Human Milk Banking Research

Reduction in Necrotizing Enterocolitis

In preterm infants, feeding with human milk (HM) is a very effective intervention for the prevention of infections and necrotizing enterocolitis (NEC), and for potentially improved neurocognitive and cardiovascular outcomes in the long term. Banked donor milk should be promoted as standard component of health care for premature infants.
long-term.

Arslanoglu, S., Ziegler, E. E., & Moro, G. E. (2010). ***Donor human milk in preterm infant feeding: evidence and recommendations.*** *Journal of perinatal medicine, 38(4), 347–51. doi:10.1515/JPM.2010.064*

Necrotizing enterocolitis

Some of the most compelling evidence supporting the use of donor milk relates to this disease. Five of the trials included in the Cochrane review comparing donor milk to formula reported on necrotizing enterocolitis. Although no single trial found a significant difference, meta-analysis showed a significantly higher incidence of NEC in the formula-fed group. The pooled data suggests that for every 33 infants fed formula milk rather than donor breast milk one extra case of necrotizing enterocolitis will occur. A review by Boyd et al of published studies also showed a protective effect of donor milk feeding against NEC. Meta-analysis of three trials comparing exclusive donor milk feeding to exclusive formula feeding suggested an exclusive diet of donor milk might reduce the risk of NEC by about 79%

Hoodbhoy, S. ***Human milk banking; current evidence and future challenges****. Paediatrics and Child Health, Volume 23, Issue 8, August 2013, Pages 337–341*

Protection against necrotizing enterocolitis

NEC is an inflammatory bowel disease predominantly of preterm infants that significantly contributes to neonatal mortality and morbidity. It is suggested that the immature gut motility, slower digestion, decreased absorption, and immature immune defences, barrier function and circulatory regulation are factors that predispose preterm infants to NEC (Neu and Walker, 2011). Breastmilk fed infants have a marked reduction in the incidence of NEC compared to formula fed infants (Henderson et al., 2007). This may be in part related to the improved feed tolerance with breastmilk, the myriad of bioactive components in human milk that may promote gut development and more optimal bowel colonization pattern. Quigley's meta-analysis demonstrated a higher incidence of NEC among low birth weight infants fed formula versus donor milk (relative risk of 2.5 [95% confidence interval 1.2, 5.1]).

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Benefits of Using Donor Milk

Recent scientific information reinforces the importance of human milk for optimal newborn nutrition and highlights the important "health, nutritional, immunologic, developmental, psychologic, social, econ-omic, and environmental benefits."[3] Donor human milk banks play an important role in providing this ideal nourishment, especially for high-risk and premature infants. "Growing evidence supports the role of donated human milk in assisting infants with special needs, such as infants in newborn intensive care units who are unable to receive their own mothers' milk, to achieve the best possible health outcome. In these situations, use of banked donor milk may protect the infant from the risks that might result from not breastfeeding."

*Kennaugh, J., Lockhart-Borman, L**. The Increasing Importance of Human Milk Banks,** E-Journal of Neonataolgy Research**, PII:** eJNR21606072v1i3p2y2011*

American Academy of Pediatrics, Section on Breastfeeding. ***Breastfeeding and the Use of Human Milk.*** Pediatrics *2005; 115:496-506.*

Further Benefits of using Donor Milk

Feeding preterm infants breast milk has been shown to lower morbidity in this vulnerable population, with reduced risks of developing necrotizing enterocolitis late onset sepsis, retinopathy of prematurity and neurodevelopmental outcomes. Studies of preterm infants who have reached adolescence and adulthood show infants fed human milk have reduced rates of metabolic syndrome, less insulin and leptin resistance, lower low-density lipoprotein levels and lower blood pressure as compared to formula fed preterm infants.

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Enhanced immunity

Very few data exist on the protective properties of donor milk compared to formula in preterm infants, however, it is plausible that the residual activity of immune modulating components post-pasteurization of human milk is sufficient to confer an advantage. Although variably altered by pasteurization, lysosyme, lactoferrin and immunoglobulins have a direct anti-infective action while other components have an indirect effect such as human milk oligosaccharides (as a prebiotic via promotion of a favorable gut microbiome) and long-chained polyunsaturated fatty acids (via induction or modification of eicosanoid production, gene expression, lipid raft composition, T-cell signaling) (Ewaschuk et al., 2011a and Ewaschuk et al., 2011b).

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Long-term health benefits

Quigley's meta-analysis showed no differences in the long-term neuro-development, however only two studies were included in this analysis and infants were neither fed nor grew in a manner we now know is consistent with normal development. Early studies suggested that donor milk promotes a reduction in blood pressure and a more favorable lipoprotein profile during adolescence compared to formula, both

prognostic of cardiovascular disease risk in adulthood (Singhal et al., 2004, 2001). Among infants (*n* = 900) randomized to donor milk or formula as a sole diet or as a supplement to mother's milk, arterial blood pressure was lower in those infants who received donor milk. The proportion of donor milk intake was inversely related to later mean blood pressure. Similarly, infants who had received donor milk had lower ratio of low-density (LDL) to high-density (HDL) lipoprotein cholesterol and this ratio was dose-dependent, with infants who received exclusively donor milk having the lowest LDL to HDL ratio.

