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Antecedents and correlates of visual field deficits in children born extremely preterm

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ABSTRACT

Aim: We sought to identify the antecedents and correlates of visual field deficits (VFDs) at age 2 years among infants born before the 28th week of gestation.
Methods: The visual fields of 1023 infants were assessed by confrontation at age 2 years. We compared the ante-and postnatal characteristics and exposures of the 65 infants with a VFD to their peers who did not have a VFD. We used time-oriented logistic regression risk models to assess the associations of potential antecedents and correlates with a VFD.
Results: In the final regression model, VFD was associated with maternal consumption of aspirin during the current pregnancy, recurring/persistent acidemia during the first 3 postnatal days, cerebral ventriculomegaly seen on neonatal ultrasound, prethreshold retinopathy of prematurity (ROP), and supplemental oxygen and ventilator dependence at 36 weeks post-menstrual age. Birth before the 27th week was also associated with increased risk, but its significance was diminished by the addition of postnatal variables.
Conclusion: In this sample of extremely preterm born infants, antenatal as well as early and late postnatal characteristics and exposures are associated with an increased risk of having a VFD. Our study adds to our knowledge about the complex etiology of visual deficits of prematurity, and supports a multifactorial cause of these deficits.

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1. Introduction

Preterm infants are at increased risk of visual impairments, including acuity deficits,[1] strabismus,[2] reduced contrast and color sensitivity,[1] refractive errors,[3] and visual field deficits (VFDs).[4] Visual problems among infants born preterm are associated with cognitive disability at 2 years of age,[2] lower IQ scores at 5 years of age,[5] and motor problems among teenagers.[6]

Cerebral visual impairment and retinopathy of prematurity (ROP) represent the two main causes of visual impairment in preterm born children, and appear to contribute to VFDs independently.[7,8] In the brain, the primary visual pathway is anatomically close to where white matter damage tends to occur, and VFDs may be a result of such injury.[9] In addition, visual field deficits are specifically associated with cerebral damage such as unilateral spastic CP.[10,11]

The increased risk of VFD in infants with ROP is probably mediated both via the pathological process of ROP itself, and an iatrogenic effect of cryotherapy or laser coagulation.[4,8,12] On the other hand, children with ROP in the ELGAN Study were at increased risk of dysfunctions associated with brain damage.[13] Further, severe ROP is associated with nonvisual disabilities such as physical and cognitive impairment at age 5,[14,15] below-grade-level academic performance at 8 years,[16] and lower health-related quality of life at 10 years.[17] These studies suggest a shared etiology for visual and non-visual developmental disabilities in preterm born children.

In this study we examined the association between maternal, perinatal, and postnatal factors and VFDs in a cohort of more than 1000 extremely low gestational age newborns (ELGANs).[18] We are not aware of any previous study that has explored this topic in such a large cohort of extremely preterm children. The identification of VFD and their preventable risk factors is crucially important so that caretakers and professionals can improve long-term visual outcomes.

2. Material and methods

2.1. Participants

The ELGAN study was designed to identify characteristics and exposures that increase the risk of structural and functional neurological disorders in infants born extremely preterm.[18] During the years 2002–2004, women who gave birth before 28 weeks gestation at one of 14 participating hospitals in 5 states in the U.S. were asked to enroll. The individual institutional review boards approved the study.

Mothers were approached for consent either upon antenatal admission or shortly after delivery, depending on clinical circumstances and institutional preference. A total of 1506 infants born to 1249 mothers were enrolled. The sample presented in this study consists of the 1023 infants who had a developmental and visual field assessment at 2 years corrected age.

2.2. Demographic and pregnancy variables

After birth, a trained research nurse interviewed each mother in her native language using a structured form. Shortly after the mother's discharge, the nurse reviewed the maternal chart using a second structured form. Circumstances that led to preterm delivery were identified using data from the maternal interview, and data abstracted from the medical record.[19]

2.3. Placenta

Placentas were biopsied under sterile conditions. Eighty-two percent of the samples were obtained within 1 h of delivery. The microbiologic and histological procedures of the placenta are described in detail elsewhere.[20,21] In keeping with guidelines,[22] representative sections were taken from all abnormal areas as well as routine sections of the umbilical cord and a membrane roll, and full thickness sections from the center and a paracentral zone of the placental disc. After training to minimize observer variability, study pathologists examined the slides for histologic characteristics listed on a standardized data form.[23,24]

2.4. Newborn variables

Gestational age (GA) was estimated based on date of embryo retrieval, intrauterine insemination, or fetal ultrasound before the 14th week (62%). When these were not available, the estimate was based on fetal ultrasound at week 14 or later (29%), last menstrual period (7%), or GA recorded in the log of the Neonatal Intensive Care Unit (NICU) (1%).

Birth weight Z-score was defined as number of standard deviations above or below the median weight of infants of same GA in referent samples not delivered for preeclampsia or fetal indications.[25] Infants with birth weight Z-score between ≥ -2 and < -1 were identified as moderately growth restricted, and infants with a Z-score ≤ -2 were identified as severely growth restricted. Physiology, laboratory, and therapy data were collected during the first 12 postnatal hours so we could calculate a Score for Neonatal Acute Physiology (SNAP-II™).[26]

The infants were classified by their most extreme blood gas measurements on postnatal days 1, 2, and 3. For each day, the lowest and highest PaO_2, PCO_2, and pH were recorded. The infants were classified by whether or not their value was in the extreme quartile for their GA (23–24, 25–26, and 27 weeks) in the cohort on each postnatal day, and whether the specimen was arterial or venous. Values in the extreme quartile on at least 2 of the 3 days were considered as "exposed." Since infants who did not have blood gas measurements on postnatal day 3 were less likely than others to have extreme measurements on postnatal day 2, we assigned these newborns to the group with non-extreme measurements on postnatal day 3. This allowed us to include children with no measurement on the 3rd postnatal day.

Blood culture results were recorded for each of the first 4 postnatal weeks. We define bacteremia in the 1st week as "early," and in weeks 2, 3 or 4 as "late."