In infants who are not 'recovering' and there are no signs of systemic illness ... protein status should be closely evaluated and supplementation be instituted

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Nutrition of Preterm Infants after Discharge

by Richard Cooke

Key Insights

The increased risk for poor growth and the nutritional challenges do not end when the preterm infant leaves the hospital, particularly for those breast-fed. This article outlines the requirements and suggests steps to ensure that protein intakes after discharge are adequate for recovering to a normal development.

Current knowledge

Programmed growth velocity is greatest in preterm infants approximately between 28 days and 1–2 months corrected age. Yet, studies examining growth after discharge show, for the most part, preterm infants do not grow as well as term counterparts at 3 and 8 years, and in adulthood. Until recently, the nutritional factors involved in the pathogenesis of this growth restriction were poorly studied.

Practical implications

Human milk fortification or nutrient-enriched formula is recommended after discharge. Regardless of how a preterm infant is fed, growth must be closely monitored, i.e. every 2–3 weeks, to ensure that they 'recover' or 'catch back' to their original birth weight percentile by 1–2 months corrected age.

Recommended reading

Cooke RJ, Griffin IJ, McCormick K: Adiposity is not altered in preterm infants fed with a nutrient-enriched formula after hospital discharge. *Pediatr Res* 2010;67:660–664.

Small for gestational age: schematic of growth restriction between preterm and term infants at hospital discharge (see text for details).

Nutrition of Preterm Infants after Discharge

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Key Message

- Regardless how an infant is fed, growth must be closely monitored after discharge so that they 'recover' to their original birth weight percentile by 1–2 months corrected age; thus, supplementation should be logically instituted as needed.

Key Words

Catch-up growth · Discharge · Nutritional support · Preterm infants

Abstract

The fundamental principle underlying nutritional support is that intake meets needs thereby ensuring the best outcome, which, in the case of the preterm infant, is optimal growth and development. Achieving this goal is problematic. Most, if not all, very-low-birth-weight infants (VLBWI) are undernourished and under-grown when they are first discharged from the hospital. This has important implications for the nutritional care of preterm, particularly the breast-fed, VLBWI after hospital discharge.

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Postnatal Growth Failure

Many preterm, if not all, very-low-birth-weight infants (VLBWI) are growth restricted at hospital discharge [1, 2]. Several factors contribute to the development of growth failure. It takes time to establish an adequate intake in the small sick infant. Once established, enteral feeding is commonly interrupted because of clinical concerns, and it takes time to re-establish full intakes. In effect, infants accrue a nutrient deficit that is not recouped before hospital discharge.

Dietary needs are not well established in preterm infants. Recommendations assume that needs are consistent throughout gestation [3, 4]. They are not; yet, Ziegler et al. [5] have noted that protein requirements are inversely related to body weight, i.e. they fall from 3.8 to 3.1 g/100 kcal in infants weighing between 500 and 1,500 g. Standard preterm formulas have a protein:energy ratio of 3.0 g/100 kcal and, therefore, do not meet the protein needs of the preterm VLBWI.

Recommended intakes are based on needs for maintenance and normal growth [3, 4]; however, no allowance is made for recovery or 'catch-up' growth. In the study by Embleton et al. [2], the accrued protein deficit at hospital discharge varied from 15 to 25 g/kg. An additional protein intake of 0.5–1.0 g/kg/day would have been required to recoup this deficit before hospital discharge, which further compounds the problem.

Reduced body size in these infants is paralleled by alterations in adiposity and/or body composition. In the

study by Uthaya et al. [6], infants were underweight and short but had increased intra-abdominal fat leading to the conclusion that adiposity was altered in these infants' length. In the study by Cooke and Griffin [7], infants were underweight, short and had an increased total and central fat mass. These infants also had a significantly decreased lean or fat-free body mass [7].

A reduced body size that is paralleled by reduced linear growth and fat-free mass suggests that dietary protein needs were not met in these infants and that close attention be paid to dietary protein and energy intake after hospital discharge. A diet with a relatively low protein-to-energy ratio may compound the situation by further blunting insulin sensitivity, and thus the development of obesity and metabolic syndrome in later life [6, 8].

Postnatal Growth and Development

Malnutrition during infancy is associated with permanent alterations in brain growth, structure and function. Brain size is reduced, the brain cortex is thinner, neuronal cell numbers are decreased, myelination is reduced and dendritic morphology is altered, all of which can be related to poorer neurodevelopmental outcome [9, 10].

Early studies indicated that poor growth between birth and hospital discharge was associated with poorer neurodevelopment [11, 12], and that better growth, as achieved by feeding a nutrient-enriched formula, was associated with better developmental outcomes in preterm infants [13]. More recently, early parenteral nutrition coupled with the early introduction and advancement of enteral feeding has improved growth but many infants continue to be small for gestational age at hospital discharge [14].

A clear relationship exists between 'catch-up' growth and development in preterm infants but the time frame within which it needs to occur is not well delineated. In most studies, infants who 'catch up' or 'catch back' by 6–9 months corrected age have better neurodevelopmental outcome than those not catching up [11, 15]. In the study by Dharmaraj et al. [16], infants who 'recovered or caught up' by 2–3 months corrected age had significantly better development than those who did not [fig. 2 in ref. 16].

The course of postnatal growth, therefore, is a critical determinant of later development. In the case of the preterm VLBWI, the critical time frame for recovery or

'catch-up' is somewhere between 28 days and 1–2 months corrected age. This is when programmed growth velocity is greatest in preterm infants and recovery or 'catch-up' to the original birth weight percentile is paralleled by better development. If infants are to 'catch up', this is the time frame within which to do it.

