Feeding Practices – Current and Improved?

Nutrient Needs for Catch-Up Growth in Low-Birthweight Infants
Ekhard E. Ziegler
Department of Pediatrics, University of Iowa, Iowa City, IA, USA

Abstract
Growth restriction among low-birthweight (LBW) infants occurs prenatally as well as postnatally. Regardless of when and how the growth restriction occurs, growth-restricted infants have the potential for catch-up growth. Catch-up growth has decidedly beneficial effects on later cognition. It also may have adverse effects on cardiovascular and metabolic health. Although the benefits for later cognition are well documented in a number of studies, growth-restricted LBW infants often do not experience catch-up growth and therefore do not enjoy its benefits. One reason is that for catch-up growth to occur, extraordinarily high protein intakes are required. Nutrient intakes have been estimated with the use of the factorial method based on the assumption that catch-up growth comprises essentially a restoration of lean body mass, with restoration of fat mass optional. The basic (no catch-up) nutritional needs of growth-restricted LBW infants are altered to a modest degree, with energy needs increased and protein needs decreased. With catch-up, however, protein needs are increased sharply. Since energy needs are only modestly increased, the protein/energy ratio of requirements is appreciably increased. The high protein needs are difficult to meet with the usual feedings for LBW infants unless special measures are taken to increase protein intakes and to increase the protein/energy ratio. Without the necessary protein intake, catch-up growth is not possible or will be delayed, which may compromise the realization of the long-term benefits on cognition.

© 2015 Nestec Ltd., Vevey/S. Karger AG, Basel

The purpose of this review is twofold. First, to make the case that in growth-restricted low-birthweight (LBW) infants catch-up growth confers benefits for cognition later in life, regardless of whether catch-up occurs following intrauter-
ine growth restriction (IUGR) or postnatal growth restriction (PGR). And second, that the nutrient requirements for catch-up growth are high, meaning that catch-up growth and its benefits will only be realized if the high nutrient intakes are met. The similarities between pre- and postnatal growth restriction and the catch-up growth that can follow either have been recognized [1]. Since it is not widely appreciated that the nutrient needs for catch-up growth, especially the needs for protein, are very high and difficult to meet, the present discussion will provide estimates of nutrient intakes needed for the realization of catch-up growth.

It is generally recognized that infants who are classified at birth as small for gestational age (SGA) constitute a heterogeneous group. Some of these infants are intrinsically small and remain small. But the majority of SGA infants are small as a result of IUGR due to causes extrinsic to the infant. It is also widely appreciated that PGR occurs commonly in VLBW infants as a result of inadequate nutrient intakes. Common to all infants who have experienced growth restriction is the potential to return to their original size once the erstwhile obstacles have been overcome. Return to the original size is commonly known as catch-up growth and is the focus of the present discussion.

The undoing of the effects of growth restriction would seem to be unconditionally desirable were it not for the findings from long-term follow-up studies. Besides showing that catch-up growth improves cognition later in life, follow-up studies are also suggesting that catch-up growth has negative effects on later cardiovascular and metabolic health. This dichotomy of findings has led to a vigorous and ongoing debate about the merits of catch-up growth following growth restriction in LBW infants. Unfortunately, the debate has been focused predominantly on the negative effects of catch-up on later cardiovascular and metabolic health. To restore some kind of balance, this discussion will focus on the effects of catch-up on later cognition.

Catch-up growth is usually understood as growth that is returning toward the original size that existed before the onset of growth restriction, even though that size is not precisely known in the case of IUGR. Size is expressed in relative terms such as weight percentile or z score. The crucial deficit in growth restriction is a decreased lean body mass. Consequently, the most important aspect of catch-up growth is the restoration of lean body mass. Fat mass may also be diminished, at least in IUGR, but its restoration is of secondary in importance. Since the cause of IUGR differs from the cause of PGR, it is not too surprising that there are differences in body composition. A well-documented difference concerns body fat, which is diminished in IUGR but is often normal or increased in infants with PGR.
Catch-Up Growth and Later Cognition in Low-Birthweight Infants

