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Effect of gentamicin and levels of ambient sound on hearing screening outcomes in the neonatal intensive care unit: A pilot study☆

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ABSTRACT

Objective: Hearing loss rates in infants admitted to neonatal intensive care units (NICU) run at 2–15%, compared to 0.3% in full-term births. The etiology of this difference remains poorly understood. We examined whether the level of ambient sound and/or cumulative gentamicin (an aminoglycoside) exposure affect NICU hearing screening results, as either exposure can cause acquired, permanent hearing loss. We hypothesized that higher levels of ambient sound in the NICU, and/or gentamicin dosing, increase the risk of referral on the distortion product otoacoustic emission (DPOAE) assessments and/or automated auditory brainstem response (AABR) screens.

Methods: This was a prospective pilot outcomes study of 82 infants (<37 weeks gestational age) admitted to the NICU at Oregon Health & Science University. An ER-200D sound pressure level dosimeter was used to collect daily sound exposure in the NICU for each neonate. Gentamicin dosing was also calculated for each infant, including the total daily dose based on body mass (mg/kg/day), as well as the total number of treatment days. DPOAE and AABR assessments were conducted prior to discharge to evaluate hearing status. Exclusion criteria included congenital infections associated with hearing loss, and congenital craniofacial or otologic abnormalities.

Results: The mean level of ambient sound was 62.9 dBA (range 51.8–70.6 dBA), greatly exceeding American Academy of Pediatrics (AAP) recommendation of <45.0 dBA. More than 80% of subjects received gentamicin treatment. The referral rate for (i) AABRs, (frequency range: ~1000–4000 Hz), was 5%; (ii) DPOAEs with a broad F2 frequency range (2063–10031 Hz) was 39%; (iii) DPOAEs with a low-frequency F2 range (<4172 Hz) was 29%, and (iv) DPOAEs with a high-frequency F2 range (>4172 Hz) was 44%. DPOAE referrals were significantly greater for infants receiving >2 days of gentamicin dosing compared to fewer doses ($p = 0.004$). The effect of sound exposure and gentamicin treatment on hearing could not be determined due to the low number of NICU infants without gentamicin exposure (for control comparisons).

Conclusion: All infants were exposed to higher levels of ambient sound that substantially exceed AAP guidelines. More referrals were generated by DPOAE assessments than with AABR screens, with

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significantly more DPOAE referrals with a high-frequency F2 range, consistent with sound- and/or gentamicin-induced cochlear dysfunction. Adding higher frequency DPOAE assessments to existing NICU hearing screening protocols could better identify infants at-risk for ototoxicity.

Abbreviations

AABR	automated auditory brainstem response
AAP	American Academy of Pediatrics
ABR	auditory brainstem response
ASHA	American-Speech Language-Hearing Association
CPAP	continuous positive airway pressure ventilation
dBA	A-weighted decibels, accounting for relative loudness to the human ear
DP	distortion product
DPOAE	distortion product otoacoustic emission
EHDI	Early Hearing Detection and Intervention
EPA	Environmental Protection Agency
L_{eq}	equivalent continuous sound level
L_{max}	maximum sound level
NBHS	Newborn Hearing Screening
NICU	neonatal intensive care unit
NIOSH	National Institute for Occupational Safety and Health
SNR	signal-to-noise ratio
WHO	World Health Organization

1. Introduction

Approximately 78 of 1000 live births are admitted into the neonatal intensive care unit (NICU) each year in the United States [1], placing them at greater risk for acquired sensorineural hearing loss [2]. The prevalence of hearing loss in NICU graduates (2–15%) is significantly higher than for full-term births (0.2–0.3%) [3]. Although management of NICU admissions is medically more challenging than regular births, the factors that contribute to this greater prevalence of hearing loss in NICU graduates remain poorly understood. Several risk factors have been identified, including low birth weight, prematurity, medications (including aminoglycosides), oxygen use, length of stay, and exposure to higher levels of ambient sounds [4–8]. This pilot study investigated two risk factors - cumulative sound exposure and aminoglycoside dosing - on the hearing of NICU neonates.

