Preterm birth: Strategies for establishing adequate milk production and successful lactation

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S U M M A R Y

Whilst human milk has not evolved to meet the unique requirements of the preterm infant there are unquestionable benefits to be gained via breast milk in terms of the development and health of the infant. Many mothers of preterm infants struggle to achieve a full milk production for many reasons the mechanisms of which are still unclear. Strategies to enhance milk volume include early, frequent simultaneous expression of milk combined with breast massage and a reduction of stress. However, these are not always successful, therefore a greater understanding of lactation physiology is required to devise more effective interventions to increase milk supply. The difficulty these infants experience transitioning to oral feeding and ultimately full breastfeeding further complicates lactation. In order to improve the health of these already compromised infants it is critical that more research be directed to this area so that they reap all the benefits that can be gained from breastfeeding.

1. Introduction

A consideration of the strategy for lactation in mammals can be best described by considering the importance of the evolution of lactation and how the pre-mammals fitted into a range of environments that favored their reproductive success. In other vertebrates, strategies have been developed that result in the young being either born or hatched into restricted environments that have sufficient special foods to ensure the survival of at least some of the young. Thus numbers of birds and fish return to special breeding grounds to achieve reproductive success. However, mammals do not require special breeding grounds because the secretion of milk ensures that the young can be fully nourished wherever the adults can thrive.

There is now strong evidence to suggest that the mammary gland evolved from the inflammatory response — the innate immune system — and that the nutrients in milk developed from components of the innate immune system quite late in the pre-mammalian lineage. Therefore mammary secretion first evolved to protect the hatchlings; later, it also provided unique and complete nourishment for the young. This has important ramifications for the nourishment of the preterm baby, whose ability to mount a defense against microbial attack is extremely limited. Thus the protection provided by mother’ milk is vital.

2. Physiology of preterm lactation

In the extremely preterm infant there are particular difficulties in establishing lactation, due to the earlier stage of breast development at parturition and the inability of the newborn infant to suckle. Some mothers may not have reached secretory activation prior to delivery, so the mammary epithelium may not be sufficiently prepared by the pregnancy hormones to synthesize milk efficiently. Poor placental function with low levels of placental lactogen may exacerbate this problem. Fortunately in the majority of mothers of preterm infants compensatory breast growth can be achieved, even if somewhat delayed, by early and frequent milk removal.2 However, many mothers still struggle to produce enough milk to meet their infant’s nutritional requirements. The reasons for this are not entirely understood, but may be related to physiological and emotional challenges that mothers face following preterm delivery.

3. Composition of preterm milk

The composition of human preterm milk differs from that of term milk. The reasons for these differences are unclear, but preterm milk typically has higher concentrations of protein, secretory IgA and lipids. Protein levels in preterm milk are documented to be 15–20% higher than in term milk, with no differences in the individual proteins4; however, epidermal growth factor and secretory IgA (sIgA) levels are higher5,6 whereas leptin levels are lower.7 sIgA,
the major immunoglobulin found in breast milk, provides immune protection for the infant via the formation of antibodies specific to those pathogens to which the mother and infant are exposed. Given the fragility and immaturity of the preterm infant and its increased predisposition to infection the extra protection provided by breast milk is essential to their health. Total lipid and total energy content is 20–30% higher in preterm milk and contains higher proportions of medium (MCFA) and long-chain polyunsaturated fatty acids (LCPUFA). LCPUFA omega-3 fatty acid docosahexaenoic acid (DHA) and the omega-6 fatty acid arachidonic acid (AA) are important as they enhance visual and neural function by their uptake into the membranes of the retina and brain. Indeed formula supplemented with DHA and AA have shown improved visual and cognitive development compared to standard formula as well as better growth and development.

Human milk also provides micronutrients in addition to macronutrients including fat- and water-soluble vitamins, minerals and trace minerals. The concentration of many micronutrients is influenced by the maternal diet and it is critical that the levels of thiamin, riboflavin, vitamins B6 and B12, vitamin A, iron and iodine in particular are adequate.

