Kent Surrey and Sussex Neonatal Operational Delivery Network

Principles of Practice Breast Milk Fortifier in Neonatal Infants

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Aim of Principles of Practice

To share evidence on the use of breast milk fortifier in the neonatal infant
To standardise the use of breast milk fortifier on all units within KSS
To ensure parents are fully informed of the benefits of BMF for optimal growth
To ensure clinician' practice remains evidence based whilst on a rotation programme

This guideline will inform nursing and medical staff about the use of breast milk fortifier, from when to introduce it, to its use in the community setting, post discharge.

Background

It is well documented, including in the recent ESPGHAN 2022 guideline, that breast milk is the feed of choice for premature infants due to improved enteral tolerance and reduced incidence of necrotising enterocolitis, amongst other benefits. However, its nutritional composition is not sufficient to meet the higher nutritional requirements of a pre-term infant and the addition of a multi-nutrient breast milk fortifier (BMF) to breastmilk is recommended for all infants born <32 weeks or 1.5kgs. For babies over 32 weeks gestation, breastmilk in sufficient volumes (up to 220ml/kg/day) may be considered nutritionally adequate, however, some vitamins and minerals remain lower than nutritional guidelines recommend.

Breast milk fortifiers provide additional nutrients to breastmilk, particularly protein, calcium, and phosphate as well as vitamins and trace minerals to meet the additional nutrient needs of the pre-term infant. A number of Cochrane studies have examined the evidence for the role of breast milk fortifiers in enhancing growth. Kuschel and Harding, 2004 and Brown et al, 2016 have both reported that supplementation of human milk with multicomponent fortifiers was associated with short-term increases in weight gain, and in linear and head growth. However, there is limited data of any benefit beyond infancy to evaluate long-term neurodevelopmental and growth outcome. There is also minimal consistent evidence of other potential benefits or harms of fortification including effects on risk of feeding or bowel problems.

Given the variation in practice in Europe and across the Atlantic the use of BMF remains inconsistent. (Klingenberg C et al, Arch Dis Child Fetal Neonatal Ed, 2011) . There is also no clear evidence for early safe fortification, i.e. < 150 ml/kg/day and as a result of this, there is a large variation in the required enteral volume tolerated (ml/kg/day) before adding HMF. In Canada approximately two thirds of the units added HMF when an enteral volume of 80–140 ml/kg/day was tolerated. In UK/Ireland approximately four fifths of the units added HMF only when an enteral volume ≥150 ml/kg/day was tolerated and 15/48 units only added HMF to human milk when the infant 'needed it', for instance because of poor weight gain or low urea values. The variation in practice across the UK population was pulished in a more recent study in the Journal of Human Nutrition and Dietetics in 2020 highlighting the inconsistencies within the UK population. The conclusion from this study was that although BMF today is used more proactively in UK neonatal units than previously, variation in practice remains.

In contrast, in UK/Ireland approximately two thirds of the units started with full strength HMF, whereas in Canada approximately two thirds of units commenced half strength HMF or less.

Individualised fortification is very uncommon and caution remains regarding risk of NEC. The development of consensus guidelines on the use of BMF would help to standardise nutritional care in neonatal units.

There are challenges in providing adequate nutrition to very low birthweight infants. Radmacher and Adamkin, 2017 suggested three strategies for fortification to provide support to all infants.

1. **Standard fortification**: the most widely used strategy is based on the assumption that the human milk being fortified has a protein content of 0.6 – 1.5g/100ml. A fixed dose of fortifier is added to milk over the entire fortification period and does not account for any changes in the energy and nutrient content of the milk being fortified. Evidence suggests that variations in the nutritional content of human milk make this an imprecise method.

2. **Adjustable fortification**: this method uses regular measurements of the plasma urea as well as the infant's growth, to assess appropriate nutritional intake and the amount of fortifier that might be required.

3. **Targeted fortification**: this method uses infrared spectroscopy to analyse human milk in real time and assess the additional energy, protein and nutrient needs. It has been shown that the nutrient profile of human milk varies between women and within the same woman and challenges assumptions that standard amounts of fortifiers are needed. Periodic human milk analysis could be helpful in supporting the nutritional plan for each infant and prevent growth faltering in the critical NICU period.

The authors point out in this review that adding standard fortification to breast milk, when it may be that just protein is the nutrient that is needed, will increase the amount of other nutrients which may impact on osmolarity (as discussed below).

Osmolarity and Osmolality

It should be noted that osmolarity and osmolality are expressed in different units, and when reading papers or comparing products it can be confusing if different figures are given.
Osmolality is the concentration of a solution in terms of osmoles of solute per kilogram of solvent, expressed as mOsm/kg.
Osmolarity is the concentration of a solution in terms of osmoles of solute per litre of solution, expressed as mOsm/L.