Catch-Up after Intrauterine Growth Restriction

In infants born close to term, the adverse effects of IUGR on later cognition are well recognized [2, 3], as are the beneficial effects of catch-up growth [4]. In pre-term and LBW infants, the negative effects of IUGR on cognition are also well recognized [5, 6]. Less well recognized is the marked positive effect that catch-up growth has on later cognition in growth-restricted LBW infants. Brandt et al. [7] showed that VLBW SGA infants who did not experience head circumference catch-up had lower IQ scores as adults than SGA infants with head circumference catch-up or appropriate for gestational age (AGA) infants. Latal-Hajnal et al. [8] followed up VLBW SGA infants to age 2 years and found that those who caught up (weight or length >10th percentile at 2 years) scored significantly higher on the psychomotor development index (PDI) than those who did not catch up. More recently, Belfort et al. [9] examined the effect of catch-up growth in a large cohort of 613 premature infants who participated in a trial assessing the effect of omega-3 fatty acid supplementation on neurodevelopmental outcome. Among SGA infants, growth from one week to term was strongly positively associated with MDI and PDI scores at 18 months. The association was also significant among AGA infants, but it was less strong than in SGA infants. The importance of this study lies in the fact that it involved a very large number of infants.

Catch-Up after Postnatal Growth Failure

Most VLBW infants experience postnatal growth failure of some degree due to insufficient nutrient intakes. Their growth shares many characteristics with that of infants born SGA, as has previously been pointed out [1]. Although growth recovery often does not occur until after discharge from the hospital, it not infrequently occurs or begins before discharge. For example, in the study by Ehrenkranz et al. [10] the majority of infants were still showing growth failure at the time of discharge. But infants who were undergoing catch-up growth before discharge showed better neurocognitive outcomes on follow-up than infants who did not. Although it is likely that even infants with late catch-up would eventually recover from their growth deficit and derive benefits for cognition from it, with regard to neurocognitive outcome early recovery may be crucial. As in the study of Ehrenkranz et al. [10], it may be assumed that in all studies that examined the association between growth and neurocognitive outcome of infants.
VLBW infants, the fastest growing infants (e.g. the top quartile in Ehrenkranz et al. [10]) were exceeding fetal growth rates and were thus showing catch-up growth.

A number of studies have examined the association of growth with developmental outcomes in VLBW infants. The age at which cognition was assessed ranged from 1 year [11] to 19 years [12]. As a result of changes in clinical practices, infants born after about 1995 have shown less postnatal growth failure than infants born before 1995. But even among infants born after 1995, follow-up studies have invariably found that cognitive development as measured between 2 and 5.5 years of age was strongly positively associated with growth before discharge [9, 13–15]. Because at least the fastest growing among theee VLBW infants may be assumed to have been catching up, these findings constitute a large body of evidence documenting that catch-up after postnatal growth failure has positive effects on cognition.

**Estimation of Nutrient Needs**

In spite of its limitations, the factorial method has been useful in obtaining at least crude estimates of nutrient needs of LBW infants. Such estimates of the nutrient needs of premature infants [16] form the basis of recommendations by official bodies [17]. The factorial method has been used to obtain estimates of nutrient needs of extremely LBW SGA infants undergoing catch-up growth [18]. Using similar assumptions, it is used here to obtain estimates of the nutrient needs of LBW infants undergoing catch-up growth.

The nutrient needs of SGA infants differ from those of normally grown LBW infants because of (1) altered body composition and (2) catch-up growth. Catch-up is best understood as recovery of lean body mass. Full recovery would be a return of lean body mass to its original (pregrowth failure) channel. Nutrient needs are considered here for three scenarios: basic needs (no catch-up); half catch-up, defined as 50% of full recovery, and full catch-up defined as return to the original channel. Because nutrient needs are expressed per unit time, the assumption is made that catch-up occurs over a period of 4 weeks. Presented are estimates of nutrient needs for each of the three scenarios and, for purposes of comparison, needs of normally grown infants of similar size. Figure 1 shows two hypothetical SGA infants weighing 1,500 g at 34 weeks’ postmenstrual age. The infant growing parallel to the percentile line does not show catch-up growth, whereas the other infant shows full catch-up over a period of 4 weeks.
Body Composition of Growth-Restricted Infants

