

Human milk banks: lights and shadows

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Abstract

Breastfeeding is the most appropriate source of nutrition also for preterm infants. When mother's own milk is not available, donor human milk (DHM), provided from a human milk bank (HMB), or formula can be used. Infants fed DHM grow at a slower rate than formula-fed infants. However, DHM has the advantage over formula to retain some of the bioactive properties of naïve human milk.

Given the wide variability of DHM content and its generally low macronutrient content, individualised fortification represents a more valid option than standard fortification in order to meet the high nutritional requirements of preterm infants.

Pasteurization is necessary to reduce bacterial count in DHM. Holder pasteurization, which is recommended in most HMB guidelines, has several limitations, because it impairs macronutrient and functional components of DHM. Alternative methods of pasteurization, which would be capable of retaining the bioactive properties of DHM with the highest level of microbiological safety, are currently under investigation.

Keywords

Human milk banks, donor human milk, breastfeeding, nutrition, preterm infants.

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Breastfeeding and the use of human milk for preterm infants

Breastfeeding is widely accepted as the gold standard for infant feeding and nutrition, due to its documented short- and long-term effects on clinical and neurodevelopmental outcomes [1-3]. Benefits of human milk (HM) feeding have been well documented also in preterm infants: preterm infants fed HM have lower risk of necrotizing enterocolitis (NEC), sepsis and retinopathy of prematurity, better feeding tolerance, and improved neurodevelopment than infants fed with formula [4, 5]. The advantage of HM over formula is related to the presence of peculiar non-nutritional factors, which promote intestinal adaptation and maturation, improve enteral feeding tolerance and protect against infective and inflammatory disorders [6].

When mother's own milk (MOM) is not available or not sufficient despite adequate lactation support, the alternatives are represented by formula and donor human milk (DHM), alone or as supplements to MOM. The choice of the alternative to MOM is critical: DHM has the advantage of retaining some of the non-nutritional properties of naïve HM, but formula feeding guarantees a consistent delivery of optimal nutrients. Furthermore, the two feeding regimens have been linked to different clinical outcomes [7]: formula feeding appears to improve short-term growth, but also to increase the risk of NEC, compared to DHM. There is currently no evidence of a difference between the two feeding regimens on longer-term growth or development.

Despite some theoretical downsides, pasteurized and fortified DHM is the recommended source of nutrition for preterm infants in the absence of fresh MOM, because the benefits in terms of improvement of clinical outcomes outweigh the risk of slow growth [1, 8]. On these bases, formula feeding should be limited to clinical settings where both MOM and DHM are unavailable [8].

There has been some concern regarding the possibility that implementing the use of DHM would discourage the mothers of preterm infants to breastfeed. However, data from the Italian Association of Human Milk Banks did not support this hypothesis, showing that exclusive breastfeeding

rate at discharge was significantly higher in NICUs with a HM bank than in NICUs without [9].

Feeding preterm infants with donor human milk vs. formula

Short-term outcomes

Several systematic reviews have investigated the role of DHM compared to formula in preventing NEC: two meta-analyses including studies performed in the 70s and 80s showed that the use of DHM resulted in a reduced risk of NEC, but also in a slower weight gain [10, 11]. Furthermore, benefits of DHM were seen exclusively when it was used as the only source of nutrition, and not as a supplement of MOM. It is important to note that unfortified DHM was used in all the studies, which can explain at least partially the reduced growth in the DHM group. The 2014 update of the Cochrane review on DHM [7], including a few more recent studies, confirmed the findings of the two previous meta-analyses, but also highlighted the limited available information regarding fortified DHM and the wide variability in the nutritional content of the formulas used as controls.

Nowadays, fortification of DHM is performed routinely in most neonatal intensive care units (NICUs): for this reason, results of previous papers are not applicable to the present preterm population, and future studies aimed at investigating growth and clinical outcome should better compare fortified DHM to a formula designed specifically for preterm infants. The same consideration also applies to feeding tolerance: limited data from the 80s reported significantly fewer episodes of feeding intolerance in infants fed unfortified DHM compared to formula [10, 11], but no data on fortified DHM are available.

Long-term outcomes

Data on long-term cardiovascular and neurodevelopmental outcome of preterm infants fed DHM derive largely from the follow-up of the original UK cohort of preterm infants enrolled in the 80s by Lucas and colleagues. These data suggest that early feeding with DHM could have a favourable effect on cardiovascular health during childhood and adolescence, by reducing arterial blood pressure and improving lipoprotein profile [12, 13], and also improve neurodevelopment [14]. Although extremely interesting, the applicability of these findings is limited by the fact that the original study

compared formula to unfortified DHM, which is not the current feeding practice for preterm infants.

Donor human milk: nutritional characteristics and supplementation

Macronutrient content of both preterm and term HM is highly variable [15] and usually not sufficient to meet the high nutritional demands of preterm infants [6]. Supplementation with standard amounts of HM fortifiers leads inevitably to the risk of under- or over-nutrition [16], depending on the nutritional characteristics of each HM sample.

DHM usually has low macronutrient content, because it is usually provided by mothers of term babies who have been lactating for some time [17]. Standard fortification does not resolve completely this issue [18], because it has been recently demonstrated that, in infants fed fortified MOM, weight gain is faster than in those fed fortified DHM [19].

