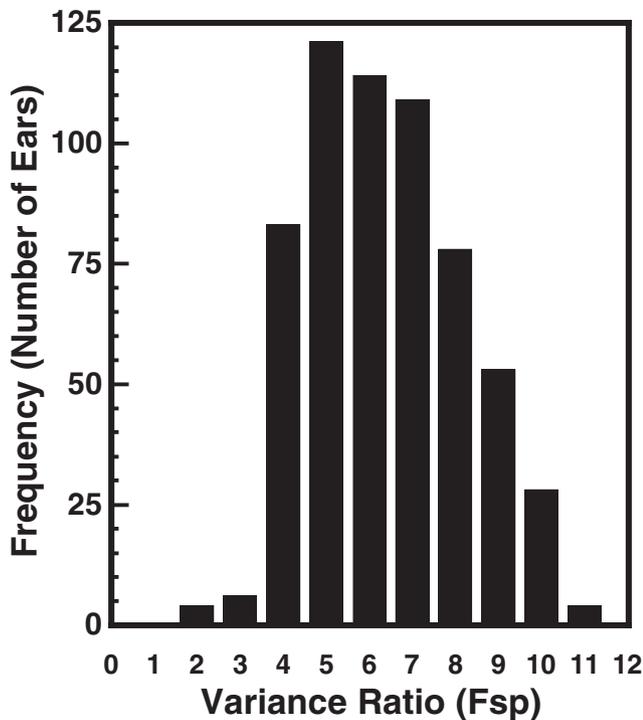


Figure 1. Frequency distribution of the auditory brainstem responses for clicks (37.1/sec at 35 dB nHL) and measured as a variance ratio (Fsp, 3000 frames) for 600 ears of 300 neonates in a well-baby nursery. The bin widths were selected so that the bins labeled 3 and lower represent Fsp values <3.2 .

in the high forehead location (noninverting) and the ipsilateral mastoid process or earlobe (inverting), and with a ground electrode located on the low forehead. Filter settings were 30 to either 1500 or 3000 Hz. The gain was typically 100,000. The analysis window was set to either 15 or 20 msec (for 500 Hz tone burst signals). For each ear of all infants, the diagnostic ABR was performed for neurodiagnosis (i.e., analysis of interwave latency values in msec) and threshold estimation (i.e., latency/intensity functions in

dB nHL). Aural immittance measurement was not performed due to unavailability of a high-frequency probe tone option required for infants under the age of six months. In some cases sound-field behavioral observation audiometry was conducted with frequency-modulated tones or narrow-band noise signals centered at standard audiometric frequencies with the infant in either an infant carrier or in the parent's lap while located between two ear level sound-field speakers.

RESULTS

A frequency distribution of the Fsp values for all ears is shown in Figure 1. The bin width was selected so that bins labeled 3 and lower represent Fsp values ≤ 3.1 , the criterion for separating "Pass" from "Refer" recommended by the large NIH study. The distribution is symmetrical and appears to be normally distributed. The distribution clearly identifies the ten ears that required a full diagnostic evaluation. The performance of the ABR screening using traditional methods for evaluating sensitivity, specificity, and positive predictive value (PPV) (called Bayesian analysis) analyzed separately by ear is shown in Table 1. Of the 600 ears that were screened, 590 yielded an ABR "Pass" (Fsp ≥ 3.2). All of these 590 ears also received a "Pass" result for the OAE measure at the time of the ABR screening providing substantial evidence that there were no hearing-impaired cases in this group. The remaining ten ears each received an ABR "Refer" outcome defined as an Fsp value <3.2 .