Differences in preterm milk composition are less pronounced after 4 weeks of lactation. Due to the immaturity of the preterm infant and its unique needs, routine fortification of breast milk is often required to provide adequate protein for growth as well as minerals such as calcium and phosphorus to enhance bone mineralization that would normally occur in the last trimester of pregnancy.

4. Optimizing lactation success

During the first post-delivery encounter, neonatal staff should include discuss the benefits of human milk, its role in the care of preterm babies and the urgency to begin a milk expression schedule. Early, frequent and effective milk expression is crucial to the initiation of preterm lactation. There is a positive relationship between milk volume and frequency and duration of pump use. Indeed mothers of very low birth weight (VLBW) infants have produced adequate milk volumes at 5 weeks postpartum, pumped at least 45 times per week (>6 expressions/day). It has also been suggested that striving for daily milk volume of 750 mL/day may, by day 10, motivates mothers to continue to express on a regular basis.

5. Interventions to improve breast milk production

Mothers of preterm infants are dependent on milk expression for weeks to months until an infant is able to breastfeed effectively. Recent evidence strongly suggests that double pumping (simultaneous) with a hospital grade breast pump is more effective than sequential pumping in the first 2 weeks. Double pumping has appeared to stimulate more milk ejections and was a more efficient and efficacious yielding milk with a higher volume and energy content when compared to single pumping.

A novel pump (which can be utilized simultaneously; Medela AG, Baar, Switzerland) mimics the sucking pattern of an infant with a two-phase programme. The initial rapid vacuum cycle rate is similar to that applied by the infant before milk ejection, and the second phase consisting of a slower cycle rate is utilized after milk ejection to improve milk removal. Mothers of preterm infants who used an experimental programme with a ‘newborn’ pattern comprised of a more random application of cycle rate demonstrated significantly greater daily and cumulative milk output at days 6–14 postpartum and greater milk output per minute spent pumping.

Although a hospital-grade electric breast pump is an effective tool to facilitate the collection of milk, it is essential that the breast shield used is a correct fit. The shield should match the anatomical configuration of the breast to eliminate friction of nipple tissue against the sides of the tunnel, which may lead to severe nipple excoriation. Milk drainage may also be compromised leading to maternal engorgement and a decrease in milk supply.

Milk ejection occurs by the release of oxytocin, which binds to the myoepithelial cells causing a contraction that expels milk from the alveoli. It is essential to effective milk removal and continued milk synthesis. When this reflex is inhibited, the average milk yield is less than 4% of available milk, and local mechanisms bring about an inhibition in milk secretion. In stressful situations, expressing mothers experience difficulty with milk ejection. The early instigation of skin-to-skin contact is thought to be beneficial in this respect with mothers experiencing the feeling of milk ejection while in contact with their infant. It has been shown that mothers of VLBW infants who practised skin-to-skin contact were less likely to discontinue lactation before discharge and lactated on average 4 weeks longer than controls. Relaxation in the form of a tape has also been shown to increase milk volumes. Interestingly, the use of nasal oxytocin spray does not markedly improve the milk yield during the first 5 days postpartum.

Pumping technique also influences milk volume. Breast massage during single and double pumping with an electric breast pump increased milk volume. Similarly a combination of hand expression of colostrum and hands-on pumping of mature milk also increased milk volume in mothers of preterm infants.

A recent systematic review suggests that milk expression is a practice likely to be influenced by many factors other than use of breast pump. Some of the critical interventions mentioned include: support and staff training, attitudes of staff, and psychological factors. A recent study evaluating peer support programmes in two neonatal intensive care units in the USA found that one of the most important aspects of the new mother’s relationship with the peer counselor was the shared experience of how difficult it can be to provide milk while coping with the emotional toll of having an infant in intensive care.