In a recent paper [20], the composition of a large number of samples of MOM and DHM was evaluated; individualized fortification was then performed and compared to standard fortification. The macronutrient variability was high for all the samples, and persisted after standard fortification. Individualized fortification allowed to maintain protein and protein:energy ratio in the range of nutritional recommendations, thus potentially reducing the consequences of both over- and under-nutrition.

Recently, the development of a HM fortifier obtained by concentrating pasteurized DHM has opened the possibility of an “all-human” diet. This exclusively HM-based diet has been compared to a diet containing bovine-derived HM fortifier and/or formula [21]: the results of that study showed that the “all-human” diet was associated with a lower risk of NEC; however, the study was not powered to NEC reduction and therefore its results require further proof.

The need for a tailored supplementation of DHM is also supported by the recent finding that DHM has low concentrations of docosahexaenoic acid [22, 23] and several free aminoacids [23], which are both essential for growth and development of preterm infants. Preliminary data have also suggested that preterm infants fed DHM and those fed MOM are likely to receive HM oligosaccharides (HMOs) in different total amounts and relative composition [24]: given the prebiotic properties of HMOs,

and their potential role in health and disease, the composition of DHM deserves further investigation also in terms of HMO content.

Human milk banks

Given the documented clinical advantages of HM feeding, the American Academy of Pediatrics (AAP) states that infant nutrition should be considered “a public health issue and not only a lifestyle choice” [1]. For this reason, strategies aimed at implementing the use of HM have been developed and the number of human milk banks (HMBs) has increased worldwide. At present, in Europe there are 186 HMBs, and new banks will be established with the support of the European Milk Bank Association (www.europeanmilkbanking.com) [8]. However, not all preterm infants have access to DHM: a recent survey conducted in the US investigated the availability of HM in advanced care neonatal units in maternal hospitals in the country. The authors documented a substantial increase over time in the number of units providing HM to $\geq 90\%$ of admitted infants; however, in 2011 only a third of the US neonatal units were routinely providing HM to most infants, and approximately 22% of them had access to a HMB [25].

HMBs are fundamental for the safe provision of HM to preterm infants: in the US, informal sharing of HM between mothers with an abundant supply and those seeking milk for their children is growing in popularity, despite both the Food and Drug Administration and the AAP discourage this practice [1, 26]. It has been shown that most samples of HM purchased via the Internet have a high overall bacterial growth, and that approximately 20% of them contains Cytomegalovirus DNA [27]; the use of contaminated milk poses infants' health on the line, especially if it is provided to preterm or sick children.

This is true also for HMBs: despite longstanding experience in HM donation, many countries lack a tight regulation for HMBs [28], probably due to the non-recognition of HM as either a food or a therapeutic product.

Quite recently, national guidelines for HMBs' creation and implementation have been developed in several countries [29, 30]; this is fundamental in order to minimize variations in procedures and ensure appropriate measures in response to unforeseen risks.

Pasteurization of donor human milk

Pasteurization of DHM is generally recommended as a standard-of-care practice in order to minimize bacterial growth [28].

Pasteurization is traditionally performed using the Holder method, which is a low-temperature, long-time heat treatment in which HM is heated in a water bath and held for 30 minutes at 62.5°C. This procedure is effective in decreasing bacterial count to non-infective levels, but at the same time reduces the concentration of beneficial bacteria which constitute the HM microbiota [31].

Furthermore, Holder pasteurization has several nutritional and immunological downsides, as it reduces significantly fat and energy content of naïve HM [32], affects the amount and activity of the main bioactive components of HM (i.e. secretory IgA, lactoferrin and lysozyme [33]), abolishes the activity of bile salt stimulated lipase (BSSL) [33], and also affects the concentration of some hormones such as adiponectin and insulin [34].

More conservative approaches to pasteurization are currently under investigation [35]: preliminary data show that high-temperature, short-time pasteurization (72-75°C for 15-16 seconds) preserves better than Holder pasteurization the profile and biological activity of some HM proteins [36], even if it retains the limitations related to heat-dependent HM treatments.

Heat-independent methods of pasteurization, such as UV-C irradiation, have shown to preserve significantly higher levels and activity of immunological proteins than Holder pasteurization, resulting in bacteriostatic properties similar to those of untreated HM [37]. These latter methods have also the advantage over Holder pasteurization to preserve heat-labile proteins such as BSSL and alkaline phosphatase [38].

Conclusions

MOM is the most valid option for feeding preterm infants. Breastfeeding the preterm infant is often problematic and requires adequate support; strategies aimed at increasing breastfeeding rates among mothers of preterm infants are a priority in the nutritional management in NICU.

When MOM is not available, DHM represents the most appropriate alternative. Actually, despite concerns related to a slower growth compared to formula-fed infants, DHM-fed infants benefit from the non-nutritional properties of DHM, which can

have positive implications in terms of developmental outcome.

DHM does not meet the high nutritional requirements of preterm infants, even if supplemented with standard amounts of HM fortifiers. For this reason, future research should focus on individualizing fortification of DHM or on developing practical methods to standardise the composition of major nutrients in DHM.

Pasteurization is necessary to reduce bacterial count in DHM; Holder pasteurization has several limitations because it also impairs macronutrient and functional components of DHM. HMBs should actively research alternative methods of pasteurization which would be capable of retaining the bioactive properties of DHM with the highest level of microbiological safety.

Declaration of interest

The Authors declare that there is no conflict of interest.

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