

The role of breast milk fortifier in the post-discharge nutrition of preterm infants

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Abstract

Infants born prematurely are often discharged from hospital before 37 weeks post menstrual age. While breastfeeding will meet all the nutritional requirements of full-term infants, these preterm infants may need enhanced levels of protein, minerals and possibly energy to ensure optimum growth, bone mineralisation and neurological development. To meet these additional nutrient needs in the neonatal unit, it is currently recommended that multinutrient breast milk fortifier is added to maternal breast milk. There may also be benefits in continuing to provide fortified milk after discharge, potentially including improved growth and preserving breastfeeding, and this is increasingly becoming a recognised practice in some neonatal units. This article presents the discussion and consensus of a multidisciplinary panel of neonatologists, neonatal dietitians, a GP and a neonatal outreach nurse. The aim is to develop guidance on providing safe and effective nutritional supplementation for preterm infants after discharge in order to maintain optimal growth. This guidance is aimed at community healthcare staff and is based on the limited evidence available, using shared best practice and expertise.

Preterm infants, particularly those weighing less than 1800 g at birth, have higher nutritional requirements than those born at term. This is because current recommendations (Ehrenkranz, 2014) aim to promote rates of growth and tissue accretion similar to that which would be achieved in utero at the same gestation. To this end, current European guidelines (Agostini et al, 2010; Koletzko et al, 2014; Moro et al, 2015; Arslanoglu et al, 2019) recommend that preterm infants born weighing less than 1800 g who are receiving milk feeds receive additional nutritional supplementation. For infants receiving maternal breast milk or donor breast milk, supplementation usually takes the form of a multicomponent breast milk fortifier, whilst those receiving formula milk should receive specialist preterm infant formula. The use of breast milk fortifier during hospital stay has been shown to help maintain head growth, length and weight gain and better overall nutritional status (O'Connor et al, 2008; Aimone et al, 2009; Brown et al, 2020), although the longer term benefits are unclear (Toftlund et al, 2018). There is also some evidence for improved visual and lung function (O'Connor et al, 2012; Toftlund et al, 2019). It should be noted that breastfeeding, or feeding with mother's own expressed breastmilk, is the best option for all low birth-weight infants (Edmond and Bahl, 2006).

Current recommendations also suggest that preterm infants who receive formula milk and who have failed to 'catch up' on the unit should be transitioned over to a specialist post-discharge preterm infant formula just before discharge with this continued for several weeks thereafter, in order to maintain higher nutrient intakes. However, there is currently no such recommendation for infants receiving fortified breast milk; these infants tend to stop receiving fortifier while establishing oral breastfeeds and so are discharged home breastfeeding without supplementation. This means that breastfed low birth weight infants receive a lower nutrient intake around the time of discharge, at a time when their sleep/wake pattern and possibly oral motor maturity is not fully developed, meaning that upregulating volume may be difficult, putting them at risk of poor growth. It is currently not standard practice to continue providing breast milk fortifier to the parents of these smaller infants after discharge, although there is some evidence to suggest that this can produce sustained improvements in various growth parameters (O'Connor et al, 2008; Aimone et al, 2009; Zachariassen et al, 2011; Marino et al, 2019). Providing breast milk fortifier to these infants around the time of discharge and beyond offers a way to try and ensure they receive adequate nutrition and achieve optimal growth. It may help prevent growth failure beyond discharge and this is important as poor growth can lead to mothers losing confidence in breastfeeding and prompt healthcare professionals to advise supplementing with formula feeds.

However, there are also potential hazards in promoting excessive growth. There is some evidence for an increased risk of insulin resistance or cardiovascular disease in later life in infants who undergo excessive weight gain and who may increase across weight percentiles in their first few months (Euser et al, 2005, 2008; Singhal et al, 2007). It is therefore important to monitor weight gain closely to ensure growth velocity is appropriate when using nutritional supplements beyond discharge. There are also concerns about the effects on the mother's willingness to continue breastfeeding if she adopts the view that her own milk is not adequately meeting the infant's needs. However, there is some evidence that use of fortifier beyond discharge does not reduce duration of breastfeeding (O'Connor et al, 2008; Zachariassen et al, 2011; King, 2014).

Which infants should receive fortified human breast milk?