6. Breastfeeding the preterm infant

To increase and maintain a milk supply that can support the normal growth of the infant it is essential that the breast is effectively emptied of milk to ensure ongoing stimulation of milk synthesis. The preterm infant is at high risk of feeding difficulties due to inherent neurological and developmental immaturity that may be compounded further by co-morbidities such as chronic lung disease and intracranial haemorrhage. These factors may limit the strength of vacuum the infant can apply to the breast as well as impact co-ordination of sucking, swallowing and breathing, thereby impeding effective feeding. Whereas it is acknowledged that feeding difficulties are common in the preterm infant (<37 weeks of gestation) a subset of infants referred to as late preterm (34–37 weeks of gestation) are often expected to progress more rapidly with oral feeding despite being up to 8 weeks younger than the full-term infant. A third of brain growth occurs in the final 6–8 weeks of gestation, therefore late preterm infants are born with ~35% less brain volume than the term infant. Rapid brain development and formation of synapses occurs between 34 and 36 weeks along with maturation of the nervous system (35–38 weeks) such that coordination of breath- or bottle-feeding improves. Given such a developmental continuum this population is at risk of feeding difficulties, and indeed a retrospective study showed that 80% of readmissions of late preterm infants were due to jaundice and that breastfed late preterm infants were 1.8 times more likely
to need hospital care compared to their breastfed full-term counterparts. Insufficient milk intake is the likely cause of jaundice in this group due to poor feeding skills, which could be exacerbated by early discharge after delivery, particularly if secretory activation has not occurred. Close observation and attention to feeding during the nursery stay as well as a good breastfeeding support post discharge may be strategies that could prevent readmission of these infants.

7. Intragastric tube feeding

Preterm infants are often fed via a nasogastric or orogastric feeding prior to and during transition to oral feeds. During the establishment of breastfeeding, supplementation via tube rather than via bottle is conducive to higher rates of breastfeeding at discharge. However, the presence of the feeding tube during a bottle feed may have detrimental cardiorespiratory effects. The provision of a pacifier during feeding has been shown to have positive effects such as increased intestinal transit time, a reduction in time to discharge and calmer behavioural state; however, a Cochrane review did not find consistent benefits, although it confirmed that transition time to bottle-feeds and bottle-feeding performance were improved. Prolonged tube feeding is not desirable as it has been associated with poor sucking ability and increased feeding difficulties later in pregnancy. Oro-gastric tubes may also distort the malleable plate, lips and gums as well as cause laryngeal trauma and subglottic stenosis further complicating feeding.

8. Initiation and establishment of breastfeeding

It is a requirement of many neonatal intensive care units (NICUs) that infants reach full oral feeds before discharge from hospital and this milestone is usually the last met prior to discharge. Rapid progression to oral feeds is highly desirable but determination of the readiness of the infant to feed can be difficult. Corrected gestational age, infant weight and infant behaviour are both common indicators. Developmental assessments are based on the premise that behavioural organization is indicative of central nervous system maturation. Alertness and the ability to maintain this state is one sign recognized to implement oral feeding as well as other oral behaviours such as mouthing, hand and tongue sucking, hand-to-mouth and hand swipes. Listening to amplified sounds of breathing and swallowing during bottle-feeding has been shown to improve the caregiver’s response to the infant resulting in better infant state and physiological responses (e.g. less desaturation episodes). Nyqvist takes a different approach by encouraging breastfeeding as soon and as frequently as possible rather than assessing readiness for oral feeding. This approach may be facilitated not only by the provision of breast milk but by the modulation of infant physiological responses with respect to sucking and skin-to-skin contact with the mother. Many preterm infants are supplemented by bottle-feeds while establishing breastfeeding, as milk intake volumes from the breast are often lower than the feed volume prescribed by the neonatologist due to weak sucking pressures, poor suck—swallow—breathe coordination and the energy expended necessitating the need for complementary feeds.

