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Review

New perspectives in human milk banks

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Proceedings

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From the womb to the adult
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Abstract

Mother's own milk (MOM) is the first choice in preterm infant feeding, and when it is not available or is insufficient, donor human milk (DHM) is recommended. It has been shown that feeding preterm infants with human milk is less related to major morbidities, enhances feeding tolerance and prevents metabolic syndrome in childhood. As The Committee on Nutrition of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) states, specific guidelines for Human Milk Banks (HMB) are needed to guarantee the best possible compromise between microbiological safety and nutritional/biological quality of human milk (HM).

Currently, Holder pasteurization (HoP: pasteurization process at 62.5-63°C for 30 minutes) is recommended by all international guidelines: this method inactivates bacterial and viral pathogens but it also affects some nutritional and biological properties of human milk. New methods to ameliorate the biological quality and safety of DHM are under investigation in the last years. High Pressure Processing (HPP) is a non- thermal process used in food industries: this technology inactivates pathogenic microorganisms by applying hydrostatic high pressure, however further researches are required before applying this technology in milk banking.

Ultraviolet-C irradiation (UV-C) is another non-thermal method capable of reducing vegetative bacteria in human milk and it also seems to preserve higher levels of immunological proteins than HoP.

High-temperature short-time pasteurization (HTST: flash pasteurization, 72°C for 5-15 seconds) currently is available only at industrial level, but it

could represent an alternative to HoP seeming to maintain the protein profile and some of the key active components of DHM.

Further researches are needed to define the optimal treatment of DHM.

Keywords

Human milk, donor human milk, preterm infants feeding, human milk banking, Holder pasteurization, UV-C, HTST.

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Introduction

Growing evidence support the use of human milk (HM) for term and preterm infants as well as for sick infants in Neonatal Intensive Care Units (NICUs) [1-3]. Mother's own milk (MOM) is the first choice in preterm infant feeding. When mother's milk is not available or is insufficient, donor human milk (DHM) is recommended [1-5]. Some authors who applied Baby-Friendly Hospital Initiatives to NICUs has considered DHM as one of the supportive measures for the establishment of breastfeeding by [6, 7].

Benefits of feeding with donor human milk

Reduction in the incidence of necrotizing enterocolitis (NEC). The main benefit deriving from the use of DHM vs. formula in preterm infant feeding is the reduction of incidence of necrotizing enterocolitis (NEC) as well explained in some meta-analyses [8-10] and also in some observational studies [10-12].

Reduction in the incidence of sepsis and other infections. A systematic review [13] underlined the protective effect of HM against infections in preterm infants. However, the studies included in this review present a wide heterogenicity regarding the definition of the milk utilized and do not allow to discriminate the effects deriving specifically from the use of DHM. A large prospective study [14] as well, showed that fresh HM or DHM feeding reduced the risk of late onset sepsis in extremely low birth weight or extremely premature infants. These findings have been confirmed only for fresh MOM in a later study [15]. Further studies evaluating specifically the anti-infective effects of DHM are needed.

Reduction in the incidence of bronchopulmonary dysplasia. It has been shown that DHM feeding significantly reduces the incidence of bronchopulmonary dysplasia in neonates born at a gestational age below 30 weeks [5, 15]. This observation shows an antioxidant activity of HM, which is likely to be maintained also after pasteurization.

Enhancement of feeding tolerance. It has been demonstrated that early initiation of enteral feeding with MOM or DHM even within the first hours of life is well tolerated [16]. In the 1980s few experimental studies observed a lower incidence of feeding intolerance and an earlier establishment of full enteral feeding in preterm infants fed with DHM compared to formula [9].

Prevention of hypertension, insulin resistance, and atherogenic lipoprotein profile. Several studies conducted in large cohorts suggest that adolescents born preterm and fed with human milk present lower risk of metabolic syndrome and lower cardiovascular risk [1-2, 17].

Promotion of breastfeeding in NICU: a recent national survey in Italy observed a positive effects of the availability of DHM on breastfeeding rate of very low birth weight (VLBW) infants at discharge [18], confirming the existing data from Australia [19], USA [20], and Spain [21] which already indicate that the presence of a HMB does not decrease the breastfeeding rate of VLBW infants, but instead, it is supportive for breastfeeding promotion.