It is important to clearly define which infants should receive fortified human breast milk. There is variation in local guidelines used around the country, but the panel proposes that infants born before 32 weeks' gestation and/or preterm infants weighing less than 1800 g should be considered suitable for ongoing fortification of maternal breast milk after discharge. A weight criterion of 1800g was also used in the ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition) recommendations (Agostini et al, 2010). In addition, fortification should also be considered for infants whose growth parameters fall down more than 1.33 standard deviations (equivalent to crossing two marked centile lines) on a UK newborn infant close monitoring (NICM) growth chart (this may be termed faltering growth, as per the National Institute for Health and Care Excellence (2020) quality standard).

Neonatal units will usually discontinue fortification when the infant is ready to be discharged. However, with the extension of outreach services nationally, preterm infants are being discharged earlier, and it is becoming a practical option to maintain fortifier treatment at home (King, 2014; King and Winter, 2014; Marino et al, 2019). The panel felt that the fortification product should be prescribed by hospital physicians rather than GPs, and monitored by the neonatal multidisciplinary team, at least while this remains a new area of practice. The hospital team will ensure that parents receive training in handling and administering the fortifier, which is mixed with expressed breast milk and delivered via a bottle, syringe or cup (depending on local practice), before the infant is discharged.

Fortification provides vital nutrients needed during the period of rapid bone mineralisation as the infant approaches term. By this time, most preterm infants will have developed a mature sleep/wake pattern and oral reflexes which mean they will successfully breastfeed. Decisions on when to discontinue fortification are likely to reflect the specific features of each individual case, as well as local guidelines. In those units currently using fortifier beyond discharge, some will recommend reducing or stopping fortification at around 46 weeks corrected gestational age, while other centres continue up to 52 weeks corrected gestational age, and some will start the process of ceasing fortification only once infants have made any catch-up growth. The infant's growth should be monitored using a UK NICM growth chart and fortification should be discontinued earlier if the weight crosses to a higher marked centile line which is out of proportion with length. Parents should be made aware that crossing down as much as a marked centile line on a UK NICM growth chart after beginning breastfeeding is not unusual. When the infant is able to maintain its weight along the same centile, it may be possible to reduce the dose of fortifier being administered. The infant's weight should not be considered in isolation as other growth parameters such as the infant's length and head circumference are equally as important. Both quantity and quality of growth need to be considered.

In the UK, the SIFT Investigators (Dorling et al, 2019) found that over 97% of infants <32 weeks' gestation or <1500 g at birth receive human milk in the first weeks of life with the majority receiving mother's own milk. However, many infants will not be exclusively breast feeding at discharge, although they may still be receiving expressed breast milk. Mothers may be offered post-discharge preterm infant formula and it is important that they are made aware of the difference between post-discharge preterm infant formula, standard formula and human breast milk fortifier. Human breast milk fortifier is a supplement and not intended as a replacement for maternal milk, since it does not contain all the macro- and micronutrients needed for healthy growth. Its use is intended to supply extra protein, minerals

and vitamins, and a little energy to enable the preterm infant to grow in a way that would approximate that seen in utero.

It should be noted that breastfeeding, or feeding with mother's own expressed breastmilk, is the best option for all low birth-weight infants (Edmond and Bahl, 2006). Partial breastfeeding at discharge, low maternal educational level and longer length of stay in the neonatal intensive care unit all increase the risk for ceasing breastfeeding during the first 12 months (Maayan-Metzger et al, 2018). There is some evidence to suggest that providing fortifier to supplement breast milk does not decrease the duration of breastfeeding, possibly because of the increased level of lactation support (O'Connor et al, 2008), and may possibly support it (King, 2014). However, it may be because infants receiving post-discharge fortifier do not have weight faltering, meaning that the addition of formula is not recommended by health professionals monitoring infants' growth post discharge. Continued breastfeeding will have positive long-term health consequences in terms of hospital readmissions, minor infections and cardiovascular disease among others, and in turn will have health economic benefits (Renfrew et al, 2012).

If, despite continued use of breast milk fortifier, an ex-preterm infant's growth appears to be faltering at 48 weeks corrected gestational age, a referral should be made for a full nutritional review with the local neonatal or paediatric dietitian, along with support and education from community services to support continued breastfeeding. At this stage other factors may be responsible for the faltering and breast milk fortifier may not be an appropriate treatment.

The role of different healthcare professionals

Close monitoring and regular follow up is required for all infants discharged on breast milk fortifier to ensure they are continuing to exhibit satisfactory growth. Infants on breast milk fortifier in the community will need regular follow up to monitor growth and tolerance, and advice on reducing dose. However, if a preterm infant is discharged at 34–38 weeks corrected gestational age they should receive earlier follow up to review feeding progression and growth. This follow up can be done by neonatal outreach teams, dietitians, community nurses or health visitors – increasingly this care will be provided by the neonatal unit's outreach staff along with their neonatal dietitian. However, in areas where these services are not yet available, community nursing staff or health visitors are advised to weigh and measure the infant at weekly intervals and relay that information to the neonatal or paediatric consultant and the dietitian on the neonatal unit, if available.