In the UK, we provide information on the osmolality (mOsm/kg) of some products but not all. Studies from other countries frequently use osmolarity (mOsm/L) as a measure, so this needs to be considered when comparing recommendations.

The osmolality of breast milk is about 300mOsm/kg but this can be increased when fortifiers, nutritional supplements or medications are added. The present guidelines of the American Academy of Pediatrics recommend that osmolarity should be no more than 400mOsm/L for breastmilk or infant formulae to minimise the risk factors for necrotising enterocolitis.

In the UK, it has been recommended that osmolality should be kept below a maximum of 500mOsm/kg in normal conditions but that this should drop below 400mOsm/kg in malabsorptive states (Shaw, 2015). A recent systematic review (Ellis et al, 2019) on milk feed osmolality looking at whether this caused adverse gastrointestinal events in newborn and low birthweight infants concluded that there was no consistent evidence that differences

in osmolality in the range 300-500 mOsm/kg are associated with adverse events in neonates.

Another study discussed the processing of breast milk and the impact on osmolarity, with thawed breastmilk/fortifier mixtures showing the highest osmolarity. The paper, published by ESPGHAN, also provides a detailed review of impacts on osmolality when a range of fortifiers and micronutrients are added. It is currently advised that BMF be added to the minimum amount of breastmilk possible, and that this is used before fortifying any more milk to avoid prolonged storage

Processes and Procedures

Expressed Breast Milk (EBM)

Use of maternal expressed breast milk (MEBM) should be prioritised at all times. Freshly expressed breast milk should always be used where available, with frozen EBM used if insufficient fresh breast milk. Where MEBM is unavailable, the use of donor expressed breast milk (DEBM) should be considered. When using EBM please refer to the units "Expressing and handling breast milk guidance"

Breast Milk Fortifier (BMF)

The decision to fortify breast milk should be made by the medical and nursing team with parental agreement. Parents should be given an information leaflet before BMF is introduced (see Appendix 1).

Human milk fortifier comes in sachets, and currently there are two brands available in the UK: Cow & Gate Nutriprem Breast Milk Fortifier, which is provided in 1g sachets of powder; and SMA Breast Milk Fortifier that is also presented in 1g sachets of powder.

Indications/Criteria for the use of BMF

- Any preterm infant born < 32 weeks and < 1.5kgs
- Infants who are tolerating a minimum of 60 and up to150mls/kg/day of enteral nutrition according to individual Trust unit guidelines.Infants born 1.5 -2.2kgs and volume restricted (<150mls/g/day) or poor growth (<15-20g/kg/day) on review of both weight and length centiles

Contraindications for the use of BMF

- Weight less than 1000g and on >50% parenteral nutrition
- Urea levels higher than 7mmols/s (note 5.7mmols/l in ESPGHAN recommendations)
- EC/suspected NEC/distended abdomen
- Parental request
- BMF should not be added directly to an infant formula
- Term infants
- Not suitable for use in cow's milk protein allergy. Whilst Nutriprem BMF contains extensively hydrolysed cow's milk protein, individual's tolerance may vary, and it is possible that some infants could react to the hydrolysed protein in BMF.
- Inborn errors of metabolism such as phenylketonuria, galactosaemia, galactokinase deficiency
- Infants on a combination of MEBM and preterm formula should not be commenced on BMF is preterm formula>50% of total daily feed volume.

Use with Caution

- Infants who have had gastrointestinal surgery/high stoma outputs post-surgery

- Infants with absent/reversed end diastolic flow (abnormal placental blood flow at birth).

When to Start BMF and Recommendations on advancing the dose

- When the infant is able to tolerate a minimum of 60 to 150mls/kg/day of breast milk (Embleton, ND. Et AL, 2022) and according to individual Neonatal Unit Guidelines, commence half strength BMF (2%)
- Ensure volume is tolerated for a minimum of 48hours before increasing the doseIncrease to full strength (4%) after 48hours/as tolerated and once tolerating 150mls/kg/day to provide appropriate macro and micronutrients in addition to growth.
- In some infants if suboptimal weight gain and growth and for those requiring higher protein intakes, consider further increasing feed volume to 165ml/kg/day

Administration of BMF / Instructions for making up BMF on the ward

NB This is a guideline only and individual KSS Trusts may have local policies on the preparation of BMF

1. Wash hands
2. Collect together a clean plastic tray (to be used as the area for milk preparation), 1 x5mls syringe, 1 x 100mls sterile infant feeding bottle, fresh or thawed breast milk and 2 x 1g sachets of BMF
3. Wash hands