The actual hearing sensitivity of these ears was determined at the time of the diagnostic evaluation. The sensitivity of the ABR screening test (the percentage of ears

Table 1. Summary of the Test Performance for an Auditory Brainstem Response Hearing Screening Technique in a Series of 300 Newborns

Diagnostic Outcome	Pass	Screening Outcome	
		Pass	Refer
Normal	590	2	592
Hearing Impaired	0	8	8
Number of Ears	590	10	600
		Sensitivity	100.0%
		Specificity	99.7%
		Refer Rate	1.7%
		Positive Predictive Value (PPV)	80.0%

Note: The "Pass" criterion was an Fsp value of ≥ 3.2 . The results are separated by individual ears.

Table 2. Summary of the Screening Test Performance for a Combined Otoacoustic Emissions and Auditory Brainstem Response Hearing Screening Technique in a Series of 300 Newborns

Diagnostic Outcome	Pass	Screening Outcome	
		Refer	Number of Neonates
Normal	294	1	295
Hearing Impaired	0	5	5
Number of Neonates	294	6	300
		Sensitivity	100.0%
		Specificity	99.7%
		Refer Rate	2.0%
		Positive Predictive Value (PPV)	83.3%

with actual hearing impairment that received a “Refer” outcome) was 100%. The specificity of the ABR screening test (the percentage of normal-hearing ears that received a “Pass” outcome) was 99.7%. The overall referral rate (the percentage of ears referred for a full diagnostic evaluation) was 1.7%. The positive predictive value (the probability that an ear that received an ABR screening “Refer” result was in fact hearing impaired) was 80.0%.

Though analyses of the data by individual ear is instructive, analyses by individual neonate would represent the actual clinical situation. Performance of the ABR screening using traditional methods for evaluating sensitivity, specificity, and positive predictive value analyzed separately by neonate is shown in Table 2. Of the 300 neonates who were screened, 294 yielded an ABR “Pass” ($F_{sp} \geq 3.2$) in both ears. All of these 294 neonates also received a “Pass” result in both ears for the OAE measure at the time of the ABR screening providing substantial evidence that there were no hearing-impaired neonates in this group. The remaining six neonates

each received an ABR “Refer” outcome defined as an F_{sp} value < 3.2 in at least one ear. The actual hearing sensitivity of these neonates was determined at the time of the diagnostic evaluation. The sensitivity of the ABR screening test (the percentage of neonates with actual hearing impairment who received a “Refer” outcome) was 100%. The specificity of the ABR screening test (the percentage of normal-hearing neonates who received a “Pass” outcome) was 99.7%. The overall referral rate (the percentage of neonates referred for a full diagnostic evaluation) was 2.0%. The positive predictive value (the probability that a neonate received an ABR screening “Refer” result was in fact hearing impaired) was 83.3%.

Findings for the full diagnostic evaluations for these six neonates are summarized in Table 3. These results were used to estimate prevalence of hearing impairment by type though caution must be used in interpretation because of the small numbers.

Table 3. Summary of Diagnostic Evaluations Following a “Refer” Outcome with Combined Otoacoustic Emissions and Auditory Brainstem Response Hearing Screening for 300 Neonates in a Well-Baby Nursery

Diagnostic Outcome	Prevalence		Per 1000
	Number	%	
Conductive	2	0.67%	6.7/1000
Sensorineural (Cochlear)	2	0.67%	6.7/1000
Sensorineural (Auditory Neuropathy)	1	0.33%	3.3/1000
Normal	1	N/A	N/A

Note: The results also were used to calculate prevalence of hearing impairment.

Case Reports

The audiologic results for each baby who received a complete diagnostic evaluation will be given in greater detail. This approach will shed more light on the screening process and allow a more direct comparison to the screening results.

Case 1. This infant initially yielded a “Refer” outcome bilaterally for both the ABR and OAE hearing screenings. The first diagnostic evaluation showed no detectable OAE. Diagnostic ABR findings, however, were consistent with a bilateral conductive hearing loss. That is, absolute latencies for ABR waves I, III, and V were proportionally prolonged in comparison to the age-appropriate normative data provided graphically with the auditory evoked response system. Analysis of the latency/intensity function for click signals confirmed the presence of a repeatable wave V down to a level of 40 dB nHL for the right ear and down to 35 dB nHL for the left ear. Neurodiagnostic ABR findings (interwave latency values) were normal with respect to the age of infant. Bone-conduction ABR threshold estimations were within normal limits. Taken together, these results were consistent with a conductive component bilaterally.