If growth appears to be faltering during this initial 6–8-week period, then it is recommended that the infant should be referred to a neonatal or paediatric dietitian, and for an assessment of breastfeeding technique and the mother's lactation. Staff at the hospital neonatal unit and/or the neonatal outreach team may provide advice to community health professionals, such as the 'healthy families team', but the GP practice will be responsible for routine care. Parents with urgent concerns over their infant's health (other than growth or feeding) should contact their GP surgery or hospital emergency department rather than seeking guidance from the neonatal unit, since these facilities will not normally re-admit patients after they have been discharged. Most infants who fit the criteria to receive breast milk fortifier will receive follow up with a neonatologist or paediatrician until they are 2 years of age. Health visitors and GPs will have a responsibility for routine monitoring of health, growth, development and any illnesses, but most infants will also be in a neonatal follow-up programme.

Supporting breastfeeding at home

Preterm infants may be at risk of faltering growth at home as a result of persistent immature feeding patterns related to the prematurity of the infant, which should improve over time. It is possible that mothers of these infants may become disheartened with breastfeeding if the infant fails to grow and may consider switching to, or supplementing with, formula milk. Therefore, adding fortifier, which provides additional protein and nutrients to support the infant's growth, may encourage mothers to maintain breastfeeding. The process of expressing breast milk and mixing in the powdered fortifier may be difficult and time consuming for many mothers, so they will need simple but specific written advice with details of who to contact with queries, as well as support and encouragement from both dietetic and outreach services.

Dosage and administration of fortifier

Currently two breast milk fortifier products are available and used for home fortification in the UK: Nutriprem Human Milk Fortifier (Nutriprem HMF) and SMA Breast Milk Fortifier (SMA BMF). Of note, Nutriprem HMF sachets contain approximately twice the amount of fortifier as SMA HMF. There may be confusion regarding the names of these products, but it is important to remember that both products are made from hydrolysed cow's milk.

Normally, for use before hospital discharge, one sachet of Nutriprem HMF or two sachets of SMA BMF is added to each 50 ml expressed breast milk. However, for home use the fortifier is added to smaller measured volumes of expressed breast milk and given to the infant alongside some breastfeeds throughout the day. The resulting fortifier solution is more concentrated than the standard dilution used before hospital discharge. For the purposes of this document, use of either product is referred to as 'BMF concentrate'.

The total number of sachets of fortifier to be used daily will vary according to the needs of the individual infant and the product used. In practice the amount of BMF concentrate per day is typically based on 50% of that which would have been required to fortify approximately 150 ml/kg/day at the infant's discharge weight. The quantity of BMF concentrate prescribed at discharge is usually continued until the infant is following a weight centile line; after which the daily quantity of BMF concentrate should be reduced gradually, for example, by one BMF concentrate per day per week until no further fortifier is required. Dietetic staffing to support these infants following discharge from hospital varies throughout the country, as does the approach to reducing and stopping fortifier. As a guide, BMF concentrate should not usually be required after term plus 6 weeks corrected age; further dietetic assessment should be sought if growth remains a concern at this time.

Ideally, BMF concentrate should be made as close as possible to the time of the feed. *Figure 1* gives an example of how to make up individual BMF concentrate using both products currently available in the UK, although local policy should be followed if such practice differs.

Figure 1. Examples of how to make up breast milk fortifier (BMF) concentrate using currently available breast milk fortifiers. This information is based on practice developed at Queen Charlottes Neonatal Unit, London.

For Nutriprem HMF (one sachet is usually added to 50ml expressed breast milk)

Example calculation for daily fortifier dosage with Nutriprem HMF for a 2.1 kg infant

- One sachet Nutriprem HMF mixed with 3 ml expressed breast milk provides a 4 ml 'BMF concentrate'

2.1 kg infant feeding 150 ml/kg/day = 315 ml per day
 315 ml ÷ 50 ml = 6.3 sachets Nutriprem HMF per day
 50% requirement = 3.1 sachets per day
 Using **one sachet** per BMF concentrate = Three Nutriprem BMF concentrate per day

- Continue three Nutriprem BMF concentrate per day until weight is following a centile
- Reduce by one Nutriprem BMF concentrate per day per week until nil concentrate is required

For SMA BMF (one sachet is usually added to 25ml expressed breast milk)