OPTION 1a (using a BMF concentrate if no BMF weighing scales available):

1. Using the 5mls syringe, draw up 5mls of MEBM and add to the 100mls sterile infant feeding bottle
2. Empty the content of 2 x 1g sachets of BMF into the 100mls bottle and replace the lid.
3. Leave for a few minutes for the BMF to dissolve. Swirl/roll gently to mix. Do not shake vigorously as the fat globules are disrupted if milk froths
4. This will make a 6ml BMF concentrate
5. Discard gloves and wash hands. Repeat this process for each feed
6. Immediately make up fortified breast milk for administration (as per table below, with kind permission of Kings College Hospital)
7. For milk storage & handling refer to relevant trust guideline: file:///T:/Dietetics & SLT/Paediatrics/Neonates/NICU Dietetics/FEEDING GUIDELINES/Part 1 Nutrition in the Neonate/Preparation, Storage, Handling, Checking and.pdf

    - Do not store BMF concentrate
    - Do not add BMF to infant formula

Total Volume of Fortified MEBM required	Half Strength		Full Strength	
	Amount of BMF concentrate required	Amount of MEBM required	Amount of BMF concentrate required	Amount of MEBM required

10mls	0.5mls	9.5mls	1ml	9mls
20mls	1.0mls	19mls	2ml	18mls
30mls	1.5mls	28.5mls	3ml	27mls
40mls	2mls	38.0mls	4ml	36mls
50mls	2.5mls	47.5mls		
60mls	3.0mls	57.0mls		
70mls	3.5mls	66.5mls		
80ml	4.0mls	76mls		
90mls	4.5mls	85.5mls		

OPTION 1b: (for larger volumes without concentrate when no BMF weighing scales available):

- Full strength (4%) = 1g and make up to 25mls
- For ½ strength (2%) = 1g sachet make up to 50mls
- Full strength (4%) = 2 x 1g sachet and make up to 50mls

- Discard any unused BMF concentrate.
- Label any unused fortified EBM with patient's details and time of milk preparation.
- BMF can be stored in the fridge for the following feed or, for the purposes of NG continuous feeding out of the fridge, for a maximum of 4 hours.
- Caution needs to be considered when using for NJ feeding. There is currently no evidence to suggest BMF is safe to use in NJ feeding, or that BMF is a contraindication in NJ continuous feeding

Fortified breast milk has an osmolality of 390-450 mOsm/Kg/H20, well within the recommended range, however, re-warming fortified expressed breast milk (EBM) and/or preparing significantly in advance of use has the potential to increase osmolality, with a further 10% increase after storage at 4 degrees C for up to 24 hours (ESPGHAN 2022). In order to minimise any potential for increased osmolality, supplements should ideally, be made immediately prior to a breast feed using freshly expressed milk, and not prepared in advance and stored in the refrigerator.

OPTION 2: (if BMF weighing scales are available)

- For babies on <25mls per feed, BMF can be weighed as an alternative to using a concentrate. It can be mixed with MEBM/DEBM directly before each feed.
- For example, a baby receiving 2% BMF (HS) and 16mls/feed = 0.32g BMF/feed
- For a baby receiving 4% BMF (FS) and 9mls/feed = 0.36g BMF/feed

Use of BMF alongside formula feeds

On occasions, when there is insufficient EBM, preterm formula may be used to make up the remaining feed volume required. BMF should not routinely be used if preterm formula makes up >50% of total daily feed volume (unless directed by a dietitian). BMF should **never** be added directly to preterm formula.
Combination feeds should be given aseither:

- Alternating feeds of EBM +BMF and preterm formula

- Use the fresh MEBM at the start of the day and then offer Preterm formula once the daily supply of fresh MEBM has been used or until the next expression.

There is no evidence to support one practice over the other, but the method that involves the least amount of milk handling is likely to be the best for individual infants.

Monitoring Anthropometrics and Biochemistry

- Growth, including weight, head circumference and length should be measured minimum weekly
- Serum biochemistry should be monitored 1-2 weekly including urea, electrolytes and bone minerals whilst infants are on BMF. Following discharge, ongoing biochemical monitoring will depend on baby's growth, MBD and the ongoing need for full fortification of breast milk.
- Feed intolerance

Administering Additional Vitamins and Minerals

(See KSS Vitamins and Additives Policy)

Weaning/Discontinuing BMF

Current recommendations suggest that preterm infants who receive pre-term formula milk and who haven't caught up with their growth should be transitioned to a nutrient enriched post discharge formula just before discharge if less than 1.8kgs, or once they are 1.8kgs. There are currently no recommendations for infants >1.8kgs and receiving fortified breast milk.

