An Evaluation of Three Nutritional Feedings in Extremely Premature Infants

Nilsa A. Collins, RD, LD, CLC, CNSC
LeeAnna Spiva, PhD, RN, PLNC
Lewis VanBrackle, PhD
Brenda Marino, MD
Emma Casanova, MD
Rachel Lipson, MD, IBCLC
Mike Metcalf, MD
Marla Camp, BSN, RN

Data Collectors: Deborah Kilday, MSN, RN; Marie Black, RN; Mary Conner, NNP; Tiffany Perry, BSN, MBA, RN
Background

Necrotizing Enterocolitis (NEC)

– Premature infant are at an increased risk due to immature GI system $^{1,2}$
– May lead to necrosis of the bowel $^{2,3}$
– Longer LOS, higher rates of mortality, morbidity, & costs $^{14-16}$
– Costs between $500 million to $1 billion $^{16}$
Background: NEC Risk Factors

- Prematurity
- Rate of enteral feedings
- Formula feedings
- Bacterial infection
- Intestinal ischemia
- Prolonged initial empirical antibiotic treatment
- Packed red blood cell transfusion
- Abnormal toll-like receptors signaling in the intestine
- Longer mechanical ventilation days 4-13
Background

• Research demonstrate the protective effects of human breast milk \(^{17-22}\)

• Further work is needed to determine nutritional interventions to prevent the devastating effects of NEC in the premature infant \(^{23}\)
Necrotizing Enterocolitis
Methods

• **Design**
  – Retrospective, descriptive

• **Setting/Sample**
  – 1 community acute care hospital Neonatal Intensive Care Unit (NICU) located in Southeast
Methods

• **Inclusion criteria**
  – Infants weighing 400 to 1250 g at birth
  – Adherence to feeding protocol
  – Adherence to one of the following nutritional interventions:
    • exclusive human breast milk and human-based HMF
    • human breast milk & bovine-based HMF
    • exclusive premature formula

• **Human Subject Protection**
  – WellStar & Kennesaw State University IRB Approvals
Methods

- **Data Collected from July 1, 2007 to July 31, 2012**
- **Sample**: 141 infants weighing less than 1250 g (47 infants per group)
- **Variables collected**:  
  - Demographic  
  - Length stay  
  - Oxygen  
  - Ventilator & central line days  
  - Antenatal steroids  
  - Parenteral nutrition days to full feeding (130-150 mL/kg/d)  
  - Apgar scores  
  - Weekly growth average (calculated from body weight & head circumference measurements recorded at time of birth & discharge)
Methods

• Late-onset sepsis & NEC defined using the Vermont Oxford Network Database definitions 24

• **Late-onset sepsis**: positive blood culture after day of life 3

• **NEC**: presence of pneumatosis in the x-ray and presence of clinical signs including abdominal distention, bilious aspirate, discolored abdomen, and/or bloody stools

• Infants followed from **birth to 34 weeks** adjusted gestational age

• **Long-term follow-up** occurred with infants **transferred** prior to 34 weeks if the transfer was due to NEC to monitor outcomes
Feeding Protocols

Group 1: **Exclusive human breast milk & human-based HMF**

- Mother’s own milk mixed with a human-based HMF (volume 130-150 mL/kg/d)
- 93% of infants received 100% mother’s own milk
- 7% received some donor milk when mother’s milk was unavailable
- When infants weaned off parenteral nutrition, a multivitamin, vitamin K, & iron were added
- At 34 weeks, a transition plan began alternating bovine & human milk-based fortifier until all feeds contained bovine-based HMF
Feeding Protocols

Group 2: Bovine-based HMF

- 100% mother’s own milk (no donor milk)
- 3% of feedings with premature formula when mother’s own milk not available
- At 1 month of life, multivitamin & iron added
Feeding Protocols

Group 3: Exclusive formula

- 97% premature formula feedings (3% feedings from mother’s own milk)
- After tolerating 100 mL/kg of 20 calories premature formula, switched to 22 kilocalories & at 1 month of life to 24 kilocalories
- Multivitamin & iron added at 1 month of life
Feeding Protocols

• Feedings mixed in a designated area in NICU
• RN mixed infant’s feeding per protocol
• RN cleaned milk prep area after each use & sanitized at least once a shift
Data Analysis Plan

• Data analyzed using SPSS 18.0 & JMP® 10
• Analysis of variance (ANOVA) & Chi-square tests examined differences between the 3 groups
• Logistic regression used to evaluate all significant factors at $P < 0.05$ & removing non-significant factors using stepwise backward selection
• Relative risks were approximated by odds ratios because NEC & late-onset sepsis endpoints were rare in this population
Demographic Findings

Prolacta Group

Lower odds of NEC (compared to a bovine-based HMF diet)

- 89.6% with 100% human milk diet
- 74.9% with premature formula diet
- NEC incidence of 2.1% (1/47)
Demographic Findings

Bovine-based HMF Group

- NEC incidence was 10.6% (5/47)
- Fewer home discharges & greater in-hospital mortality, compared to the other 2 groups ($P = 0.001$)
- Greater incidence of anemia requiring treatment with epogen ($P = 0.03$) compared to the other 2 groups
- Greater number of ventilator days ($P = 0.07$) than formula group
Demographic Findings

Formula Group

- NEC incidence of 6.4% (3/47)
- Fewer private payers & more Medicaid payers compared to the other 2 groups ($P = 0.01$)
- Larger birth weight (111 g) than the human-based HMF group ($P = 0.08$)
- Larger birth head circumference compared to the other 2 groups ($P = 0.02$)
- Larger weekly weight gain than the bovine-based HMF group ($P = 0.01$)
- Fewer O2 therapy days than the human-based HMF group ($P = 0.008$)
Findings

• No significant findings among the 3 groups for NEC or late-onset sepsis
• Bovine-based HMF group ($P = 0.06$) more likely to develop NEC
• Birth weight- Only significant predictor for NEC ($P = 0.13$, OR = 0.994) & late-onset sepsis ($P = 0.043$, OR = 0.997). Each additional gram of weight reduced the odds of NEC by 0.6% & late-onset sepsis by 0.3%
# NEC Outcomes

<table>
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<th>Group Name</th>
<th>Surgical Intervention</th>
<th>Survived NEC</th>
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<tr>
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<tr>
<td>Bovine HMF Group</td>
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<tr>
<td>Formula Group</td>
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</tbody>
</table>
Discussion

• Unable to demonstrate significant differences among the 3 groups for the incidence of NEC

• Lower incidence of NEC in infants fed an exclusive human milk diet consistent with earlier studies
Discussion

• Infants fed predominantly human milk had less incidence of NEC compared to infants fed premature formula \(^{18}\)

• Infants who received bovine-based products had a higher rates of NEC & death than infants who received only human milk-based diet \(^{21,25}\)
Discussion

Low birth weight was associated with higher odds of developing late onset sepsis & NEC.
Limitations

• **Retrospective** query of database information, lacked randomization, & blinding

• **Sample size** for the endpoints, NEC & late-onset sepsis, remained **small**, limiting the ability to evaluate some variables for associations

• **Bovine group received powder HMF** which could influence the development of late onset sepsis because powder is not a sterile product
Conclusion

• **Findings** provide further evidence supporting the use of an exclusive human breast milk diet in premature infants

• Infants fed an **exclusive human milk diet had a lower incidence of NEC** compared to the premature formula & bovine-based HMF groups

• Further research is warranted in larger, diverse premature infant populations
References