Catch-Up Growth

Although catch-up growth may be related to better neurodevelopment, concern has been expressed about 'catch-up' growth and the development of insulin resistance and metabolic syndrome X [17] leading to the idea that 'bigger might not be better', even in preterm infants. Some confusion exists when the term 'catch-up' is used to describe growth during infancy.

In most instances, it is related to weight gain and then to the subsequent risk of obesity [17]. It has been interpreted more as a pathologic rather than physiologic phenomenon and, therefore, best avoided. But weight gain per se reveals little information on the nature of the gain. It also may not be preventable, i.e. after a period of growth

faltering, all infants 'recover' or 'catch up' to some degree when the underlying cause is treated and adequate nutrition is provided.

The extent to which it occurs depends on many factors; most pertinent to this discussion is the severity and

duration of the insult, i.e. the more severe and prolonged the insult the greater the accrued nutritional deficit. Subsequent intake must not only replace the accrued nutritional deficit but also meet the needs for maintenance and normal growth.

With acute illness, as occurs in preterm infants, there is an acute depletion of body protein to meet energy needs. During recovery, they are fed a diet that is relatively low in protein and, thus, are protein-energy malnourished at hospital discharge [2]. The ensuing feeding with a diet that is relatively low in protein but high in fat will be paralleled by increased weight gain and body fat.

Studies Examining Nutritional Support after Discharge in the Preterm Infant

Several studies have examined growth after discharge in preterm infants. Although some 'catch-up' growth has been observed, preterm infants do not grow as well as

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Fig. 1. Examining nutritional support after discharge in the preterm infant. The challenge is moving towards the right side of the balance, particularly in infants recovering or showing signs of systemic illness.

their term counterparts and are smaller at 3 and 8 years, and in adulthood. There are several possible reasons for this.

As noted before, under current in-hospital feeding practices, most, if not all, VLBWI are undernourished and growth restricted at initial hospital discharge [2]. A ‘critical epoch’ of growth may, therefore, have been missed. Preterm infants also have greater morbidity than term infants during the first year of life [18] and intercurrent illness will affect growth, irrespective of whether infants are admitted to the hospital or not.

Until recently, little attention had been paid to nutritional factors in the pathogenesis of this problem. For most early studies, infants were fed either human milk or a term-infant formula after hospital discharge [19]. Both feeding regimens were designed to meet maintenance and normal growth needs of the term rather than the more rapidly growing preterm infant with significant ‘catch-up’ requirements. These infants, therefore, are likely to be partly underfed during the first 6–12 months of life.

Several studies have examined the effects of feeding nutrient-enriched formulas, i.e. formulas with a greater nutrient density than a term-infant formula, to preterm infants after hospital discharge [20–32]. Although protein content of the formulas (2.4–3.0 g/100 kcal), sample size (32–229 infants) and duration of feeding (term to 12 months corrected age) varied between the studies, improved growth, primarily in boys and infants weighing $\leq 1,250$ g at birth, was noted in 8 of the 10 studies.

Recently, Cooke et al. [33] compared growth and body composition in preterm infants fed a nutrient-enriched formula to a term formula to a control group of breast-fed preterm infants. Infants fed the nutrient-enriched formula

were heavier, longer and had a greater head circumference than the other groups. Increased body size was paralleled by increased lean and total mass (in grams) but not central or percent fat mass. Feeding a nutrient-enriched formula with a protein content of 2.7 g/100 kcal, therefore, is not associated with altered adiposity but an increase in lean mass accretion (fig. 1).

The Breast-Fed Infant

Before hospital discharge, preterm infants fed human milk do not grow as well as infants fed nutrient-enriched formulas. It is, therefore, recommended that human milk be fortified with additional nutrients [4]. Growth improves but it is still not as good as in infants fed a preterm-infant formula [34]. The reasons for this are not entirely clear.

The composition of human milk varies widely and because it is not consistently measured there is no way of knowing what the infant is really receiving.

Fortifiers differ in nutrient composition and it is unclear which, if any, really meets requirements. The composition of human milk varies widely and because it is not consistently measured there is no way of knowing what the infant is really receiving. In effect, intake less adequately meets requirements and growth is poorer.

After hospital discharge, breast-fed infants also grow more poorly than those fed nutrient-enriched formulas

[26]. This, perhaps, is not so surprising. Before discharge, intake less adequately meets requirements. The accrued nutritional deficit and, therefore, needs for 'recovery' are greater. Mature human milk is designed to meet the needs of the term infant and not the preterm infant – in whom intake must meet needs for maintenance, normal growth, and 'catch-up' growth.

In a recent stratified and randomized controlled pilot trial, preterm infants (750–1,800 g) were fed unfortified (n = 20) or fortified (n = 19) human milk after hospital discharge to 12 weeks [35]. A multi-nutrient fortifier, estimated to ensure an energy and protein density of 80 kcal and 2.2 g/100 ml, was added to 50% of feeds. Growth was somewhat improved in the fortified group, supporting the idea that preterm infants be fed fortified human milk after hospital discharge.

Conclusion

Preterm, particularly breast-fed, VLBWI are likely to be under-grown at hospital discharge and, therefore, are at an increased risk for poor growth after hospital discharge. Because poor growth is associated with poor development it is recommended that they are fed fortified human milk if they are breast-fed or a nutrient-enriched formula if they are formula fed after hospital discharge [36]. Irrespective of how an infant is fed, growth must be closely monitored, i.e. every 2–3 weeks, to ensure that they 'recover' or 'catch back' to their original birth weight percentile by 1–2 months corrected age. In infants who are not 'recovering' and there are no signs of systemic illness, e.g. urinary tract infection, etc., protein status should be closely evaluated and supplementation be instituted.

Disclosure Statement

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