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## **Optimization of the human milk composition intended for the prematurely born infant**

### **Abstract**

**Introduction:** Natural feeding of preterm infants can be challenging for members of therapeutic teams due to the high demand for nutrients and limited volume of enteral feeding. The composition of breastmilk is highly diverse, and mothers of preterm infants will have higher concentration of certain nutrients in their milk. In the case of children weighing less than 1500 grams and/or born before the end of the 32nd week of pregnancy, the nutritional value may not reach the recommended levels, and human milk may require adequate supplementation. Best results are achieved through the use of individualized fortification strategies as target fortification based on analysis of mother's milk. For maximum clinical benefits, when a mother's own milk is unavailable, the use of milk from the human milk bank (HMB) should be the first alternative. Its nutritional value is closely related to the profile of recruited donors, breastmilk donated in HMBs is usually mature milk, whose nutrient content is much lower than the mother's own milk. Furthermore, the composition of milk from HMBs is changed due to the processes to which it is subject before it reaches the recipient. These include holder pasteurization (HoP), which ensures microbiological purity, but at the same time reduces nutritional quality and significantly decreases the content of bioactive components.

**The aim of the study:** The aim of the study was to evaluate and develop the methods for optimizing the composition of human milk intended for infants born prematurely.

**Material and methods:** Material and methods: This dissertation consists of a series of three original papers, including an evaluation of the implemented procedures for analyzing the composition of breastmilk (paper 1), an retrospective study analyzing the first year of human milk operation in one of the institutions in Poland (paper 2) and an experimental study on the impact of a new preservation method with the use of high-pressure processing

(HPP) on the concentration of bioactive components of human milk (paper 3). Evaluation of the human milk analysis procedures was carried out on the basis of breastmilk composition measurements of preterm infants mother's milk (<37 weeks of pregnancy, n = 70). The analyses were performed with the human milk analyzer (MIRIS HMA, Uppsala, Sweden). It was accompanied by statistical analysis of the averaged measurements and the correlations between three replications of each measurement. In order to evaluate the operation of the human milk bank, data on honorary donors (n = 45) and recipients (n = 154) were obtained from the hospital and HMB's documentation. Paper 3 compares the effect of standard pasteurisation (HoP), which is routinely used in HMBs in Poland and around the world, and 4 variants of high-pressure processing (HPP) on the content of selected bioactive components, with the hormones of leptin, adiponectin, insulin and immunological factors of HGF (hepatocyte growth factor), lactoferrin and IgG (immunoglobulin G) selected as markers. The research was conducted as part of the project "Lactotechnology as a response to the special nutritional needs of prematurely born children" (pol. Laktotechnologia jako odpowiedź na specjalne potrzeby żywieniowe dzieci urodzonych przedwcześnie), carried out under the grant of the National Center for Research and Development (IS/2/81/NCBR/2015) by the consortium: Human Milk Bank Foundation, Warsaw University of Life Sciences, Medical University of Warsaw and the Institute of High Pressure Physics Unipress.

**Results:** In the study verifying the procedures for human milk analysis for the purpose of target fortification (paper 1), correlations between three independent measurements of total and crude protein, fat, total solids and energy reached from 0.876 to 0.987, correlations between measurements of carbohydrates ranged from 0.620 to 0.726. The average protein and fat content in milk from HMB were lower than in the mothers own milk (crude protein  $0.7 \pm 0.2$  vs  $1.2 \pm 0.3$ , fat  $3.1 \pm 0.8$  vs  $3.9 \pm 0.8$ ), and the carbohydrate content was higher ( $7.3 \pm 0.3$  vs  $6.9 \pm 0.3$ ). Donors (n = 45) were recruited between the first and forty-fourth week of lactation (mean the fourteenth week). The period of cooperation ranged from 2 to 26 weeks, the volume of milk collected during this period ranged from 650 to 32030 ml. 11 of the donors (24.4%) were mothers of preterm infants, while 91.5% of recipients were born prematurely. In the experimental study on human milk preservation with the use of high-pressure processing, the effects of HoP and HPP were compared in four variants: 1) 600 MPa, 10 min 2) 100 MPa, 10 min, interval 10 min., 600 MPa, 10 min 3) 200

MPa, 10 min, interval 10 min., 400 MPa, 10 min 4) 200 MPa, 10 min., interval 10 min., 600 MPa, 10 min (paper 3). In the milk subjected to HoP, the leptin concentration was 77.86%, adiponectin 32.79%, insulin 32.40%, HGF 88.72%, lactoferrin 60.31%, IgG 49.04%. All HPP variants increased leptin concentration by 47.96-90.01%. HPP allowed to maintain 81.98%-94.76% of insulin concentration; 36.15% - 97.15% of HGF and 55.78% -78.77% of lactoferrin. Only the third variant - 200 MPa, 10 minutes, 10 minutes break, 400 MPa - allowed to maintain higher concentration of IgG (82.24%) than HoP. All HPP variants decreased adiponectin concentration. However, in the variant of 200 MPa, 10 minutes, 10 minutes break, 400 MPa, the difference was not statistically significant.

**Conclusions:** Mother's own milk usually contains a greater amount of protein than milk from a human milk bank, however, regardless of the source, the composition of breastmilk is highly diverse (paper 1, paper 2). When deciding on fortification, this variability should be taken into account. For this purpose, targeted fortification on the basis of human milk analysis may be applied, but it must be carried out in accordance with the principles of good laboratory practice (paper 1). If the milk from an HMB is used, the profile of registered donors is essential for the composition. Recruiting mothers of preterm infants as donors and starting cooperation in the early lactation phase, immediately after stabilization, may increase the nutritional value of HMB milk (paper 2). Better retention of the donor human milk bioactive factors is possible due to the use of high-pressure processing (HPP) instead of the commonly used holder pasteurization (HoP). Implementation of this method will allow for further optimization of the human milk composition intended for a prematurely born infant (paper 3).