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Randomized Controlled Trial

Impact of homogenization of pasteurized human milk on gastric digestion in the preterm infant: A randomized controlled trial

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SUMMARY

Background & aims: It has been suggested that homogenization of Holder-pasteurized human milk (PHM) could improve fat absorption and weight gain in preterm infants, but the impact on the PHM digestive kinetics has never been studied. Our objective was to determine the impact of PHM homogenization on gastric digestion in preterm infants.
Methods: In a randomized controlled trial, eight hospitalized tube-fed preterm infants were their own control to compare the gastric digestion of PHM and of homogenized PHM (PHHM). PHM was obtained from donors and, for half of it, was homogenized by ultrasonication. Over a six-day sequence, gastric aspirates were collected twice a day, before and 35, 60 or 90 min after the start of PHM or PHHM ingestion. The impact of homogenization on PHM digestive kinetics and disintegration was tested using a general linear mixed model. Results were expressed as means ± SD.
Results: Homogenization leaded to a six-fold increase in the specific surface ($P < 0.01$) of lipid droplets. The types of aggregates formed during digestion were different between PHM and PHHM, but the lipid fraction kept its initial structure all over the gastric digestion (native globules in PHM *vs.* blend of droplets in PHHM). Homogenization increased the gastric lipolysis level ($P < 0.01$), particularly at 35 and 60 min (22 and 24% higher for PHHM, respectively). Homogenization enhanced the proteolysis of serum albumin ($P < 0.05$) and reduced the meal emptying rate ($P < 0.001$, half-time estimated at 30 min for PHM and 38 min for PHHM). The postprandial gastric pH was not affected (4.7 ± 0.9 at 90 min).
Conclusions: Homogenization of PHM increased the gastric lipolysis level. This could be a potential strategy to improve fat absorption, and thus growth and development in infants fed with PHM; however, its gastrointestinal tolerance needs to be investigated further.
This trial was registered at clinicaltrials.gov as NCT02112331.

1. Introduction

Progress in neonatal care over the last decades, including the establishment of human milk banks (HMB), has reduced morbidity and improved the survival of vulnerable and high-risk infants, such as preterm and very low birth weight (VLBW) neonates. Ensuring adequate postnatal growth is crucial for better nutritional and clinical outcomes of preterm neonates [1], mainly avoiding impaired neurological development and reducing the risk of

Abbreviations: BSSL, bile-salt stimulated lipase; CLSM, confocal laser scanning microscopy; FA, fatty acid; HMB, human milk bank; MFG, milk fat globule; PHM, pasteurized human milk; PHHM, pasteurized and homogenized human milk; VLBW, very low birth weight.

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adverse metabolic consequences [2,3]. However, an important part of these infants still experiences postnatal growth restrictions [4].

Human milk given either fresh (from the own mother) or pasteurized (mainly from donors) offers several benefits and better outcomes than infant formulas [5–7]. However, achieving the high requirement in proteins, energy and micronutrients for preterm newborns remains a challenge. Firstly, most of the donors of banked-human milk delivers at term and are at advanced stage of lactation, which usually does not correspond to the specific requirements of preterm newborns [8,9]. Secondly, steps following expression (*e.g.* freeze-thaw cycles and Holder pasteurization) affect both the milk structure and its nutritional quality [10–12]. Finally, nutrient losses can occur by adherence during tube feeding [13]. In this context, fortification of human milk is considered as a strategy to ensure adequate postnatal growth rate [7], although this practice remains a source of debate [14–17].

Some authors have suggested the homogenization of banked-PHM as a strategy for improving fat absorption [20] and weight gain [21] in preterm infants fed with PHM. Homogenization fragments the native milk fat globule (MFG, mean diameter of 4 μm) in smaller and uniformly distributed lipid droplets (from 0.1 to 1 μm), and leads to an increase in the surface available for digestive enzymes adsorption [22]. This structural modification could increase the digestibility of milk fat and compensate for the heat-inactivation of BSSL [23]. Additionally, it could minimize the nutrients losses during tube feeding [21,24]. However, the impact of homogenization of PHM on its digestive kinetics has never been studied.

