Benefits and Challenges of the Use of Human Milk for Premature Infants

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• Dr. Rhine has indicated that he has nothing to disclose
Talk Objectives

• Review the benefits of human milk for all infants
• Describe the role of human milk in meeting the unique physiologic and nutritional needs of premature infants
• Share strategies for optimizing the use of human milk for premature infants
• Review nutritional monitoring of premature infants
Clinical Impact of Human Milk for Term Infants—Short-term

- Respiratory – URI (60% reduction), LRI (72-77% reduction), RSV bronchiolitis (74% reduction)
- SIDS – 36% reduction
- Otitis media – 23-50% reduction (77% reduction in recurrent OM)
- Allergies – atopic dermatitis (27-42% reduction)
- GI – gastroenteritis (64% reduction)

Clinical Impact of Human Milk for Term Infants–Long-term

- GI – celiac disease (52% reduction); inflammatory bowel disease (31% reduction)
- Allergy – asthma (26-40% reduction)
- Obesity – 24% reduction
- Diabetes – Type 1 (30% reduction); Type 2 (40% reduction)
Clinical Impact of Human Milk for Term Infants—Long-term

- Cancer – leukemia (15% reduction AML, 20% reduction ALL)
- Cardiovascular – reduced BP by 3.2 mmHg - more than weight loss (2.8 mmHg), alcohol reduction (2.1 mmHg), salt restriction (1.3 mmHg), exercise (0.2 mmHg)
- Neurodevelopmental outcomes – improved IQ scores and teacher ratings
- Maternal benefits include reduction in diabetes, HTN, breast and ovarian cancer

Gold Standard of Growth for Premature Infants

• The ideal goal of providing nutrition to premature infants is to approximate the *in utero* growth of a normal fetus of the same post-conceptional age
  – Body weight and length
  – Body composition and organ development

Unique Nutritional Aspects of the Premature Infant

- Higher organ: muscle mass ratio
- Higher rate of protein synthesis and turnover
- Greater oxygen consumption during growth
- Higher energy cost due to transepidermal water loss
- Higher rate of fat deposition
- Prone to hyperglycemia
- Higher total body water content
Unique Nutritional Aspects of Premature Infants - Brain Growth

Brain growth over 8 weeks:
- At 28 wks. 100% Increase
- At term 40% Increase
- At 3 mo. 25% Increase

Preventing Feeding-Related Morbidities in Premature Infants

- Necrotizing enterocolitis
- Osteopenia/rickets of prematurity
- Vitamin and mineral deficiencies
- Feeding intolerance
- Prolonged TPN and related cholestasis
- Nosocomial infections
- Prolonged hospitalization
Optimal Growth of Premature Infants Influences Long-term Health and Disease

- Premature infants receiving breast milk are less likely to have excessive growth.
- Adverse effects of excessive growth acceleration:
  - Obesity
  - Elevated blood pressure
  - Insulin resistance and diabetes
  - Cardiovascular mortality

Clinical Benefits of Human Milk for Preterm Infants

- Improve Host Defense – reduced infections
- Promote Gastrointestinal Development
- Provide Special Nutritional Needs
- Improve Neurodevelopmental Outcome
- Support Physically & Psychologically Healthier Mother
Human Milk Provides Protection from Infection in Premature Infants

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>Fortified BM</th>
<th>Formula</th>
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<tbody>
<tr>
<td>Oxygen Rx (days)</td>
<td>19</td>
<td>33</td>
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<tr>
<td>NEC</td>
<td>1.6%</td>
<td>13%</td>
</tr>
<tr>
<td>Late-onset sepsis</td>
<td>31%</td>
<td>48%</td>
</tr>
<tr>
<td>NEC or sepsis</td>
<td>31%</td>
<td>54%</td>
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GI Benefits of Human Milk for the Premature Infant

• Gastrointestinal development
  – Reduces intestinal permeability faster
  – Induces lactase activity
  – Multiple factors to stimulate growth, motility and maturation of the intestine
  – Human milk empties from the stomach faster than artificial milks
  – Less residuals and faster realization of full enteral feedings
Nutrition of Premature Infants: Cognitive Development

• Many studies have evaluated impact of receiving breast milk (especially fortified) on cognitive development, specifically higher IQ or Bayley score (MDI improved 0.53 per 10ml/kg/day of breast milk)
• Benefit was strongest for children of low birth weight and in males
• Improvement in developmental achievements associated with breast milk persisted at least through adolescence
• Postnatal growth lag and suboptimal HC associated with neurological and sensory handicaps and poor school performance

Human Milk Fortification

- Expressed human milk has variable nutritional content, and does not provide adequate nutrition for premature infants
- Must fortify human milk to provide adequate energy, protein, minerals and vitamins for the growing premature infant
- Starting fortifier before being on full feeds (40-100 ml/kg/day total fluids) will allow for transition from parenteral to enteral nutrition without accumulating deficits
## Human Milk Fortification

<table>
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<tr>
<th></th>
<th>HM</th>
<th>Pro</th>
<th>Sim</th>
<th>Enf</th>
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</thead>
<tbody>
<tr>
<td><strong>Energy (kcal)</strong></td>
<td>67</td>
<td>83</td>
<td>79</td>
<td>81</td>
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<tr>
<td><strong>Protein (g)</strong></td>
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<td>2.3</td>
<td>2.3</td>
<td>2.5</td>
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<tr>
<td><strong>Carbohydrate (g)</strong></td>
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<td>7.3</td>
<td>8.2</td>
<td>7.0</td>
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<tr>
<td><strong>Fat (g)</strong></td>
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<td>4.9</td>
<td>4.1</td>
<td>4.9</td>
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<td><strong>Calcium (mg)</strong></td>
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<td>110</td>
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<td>115</td>
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<td><strong>Phosphorus (mg)</strong></td>
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<td>59</td>
<td>78</td>
<td>63</td>
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<td><strong>Osmolality§</strong></td>
<td>290</td>
<td>&lt;360*</td>
<td>385</td>
<td>325</td>
</tr>
</tbody>
</table>