Whilst on the Neonatal unit, infants should gradually be weaned from BMF once:

- > 50% feeds as preterm formula unless poor growth or fluid restricted
- Weight gain optimal (growth tracking centiles for length, weight and head circumference) and nearing term age/discharge

BMF should not usually be required after term plus 6-12 weeks corrected age (K McCormick 2021).

The Provision of BMF on discharge (LINK: KSS parent information leaflet)

There is some evidence that use of fortifier beyond discharge may help to prevent growth failure and achieve optimal growth at the time of discharge and beyond. It may also have a positive impact on the duration of breastfeeding and have the potential to further protect breast-feeding in the preterm population

BMF can continue to be provided to infants on discharge with the support of a Neonatal Dietitian and/or outreach team or following local guidelines. When there is no neonatal outreach team or Dietitian available, BMF will gradually be weaned following a standardised guideline see example below. This is an alternative to targeted advice with a supportive discharge team

Example :
Nutriprem/SMA Gold Prem BMF (it is recommended that one sachet e added to 25ml EBM or on advice of the Neonatal unit team)

- Example calculation for daily fortifier dosage with BMF for 2kg infant

One sachet BMF mixed with 3-4ml EBM makes a booster
2kg infant feeding 150ml/kg/day = 300ml per day
300ml ÷ 25ml = 12 sachets per day
50% requirement = 6 sachets per day
Using one sachet per BMF booster = 6 BMF boosters per day

- Continue 6 BMF booster per day until weight is following a centile
- Reduce by 1 BMF booster per day per week or as advised by the Dietitian/NCOT until nil concentrate is required

The quantity of BMF prescribed at discharge should be continued until the infant is following a weight centile line, after which the daily quantity of BMF boosters should be reduced gradually.

- Weight gain optimal. Weight gain of 15-20g/kg/day until term and 30g per day thereafter can also be used as a guide. The infant's growth should be monitored using a UK NICM growth chart and fortification should be discontinued when weight is optimal with length centile or be maintaining their weight long the same centile. Both quantity and quality of growth should be considered

- BMF boosters should aim to be discontinued between 6-12 weeks post term when infants have developed a mature sleep/wake pattern and oral reflexes mean they are more likely to successfully breastfeed (K McCormick 2021). Further dietetic assessment should be sought if growth remains a concern. There may be circumstances whereby the dietitian advises the use of BMF for a longer duration.

- Mother's preference to transition onto formula. This may be a standard pre-term or high energy formula if weight gain is suboptimal

Practical aspects of BMF use at home

- BMF can be added either to expressed breast milk in a bottle or given as a BMF concentrate in a syringe or teat just before a breast feed
- Parents will be shown how to give the fortifier prior to discharge and provided with the leaflet 'Using breast milk fortifier at home' (KSS Supporting breastfeeding your baby when you go home LINK).
- Initial supplies of BMF will be provided by the neonatal unit on discharge; further supplies ***may*** be available on prescription from the GP as required
- The initial dose will be decided by the neonatal dietitian depending on clinical need and parents/carers will be advised on how to decrease the dose over the following weeks as decreasing number of sachets per day.
- Follow up may by arranged with either the community outreach team or Dietitian
- If infants weight gain remains sub optimal at this time, they should be continue to be managed by the neonatal dietitian/referred to the paediatric dietitian for ongoing nutritional management

- It is important that parents realise that ‘more is not necessarily better’ and that their infant’s appetite and feeding behaviour will change as they reach full term. Infants are likely to feed more frequently as feeding skills and stamina mature, so parents should be advised not to add extra fortifier beyond that recommended by the hospital team

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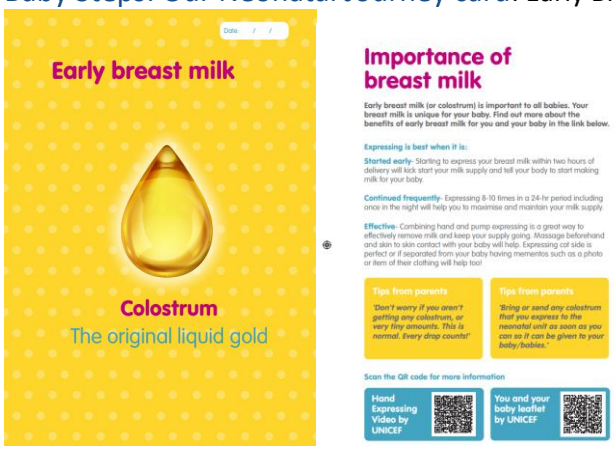
Resources

Baby Steps: Our Neonatal Journey card: Early Breast Milk



Baby Steps: Our Neonatal Journey card: Breast Milk Fortifier