Otolaryngology examination showed bilateral clear middle ear fluid with slight vernix impaction upon the tympanic membrane. Vernix was removed and the infant was followed up audiologically in three weeks. Upon return, subsequent screening with OAEs and ABR produced a “Pass” outcome bilaterally. A full ABR latency/intensity function was repeated showing the presence of a clear and repeatable wave V down to an intensity of 15 dB nHL bilaterally. Otologic examination yielded normal findings, consistent with resolution of middle ear pathology. There is substantial evidence that this case had a bilaterally conductive hearing loss at the time of the screening and even after hospital discharge. It also demonstrates that ABR screening is not always insensitive to conductive conditions as is commonly believed.

Case 2. For this infant, the initial screening yielded a “Refer” outcome bilaterally for both ABRs and OAEs. A secondary screening

yielded a “Pass” outcome bilaterally for ABR and OAEs. A later diagnostic ABR also showed normal wave I, III, and V latency values (in comparison to the age-appropriate normative database) and a normal latency/intensity function with a reliable wave V down to a level of 15 dB nHL for each ear.

Otologic examination confirmed normal appearing tympanic membranes with no obvious debris in the external ear canal or middle ear fluid. The child passed bilaterally a subsequent OAE screening five months later. This case demonstrates a true screening false positive result, although it is possible that bilateral middle ear fluid resolved spontaneously during the interval between the screening and follow-up diagnostic assessment.

Case 3. This infant was referred for diagnostic follow-up after screening in the well-baby nursery yielded bilateral “Refer” outcomes for the ABR and OAE techniques. Diagnostic audiologic evaluation yielded no measurable OAEs. In addition, there were no observable behavioral responses in the sound field to pure-tone, warble-tone, or narrow band noise signals. There was no reliable ABR for air-conduction clicks or tone bursts, or bone-conduction clicks at the intensity limits of the evoked response system for each signal.

Otologic examination findings were reported as normal with no observed external or middle ear pathology. The infant was referred to a regional Children's Hospital and subsequently followed there by audiology and pediatric otolaryngology. The infant initially was provided with amplification at 5 months of age and then, when amplification was not successful, underwent a cochlear implantation at 12 months of age. This case demonstrates a true correct referral.

Case 4. At the initial screening in the well-baby nursery, this infant yielded a “Refer” outcome only for the right ear with the ABR technique. The infant passed OAE screening bilaterally and the ABR screening for the left ear. Subsequent diagnostic audiologic evaluation produced normal OAE findings bilaterally. The diagnostic ABR assessment indicated the presence of waves I, III, and V at normal age-corrected latencies for the left ear, and the latency/intensity function showed

a clear wave V down to an intensity level of 15 dB nHL for click stimuli. ABR thresholds were also obtained at normal levels for tone-burst signals of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz. For right ear stimulation, there was no detectable ABR at the limits of the evoked response system (95 dB nHL) for click signals, and for tone-burst signals at 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz. However, during ABR assessment the presence of a cochlear microphonic provided evidence of some cochlear function, presumably due to outer hair cell integrity further indicating this may not be a sensory hearing loss.

Otologic examination indicated normal findings with no external or middle ear abnormalities noted. Due to the presence of repeatable OAEs and the subsequent abnormal right ear ABR, the infant was referred to Children's Hospital for further testing. Radiographic imaging yielded no abnormalities within the cochlea or brainstem, such as a retrocochlear lesion. Auditory neuropathy cannot be ruled out and presently is the current diagnosis. This case demonstrates clearly that the combination of OAE and ABR testing can detect correctly all auditory disorders up to the level of the brainstem.