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Feed intolerance and establishing breastfeeding

There are few data on the time taken to establish full enteral feeds, or the duration of donor milk use. Lucas et al reported significantly more infants in the formula-fed group failed to tolerate full enteral feeds by 2 weeks after birth, and by 3 weeks after birth. Meta-analysis in the Cochrane review demonstrated a statistically higher risk of feed intolerance (requirement to cease enteral feeds and commence parenteral nutrition) in the formula-fed group.

In most cases, donor milk is instituted to supplement maternal breast milk until the mother's own milk supply increases. Data on rates of successful breastfeeding following use of donor milk is scarce. Previous authors have reported personal communications suggesting availability of donor milk increased the rate of breastfeeding at 4 weeks of age and at discharge. Recently Utrera Torres et al studied the effects of opening a milk bank in a neonatal unit on feeding patterns in infants born at less than 32 weeks gestation or birthweight less than 1500 g. Availability of donor milk enabled earlier commencement of enteral feeding, and although it did not alter the proportion of infants exclusively breast milk fed with at discharge, there was a significant reduction in the proportion of infants that received infant formula during the first 4 weeks of life.

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Safety of donor milk

One of the main concerns regarding the use of donor milk is the potential for transmission of infective agents. Transmission of CMV and HIV via the breast milk of seropositive mothers is well documented. Internationally, there is variation in practice regarding donor selection, screening and processing of milk. Studies have shown that freezing alone does not inactivate CMV, and there are case reports of infants developing CMV after being exclusively fed unpasteurized thawed frozen human breast milk.

The NICE guidelines (UK) include recommendations for a stepped screening process to minimize risks to recipients and serological testing of potential donors. Currently donors are screened for HIV 1 and 2, Hepatitis B and C, HTLV I and II and syphilis. Milk from suitable donors is then pasteurized and frozen.

Microbiological surveillance of milk before and after pasteurization further reduces the risk of infants receiving contaminated milk. To date there are no reports of transmission of these viruses through pasteurized donor milk. However, to ensure rapid response to any future unforeseen risks, NICE recommends milk banks follow Hazard Analysis and Critical Control Point (HACCP) principles ensuring donor traceability with careful documentation and process control. This approach is becoming increasingly common in milk banking internationally.

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Cost savings

Wight analyzed the cost of using donor milk in an NICU in San Diego, California. Using data from a study by Schanler et al on differences in(1)length of stay,(2) number of cases of NEC per infant, and (3) number of cases of late-onset sepsis per infant, Wight calculated that after factoring the cost of the donor milk, approximately $8800 could be saved per infant. Costs used for these calculations were direct costs only for her hospital. Direct costs will differ from one institution to another, depending on the method of accounting used. Wight estimated that if donor milk is as effective in preventing NEC and sepsis and shortening hospital stay as Mothers own milk, then for every $ spent on donor milk the NICU saves between $6 and $19 in NICU costs. Wight estimated that "donor human milk for very low birth weight infants could save almost $200,000 per year.

Wight NE. ***Donor human milk for preterm infants.*** *J Perinatol. 2001; 21:249-254. 11.*

*Schanler R, et al****. Feeding strategies for premature infants: beneficial outcomes of feeding fortified human milk versus preterm formula.*** *Pediatrics. 1999;103:1150-1157.*

Societal/cost benefits

Although all milk is donated to milk banks in North America, significant costs accrue from testing donors and from processing their milk. The average cost of donor milk from a private, not for profit milk bank is variable but generally greater than $4.00 per ounce (Rosenbaum, 2012). Although these costs are not trivial, it is argued that the benefits of reducing length of stay (Ganapathy et al., 2012; Wight, 2001), sepsis (Wight, 2001) and NEC (Ganapathy et al., 2012; Wight, 2001; Neu and Walker, 2011), outweigh the costs of donor milk.

While it is known that donor milk is not as effective as mother's milk, the cost savings remain substantial. In Sullivan's study (Sullivan et al., 2010) the 100% human milk-based diet (mother's milk and donor milk fortified with human milk protein-based fortifier) led to a reduction in the NICU length of stay by 3.9 days compared to the diet of mother's milk supplemented with formula and bovine based fortifier. The main factors leading to this reduction in NICU length of stay, and therefore to the direct net savings, was the reduction in NEC rates and the reduction of NEC cases requiring surgical intervention. The full financial impact of promoting breastfeeding and using human donor milk in the NICU may thus go much beyond the boundaries of the NICU

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Future Evidence

It is unlikely that future evidence for HMB will come exclusively from RCT of PDHM. Clinicians working in NICU's with access to donor milk have difficulty randomising high risk patients to artificial formulas where the risks are known, and where their own clinical experience suggests fewer complications when donor milk is used. Because these PTF are constantly changing, it could always be argued that to ensure scientific rigour, RCTs would need be repeated regularly to evaluate potential improvements.

We suggest that it time to accept the evidence of potential and reasonable clinical benefit of donor human milk for preterm and ill hospitalised infants. The evidence to date carries enough weight to encourage the establishment human milk banks where they are managed to an appropriate standard. We also propose that it is the responsibility of these donor human milk banks and the neonatal units to which they provide product, to engage in research to better assess potential benefits of donor human milk and improve the products provided by human milk banks.

Simmer, K., Hartmann, B. ***The knowns and unknowns of human milk banking.*** *Early Human Development. Volume 85, Issue 11, November 2009, Pages 701–704*.