



Benefits of donor human milk for preterm infants: Current evidence

Enrico Bertino*, Francesca Giuliani, Luciana Occhi, Alessandra Coscia, Paola Tonetto, Federica Marchino, Claudio Fabris

Cattedra di Neonatologia, Dipartimento di Scienze Pediatriche e dell'Adolescenza, Università di Torino, Italy

ARTICLE INFO

Keywords:
Human milk
Bank milk
Preterm infant

ABSTRACT

It's undoubted that optimum nutrition for term infants is breastfeeding, exclusive for the first six months, then followed by a complementary diet and carried on, if possible, for the first year of life or even more. During the last decades several data confirmed the great advantages of fresh mother's milk use also for feeding very low and extremely low birthweight preterm infants. When mother's milk is unavailable or in short supply, pasteurized donor breast milk is widely used in neonatal intensive care units. Pasteurization partially affects nutritional and immunological properties of breast milk, however it is known that pasteurized milk maintains some biological properties and clinical benefits. The substantial benefits of mother's own milk feeding of preterm infants are supported by strong evidence. However, there is increasing evidence also on specific benefits of donor breast milk. Future research is needed to compare formula vs. nutrient fortified donor breast milk, to compare formula and DM as supplements to maternal milk rather than as sole diet and to compare effects of different methods of heat treatments on donor human milk quality.

© 2009 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

It's undoubted that optimum nutrition for term infants is breastfeeding, exclusive for the first six months, then followed by a complementary diet and carried on, if possible, for the first year of life or even more [1]. During the last decades several data confirmed the great advantages of fresh mother's milk use also for feeding very low and extremely low birthweight preterm infants [2]. When mother's milk is unavailable or in short supply, pasteurized donor breast milk is widely used in neonatal intensive care units. Pasteurization partially affects nutritional and immunological properties of breast milk, however it is known that pasteurized milk maintains some biological properties and clinical benefits.

2. Biological aspects

Human milk is at present considered not only a food, but also a dynamic biological system. A special interest exists for human milk bioactive and immune factors, e.g. Ig, lactoferrin, lysozyme, oligosaccharides, nucleotides, growth factors, enzymes, antioxidant factors and cellular components that provide adequate host defence against infections and that actively modulate immune response and favour-

ably modify intestinal bacterial colonization [3–7]. A beneficial effect of maternal milk use on lymphocytic response of VLBW preterm infants has also been observed [8]. Pasteurization partially affects nutritional and immunological properties of breast milk [9]: Holder method is the most widely employed in human milk banks. This method inactivates immunological and anti-infectious factors; nevertheless, other key nutritional and biological compounds [10,11] are not affected by temperature, as shown by our recent studies on oligosaccharides.

Oligosaccharides play an emerging leading role among biological components of human milk, for their prebiotic, immunomodulatory and antimicrobial effects [12,13]. Human milk oligosaccharides have a proven prebiotic effect since they are resistant to digestion and reach the colon, where undigested oligosaccharides are metabolized by the microflora thus producing a “biomass effect” characterized by selective development of the bifidogenic flora [14]. Moreover, bacterial fermentation processes lead to the production of short-chain fatty acids that have a trophic effect on the intestinal mucosa [14]. Milk oligosaccharides can also compete with cell receptors in binding pathogenic agents. They are in fact adhesion ligand analogs, since their structure mimics the carbohydrate portion of glycoproteins and glycolipids of epithelial cell membranes, inhibiting binding of pathogenic microorganisms to the infants epithelial cell surface [15], thus preventing pathogens from developing their full pathogenic potential. Furthermore, breast milk oligosaccharides have an immunomodulatory effect, as long as they reduce the formation of selectin-initiated platelet–neutrophil complexes, leukocyte activation and transmigration [15].

* Corresponding author. Cattedra di Neonatologia, Dipartimento di Scienze Pediatriche e dell'Adolescenza dell'Università, di Torino, Piazza Polonia 94, 10126 Torino, Italy. Tel.: +39 0113135775; fax: +39 0113134882.

E-mail address: enrico.bertino@unito.it (E. Bertino).