Case 5. This infant yielded a "Refer" outcome bilaterally for ABR and OAE hearing screening in the well-baby nursery. On diagnostic audiologic evaluation, OAEs were not observed for the right and left ears. An ABR assessment revealed a wave V for a stimulus level of 95 dB nHL bilaterally, and down to 60 dB nHL for the right ear and down to 85 dB nHL for the left ear. An ABR for tone-burst stimulation was observed for the right ear at stimulus levels down to 65 dB nHL for 2000 Hz and 4000 Hz. No response was obtained for tone-burst signals of 500 or 1000 Hz, and no response was observed bilaterally for air-conduction or bone-conduction signals. For the left ear, there was no detectable ABR for tone-burst or bone-conduction stimulation. In addition, the child showed no observable behavioral response to sound-field auditory stimulation.

Findings for the otologic evaluation were reported as normal. Audiology recommended a hearing aid consultation and assessment, and the infant was referred back to the pediatrician for approval of hearing aid fitting. This child was then placed into the

Children's Rehabilitative Services for early intervention. This case demonstrates that the current screening pass criteria are adequate for detecting even moderate sensorineural hearing losses.

Case 6. This infant was scheduled for follow-up audiologic assessment due to a "Refer" outcome on ABR and OAE hearing screening. A secondary screening resulted in a "Pass" outcome for the left ear on both ABR and OAE, and a "Refer" outcome on both the ABR and the OAE for the right ear. Follow-up diagnostic ABR and OAE assessment yielded absent OAEs. Diagnostic ABR showed normal waveforms for the left ear, and the presence of a wave V down to a level of 10 dB nHL. ABR latencies were analyzed with respect to age-appropriate normative data. With tone-burst stimulation at 2000 and 4000 Hz of the left ear, there was a reliable wave V down to 20 dB nHL. The infant awoke before an ABR could be evoked for tone-burst stimulation of the left ear at 500 or 1000 Hz.

With right ear stimulation, ABR waves I, III, and V were observed for a click signal presented at 80 dB nHL. Latencies were slightly delayed, consistent with a possible conductive loss. A latency/intensity function indicated the presence of a wave V down to an intensity level of 40 dB nHL. With tone bursts of 1000 and 4000 Hz, there was an ABR wave V at 40 and 45 dB nHL, respectively. An ABR recording for 500 Hz tone-burst signals could not be completed due to high activity level from the infant. Bone-conduction ABRs were recorded for levels better than 20 dB nHL, suggesting the presence of a conductive component, rather than a sensory loss.

Otologic examination indicated significant right ear middle ear fluid upon microscopic evaluation. No other abnormalities were noted for the external or middle ear.

Follow up diagnostic audiologic assessment four weeks later yielded normal OAEs for both the right and left ears. Another screening ABR produced a "Pass" outcome for both the right and left ears. A repeat diagnostic ABR assessment further indicated the presence of wave V down to a level of 15 dB nHL for both ears. This case demonstrates that unilateral hearing loss also can be detected accurately in a neonatal hearing screening program.

DISCUSSION AND CONCLUSIONS

Neonatal hearing screening performance can be assessed accurately by integrating two types of screening measures to circumvent the requirement that all babies receive a complete diagnostic evaluation. Peripheral auditory function can be accurately defined by otoacoustic emission results. The approach has the added advantage that the measure used to estimate cochlear function, an OAE measure, is obtained within seconds of the measure that is used to quantify neural function, the ABR screening. The use of a combined approach improves the overall effectiveness of a hearing screening program compared to the use of either measure alone.

ABRs can be measured accurately with a battery-operated handheld device. The results obtained in a typical hospital nursery are comparable to those obtained in the well-controlled large multicenter NIH study. In addition, Fsp values computed in a battery-operated handheld device are equivalent to those obtained with large, desktop computer systems in the NIH multicenter study.

