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ORIGINAL ARTICLE

Maternal and Placental Factors Associated with Congenital Hearing Loss in Very Preterm Neonates

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refer

Background: Sensorineural hearing loss (SNHL) is a multifactorial disease that more frequently affects preterm newborns. Although a number of maternal conditions have been reported to be associated with preterm birth, little information is available concerning maternal risk factors for the development of SNHL. We aimed to identify maternal and placental risk factors associated with a "refer" result on the newborn hearing screening (NHS) test and subsequently confirmed SNHL in very preterm neonates.
Methods: This retrospective cohort study included 267 singleton neonates who were born alive after ≤ 32 weeks. Histopathologic examination of the placenta was performed, and clinical data were retrieved from a computerized perinatal database. Cases with two abnormal findings, "refer" on the NHS test, and presence of SNHL on the confirmation test were retrospectively reviewed based on electronic medical records.
Results: Forty-two neonates (15.7%) showed a "refer" result, and, on the confirmation test, permanent SNHL was identified in 1.87% (5/267) of all neonates. Multivariate regression analysis revealed that the presence of funisitis was independently associated with a "refer" on the NHS test, whereas use of antenatal corticosteroids was statistically significantly associated with a reduced incidence of "refer" on the screening test. Neither histologic chorioamnionitis nor prematurity (as defined by low gestational age and birth weight) was associated with a "refer" on the NHS test. By contrast, multivariate analysis with occurrence of SNHL as a dependent variable identified no significant associations with the parameters studied, probably owing to the small total number of neonates with permanent SNHL.

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Conclusion: Presence of funisitis was significantly and independently associated with increased risk of abnormal NHS results, while administration of antenatal corticosteroids was related to a normal NHS result. These findings support the hypothesis that a systemic fetal inflammatory response, manifested as funisitis, might play a role in the pathogenesis of SNHL in preterm neonates.

1. Introduction

It has been estimated that bilateral sensorineural hearing loss (SNHL) occurs in approximately 1.86 of 1000 newborns.[1] The prevalence of bilateral severe SNHL was previously reported to be 9.7% in neonates who survived with a very low birth weight ($\leq$ 1500 g) and 16.7% in neonates who survived after neonatal seizure.[2] Although the prevalence of severe SNHL in very low birth weight or preterm neonates has decreased in the past decade, it still remains significant, ranging from 0% to 4%.[3] The observed decline in these numbers is due to the improvement in control of risk factors such as infection and implementation of oxygen supply monitoring at neonatal intensive care units (NICUs).

Many studies have addressed the causes of neonatal SNHL. Morton and Nance[1] reported that Mendelian genetic causes accounted for at least 50–60% of cases of neonatal SNHL. Furutate et al[4] and Park et al[5] reported that cytomegalovirus infection also accounted for 10–30% of neonatal SNHL cases. In addition to genetic causes and cytomegalovirus infection, Swigonski et al[6] identified exposure to ototoxic drugs as one of the most common risk factors of neonatal SNHL. According to Borradori and colleagues,[7] dopamine and furosemide are especially dangerous ototoxic drugs associated with neonatal SNHL.

There have been reports suggesting that prematurity itself is a cause of neonatal SNHL. Ari-Even Roth et al[8] published the incidence of SNHL in neonates with extremely low birth weight. Ten (3.0%) out of 337 such neonates were documented to have a hearing impairment. Of these, one infant (0.3%) showed bilateral moderate-to-severe SNHL, while the other nine infants (2.7%) turned out to have conductive hearing loss. Pereira et al[9] suggested that low gestational age (GA) and low birth weight resulted in a higher rate of no response to transient-evoked otoacoustic emission: the odds ratios for an abnormal transient-evoked otoacoustic emission result were 1.76 and 1.58, respectively, in neonates with $<$ 30 weeks of gestation and birth weight $<$ 1500 g. Finally, a statistically significant difference in the prevalence of SNHL was observed between normal full-term neonates and premature neonates (0.82% vs. 3.1%).[9]

In light of this higher prevalence of SNHL among premature neonates, several researchers tried to delineate factors related to prematurity that contributed to the increased risk of SNHL. Of neonatal factors, hyperbilirubinemia,[10,11] surgical ligation of patent ductus arteriosus,[12] and respiratory status (duration of ventilation and oxygen treatment) appeared to be associated with significant SNHL.[3,13] However, although a number of maternal conditions have been reported to be associated with preterm birth (e.g., intrauterine infection and preeclampsia), little information is available concerning maternal risk factors for the development of SNHL. In particular, several reports provided somewhat contradictory results with regard to the role of histological chorioamnionitis in the development of SNHL.[12,14,15]

In recent years, the technology and protocols of the newborn hearing screening (NHS) test have been significantly improved, which has made the NHS test the main modality for early detection of SNHL. Accordingly, this study aimed to identify maternal and placental risk factors associated with abnormal NHS results and subsequently confirmed SNHL in very preterm neonates.

2. Methods

This was a single-center retrospective cohort study of neonates admitted to the NICU at Seoul National University Bundang Hospital (Seongnam, Korea) from January 2004 to January 2013. Since 2003, we have routinely performed pathological examinations of the placenta for all cases of preterm delivery at our institution and maintained a database that prospectively collects clinical data on all obstetric women and their neonates admitted to the NICU. From this database, we retrospectively identified all singleton infants born alive at $\leq$ 32.0 weeks of gestation who: (1) survived for at least 90 days after birth; (2) underwent hearing screening examinations; and (3) did not have major congenital anomalies. We excluded neonates without histologic examination of the placenta, twins or higher-order multiple births, and out-born infants. GA was calculated based on the last menstrual period and confirmed by the first or second trimester ultrasound examination. The study was approved by the Institutional Review Board (IRB) of the Seoul National University Bundang Hospital (IRB number: B-1006/103-102). The requirement to obtain informed consent was waived by the IRB.

Electronic medical records regarding hearing loss in one or both ears of the included preterm singleton neonates were reviewed twice by two audiologists (S.H.K and J.H.P.) who were blinded to the maternal and neonatal details and results of placental pathological examination. Either automated auditory brainstem response (ABR) or automated otoacoustic emission (OAE) test was performed as an NHS test, and the results were recorded as either "refer" (further confirmatory tests needed) or "pass" (normal). As a confirmatory test, auditory brainstem response threshold

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