In this context, our objective was to investigate the impact of homogenization of PHM from donors on its *in vivo* gastric digestion in preterm infants. More specifically, we studied the gastric functions, the kinetics of lipolysis, the proteolysis and the structural disintegration of pasteurized or pasteurized and homogenized human milk.

2. Materials and methods

2.1. Study design and participants

This study was a randomized controlled trial (NCT02112331) conducted from April 2014 to August 2015 at the pediatric department of the University Hospital Center of Rennes, France, after approval by the Institutional Review Board of University Hospital Center of Nantes (CPP Ouest IV), France.

Fig. 1 shows the flow diagram of the infants included, as well as the criteria for eligibility and inclusion in the study. Briefly, eligible infants were hospitalized preterm newborns born before 32 weeks of gestation at the Hospital Center of Rennes, fed by a nasogastric tube and their mothers had no intention or no possibility to breastfeed during the hospital stay; infants were then assessed for eligibility within 72 h from birth, after their parents received oral and written information by the pediatricians, and gave informed written consent. Once an infant reached an enteral feeding of at least 120 mL/kg/d at 3 h intervals, a medical visit was performed to assess the infant for inclusion in the study. Exclusion criteria were: 1) any significant digestive disease or malformation, including a previous history of necrotizing enterocolitis, 2) abdominal bloating with abdominal tension during experimental protocol, 3) treatment with catecholamine or morphine during experimental protocol, 4) sampling failure (volume < 4 mL) on two samples taken at the same postprandial time point (except 90 min) and for the same type of milk.

Each infant was his or her own control in the comparison of the gastric digestion of PHM and PHHM. A power analysis study showed that a sample size of 12 infants was needed to detect a clinically significant difference in the gastric lipolysis degree between PHM and PHHM, with 80% power at the significance level of 0.05. The study of Armand et al. [25] in preterm infants served as a basis for the power analysis. These authors detected ~40% of reduction in the lipolysis level after ingestion of an infant formula, which is a homogenized emulsion, compared to raw human milk. At the end of the inclusion time (two years), eight infants had completed the six days of follow-up.

2.2. Test meals

Anonymous donors collected their milk following the recommendations of the HMB, froze (−18 °C) at most within 24 h and then transferred to the HMB in cooled boxes within less than 1 h. Milk samples from the same mother were thawed in a 4 °C temperature-controlled room over a period not exceeding 24 h, pooled and divided into bottles of 60–75 mL. All the bottles

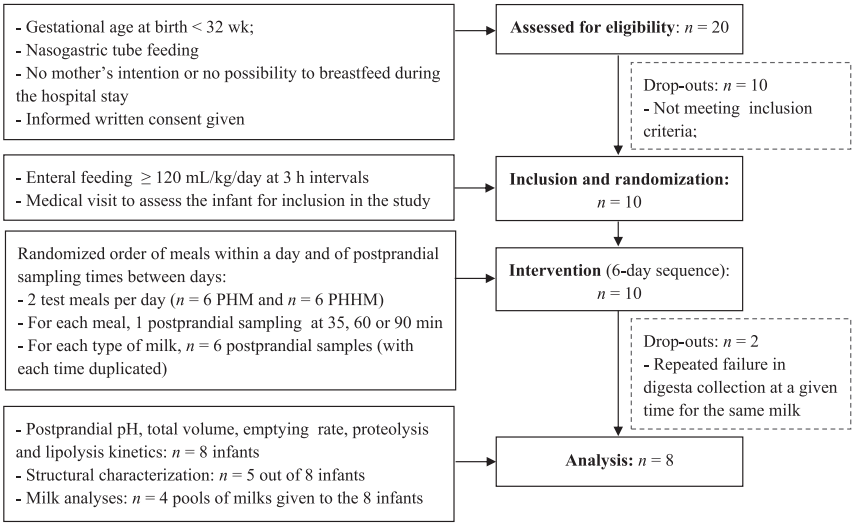

Fig. 1. Flow diagram of infants included in the study. The number of samples potentially collected per modality is indicated. Only one group was formed: each infant was his or her own control to compare the gastric digestion of pasteurized and pasteurized-homogenized human milk (PHM and PHHM).