

Beneficial effects of breast milk in the neonatal intensive care unit on the developmental outcome of extremely low birth weight infants at 18 months of age.

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OBJECTIVE: Beneficial effects of breast milk on cognitive skills and behavior ratings have been demonstrated previously in term and very low birth weight infants. Extremely low birth weight infants are known to be at increased risk for developmental and behavior morbidities. The benefits of breast milk that is ingested in the NICU by extremely low birth weight infants on development and behavior have not been evaluated previously.

METHODS: Nutrition data including enteral and parenteral feeds were collected prospectively, and follow-up assessments of 1035 extremely low birth weight infants at 18 months' corrected age were completed at 15 sites that were participants in the National Institute of Child Health and Human Development Neonatal Research Network Glutamine Trial between October 14, 1999, and June 25, 2001. Total volume of breast milk feeds (mL/kg per day) during hospitalization was calculated. Neonatal characteristics and morbidities, interim history, and neurodevelopmental and growth outcomes at 18 to 22 months' corrected age were assessed. **RESULTS:** There were 775 (74.9%) infants in the breast milk and 260 (25.1%) infants in the no breast milk group. Infants in the breast milk group were similar to those in the no breast milk group in every neonatal characteristic and morbidity, including number of days of hospitalization. Mean age of first day of breast milk for the breast milk infants was 9.3 +/- 9 days. Infants in the breast milk group began to ingest non-breast milk formula later (22.8 vs 7.3 days) compared with the non-breast milk group. Age at achieving full enteral feeds was similar between the breast milk and non-breast milk groups (29.0 +/- 18 vs 27.4 +/- 15). Energy intakes of 107.5 kg/day and 105.9 kg/day during the hospitalization did not differ between the breast milk and non-breast milk groups, respectively. At discharge, 30.6% of infants in the breast milk group still were receiving breast milk. Mothers in the breast milk group were significantly more likely to be white (42% vs 27%), be married (50% vs 30%), have a college degree (22% vs 6%), and have private health insurance (34% vs 18%) compared with the no breast milk group. Mothers who were black, had a low household income (< or = dollar 20000), or had higher parity were less likely to provide breast milk feeds. The analysis of outcomes between the any human milk and no human milk groups were adjusted for maternal age, maternal education, marital status, race/ethnicity, and the other standard covariates. Children in the breast milk group were more likely to have a Bayley Mental Development Index > or = 85, higher mean Bayley Psychomotor Development Index, and higher Bayley Behavior Rating Scale percentile scores for orientation/engagement, motor regulation, and total score. There were no differences in the rates of moderate to severe cerebral palsy or blindness or hearing

impairment between the 2 study groups. There were no differences in the mean weight (10.4 kg vs 10.4 kg), length (80.5 cm vs 80.5 cm), or head circumference (46.8 cm vs 46.6 cm) for the breast milk and no breast milk groups, respectively, at 18 months. Multivariate analyses, adjusting for confounders, confirmed a significant independent association of breast milk on all 4 primary outcomes: the mean Bayley (Mental Development Index, Psychomotor Development Index, Behavior Rating Scale, and incidence of rehospitalization). For every 10-mL/kg per day increase in breast milk ingestion, the Mental Development Index increased by 0.53 points, the Psychomotor Development Index increased by 0.63 points, the Behavior Rating Scale percentile score increased by 0.82 points, and the likelihood of rehospitalization decreased by 6%. In an effort to identify a threshold effect of breast milk on Bayley Mental Development Index and Psychomotor Development Index scores and Behavior Rating Scale percentile scores, the mean volume of breast milk per kilogram per day during the hospitalization was calculated, and infants in the breast milk group were divided into quintiles of breast milk ingestion adjusted for confounders. Overall, the differences across the feeding quintiles of Mental Development Index and Psychomotor Development Index were significant. There was a 14.0% difference in Behavior Rating Scale scores between the lowest and highest quintiles. For the outcomes (Mental Development Index, Psychomotor Development Index, Behavior Rating Scale, and Rehospitalization <1 year), only the values for the >80th percentile quintile of breast milk feeding were significantly different from the no breast milk values. In our adjusted regression analyses, every 10 mL/kg per day breast milk contributed 0.53 points to the Bayley Mental Development Index; therefore, the impact of breast milk ingestion during the hospitalization for infants in the highest quintile (110 mL/kg per day) on the Bayley Mental Development Index would be 10 x 0.53, or 5.3 points. CONCLUSIONS: An increase of 5 points potentially would optimize outcomes and decrease costs by decreasing the number of very low birth weight children who require special education services. The societal implications of a 5-point potential difference (one third of an SD) in IQ are substantial. The potential long-term benefit of receiving breast milk in the NICU for extremely low birth weight infants may be to optimize cognitive potential and reduce the need for early intervention and special education services.

