The Canadian Neonatal Network™/Le Réseau Néonatal Canadien™

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Research Proposal

Early Exclusive Enteral Feeding versus Intravenous Fluids with Gradual Feeding for Preterm Infants Born at 30-32 Weeks Gestation: A Stepped-Wedge Cluster Randomized Trial

Investigators: Belal Alshaikh
Email: Belal.Alshaikh@albertahealthservices.ca

Hospital discharge for preterm infants is primarily determined by the achievement of physiological milestones, with feeding and oxygen requirements being the final hurdles. Among infants born at ≥30 weeks of gestation, neonatal morbidities such as oxygen dependency from bronchopulmonary dysplasia are rare, making delayed attainment of feeding milestones the leading cause of prolonged hospital stays. Preterm infants born between 30 and 32 weeks account for approximately 50% of the workload in tertiary NICUs, underscoring the need for optimized feeding strategies in this population.
The conventional nutritional approach—characterized by intravenous (IV) nutrition, delayed initiation, and slow progression of milk feeds—may be unnecessary for these infants and could even pose risks. A shift toward exclusive enteral feeding from birth has the potential to significantly improve outcomes, including shorter hospital stays, reduced pain and stress, enhanced breastfeeding success, and strengthened parent-infant bonding. These benefits highlight the importance of reevaluating current feeding practices to support earlier physiological maturation and discharge in this population.

Research Question

In preterm infants of 300/7-326/7weeks' gestation, does exclusive enteral feeds initiated within 3 hours of birth, compared to the current standard approach of initiation with intravenous fluids with a gradual increment of enteral feeds, reduce total length of hospital stay?

Objectives

Primary:

To evaluate the efficacy of EEEF for preterm infants 30-32 weeks gestation on the total length of hospital stay.

Secondary:

1) To evaluate secondary efficacy outcomes: Breastfeeding, time to achieve full milk feeds, length of stay in level III NICU, parents satisfaction, and total cost.
2) To evaluate safety outcomes: survival, hypoglycemia, late-onset sepsis, and NEC.

Primary outcome

Total length of hospital (level III and level II) stay.

Secondary outcomes:

1) *Effectiveness outcomes:*
    - Time to achieve full milk feeding (reaching140 ml/kg/day that is sustained for 3 consecutive days),
    - Number of CVCs inserted,
    - Growth anthropometrics at 36 weeks corrected gestation,
    - Breastfeeding (nursing) at discharge,
    - Mother's breastmilk feeding (type of milk: any usage of mother's milk regardless of delivery method) at discharge, and
    - Total costs per patient;
2) *Parent satisfaction of care:*
    - EMPATHIC-N questionnaire will be administered for parents at 3-4 weeks after discharge;
3) *Safety:*
    - Survival to hospital discharge,

- Any hypoglycemia in the first 72 hours,
- Incidences of culture-proven late-onset sepsis, necrotizing enterocolitis, and spontaneous intestinal perforation.

Study design
Stepped-wedge cluster randomized trial (SW-CRT) design. Nine NICUs are included.

Consent
Since the intervention will be randomized at the site level, patient consent will be obtained between 2 and 7 days post-exposure for inclusion in data collection.

Control period
When NICU is randomized to the control phase, preterm infants meeting inclusion criteria will receive fluids and nutrition as per standard practice at the NICU.

Intervention period
When NICU is randomized to the EEEF phase, infants eligible for the study will have their nutrition fluids started as milk at 60-80 ml/kg/day and increased per the infant's fluid needs.

Inclusion criteria:
1) Infants born between 30 0/7and 32 6/7weeks gestation, and
2) Infants less than 180 minutes from birth.

Exclusion criteria
Major congenital abnormalities, infants born outside the participating NICUs, antenatal diagnosis of absent or reversed umbilical arterial end-diastolic blood flow or extremely small for gestational age (birthweight <3rd percentile), moderate to severe respiratory distress or hemodynamic instability that would preclude feeding, symptomatic or severe hypoglycemia, evidence of perinatal acidosis.

Sample size

Our anticipated sample size is 1440 infants over the 3 years. Our power calculations account for the design effect determined by the number of sites (#9), the size of the clusters, the intra-cluster correlation coefficient (ICC), and the relative efficiency imposed by unequal cluster sizes.