Human milk banks

The recent commentary of The Committee on Nutrition of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) states that "DHM should be obtained from established Human Milk Banks (HMBs)

that follow specific guidelines for screening, storage, and handling procedures to optimize its composition while ensuring its safety for the recipient" [5].

Milk handling and processing should always follow the principles of Hazard Analysis and Critical Control Points (HACCP) and should represent the best possible compromise between safety and nutritional/biological quality of the product.

Many countries now have their own HMBs guidelines [23-27].

Donor human milk treatment in human milk banks

Milk delivered to the HMBs should be pasteurized to inactivate viral and bacterial agents [5]. The ideal pasteurization process should consist of a phase of rapid heating, followed by a phase in which the temperature is maintained constant, and a final phase of rapid cooling.

Currently, a pasteurization process at 62.5-63°C for 30 minutes (i.e. the Holder pasteurization [HoP]) is recommended by all international guidelines for constitution of HMBs [27] (level of evidence A: at least two good quality coherent studies, where bias or confounding factors are not present). Pasteurized milk is known to retain many beneficial and protective effects of HM. This method allows a good compromise between microbiological safety and nutritional/biological quality of DHM [2, 4-5, 27]. In fact, it destroys pathogens in milk, including *M. tuberculosis*, and *B. cereus*, as well as some viruses (HIV, HTVL 1-2, Cytomegalovirus, Herpes Simplex and Rubella) [25, 33-39]. But it is also well known that HoP affects some of the nutritional and biological properties of human milk. Several studies have been performed to investigate the effects of Holder pasteurization on these properties of HM and a significant variability in the data is reported in the scientific literature. A possible explanation for the different results may be the heterogeneity of the test protocols applied in the studies (e.g. in terms of sample origin, storage conditions or methods of analysis). Another important source of variability is represented by the fact that often HoP of DHM is simulated on small aliquots, rather than being performed following HMB-implemented protocols. Moreover, modern pasteurizers required significantly less time for heating and cooling than older ones, thus changing the kinetics of the thermal response for many heat-sensible compounds. Additionally, it appears that some biochemical patterns were investigated more extensively than others, while some other milk components were not considered at all.

The available data confirm that the HoP affects several components of HM (such as immunoglobulins, specific enzymatic activities, vitamins, growth factors and cytokines), even if it is rather difficult to quantify the degradation degree [2, 5].

Furthermore, HoP maintains the bactericidal activity of the milk against *E. coli* better than high temperature short term pasteurization (HTST) [53]. Moreover, although HoP decreases IgA concentration, the remaining molecules effectively inhibit bacterial adhesion (enteropathogenic *E. coli*) [54]. Nonetheless, clinical practice demonstrates that many beneficial properties of HM remains even after pasteurization.

The optimal treatment of DHM should aim to maintain microbiological safety while preserving the highest amount and activity of the milk bioactive components. New methods to improve the biological quality and safety of DHM are under investigation.

High Pressure Processing (HPP) has recently received attention as a novel food preservation method. This non thermal process is an emerging food processing method that can be applied to liquid foods to provide microbiologically safe, nutritionally intact and organoleptically high quality products. This technology inactivates pathogenic microorganisms by applying hydrostatic high pressure (usually 400-800 MPa) to food for short-term treatments (less than 5-10 min). However, further researches are required before applying this technology in milk banking [40-41].

Ultraviolet-C irradiation (UV-C), classified as a non thermal method, seems to be capable of reducing vegetative bacteria in HM as required in HMBs guidelines with no loss of bile salt stimulated lipase (BSSL) and alkaline phosphatase (ALP) activity and no change of fatty acids (FA) [42]. This method also seems to preserve significantly higher levels of immunological proteins than HoP, resulting in bacteriostatic properties similar to those of untreated HM [43].

HTST (flash pasteurization, 72°C for 5-15 seconds) is a pasteurization method in use in the food industries and this thermal treatment has been suggested as an alternative to the HoP.

HTST seems to better retain the protein profile and some of the key active components of DHM (bile salt-stimulated lipase, lactoferrin, IgA, IGFs) if compared to HoP [44-57]. However, this method requires technological investment (a thin layer of milk between two heated metallic walls) and currently is available only at industrial level.

A new high-tech method of flash pasteurization for low quantity of HM has been recently patented by our group and is, at present, ongoing validation.

Declaration of interest

The Authors declare that there is no conflict of interest.

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