



The Canadian Neonatal Network™/Le Réseau Néonatal Canadien™

2025 CNN-CPTBN Annual Meeting

Research Proposal

Early targeted treatment versus expectant management of patent ductus arteriosus in extremely preterm infants: A National Comparative Effectiveness Research (CER) Project

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Background

The most common cardiovascular problem that infants born extremely preterm experience early in life is a patent ductus arteriosus (PDA). According to the 2023 CNN annual report, among infants born <1000 g birth weight and diagnosed with a PDA, 63% (475/758) received some form of therapy. Despite recent RCTs suggesting possible harm with early PDA treatment, a substantial proportion of extremely low birth weight infants in Canada continue to receive treatment for a PDA. Preliminary data from the recently concluded SMART-PDA RCT suggests possible benefit with an early screening and treatment approach based on a combination of clinical and echocardiographic criteria in extremely preterm infants born <26 weeks GA. The posterior probability of the SMART strategy leading to a better WIN ratio with regards to the most patient-important outcomes (death, sepsis, NEC and ROP) was 88%. Similarly, in a recently concluded large QI project (n=538) from Mt Sinai Hospital, Toronto, implantation of an early hemodynamic screening and treatment approach in infants born <29 weeks GA resulted in a significant reduction in severe IVH (aOR 0.51, 95% CI 0.28 to 0.94). Evidence from such recent pan-Canadian studies lends credence to the hypothesis that though indiscriminate use of NSAIDs may be harmful, selective early treatment of PDA using NSAIDs within the first 72 h of age may be beneficial in the smallest infants. Therefore, we propose a comparative effectiveness study to understand the effectiveness of an early targeted PDA treatment in the real-world.

Research Question

In extremely low birth weight infants born <1000 g, does an early targeted treatment approach based on a combination of screening echocardiogram and clinical signs within the first 72h of life, when compared to an expectant management approach in the first week of life, improve survival without major morbidity (sIVH, NEC, ROP, sepsis)?

Participants

Infants born at or admitted to (within the first 72 h of birth) participating CNN sites with a birth weight of <1000 g

Interventions

- **Early targeted PDA treatment** – with IV/oral ibuprofen or acetaminophen based on a combination of early screening echocardiography and clinical signs
- **Expectant management** – no pharmacotherapy for PDA for at least 7 days, symptomatic management at the discretion of the medical team beyond 7 days

Primary Outcome

Survival without major morbidity (sIVH, NEC, ROP, sepsis)

Method

In this CER study participating sites will self-select and adhere to one of the above management approaches for all preterm babies born <1000 g birth weight. To mimic the real-world scenario, choice of pharmacotherapy (ibuprofen/acetaminophen/indomethacin) will be left up to the medical team. Infants who received prophylactic NSAIDs in the first 24 hours after birth for prevention of intraventricular hemorrhage will be included. The participating centers will also be allowed to continue the use of concomitant neonatal interventions such as prophylactic and rescue



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corticosteroids, blood product transfusion practices, enteral feeding practices including use of donor breast milk and probiotics as per their usual NICU policy. This information is collected as routine in the CNN database and will be compared between groups and any imbalances will be adjusted at the analyses stage.