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Persistent beneficial effects of breast milk ingested in the neonatal intensive care unit on outcomes of extremely low birth weight infants at 30 months of age.

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BACKGROUND: We previously reported beneficial effects of breast milk ingestion by infants with extremely low birth weight in the NICU on developmental outcomes at 18 months' corrected age. The objective of this study was to determine whether these effects of breast milk in infants with extremely low birth weight persisted at 30 months' corrected age. **METHODS:** Nutrition data, including enteral and parenteral feeds, were prospectively collected, and 30 months' corrected age follow-up assessments were completed on 773 infants with extremely low birth weight who participated in the National Institute of Child Health and Human Development Neonatal Research Network Glutamine Trial. A total of 593 ingested some breast milk during the neonatal hospitalization, and 180 ingested none. Neonatal feeding characteristics and morbidities and 30-month interim history, neurodevelopmental outcomes, and growth parameters were analyzed. Children were divided into quintiles of breast milk volume to evaluate the effects of volume of human milk ingested during the NICU hospitalization. **RESULTS:** At 30 months, increased ingestion of breast milk was associated with higher Bayley Mental Developmental Index scores, higher Bayley behavior score percentiles for emotional regulation, and fewer rehospitalizations between discharge and 30 months. There were no differences in growth parameters or cerebral palsy. For every 10 mL/kg per day increase in breast milk, the Mental Developmental Index increased by 0.59 points, the Psychomotor Developmental Index by 0.56 points, and the total behavior percentile score by 0.99 points, and the risk of rehospitalization between discharge and 30 months decreased by 5%. **CONCLUSIONS:** Beneficial effects of ingestion of breast milk in the NICU persist at 30 months' corrected age in this vulnerable extremely low birth weight population. Continued efforts must be made to offer breast milk to all extremely low birth weight infants both in the NICU and after discharge.

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Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants.

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OBJECTIVES: The objectives of this study were to assess whether (1) in-hospital growth velocity is predictive of neurodevelopmental and growth outcomes at 18 to 22 months' corrected age among extremely low birth weight (ELBW) infants and (2) in-hospital growth velocity contributes to these outcomes after controlling for confounding demographic and clinical variables. **METHODS:** Infants 501 to 1000 g birth weight from a multicenter cohort study were divided into quartiles of in-hospital growth velocity rates. Variables considered for the logistic-regression models included gender, race, gestational age, small for gestational age, mother's education, severe intraventricular hemorrhage, periventricular leukomalacia, age at regaining birth weight, necrotizing enterocolitis, late-onset infection, bronchopulmonary dysplasia, postnatal steroid therapy for pulmonary disease, and center. **RESULTS:** Of the 600 discharged infants, 495 (83%) were evaluated at 18 to 22 months' corrected age. As the rate of weight gain increased between quartile 1 and quartile 4, from 12.0 to 21.2 g/kg per day, the incidence of cerebral palsy, Bayley II Mental Developmental Index (MDI) <70 and Psychomotor Developmental Index (PDI) <70, abnormal neurologic examination, neurodevelopmental impairment, and need for rehospitalization fell

significantly. Similar findings were observed as the rate of head circumference growth increased. The in-hospital rate of growth was associated with the likelihood of anthropometric measurements at 18 months' corrected age below the 10th percentile values of the Centers for Disease Control and Prevention 2000 growth curve. Logistic-regression analyses, controlling for potential demographic or clinical cofounders, and adjusted for center, identified a significant relationship between growth velocity and the likelihood of cerebral palsy, MDI and PDI scores of <70, and neurodevelopmental impairment. CONCLUSIONS: These analyses suggest that growth velocity during an ELBW infant's NICU hospitalization exerts a significant, and possibly independent, effect on neurodevelopmental and growth outcomes at 18 to 22 months' corrected age.

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