Got Milk? Optimizing Nutrition of Human Milk for Premature Infants
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Abbott Nutrition – Speakers Bureau

It is my obligation to disclose to you that I am on the Speakers Bureau for Abbott Nutrition. However, I acknowledge that today’s activity is certified for CME credit and thus cannot be promotional. I will give a balanced presentation using the best available evidence to support my conclusions and recommendations.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

Objectives
• Review the nutritional goals for premature infants.
• List the macronutrient requirements for premature infants.
• Describe the unique nutritional challenges of premature infants.
• Describe the need for fortification of human milk to meet the nutritional goals of premature infants.
• Identify key differences between human milk fortifiers.

Human Milk is Preferred Feeding for All Infants
• American Academy of Pediatrics support feeding of human milk for all infants, term and preterm
• And….
• Human milk is nutritionally insufficient to fully support the growth needs of very low birth weight and extremely low birth weight infants

Human Milk and Prematurity
• Over 63,000 very preterm (<32 weeks) infants born in US
• At risk for undernutrition during long NICU stay
• Critical time for organ development
• Short- and long- term benefits of HM for preterm infants
• Addition of fortifiers to HM is standard practice
• Fortifiers designed to meet recommended nutrient goals when added to milk with average nutrient values at typical volumes
• Several products and strategies are available to fortify HM

Human Milk and Prematurity
Benefits of HM in Premature Infants
Preterm Infant Nutrition and Growth Goals
Human Milk and Prematurity

- NICU growth outcomes have improved in recent years
- Fortified HM-fed infants have shown slower weight gain and head growth compared to preterm formula-fed infants
- Current fortification strategies may not meet nutritional requirements for all infants
- Increase in use of maternal and donor human milk
- Macronutrient content of HM highly variable

Human Milk Benefits for Preterm

- Protection against Necrotizing Enterocolitis
- Protection against Late Onset Sepsis
- Priming of the immature gut
- Protection against Severe Retinopathy of Prematurity
- Protection against Bronchopulmonary Dysplasia
- Improvement of long-term Retinopathy of Prematurity
- Improvement of Cardiovascular Health

Preterm Nutrition and Growth Goals

- Meet goals of in utero growth of normal fetus of same post-conceptional age
  - Body weight and length
  - Body composition
  - Organ development and maturity
  - Catch up growth for deficiencies

Preterm Nutrition and Growth Goals

- Achieving adequate/optimal growth in preterm infants
- Extremely relevant for long-term neurodevelopment
- Reducing extrauterine growth restriction (EUGR)
- Goal not to lose more than 1 standard deviation in weight and HC from birth to discharge
- Growth: only weight gain, don't forget length and HC

Preterm Nutritional Requirements

- Energy
- Protein
- Fat
- Carbohydrates
- Oligosaccharides

Preterm Nutritional Requirements

| Requirement for protein and energy, based on factorial and empirical methods (g/l)
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, g</td>
</tr>
<tr>
<td>Protein, g/l</td>
</tr>
<tr>
<td>Energy, kcal/l</td>
</tr>
<tr>
<td>Protein energy, g/l ( additions)</td>
</tr>
</tbody>
</table>
Preterm Nutritional Requirements

| Nutrient   | Requirements for Major Micro and Macro Nutrients Determined by Faecal Method, Laid to body weight |
|------------|-------------------------------------------------------------------------------------------------|---|
| Energy (kcal/kg) | 105-110 | 110-120 | 115-117 | 119-127 | 121-123 |
| Protein (g/kg) | 2.0-2.1 | 2.0-2.1 | 2.0-2.1 | 2.0-2.1 | 2.0-2.1 |
| Lipids (g/kg) | 4.0-4.5 | 4.5-5.0 | 5.0-5.5 | 5.5-6.0 | 6.0-6.5 |
| Carbohydrates (g/kg) | 3.0-3.5 | 3.5-4.0 | 4.0-4.5 | 4.5-5.0 | 5.0-5.5 |

Human Milk: Known vs Unknown

Table 2

Table 3

Macronutrient Intake from HM Varies

- Longitudinal study
- 37 infants <32 weeks gestation
- Analyzed 1626 HM samples
- Study aims:
  - Determine between-infant variation in macronutrient intake from HM
  - Examine associations of macronutrient intake with growth outcomes
Macronutrient Intake from HM Varies

• Greater intakes of fat and energy associated with higher weight
• Greater protein intake associated with greater body length
• Higher fat intake associated with higher fat mass and fat-free mass
• Macronutrient intakes from HM highly variable and associated with growth outcomes despite routine fortification

Sources of Human Milk

Mother’s Milk
Donor Milk

Sources of Human Milk

• Mother’s milk
• Donor milk
• **NOT** the internet

Breastmilk Black Market

• Discourage families from direct HM sharing/purchasing online
• Increased risks of bacterial or viral contamination
• Exposure to medications, drugs, other substances
• No guarantee it was stored properly
• Cow’s milk Contamination

Donor Human Milk

• Prioritization for preterm infants <1500 g
• Ideally a temporary bridge to obtaining mother’s milk
• Does not compete with mother’s own milk
• Growth outcomes:
  • Lower protein content
  • Lower energy content
  • Loss of bile salt-dependent lipase activity
• Pasteurization:
  • Loss of nutrients
  • Anti-inflammatory factors
  • Can eliminate bacterial strains with probiotic properties
  • Bioactive components substantially decreased
  • Much less effect on macro- and micro- nutrients