Example calculation for daily fortifier dosage with SMA HMF for a 2.1 kg infant

- Two sachets SMA BMF mixed with 3 ml expressed breast milk provides a 4 ml BMF concentrate

2.1 kg infant feeding 150 ml/kg/day = 315 ml per day
 315 ml ÷ 25 ml = 12.6 sachets SMA BMF per day
 50% requirement = 6.3 sachets per day
 Using **two sachets** per BMF concentrate = Three SMA BMF concentrate per day

- Continue three SMA BMF concentrate per day until weight is following a centile
- Reduce by one SMA BMF concentrate per day per week until nil concentrate is required

Table 1 provides the nutritional composition of the two products currently available in the UK and used for home fortification (macronutrients and a selection of micronutrients are included). The analysis is given per sachet and should be considered when comparing the products.

Table 1. Nutritional composition (per sachet) of breast milk fortifiers (BMF) available in the UK

Product	Sachet size (g)	Nutritional composition of fortifier (per sachet)										
		Energy (kcal)	Protein (g)	CHO (g)	Fat (g)	Na (mg)	K (mg)	Ca (mg)	P (mg)	Fe (mg)	Zn (mg)	V (mg)
Nutriprem HMF	2.2	8	0.6	1.4	0	18	12	33	19	0	0.31	11
SMA BMF	1	4.3	0.36	0.32	0.18	9.2	12	19	11	0.45	0.24	9.5

From Nutricia (2020), SMA Nutrition (2019)

Parents should be warned that 'more is not necessarily better' when serving the nutritional needs of their preterm infant. The infant's appetite and feeding behaviour will change as they reach full term age. The infant is likely to feed more frequently as its feeding skills and stamina mature, but mothers should not add extra fortifier beyond that recommended by the hospital, and should be reminded of the importance of following each BMF concentrate with a breast feed. BMF concentrate should not be given alongside formula feeds. Advice should be sought if mothers reduce or stop breast feeding any point during this treatment.

It is also important to note that SMA BMF contains more iron than Nutriprem HMF and this should be considered when prescribing iron supplementation.

Guidance for parents

Before taking their infant home, parents should be congratulated on having reached this stage of their breastfeeding journey. It should be emphasised how important breastfeeding will be in this process and how it can provide longer term benefits for both infant and mother if continued for as long as the mother and infant are able. It should be emphasised that while some preterm infants will thrive on breast milk alone, others may benefit from the time and effort taken by their parents to mix and administer the fortified maternal milk.

Parents should appreciate that preterm infants who have reached an appropriate weight for their age may still face considerable health challenges. Moreover, all infants may experience common childhood illnesses that are completely unrelated to their developmental age. It is appropriate for parents to be given the contact details of the outreach team, dietetic team, or equivalent service, for advice on non-urgent issues related to the infant's growth and the use and supply fortifier, which is normally supplied by the neonatal unit. It is important to advise parents of the potential implications of overnutrition.

Priorities for further research

Breast milk fortification is a major nutritional intervention with significant potential benefits for the infant concerned. There is a need for further research to provide high quality evidence on the long-term impact of this practice on the future health of preterm infants. In particular, questions remain about whether the use of breast milk fortifier around the time of discharge and beyond can improve both the quantity and quality of growth in preterm infants. Furthermore, whether any such improvements can lead to better neurodevelopmental outcomes is also key, and there is a need to consider the impact of such changes in growth in relation to the use of home fortifier regarding long-term cardiovascular health and the risk of metabolic disease in later life. Finally, as breastfeeding is associated with improvements in both short- and long-term health in all infants, the impact of home fortifier use on breastfeeding rates and duration needs to be formally evaluated. High quality randomised controlled trials are needed to address all these issues.

Breast milk fortifiers are not currently prescribed by GPs. This group believe that the use of these products as described in this document, which is outside of the manufacturer recommendations, should be directed by staff within neonatal services and be limited to infants who remain under hospital follow up.

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Key points

- Current European guidelines recommend that preterm infants born weighing less than 1800 g who are receiving milk feeds receive additional nutritional supplementation. For infants receiving breast milk, this may take the form of a multinutrient breast milk fortifier.
- Fortification provides protein, minerals and vital micronutrients needed during the period of rapid bone mineralisation as the infant approaches normal term.
- Continuing fortification after discharge from hospital aims to optimise growth and may help supporting breastfeeding during a time when infants are developing mature feeding skills.
- Decisions on when to discontinue fortification are likely to reflect the specific features of each individual case, as well as local guidelines.

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