In a recent study we evaluated the effects of Holder pasteurization on lactose concentration and on the pattern of 24 different oligosaccharides, quantitatively representing the big majority of those so far identified in human milk. Our study demonstrated that concentration and pattern of human milk oligosaccharides are not affected by Holder pasteurization [16]. In conclusion, as concerns oligosaccharides our study confirms the persistence of the biological value of human milk even after pasteurization.

3. Clinical aspects

3.1. Necrotizing enterocolitis

Two meta-analysis have shown a reduction in necrotizing enterocolitis incidence in preterm or low birthweight babies fed donor milk versus compared to those fed preterm formula [17,18].

3.2. Feed tolerance

Data about feeding tolerance in VLBWI and especially in ELBWI are based only on observational studies, mainly because of the impossibility to randomize to formula or human milk and the dishomogeneity of feeding tolerance definition in different studies [19]. No published study provides definitive data about the comparison, for what concerns feeding tolerance, among mother's milk, donor milk and pre-term formula [20–22,19].

3.3. Infections

Both the systematic review of De Silva et al. [23], and the subsequent national cohort study of Rønnestad et al. [24] do not provide conclusive information about specific effects of donor milk, mostly because infants are not exclusively fed donor milk. In 2005 Schanler et al. in a randomized blinded trial found that infants fed DM had similar rates of LOS and NEC, considered together, compared with infants fed preterm formula [25]. However, also this study does not reach definitive results, as long as some methodological flaws can be outlined [26].

3.4. Long term health benefits

It was observed in a meta-analysis by Martin et al. [27] a small reduction in diastolic blood pressure associated with breastfeeding in infancy. Among studies included in the meta-analysis there is also the one of Singhal et al. on preterm infants aged 13–16 years fed donor milk [28]. Singhal also observed a better lipoprotein profile in adolescents born preterm randomized to donor human milk versus formula [29]. The positive effect was associated with increased consumption of donor bank milk. If confirmed, these effects could have relevant benefits on cardiovascular health at a population level.

3.5. Bronchopulmonary dysplasia

In the already mentioned study by Schanler et al. "Some but significantly less chronic lung disease was observed in groups" fed maternal or donor milk. This observation suggests "antioxidant protection from MM, protection that may remain despite pasteurization. Although this study was not designed to evaluate these observations as primary outcomes, additional studies in this area are warranted, to determine whether presumed antioxidant protection is a short-term outcome of feeding human milk" [25].

4. Conclusion

The substantial benefits of mother's own milk feeding of preterm infants are supported by strong evidence. However, there is increasing

evidence also on specific benefits of donor breast milk. Future research is needed to compare formula vs. nutrient fortified donor breast milk, to compare formula and DM as supplements to maternal milk rather than as sole diet and to compare effects of different methods of heat treatments on donor human milk quality.

