Impact of Nutrition on Bronchopulmonary Dysplasia

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KEYWORDS

• Nutrition • Bronchopulmonary dysplasia • Growth • Premature infants

KEY POINTS

- Suboptimal intrauterine and postnatal growth is associated with an increased risk of bronchopulmonary dysplasia (BPD).
- Premature infants with BPD are at high risk for poor growth attainment after discharge from the neonatal intensive care unit.
- A multidisciplinary approach to postdischarge management is critical to optimize nutrition, growth, and medical outcomes.
- Pilot human data and animal data support the critical role of specific immunonutrients in lung development and in the protection from lung injury. Additional research and bedside translation are needed to optimize nutritional strategies in the neonatal intensive care unit and following hospital discharge.

INTRODUCTION

Bronchopulmonary dysplasia (BPD) remains a common morbidity of prematurity. Although the pathogenesis of BPD is recognized to be both multifactorial and complex, much of the focus is traditionally on injurious factors, such as oxygen toxicity, volutrauma, and inflammation. Discussion of the role of nutrition in the pathophysiology of BPD is typically limited to management after a diagnosis has been made. In this article, the association between growth and pulmonary outcomes is reviewed, including the role of nutrition in lung development and function, the consequences of various treatments for lung disease on nutritional status, and the nutritional strategies to optimize growth of infants at risk for or diagnosed with BPD, including management

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following hospital discharge. Finally, research opportunities on the role of nutrition and lung disease are considered.

INTRAUTERINE GROWTH AND PULMONARY OUTCOMES

Although infants with BPD are more likely to experience postnatal growth failure, it is important to recognize that suboptimal intrauterine growth is also associated with an increased risk of adverse pulmonary outcomes. Although the incidence of small for gestational age (weight less than the 10th percentile) among very low birth weight infants is approximately 20%,[1] large cohort and observational studies have demonstrated significantly higher neonatal mortality and rates of BPD in small-for-gestational-age neonates compared with preterm infants born appropriate for gestational age.[2,3]

Indeed, fetal growth restriction based on birth weight *z* scores was found to be independently associated with the risk of chronic lung disease in the (ELGAN) Extremely Low Gestational Age Newborn study cohort.[4] Although not completely understood, decreased lung growth is hypothesized to be the mechanism. Using a well-established animal model of placental insufficiency, Rozance and colleagues[5] found decreased alveolar and vascular growth in fetal lambs with intrauterine growth restriction. These investigators hypothesize that a similar mechanism may contribute to the increased risk of BPD in infants with suboptimal intrauterine growth. A review of clinical and animal data discussed later in greater detail suggests that these changes in lung growth may be amenable to nutritional interventions.

POSTNATAL GROWTH AND CLINICAL OUTCOMES

Postnatal growth failure, typically defined as weight less than the tenth percentile for gestational age at 36 weeks postmenstrual age (PMA), is an all too common by-product of several months in the neonatal intensive care unit (NICU). Although the incidence of postnatal growth failure in extremely premature infants has steadily declined over the past 2 decades,[1,6,7] further efforts to decrease growth faltering are urgently needed. In a recent cohort of more than 2000 infants less than 27 weeks' gestation reported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network, 55% were found to have weight less than the tenth percentile at 36 weeks PMA based on the Olsen postnatal growth curves.[6,8] Infants who have experienced one or more major morbidity, such as BPD, necrotizing enterocolitis, severe intracranial hemorrhage, or late-onset sepsis, have a higher incidence of postnatal growth failure than infants who survive without a major morbidity. Factors commonly associated with postnatal growth failure include male gender, need for assisted ventilation on the first day of life, necrotizing enterocolitis, need for respiratory support at 28 days of age, and treatment with postnatal corticosteroids.[9]

Ehrenkranz and colleagues[10] evaluated the relationship between in-hospital weight gain and neonatal morbidities in a cohort of extremely low birth weight (501–1000 g) infants cared for in centers participating in the Eunice Kennedy Shriver NICHD Neonatal Research Network. Infants were divided into quartiles of weight gain, with those in the lowest quartile gaining an average of 12 g/kg/d, whereas those in the highest quartile gaining an average of 21 g/kg/d. Not surprisingly, the incidence of BPD and receipt of postnatal corticosteroids were higher in the infants in the lowest quartile of in-hospital weight gain (BPD: 56% vs 31%; postnatal steroids: 64% vs 30% for lowest weight gain quartile and highest weight gain quartile, respectively). In-hospital weight gain was also found to have a significant and independent effect on