Middle ear fluid can occur at birth and persist even several weeks later. Published estimates of the prevalence in the newborn period of middle ear fluid vary widely (de Sa, 1973; Eavey, 1993; Roberts et al, 1995). Although there is some agreement that middle ear disorders are more common among infants with extended stays in the intensive care nursery, consensus is lacking on the likelihood of these disorders in the well-baby population (Eavey, 1993; Roberts et al, 1995; Priner et al, 2003). With reliance on a single newborn hearing screening technology, detection of auditory dysfunction secondary to middle ear disorders is rarely possible. That is, a "Refer" outcome for OAE screening may be due to auditory dysfunction in multiple sites, such as the external ear canal (vernix), middle ear, and/or the cochlea. Yet a "Pass" outcome with ABR does not necessarily rule out middle ear disorder. The combination of a "Refer" finding for an OAE screening and a "Pass" outcome for ABR screening raises the distinct possibility of either external or middle ear disorder. This possibility can be confirmed with diagnostic ABR techniques, including bone-conduction stimulation, along with tympanometry and otoscopic examination.

We also present evidence, however, that conductive hearing loss associated with neonatal middle ear disorder can produce an ABR screening "Refer" outcome. Although data are generally lacking, the conventional opinion expressed in the literature is that the ABR will be detected in infants with modest degrees of conductive hearing loss (Hall, 1992). To be sure, if the ABR wave I latency were calculated in these cases, the analysis would reveal the delay associated with a conductive hearing loss component. Decisions on screening outcome, however, are invariably based not on ABR latency values but, rather, on some statistical measure of the simple presence of a wave V component. It is clear that ABR screening can be affected by neonatal conductive problems.

Consistent with previous citations in the literature (Feinmesser and Tell, 1976; Feinmesser et al, 1982; NIH, 1993; Cone-Wesson et al, 2000), we report in this modest sized sample of newborn infants that the prevalence of bilateral deafness (profound hearing impairment) is 0.33%, or about 3/1000, and the prevalence of bilateral severe or greater sensorineural hearing impairment is 0.67%, or about 6/1000.

Finally, the longitudinal diagnostic findings for one infant in the present study show that unilateral auditory neuropathy can occur, as reported in the literature (Sininger et al, 2000; Sininger and Starr, 2001). The case (number 4) reported in this paper would have been missed with OAE screening alone or with a policy of unilateral hearing screening as followed in some hospitals. The question of auditory neuropathy is often raised in discussions of newborn hearing screening strategy. Clearly, with total reliance on OAEs as a screening technique, auditory neuropathy will go undetected. That is, the rare infants with auditory neuropathy will yield a "Pass" outcome along with the large numbers of infants with normal (cochlear and retrocochlear) auditory function. A logical approach for minimizing the number of babies with auditory neuropathy who are missed during hearing screening is to perform ABR screenings in populations likely to include these infants, for example, infants with neurologic risk factors (e.g., hyperbilirubinemia, asphyxia, degenerative neurologic disease) or, conservatively, all infants in the intensive care nursery. This

approach, however, does not immediately differentiate babies with auditory neuropathy from those with sensory or serious conductive hearing loss, as all will yield a "Refer" ABR screening outcome. The use of neurologic risk factors as a factor in the detection of auditory neuropathy, and the decision about when to use the ABR versus OAE screening technique, also is of very limited value in the identification of auditory neuropathy in the well-baby population. Although the prevalence of auditory neuropathy in apparently healthy children is not known, it will no doubt be exceedingly low. Nonetheless, auditory neuropathy has been reported in well-baby screening populations. We demonstrate herein that the surest and most feasible strategy for early detection of auditory neuropathy is to utilize a combined OAE and ABR screening technique for all infants. A combination OAE/ABR device offers the clinician multiple options for newborn hearing screening, depending on characteristics of the infant population, the availability of other diagnostic instrumentation, and the overall objective of the screening program

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