9. Breastfeeding versus bottle-feeding

Supporting the immature infant to achieve oral feeding is challenging for support staff as they work to improve sucking skills according to the infant’s development and health. Recognition of the differences between feeding modes will allow adjustment of feeding strategies accordingly. There are marked differences between breastfeeding and bottle-feeding. Generally stronger vacuums are applied to the breast compared to the bottle for reasons such as the necessity to extend the nipple to both facilitate milk flow and position the nipple correctly in order to collect an appropriately sized oral bolus and achieve clearance of milk from the oral cavity. During breastfeeding the availability of milk is transient and flow rates are variable due to the milk ejection reflex; thus, a preterm infant must suck effectively and coordinate sucking—swallowing and breathing during the period in which milk is available. By contrast, milk is always available from the bottle and sometimes flows without the application of vacuum, explaining in part the lower vacuums applied and the more effective and efficient feeds compared to breast feeding, at least during the establishment of breastfeeding. Strength of vacuum applied to the bottle is positively related to the volume of milk ingested and efficiency of milk transfer. Nevertheless, breastfeeding elicits better physiological responses in that infants experience fewer desaturation episodes compared to bottle-feeding.

Little work has been carried out during breastfeeding in the preterm infant. Geddes et al. have recently shown that breastfeeding vacuums are typically lower in the preterm infant compared to the term infant. Further evidence of the importance of vacuum comes from studies of conditions that typically impede oral feeding such as prematurity, bronchopulmonary disease and cleft lip and/or palate infants. Weaker intra-oral vacuums have been associated with these conditions compared to infants with no feeding issues or more mild disease.

10. Nipple shields

Preterm infants often have difficulty attaining and maintaining good attachment to the breast, sustaining long suck bursts, and they tire easily, falling asleep at the breast. Nipple shields are often used to assist infants to breastfeed by enabling the infant to attach to the breast for sustained periods and increase milk transfer. The mechanism by which the nipple shield confers these benefits has not yet been elucidated. Further, long-term studies of nipple shield use have not been carried out, although Meier et al.’s data do not suggest that they have a detrimental effect in this population.

11. Alternative methods of feeding during the establishment of breastfeeding

Bottle-feeds still tend to be the preferred method of suck feeding in the absence of the mother or as a supplement to breastfeeding rather than intragastric tube feeds. No particular bottle-feeding system has been proven to be beneficial for the preterm population as a whole, and this may simply reflect the variability in development and health status of the infants.

Cup feeding is used in some nurseries with the intention of avoiding nipple confusion. The ‘cups’ vary in size and shape; however, for the technique to be effective it requires patience and experience as research has shown that ingested volumes may be small due to a large amount of milk lost during feeding. Nevertheless, studies have shown both fewer desaturation episodes and a greater incidence of breastfeeding at 3 months compared to bottle-feeding.

Supplemental milk can also be delivered via a tube taped to the side of the nipple or the caregiver’s finger. The tube is attached to a milk reservoir or a milk-filled syringe (finger feeding) or reservoir and the infant siphons the milk while sucking on the mother’s finger. This method was devised to reduce nipple confusion, but there appears to be only one study showing an increase in breastfeeding rates at discharge. Alternative methods of feeding (excluding the artificial teat) have been favored with the intention of avoiding nipple confusion, the incidence of which is not known. There has been no systematic
or mechanistic study of this phenomenon in either term or preterm infants and with current knowledge severely lacking it is difficult to develop feeding methods that will enhance feeding development, particularly in the absence of breastfeeding as with the preterm infant.

12. Interventions to enhance feeding

There has been concerted effort in the last few years to accelerate maturation of oral feeding with the application of a stimulus. One intervention to improve times to oral feeding involves the application of a non-nutritive suck-burst pattern via an ‘active’ pacifier and is based on the premise that this input primes swallow circuits as well as improving orofacial motor control. This patterned orocutaneous simulation enhances oral feeding skills beyond those expected by maturation alone especially in infants with sucking difficulties and those with respiratory distress syndrome.43