References

- [1] Dewey KG. Nutrition, growth and complementary feeding of the breastfed infant. *Pediatr Clin North Am* 2001;48:87–104.
- [2] Morales Y, Schanler RJ. Human milk and clinical outcomes in VLBW infants: how compelling is the evidence of benefit? *Semin Perinatol* 2007;31:83.
- [3] Rosetta L, Baldi A. On the role of breastfeeding in health promotion and the prevention of allergic diseases. *Adv Exp Med Biol* 2008;606:467–83.
- [4] López Alvarez MJ. Proteins in human milk. *Breastfeed Rev Mar* 2007;15(1):5–16.
- [5] Agostoni. *La Nutrizione del Neonato*. EDITEAM; 2006.
- [6] Field CJ. The immunological components of human milk and their effect on immune development in infants. *J Nutr* 2005;135(1):1–4.
- [7] Diehl-Jones WL, Askin DF. Nutritional modulation of neonatal outcomes. *AACN Clin Issues* 2004;15(1):83–96.
- [8] Tarcan A, Gurakan B, Tiker F, Ozbek N. Influence of feeding formula and breast milk fortifier on lymphocyte subsets in very low birth weight premature newborns. *Biol Neonate* 2004;86(1):22–8.
- [9] Wight NE. Donor human milk for preterm infants. *J Perinatol* 2001;21:249.
- [10] Henderson TR, Fay TN, Hamosh M. Effect of pasteurization on long chain polyunsaturated fatty acid levels and enzyme activities of human milk. *J Pediatr* 1998;132:876.
- [11] Van Zoeren-Grobben D, Schrijver J, Van Den Berg H, Berger HM. Human milk vitamin content after pasteurisation, storage, or tube feeding. *Arch Dis Child* 1987;62:161.
- [12] Kunz C, Rudloff S, Baier W, Klein N, Strobel S. Oligosaccharides in human milk: structural, functional, and metabolic aspects. *Annu Rev Nutr* 2000;20:699.
- [13] Kunz C, Rudloff S. Potential anti-inflammatory and anti-infectious effects of human milk oligosaccharides. *Adv Exp Med Biol* 2008;606:455–65.
- [14] Coppa GV, Bruni S, Morelli L, Soldi S, Gabrielli O. The first prebiotics in humans: human milk oligosaccharides. *J Clin Gastroenterol* 2004;38:S80–3.
- [15] Bode L. Recent advances on structure, metabolism, and function of human milk oligosaccharides. *J Nutr* 2006;136:2127.
- [16] Bertino E, Coppa GV, Giuliani F, Coscia A, Gabrielli O, Sabatino G, et al. Effects of Holder pasteurization on human milk oligosaccharides. *Int J Immunopathol Pharmacol* 2008;21(2).
- [17] Boyd CA, Quigley MA, Brocklehurst P. Donor breast milk versus infant formula for preterm infants: systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2007;92:F169.
- [18] Quigley MA, Henderson G, Anthony MY, Mc Guire W. Formula milk versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev* 2007;(4):CD002971.
- [19] Premji S, Chessell L. Continuous nasogastric milk feeding versus intermittent bolus milk feeding for premature infants less than 1500 grams. *The Cochrane library*; 2004.
- [20] McGuire W, Bombell S. Slow advancement of enteral feed volumes to prevent necrotizing enterocolitis in very low-birth-weight infants. *Cochrane Database Syst Rev* 2008;(2):CD001241.
- [21] Tyson JE, Kennedy KA. Trophic feedings for parenterally fed infants. *Cochrane Database Syst Rev* 2005(3).
- [22] Kennedy KA, Tyson JE, Chamnanvanikij S. Early versus delayed initiation of progressive enteral feedings for parenterally fed low birth weight or preterm infants. *Cochrane Database Syst Rev* 2008(2).
- [23] De Silva A, Jones PW, Spencer SA. Does human milk reduce infection rates in preterm infants? A systematic review. *Arch Dis Fetal Neonatal Ed* 2004;89:F509.
- [24] Rønnestad A, Abrahamsen TG, Medbø S, et al. Late-onset septicaemia in Norwegian national cohort of extremely premature infants receiving very early full human milk feeding. *Pediatrics* 2005;115:269.
- [25] Schanler Richard J, Lau Chantal, Hurst Nancy M, O'Brian Smith Elliot. Randomized trial of donor human milk versus preterm formula as substitutes for mothers' own milk in the feeding of extremely premature infants. *Pediatrics* 2005;116:400–6.
- [26] Bertino E, Giuliani F, Tonetto P, Fabris C, Profeti C, Magnani C, et al. Letter to the editor. *Pediatrics* 2006;117(3):985–6.
- [27] Martin RM, Gunnell D, Smith GD. Breastfeeding in infancy and blood pressure in later life: systematic review and meta-analysis. *Am J Epidemiol* 2005;161(1):15–26.
- [28] Singhal A, Cole TJ, Lucas A. Early nutrition in preterm infants and later blood pressure: two cohorts after randomised trials. *Lancet* 2001;357:413.
- [29] Singhal A, Cole TJ, Fewtrell M, Lucas A. Breastmilk feeding and lipoprotein profile in adolescents born preterm: follow-up of a prospective randomised study. *Lancet* 2004;363(9421):1571–8.