מרץ, 2019

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Research Number: 3-15657
Title: The role of oligosaccharides in preterm and term human breast milk in the inhibition of experimental necrotizing enterocolitis in neonatal mice model
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Year (Start): 2020 Year (End): 2021 (extended one year due to Covid-19)

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Abstract

Background: Necrotizing enterocolitis (NEC) is a leading cause of mortality in preterm infants, occurring more often in formula-fed than breastfed infants. Studies show that human milk oligosaccharides (HMOs) lower the incidence of NEC and affect immune function. Maternal HMO composition varies depending on the time of lactation, the mother's genetic makeup and potential environmental exposures. It is not feasible to replicate HMO's complete profile by synthetic methods.

Research Hypothesis

We hypothesize that oligosaccharides from HBM regulate barrier function in NEC models in mice.

Aims

This work aims to evaluate the effect of oligosaccharides from HBM in NEC models on gut barrier function. Additionally, for the first time, we aim to investigate the HMO profile and maternal characteristics of Israeli women.

Methods: Pooled HBM were collected, and OS were extracted and isolated from fat, proteins, salts, lactose, and endotoxins, followed using FPLC. Chemical analysis was conducted by Negative ESI LC-MS chromatograms to profile the OS. The OS was supplemented in a neonatal mice diet, and the impact of HMOs was investigated. To this end model for hand feeding and rearing neonatal mice pups were developed. Six-day-old C57BL/6 mouse pups were fed with Esbilac formula 2-4 times a day and were separated from their mothers for increasing time intervals. Pups were subjected to hypoxia twice daily, followed by cold stress. Mother reared pups served as controls. Pups were maintained for 72 hours and sacrificed after the treatments followed by dextran administration; intestines and plasma were removed for experiments. The successful induction of NEC was confirmed by histopathology. Changes in tight junction proteins in NEC intestines were studied by western blotting and Alcian Blue - PAS staining

Results

64.28% of the mothers were secretors. Most HMO concentrations were lower in milk collected later in lactation, except for LNT. Independent of Secretor status and lactation stage, infant sex variation was observed for 2'FL. Our in vivo study results demonstrate that we induced NEC in experimental pups that did not gain weight, and their intestines showed gross changes and microscopic changes associated with NEC. There was increased permeability of the gut with disruption of tight junction occludin protein and loss of goblet cells number and secretions in the ileum. The effect of HMO was notorious.

Discussion

NEC leads to the epithelial barrier breakdown due to increased leakiness of the gut and changes in tight junction occludin with disruption in goblet cells. Understanding the importance of OS from humans on NEC prevention can be crucial in planning the preterm infant diet to reduce mortality rate and known complications.

Key words: (up to 5) NEC, HMO, Tight junctions, permeability

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Publications associated with the project (PubMed Format):

No publications jet. All are in preparation