Other combinations of oral and non-oral stimulation include sucking on a pacifier; stroking the cheeks, lips, gums and tongue; stroking the head, neck, back, arms and legs; passive movement of the limbs.44 All of these interventions improved the volume and efficiency of milk intake as well as transition time to oral feeding. Furthermore it was found that oral stimulation alone improved both sucking and expression pressures as well as the coordination of swallowing and respiration compared to the non-oral and combined groups.44 It is encouraging that a small pilot study has been successful in the application of stimulus by the mother or a family member indicating the potential for a family-centered approach.45

13. Assessments of feeding

Despite the importance of the development of safe and efficient oral feeding in the preterm infant there are still few accurate and reliable assessment tools available to the clinician to determine the success of an intervention. Most are based on bottle-feeding with few specifically designed for breastfeeding. Rigorous testing has not been carried out and ideally more objective measures of feeding are required that are not biased by observer error.

The Neonatal Oral Motor Assessment Score is designed to identify and classify oral-motor patterns associated with poor feeding. Despite contrasting results pertaining to validity of the tool and its poor predictability46 it has been used for longitudinal studies of term breastfed and bottle-fed infants,47 progression of feeding in small-for-gestational-age preterm infants48 and infants with bronchopulmonary dysplasia.49

The Infant Breastfeeding Assessment Tool (IBAT) subjectively assesses infant behaviour, attachment, feeding and the mother’s perception of feeding. IBAT has variable reliability, lacks predictive validity and has a low association with milk intake in VLBW preterm infants.46

The Preterm Infant Breastfeeding Behavior Scale assesses infant behaviour, attachment, sucking bursts and swallowing. It has adequate inter-rater reliability between health professionals but is poor between mothers and health professionals.46

The Early Feeding Skills assessment (EFS) focuses on specific feeding skills such as the ability to remain engaged, organization of oral motor movements, coordination of sucking, swallowing and breathing as well as the maintenance of physiological stability. EFS consists of a three-part 36-item checklist measuring oral feeding readiness, oral feeding skill and oral feeding recovery and has not been tested for validity.46

Test weighing is an objective method that measures the effectiveness of breastfeeding by weighing the infant before and after breastfeeding to determine the volume of milk ingested. This method has proven feasible in the preterm population50 as well as more accurate and reliable than clinical indicators.51 Test weighing has the potential to improve transition to full breastfeeding by bolstering the mother’s confidence as infant milk intakes increase over time44 and facilitates calculated reduction of supplementation as breastfeeding is established. This measurement has the potential to enhance breastfeeding if managed well within the NICU and is currently being employed as a routine measure in some nurseries in the USA and Europe.

14. Conclusions

In spite of the importance of the evolution of lactation in mammals, it has not been a factor in the improved survival of premature infants. In the past, premature babies did not survive so it cannot be claimed that breast milk has evolved to provide benefits for preterm babies. However, recent research has shown that modified mother’s breast milk is the preferred food for these infants. The establishment of breastfeeding in premature babies not only provides the infant with protection and nourishment but also provides a multitude of positive stimuli for the infant. The normal function of the milk ejection reflex is crucial to successful breast expression and breastfeeding. This reflex is facilitated by the release of oxytocin. This hormone also has calming and connecting functions that oppose the flight, freeze or fight response and facilitates bonding between mother and infant. Given the multitude of benefits conferred by breastfeeding it is imperative that research is directed to understanding lactation physiology, particularly after preterm birth, in order to ensure that these at-risk infants reap the benefits of both breast milk and breastfeeding.

**Practice points**

- Early and effective milk removal is crucial for the initiation of lactation.
- Triggering the milk ejection reflex is essential for effective milk removal.
- Skin-to-skin contact increases milk production and facilitates feeding at the breast.
- Effective and efficient oral feeding depends on the development of adequate infant vacuum.
- There are no accurate subjective clinical assessments of effective breastfeeding.
- Test weighing of infants before and after breastfeeding measures milk intake.

**Research directions**

- Methods of enhancing breast milk production.
- Interventions to accelerate oral feeding and breastfeeding duration.
- Accurate clinical assessments/measurements of breastfeeding the preterm infant.

**Conflict of interest statement**

None declared.

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