The Environmental Protection Agency (EPA) published data in 1974 to protect patients and staff in hospital environments from damaging levels of ambient sound [9]. The levels of ambient sound were measured over a 24 h period in decibels (dB) with an A-weighted filter, dBA, that is less sensitive to higher (typically >6 kHz) and lower frequencies (typically <1 kHz). This weighted filter is intended to be comparable to the loudness and frequency sensitivity of the human ear, and therefore has been used for developing national standards for sound exposures [10–12]. These levels are further reported as the steady sound level that has the same acoustic energy as the fluctuating level actually measured over a period of time, L_{eq}, or the maximum level, L_{max}. Based on these measurement standards, the EPA reported that levels of ambient sound be < 45 dBA in hospitals to provide a suitable environment for healing, development, staff communication and healthy family interactions. The EPA also reported that exposure to sounds >45 dBA put infants at risk for cochlear damage and abnormal development [9,13].

In 1997, the *American Academy of Pediatrics* (AAP) recommended that the mean level of ambient sound in the NICU should not exceed 45 dBA over 24 h based on EPA criteria [9,13]. However, recent studies in 2008 have reported that the average NICU has sustained levels of ambient sound (e.g., mostly generated by monitors, ventilators, and alarms) ranging between 53.9 dBA and 60.6 dBA [14,15]. Sustained higher levels of ambient sound cause significant changes in vital signs, physiology and behaviors of infants in the NICU, including drops in oxygen saturation, altered heart rate, blood pressure, and disturbed sleep, with reduced healing and growth rates [16,17]. Graven [18] recommended that the L_{eq} be $\leq$ 50 dBA with an L_{max} of 70 dBA, as these criteria would "protect sleep, support stable vital signs, and improve speech intelligibility for many infants."

These recommended levels for ambient sound in the NICU are much lower than the standards established for adults by the National Institute for Occupational Safety and Health (NIOSH) in 1998, which recommended a workplace exposure limit of 85 dBA as an 8-h time-weighted average (TWA) [19]. This limit differs slightly from the EPA and AAP guidelines due to differences in measurement. NIOSH recorded levels of ambient sound using special-purpose sound level meters called dosimeters, with a TWA output and/or "dose" expressed as a percent of the total permissible daily exposure and corresponds to an average level of 90 dB over 8 h. However, the World Health Organization (WHO) report that ambient sound exposures >70 dBA L_{eq} over a 24 h period (comparable to EPA measures) negatively impact stress and behavior, including increased risk of hearing loss, reduced performance of cognitive tasks, hypertension, neurosis, and sleep disturbance [20]. Taken together, these standards for adults (i.e., <70 dBA L_{eq}) allow for a much greater tolerance of sound exposure compared to those recommended for infants in the NICU (i.e., 45 dBA L_{eq}). Table 1 summarizes both adult and infant sound exposure recommendations for each organization.

Although previous studies have measured the levels of ambient sound in NICU settings, there are inconsistencies in study design, such as placing the dosimeter or sound level meter away from the occupied isolette [21,22], recording sound levels <24 h each day [14,15,17], or completing sound measurements in empty isolettes or empty rooms without ventilator noise [23]. Little to no evidence exists on the long-term effects of the higher levels of ambient sounds on the hearing of NICU infants. This is critical, as exposure to sustained levels of ambient sound can induce significant temporary and permanent hearing losses in adults and may have the same, or greater, effect on hearing in infants [24].

In addition to ambient sounds, as many as 57.5% of neonates receive gentamicin - an aminoglycoside antibiotic - for suspected or confirmed bacterial infections, because of its low-cost, broad spectrum and high bactericidal efficacy [25,26]. However, aminoglycosides can have deleterious effects on cochlear outer hair cells, initially resulting in, a higher frequency ($\geq$8 kHz) sensorineural hearing loss known as ototoxicity [27,28]. Aminoglycoside ototoxicity has been widely researched in adults, and despite some conflicting studies, substantial evidence for gentamicin-induced