Donor Human Milk

• Donor HM should be obtained from a well-established milk bank
• HMB must follow specific safety guidelines
• Collection, treatment, distribution of DHM processes
• Need universal quality principles for all HMB
• DHM currently requires pasteurization, freezing, thawing
• Currently recommend Holder pasteurization for DHM
• New methods of DHM treatment are under investigation
Promotion of Breast Feeding in the NICU

• Begin milk expression as soon after delivery as possible
• Use colostrum for oral cares
• Encourage kangaroo care
• Strategies to promote and support breast-feeding for preterm infants in every maternity or children’s hospital
• Hospital-based lactation programs
• Fresh mother’s own milk is first choice
• Ensure processes in place for safe centralized handling of HM

Fortification of Human Milk

Multi-nutrient Fortifiers

• Most multi-nutrient fortifiers contain bovine milk protein
• Donkey milk recently proposed as composition similar to HM
• HM based fortifier

Human Milk Fortifiers

• Formula
• Human Milk Fortifier
  • Powder vs Liquid
  • Sterilization: heat vs acidification
  • Human vs Bovine vs Donkey?
• Supplements
  • Protein
  • Lipids
  • Carbohydrates

Multi-Nutrient Fortifiers

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Powder</th>
<th>Donkey</th>
<th>HM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>10.5</td>
<td>10.2</td>
<td>10.0</td>
</tr>
<tr>
<td>Lipids</td>
<td>4.5</td>
<td>4.3</td>
<td>4.0</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>20.5</td>
<td>20.3</td>
<td>20.0</td>
</tr>
</tbody>
</table>

Table 4: Nutrient composition of selected fortifiers and ingredients.

Single-Nutrient Supplements

• Protein
  • Many protein supplements not specifically designed for neonates
  • +/- Partially or extensively hydrolyzed protein
  • New products designed for preterm infants
  • No consensus on how to use these products

• Lipids
  • Medium chain triglycerides
  • HM derived cream supplement

• Carbohydrates
  • Dextrin maltose
Fortification Strategies

• Standard Fortification
• Individualized Fortification
• Adjustable Fortification
• Targeted Fortification

Conclusions/Comments EBMA

• HM is first choice in preterm feeding
• Unfortified HM insufficient amount of nutrients when fed at usual feeding volumes
• To prevent EUGR, poor neurocognitive outcome and specific nutrient deficiencies, need fortification of HM
• Despite standard fortification, many VLBW infants continue to have suboptimal growth
• Targeted fortification needs to be improved
• HM-based fortification seems promising, still concerns on efficacy, safety, ethical issues
• No strong evidence to support use of hydrolyzed protein source

Recommendations EBMA

• HM feeding is basic right for preterm infants
• Mother’s own milk is first choice in preterm infant feeding
• When mother’s milk unavailable, donor HM is best alternative
• HM fortification recommended for preterm with BW <1800g
• HM fortification can be started when feeds 50-80 ml/kg/day
• Optimization of HM fortification is required
Conclusions/Comments JPGN

• All preterm infants <1800 grams should be fed fortified HM
• HM should be fortified with protein, vitamins and minerals
• Quantity of HM fortification should optimize growth in NICU stay
• HM fortification should start with standard fortification
• If infants do not grow appropriately, advise individualized fortification
  • Targeted fortification (based on milk analysis)
  • Adjustable fortification (based on BUN measurements)
  • Both advisable depending on the NICU experience and facilities

Future Research

• Address nutritional management in specific preterm groups
• Randomized controlled trials assessing efficacy/safety of HM fortification
  • After discharge
  • Adjusted vs targeted
• Defining reasonable and replicable study endpoints in large cohorts
  • Neurocognitive outcomes
  • Body composition
• Optimization of quality of fortifiers

Nutrition at Discharge

• No consensus about post discharge nutrition
• Nutritional supplementation for premature infants should be continued for 3-6 months to optimize growth and development
• Studies that evaluated post discharge HM fortification showed no deleterious effect on breastfeeding rates
  • Suggested some advantages

Changes You May Wish to Make in Practice

CPQCC Potentially Better Practices

PBP #15: Start Fortification Before Full Feeds are Reached

• Early fortification of HM minimizes nutrition gap
• Best to follow standardized local guidelines
• No clear evidence when it is safe to introduce fortification
• Protocols have increasing used earlier fortification steps without intestinal complications
• Increase in osmolality with addition of fortifiers does not exceed significant levels of risk that were associated with NEC
• Powdered fortifiers no longer recommended in NICU

PBP #16: Enteral Feeds Should be Advanced and Concentrated Until Providing Adequate Nutrition to Sustain Optimal Growth

• Provide optimal nutrition/growth, replace need for TPN
• Advance volume to deliver more nutrients 150-200 ml/kg/d +/-
• May need fortification beyond 24 kcal/oz
  • Not well evaluated, but common practice
• Proactive rather than reactive approach
• Adjust feedings based on daily weights
• Customized fortification may be required
  • Adjustable approach: growth and BUN <9 mg/dL
  • Targeted approach: technology to measure macronutrients in milk*
References


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