Issues in nutrient supplementation of breast-milk fed low birth weight infants

Of the 20.6 million low birth weight (LBW) infants born every year, about 8 million are born in India. Low birth weight is the most important risk factor for neonatal mortality, contributing to about three quarters of neonatal deaths in India. In order to survive through infancy, LBW infants need additional care particularly with regard to breathing, temperature maintenance, feeding, hygiene and early recognition and treatment of infections. LBW infants are a heterogeneous group - born too early, born too small, or both - and the spectrum varies for developing and developed countries. In India, over two thirds of LBW infants are term.

In this issue Elizabeth and colleagues report the findings of a study of umbilical cord blood nutrients in preterm and term LBW infants. Blood concentrations of all nutrients including proteins, fats, calcium, magnesium, zinc and iron were lower in LBW infants, particularly in preterm LBW infants. These are important findings, but their implications for recommendations for feeding of LBW infants need to be carefully considered. Lower nutrient levels in LBW infants should not automatically lead to a recommendation for nutrient supplementation.

First, one must consider physiological issues most important of which is that the composition of breast milk is best suited to the needs of the baby. It is important to note that breast milk of mothers who have preterm babies has higher concentrations of several nutrients such as energy, protein, calcium and folate. There is little justification for supplementation of these nutrients in breast-milk fed LBW infants. However, there is no increase in the concentrations of phosphorus, magnesium, iron, zinc and vitamins A and D in preterm breast milk.

Second, the relevance of biochemical concentrations of nutrients in defining nutrient deficiency is uncertain. The safety and efficacy of nutrient supplementation in improving functional measures such as infant mortality, morbidity, growth and development are therefore considered more appropriate evidence to base recommendations for possible supplementation. A systematic review of such evidence for human milk supplementation is available as a WHO publication, some of the key findings of which are summarized below.

There is strong and consistent evidence that feeding mother’s own milk to preterm infants of any gestation is associated with a lower incidence of infections and necrotising enterocolitis, and improved neurodevelopmental outcome as compared with formula feeding. While feeding unsupplemented mother’s own milk to very low birth weight infants (birth weight <1500 g) has been shown to result in slower weight and length gains, the implications of this slower growth are unclear and there is not enough evidence to assess if it increased the risk of malnutrition. Long-term beneficial effects of breastfeeding on blood pressure, serum lipid profile or pro-insulin levels have also been reported for pre-term infants. There are limited data on most outcomes in term LBW infants; the available data suggest that improved infection and neurodevelopmental outcomes associated with feeding mother’s milk in pre-term infants are also seen in this group.

Multi-component human milk fortifiers, which contain proteins as well as several micronutrients, are used in developed countries for very low birth weight infants with gestation less than 32 wk. There is evidence that use of multi-component fortifier leads to short-term increases in weight gain, linear growth, head growth and bone mineralization in very low birth weight infants. There are insufficient data to evaluate the long-term neurodevelopmental and growth outcomes,
although there appears to be no effect on growth beyond one year of age\(^{21,22}\). The safety of multi-component fortifiers has been questioned as some studies have reported an increased risk of mortality and necrotising enterocolitis associated with its use. However, a meta-analysis of all available studies did not find a statistically significant increased risk of mortality or necrotizing enterocolitis, although the small number of infants and the large amount of missing data in the studies reduce confidence in this conclusion\(^{20}\). There are no data examining the efficacy of multi-component fortifier in infants of 32-36 wk gestation or in term LBW infants.

There is some evidence of reduced linear growth and increased risk of rickets in very low birth weight infants fed ununsupplemented human milk\(^{23,24}\). There are no clinical trial data on the effect of vitamin D on key clinical outcomes in infants with birth weight greater than 1500 g.

There is some evidence that phosphorus and calcium supplementation reduces the risk of metabolic bone disease in preterm infants and leads to short-term increases in bone mineralization in very low birth weight infants\(^{25-27}\). There are no data on the effect of phosphorus and calcium supplementation on key clinical outcomes in infants with a birth weight greater than 1500 g.

Iron supplementation, started at 2-8 wk of age, is effective in preventing anaemia during infancy in LBW infants\(^{28-30}\). However, there are insufficient data on the safety of iron supplementation during the first two months of life. There are no data on the effects of iron supplementation on mortality, common childhood illnesses or neurodevelopment in LBW infants.

A systematic review concluded that supplementing very low birth weight infants (<1500 g) with vitamin A was associated with a reduction in death or oxygen requirement at one month of age\(^{32}\). Three published community-based studies have examined the effects of vitamin A supplements given in the first few days of life to LBW infants. Findings from a large trial conducted in south India\(^{32}\) suggest that vitamin A (50,000 IU in one or two divided doses) during the first days of life may have a survival advantage, particularly in infants with birth weights less than 2000 g. Two smaller studies showed no mortality benefit but their sample size was insufficient to detect a reasonable difference in mortality between groups\(^{33,34}\). Findings from two large community studies done in Guinea-Bissau and Bangladesh are under publication and may provide more evidence on this issue.

There are no data on the effect of zinc on key clinical outcomes in preterm infants. Data from two Indian trials suggest that term LBW infants may have lower mortality\(^{35}\) and morbidity\(^{36}\) if they receive zinc supplementation. Findings from another large study done in Delhi are being analysed and may provide more evidence on this issue. There seems to be little evidence that zinc supplementation improves neurodevelopment or affects growth.

What are the implications of the above evidence for feeding of LBW infants in developing countries? First, it is clear that breast-milk feeding should be recommended for all LBW infants, directly, by alternative methods of oral feeding such as a cup or paladai, or by intragastric tube feeding. Second, supplementary formula feeding should not be recommended. Third, uncertainty about safety and effectiveness of multicomponent human milk fortifiers does not allow a recommendation on its routine use in developing countries. Fourth, there is some evidence for supplementation of very low birth weight infants with vitamin A, vitamin D, calcium and phosphorus starting as soon as feeding is established, and for all low birth weight infants with iron starting after 8 wk of age. Finally, more research is required on the benefits of routine zinc and vitamin A supplementation of preterm and term LBW infants.

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References


