

# Mode of delivery at periviability and early childhood neurodevelopment

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**OBJECTIVE:** Little is known regarding the impact of mode of delivery in the periviable period. Even less is understood regarding the effect of mode of delivery on neurodevelopment. Our objective is to determine if the mode of delivery at time of periviability impacts Bayley II scores at 2 years of age.

**STUDY DESIGN:** This is a secondary analysis of a randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy, a multicenter trial where women at imminent risk for delivery were assigned to receive magnesium sulfate or placebo. For this secondary analysis we included nonanomalous singleton gestations delivered between 23 4/7 and 25 6/7 weeks. We excluded women with missing exposure or outcome data. The primary exposure of interest was mode of delivery. The primary outcome was Bayley II scores <70 (mental and motor) at 2 years of age. Log binomial regression was used to control for possible confounders including gestational age at delivery, presentation

at time of delivery, chorioamnionitis, years of maternal education, maternal body mass index, and original study treatment group.

**RESULTS:** A total of 158 women met inclusion criteria. In all, 91 had a vaginal delivery and 67 had a cesarean delivery. Exposure to magnesium sulfate, maternal education, chorioamnionitis, years of maternal education, and maternal body mass index were similar in both groups. There was no difference in either mental or motor Bayley II scores <70 or <85 by mode of delivery in either univariable or multivariable analysis.

**CONCLUSION:** There is no detectable difference in Bayley II scores between mode of delivery at time of periviability. This adds to the literature supporting obstetric indications dictating mode of delivery at this gestational age.

**Key words:** Bayley II, mode of delivery, neonatal outcomes, periviability

Cite this article as: Običan SG, Small A, Smith D, et al. Mode of delivery at periviability and early childhood neurodevelopment. *Am J Obstet Gynecol* 2015;213:x.ex-x.ex.

There is much debate in the field of maternal-fetal medicine about the optimal mode of delivery for the periviable infant, defined as an infant delivered between 22 0/7 and 25 6/7 weeks' gestation.<sup>1,2</sup> Very preterm infants born <32 weeks of gestation and especially extremely preterm infants born <28 weeks of gestation are at particularly high risk for mortality and morbidity.<sup>1</sup> One of the most devastating consequences of a preterm delivery is the

potential effect on the future neurodevelopment of the child. Preterm birth has been associated with decreased IQ in the offspring with a dose-response relationship based on gestational age.<sup>2</sup> This risk is particularly concerning for the periviable infant, since the risk of neurodevelopmental disability increases with decreasing gestational age.<sup>3</sup> The optimal route of delivery for the periviable infant is not known, especially in regards to how mode of delivery might

affect the future neurodevelopment of this delicate population.

Despite the uncertainty regarding the optimal delivery method of the periviable infant, cesarean delivery is 57% for this group.<sup>3</sup> Cesarean deliveries are thought to have a theoretical advantage over vaginal deliveries in premature infants due to the avoidance of prolonged labor, which would allow for a less traumatic birth.<sup>4</sup> In 1 study of early preterm infants, including periviable infants, cesarean delivery was associated with lower mortality rates, higher 1-minute Apgar scores, and fewer instances of intraventricular hemorrhage.<sup>5</sup> However, preterm cesarean deliveries are not without risk. They can be technically difficult and carry increased maternal risks over vaginal deliveries including the need for a classic incision, maternal hemorrhage, and bladder injuries. On the other hand, vaginal deliveries have also been linked to various risks including hypoxia and future neurodisability of the infant.<sup>6</sup> Since each delivery is unique, the complexity of these issues relies on balancing the risks to both mother and child.

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Received March 7, 2015; revised May 27, 2015; accepted June 17, 2015.

This manuscript could not have been completed without the assistance of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the Maternal-Fetal Medicine Units (MFMU) Network, and the study protocol subcommittee. However, the contents of this report represent the views of the authors and not necessarily those of the NICHD MFMU Network or the National Institutes of Health.

The authors report no conflict of interest.

Presented in poster format at the 35th annual meeting of the Society for Maternal-Fetal Medicine, San Diego, CA, Feb. 2-7, 2015.

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0002-9378/\$36.00 • © 2015 Elsevier Inc. All rights reserved. • <http://dx.doi.org/10.1016/j.ajog.2015.06.047>

The purpose of our study is to determine whether the mode of delivery at the time of periviability impacts the neurodevelopment of the infant. We hypothesized that mode of delivery for periviable infants would not significantly impact future neurodevelopment as measured by Bayley II scores.

