

## Human milk benefits for preterm infants in the NICU

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One of the main issues with preterm infant nutrition is the analysis of the concerns and benefits of human milk (HM) compared to preterm formula (PF). This issue requires a scientific and not preconceived approach that weighs the benefits and concerns of the different choices.

The main concern with feeding preterm infants with human milk is the slower growth, well demonstrated both during the hospital stay and at later follow up <sup>1</sup>. This slower growth is due to several causes:

- 1) The nutritional content of HM is lower than the nutrient content of formula and often remains lower also after the addition of standard fortification <sup>2</sup>.
- 2) The actual intake is often lower than the theoretical, previously planned, intake, because of frequent and sometimes inappropriate reduction of the daily intake due to some feeding intolerance signs such as gastric residuals, abdominal distension, etc.
- 3) The native nutritional contents of raw milk decreases during the sequential milk manipulations such as freezing, thawing, pasteurization and tube administration.

For example, regarding fat, a 45 % pre-exposure loss is calculated, mainly due to the continuous feeding administration <sup>3</sup>. During continuous feeding the milk fat tends to accumulate in the administration kit. We recently calculated the in-vitro fatty acids intake in three different conditions compared to baseline:

1. Bolus feeding
2. Continuous feeding
3. Continuous feeding with a 45° tilt

We found that continuous feeding strongly impairs fat intake. Particularly relevant is the LCPUFA reduction because of their involvement in central nervous system and retinal structure and function. The use of bolus feeding can significantly reduce this loss. A certain advantage may be also obtained by the 45° tilting of the nutrition pump.

Other nutritional interventions can be planned with the aim to minimize this growth problem:

If the patient fails to gain weight an individualized fortification protocol may be adopted. An additional amount of multicomponent or protein fortifier can be added to milk. This additional amount may be defined by directly measuring the raw milk nutritional contents by means of an infrared analysis (Targeted Fortification) or evaluating the metabolic individual response of the neonate by the BUN (Adjustable Fortification) <sup>4</sup>.

Regarding the benefits of HM we can include: Neurodevelopment, decreased Retinopathy of Prematurity (ROP), decreased Bronchopulmonary Dysplasia (BPD) and Necrotizing Enterocolitis (NEC).

Regarding neurodevelopment: Some follow-up studies conducted in France showed slower growth in HM fed preterm infants but better neurodevelopment at 2 and 5 years of age <sup>1</sup>. A large English study showed a significant improvement in neurodevelopmental scores related to the duration of human milk usage <sup>5</sup>. Furthermore, five out of seven recently reviewed studies that aimed at assessing a correlation between HM and neurodevelopment confirmed neurodevelopmental improvements <sup>6</sup>. Our group recently assessed this issue in a follow up study. Our results also demonstrated that feeding HM during the hospital stay significantly improved the general quotient score at 24 months of age <sup>7</sup>.

Regarding ROP, a recent meta-analysis demonstrated a significant reduction of retinopathy of prematurity with HM use <sup>8</sup>. Recent evidence has provided similar results for a reduction in BPD <sup>9</sup>.

With regard to NEC several studies showed a significant reduction of NEC in HM fed preterm infants <sup>10</sup>.

The pathogenesis of NEC is multifactorial and the reduction may be attributed to several factors such as:

1. Early enteral nutrition initiation without wasting time waiting for the own mother's milk
2. Avoidance of early exposure to cow milk proteins
3. Bioactive compounds

The early introduction of nutrition counteracts the effect of fasting and parenteral nutrition on the gut. Furthermore, the prolonged enteral nutrition deprivation leads to increased inflammatory status, loss of mucosal integrity, possible bacterial translocation<sup>11</sup>. The theoretical promoting effect of cow milk protein on NEC could be due to:

1. Demonstrated increase of gut permeability because of a reduction of the mucosal integrity
2. An up-regulatory effect on gut inflammation
3. And a dysbiotic colonization

Lastly, the list of bioactive components potentially affecting the NEC pathogenesis is growing every day. However, many of these compounds are partially destroyed during Holder pasteurization, which raises concerns about the protective qualities of the pasteurized human milk. Although, in a recent review an effect similar to the Mother's Own Milk (MOM) on NEC was demonstrated for Donor Human Milk, when compared with formula feeding<sup>12</sup>.

In conclusion:

- The slower growth in HM vs formula milk fed infants could be minimized with optimal fortification and optimization of enteral feeding protocols
- The benefits of human milk feeding in NICU clearly outweigh the concerns for growth
- Fortified fresh Mother's Own Milk is the gold standard for preterm infant nutrition with Donor Human Milk being the second choice in preference to Preterm Formula

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