*estimated

**HM**=Human Milk;  **Pro**=Prolacta;  **Sim**=Similac;  **Enf**=Enfamil

Human Milk Fortification

- Babies randomized to receive human milk-based fortifier had 50% reduction in medical NEC (p<0.03) and 90% reduction in surgical NEC (p<0.007) compared to bovine-based
- No difference in feeding intolerance or NEC in those infants receiving human milk-based fortifier starting at 40 mL/kg/day of feeds vs. 100 mL/kg/day

Reduced NEC with HM-Based Fortifier

Human Milk-Based Fortifier Cost/Benefits

• Recent cost analysis predicts savings of 3.9 NICU days and $8,167 per patient, based on cost estimates of medical and surgical NEC within California 2007 dataset
• Factors that influence costs include patient selection, duration of fortifier use, and baseline NEC rate
• Calculator program to estimate unit-specific costs/benefits available at vtoxford.org NICQpedia
• Estimated cost per patient at LPCH=$3,750
Use of Human Milk for Premature Infants – Optimizing Commitment

- Need to start education around human milk and pumping before delivery—by Obstetrical Services and during Neonatology consultations
- Hospital policy support of WHO/UNICEF Ten Steps to Successful Breastfeeding (<5% of hospitals support 9-10 steps) for all babies
- Resource allocation includes facilitating breast pump availability, appropriate milk storage
- Post partum and NICU staff education and support of breastfeeding and pumping, as directed by adequate lactation consulting services

Human Milk Availability - Recent Studies

• Best way of optimizing milk production is a combination of hand expression and breast pump

• This combination also increases the caloric content of human milk available to premature infants

• Bundle of practices to improve breast milk availability can be found at cpqcc.org – these were associated with relative 13% improvement in % of VLBW infants being sent home on breast milk
Challenges to the Use of Mother’s Breast Milk for Premature Infants

- Neonatal transports
- Maternal diseases/colonization
- Maternal medications
- Concerns about CMV
- Safety of transport and storage of maternal milk
Alternatives to Specialty Fortifiers

• Protein fortifiers—liquid formulation recently available; lack many nutrients including Ca$^{+2}$ and phosphorus that may be necessary for optimal fortification of breast milk

• Thickeners—recent warning by FDA against use of Simply Thick thickener for VLBW infants due to association with NEC; expressed concern that xantham gum may affect GI flora

Nutritional Care/Outcomes in Premature Infants-LPCH at Stanford

• Feeding pathway and nutrition bundle used at Stanford described by McCallie et al.
• Encourage use of human milk and fortification
• “Early” TPN
• GI priming/trophic feeds
• Defined feeding advance schedule
• Standardized fortification
• Consensus around residuals, feeding intolerance

Human Milk Use and Fortification at LPCH

• Over 90% of the mothers of our VLBW infants provide breast milk; if mother’s milk not available, we recommend banked breast milk
• Per FDA recommendations, we seek to avoid powdered fortifier products, which until recently limited options
• In past 2+ years we have used Prolacta fortifier up to 1500 gm/34-35 weeks gestational age, then transitioned to other liquid fortifiers
• 85% of inborn VLBW infants are discharged on at least some breast milk
LPCH vs. VON
Inborn NEC
Nutritional Practices Supporting Breast Milk-Individual Patient Level

• Careful monitoring of nutrition
  – Intake-fluid volume, calories, protein
  – Growth-measuring weight, length (using board), head circumference

• Adjust intake volume to anticipate growth instead of reacting to decreases in growth rate

• Track breast milk production- use pumping log

• No definitive evidence about selection and benefits of nutrition lab monitoring, e.g. alkaline phosphatase
Nutritional Practices Supporting Breast Milk - Individual Patient Level

- Should aim for weight gain of 15-18+ gm/kg/day during growth phase after weight nadir
- Premature infants being discharged home should have careful follow-up of their nutrition and growth
- Nutritional supplementation for premature infants should be continued for 3-6 months to optimize growth and development
Nutritional Practices Supporting Breast Milk-NICU Level

• Average weight gain for VLBW infants*
• NEC rate for VLBW infants*
• Track and benchmark percentage of babies starting on human milk (mom’s or banked)
• Track and benchmark percentage of babies discharged on human milk*
• Other nutritionally-related measures include day of first feed, TPN days, length of stay*

* Data available on VON, Pediatrix NICU databases
Alternatives to Mother’s Breast Milk

• Banked breast milk-usually in conjunction with HMBANA milk bank
  – Usually selected population for use, e.g. VLBW infants
  – Informed assent/consent should be obtained describing pros and cons of donated milk compared to formulas

• Special premature formulas-superior to term formulas as far as growth; nutritional content better meets the needs of premature infants
Summary

• Nutrition is critically important for the optimal growth and development of premature babies.
• Ideal food for premature infants is mother’s breast milk that should be fortified, or donated breast milk (fortified prn), or else premature specialty formula.
• Successful use of breast milk depends on institutional promotion and support and maximizing availability.
• Should have standardized approach based on providing optimal nutrition, mainly human milk for premature infants; at Stanford this has been associated with improved growth velocity and reduced NEC.