## MATERIALS AND METHODS

This is a secondary analysis of the Beneficial Effects of Antenatal Magnesium randomized, controlled trial conducted through the *Eunice Kennedy Shriver* National Institute of Child Health and Development's Maternal-Fetal Medicine Units (MFMU) Network performed at 20 US academic centers from December 1997 through May 2004. The objective of the parent study was to assess whether administration of antenatal magnesium decreased the rate of cerebral palsy or death in children likely to be born preterm. Data were collected for women randomized between 22-31 weeks of gestation at risk of preterm birth due to rupture of membranes, spontaneous labor, or anticipated indicated preterm delivery within 2-24 hours. The details of the study have previously been reported.<sup>7</sup>

The current study was approved by the institutional review board at Columbia University Medical Center. We included nonanomalous singleton gestations delivered between 23 4/7 and 25 6/7 weeks, as the earliest survivor in our cohort was delivered at 23 4/7 weeks. We excluded women with missing exposure (mode of delivery) or outcome data (Bayley II scores). Our primary exposure of interest was mode of delivery. The primary outcomes were mental and psychomotor Bayley II scores <70 at 2 years of age.

The Bayley Scales of Infant and Toddler Development are an individually administered instrument to assess neurodevelopmental functioning of infants and young children between 1-42 months of age. It is used both clinically and in the research setting.<sup>8</sup> Clinically, its primary goal is to identify children with developmental delay and allow for intervention planning. As a research tool, it is used to determine the developmental outcomes associated with a history of prematurity and drug exposures.<sup>9,10</sup> Prior to 2006

and the introduction of the Bayley III, the Bayley II was considered the standard neurodevelopmental tool in young children. The Bayley II evaluates sensory-perception, knowledge, memory, problem solving, and early language.<sup>8</sup>

In the parent study, all children were evaluated by Bayley II as a prespecified secondary outcome. The test was administered by either a trained psychologist or psychometrist at 2 years of age, corrected for prematurity.

The Strengthening the Reporting of Observational Studies in Epidemiology guidelines were followed. Continuous variables were compared with the Student *t* test or Wilcoxon rank sum and categorical variables with  $\chi^2$  or Fisher exact test as appropriate. Bivariate analyses were used to identify independent variables that were associated with mode of delivery and neurodevelopmental outcomes defined by the Bayley II scores. The association between mode of delivery and Bayley scores was estimated using log linear regression adjusting for potential confounding variables, including gestational age at delivery, presentation at time of delivery, chorioamnionitis, years of maternal education, maternal body mass index (BMI), and original study treatment group. Our sample size was fixed by the parent study and our necessary exclusions, with 67 patients undergoing a cesarean delivery and 91 delivered vaginally. Prior data suggest that approximately 35% of early preterm infants would have an abnormal Bayley II score. Thus, with a power of 80% and a type I error rate of 0.05, we would be able to detect true relative risks of  $\leq 0.408$  or  $\geq 1.674$  in exposed subjects relative to unexposed subjects. We used a continuity-corrected  $\chi^2$  statistic or Fisher exact test to evaluate this null hypothesis. All tests were 2-tailed. We calculated adjusted odds ratios with 95% confidence intervals (CIs) for variables of interest. We then fit a log linear regression model to adjust for possible confounders. Software (SAS, version 8; SAS Institute, Cary, NC) was used for the analysis.

## RESULTS

From the original population of 2444 neonates in the parent trial, we sequentially

excluded 406 twins, 1775 infants delivered at  $\geq 26$  weeks, 103 infants without Bayley II scores, and 2 infants with major congenital anomalies yielding a total of 158 meeting our inclusion and exclusion criteria. Our analysis group contained 91 neonates delivered vaginally and 67 neonates delivered by cesarean. The earliest gestational age of delivery of eligible patients was 23 4/7 weeks in the vaginal delivery group and 24 2/7 weeks in those delivered by cesarean.

Demographic and obstetric characteristics of the study population are presented in Table 1. Exposure to magnesium sulfate, maternal education, chorioamnionitis, years of maternal education, and maternal BMI were similar in both groups. There is a significant difference between groups in presentation at time of delivery with vertex presentation by far the most common in the vaginal delivery group and breech presentation being the most common in the cesarean delivery group (Table 1).

Neurodevelopmental outcomes by Bayley II scores are presented in Table 2. On unadjusted analyses, children of women who delivered vaginally or by cesarean delivery did not show a difference in Bayley Mental Developmental Index (MDI) <70 or Psychomotor Developmental Index (PDI) <70 at 2 years of age. Additionally, there was no difference in MDI or PDI <85 between vaginal and cesarean deliveries. The mean Bayley MDI and PDI scores also did not significantly differ between groups.

After controlling for potential confounders including gestational age at delivery, presentation at time of delivery, chorioamnionitis, years of maternal education, maternal BMI, and original study treatment group, all of the study outcomes remained nonsignificantly different between the 2 groups. The adjusted relative risks for Bayley MDI <70 and <85 were 0.78 (95% CI, 0.47–1.31) and 0.92 (95% CI, 0.70–1.21), respectively. The adjusted relative risks for Bayley PDI <70 and <85 were 0.98 (95% CI, 0.54–1.77) and 1.02 (95% CI, 0.72–1.45), respectively.

## COMMENT

Our study provides evidence that among periviable pregnancies, the mode of

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