The hallmark of growth restriction is reduction of lean body mass relative to normally grown infants of the same age. In the case of IUGR, there is also a reduction of fat mass [19–21], whereas in infants with PGR fat mass is unchanged or often even increased [22]. This is explained by normal or increased energy intakes which typically accompany the insufficient protein intakes that are causing growth failure. In spite of its reduction in mass, the composition of lean body mass is commensurate with gestational age, meaning that its water content is lower, its protein content is higher and its resting energy expenditure higher than normally grown infants of the same size.

Basic Nutrient Needs

Because of the higher metabolic rate of the lean body mass, and also as a consequence of the reduced fat mass relative to lean mass, resting energy expenditure per unit of body mass is higher in growth-restricted infants than in normally grown infants, as has been documented in a number of studies [23–25]. Therefore, resting energy expenditure is increased and total energy needs are increased in SGA infants (table 1). Because the rate of growth per unit body weight is lower at 34 weeks’ postmenstrual age than at 30 weeks, protein needed for growth (accretion) is less per unit body mass in SGA without
catch-up than in AGA infants of similar weight. The net effect of these changes in basic needs in SGA infants is that the required protein/energy ratio is somewhat decreased.

**Nutrient Needs for Catch-Up**

Shown in table 1 are the nutrient needs of infants undergoing one-half catch-up and full catch-up within a period of 4 weeks. Compared to the modest impact on needs of just being SGA, the impact of catch-up growth is large, especially with regard to needs for protein as protein is needed for the restoration of lean body mass. As indicated in table 1, for full catch-up of lean mass within in 4 weeks, the protein requirement jumps to 5.1 g/kg per day, while for half catch-up it still is 4.2 g/kg per day. Restoration of energy stores (fat mass) is not essential in catch-up growth, and the increase in fat can therefore be variable. Energy intakes shown in table 1 are only modestly increased over basic needs, assuming that only a small fraction of the fat mass deficit is being restored. Greater energy intakes will of course permit more rapid restoration of fat mass. It is important
to distinguish between the essentiality of protein for the restoration of lean body mass and the optional nature of energy needed for restoration of fat mass. The disproportionately increased needs for protein due to catch-up necessitate substantial increases in the protein/energy ratio of feeds (table 1).

Comment on Nutrient Needs

The estimates of nutrient needs presented above cannot claim to be quantitatively accurate. For one thing, they depend on a number of assumptions that, if chosen differently, would alter the outcome. The use of a theoretical model has, of course, the advantage of allowing the examination of the effects of different assumptions. In spite of these limitations, the main conclusion derived from the model is robust enough to support recommendations for nutritional management of growth-retarded LBW infants. There can be no doubt that catch-up growth requires very high intakes of protein. If these protein needs are not met, catch-up will not occur. If they are met partially, catch-up will proceed at slower pace. Without the necessary protein, catch-up simply cannot take place. In practice, the high protein needs are probably seldom met, not least because the means for increasing the intake of protein are limited. Perhaps herein lies a reason why catch-up growth does not always occur, or proceeds more slowly than would seem desirable.

Nutritional Recommendations

The exorbitantly high amounts of protein necessary for catch-up growth are difficult to achieve. They can be achieved only with feedings with a suitably high protein/energy ratio. Such high ratios can be achieved only by selectively increasing the protein content of feedings. Whether the required protein intakes can be achieved with feedings with the usual protein/energy ratios is questionable as the required very high feeding volumes are probably beyond the ability of most LBW infants. One advantage of lower-protein feedings, if adequate protein intakes could be achieved, would be a more rapid restoration of fat mass. However, given the primacy of restoration of lean body mass, the use of high-protein feedings would still be preferred. Without high intakes of protein, catch-up growth is not possible and the infant’s ability to reap cognitive benefits is compromised. Although most growth-restricted infants may catch up eventually, the existing evidence suggests that delaying catch-up may compromise long-term cognitive benefits.
Disclosure Statement

The author reports no conflict of interest.

References


