Title: Evaluation of Continuous Morphine Versus Dexmedetomidine in Neonates with Encephalopathy Undergoing Therapeutic Hypothermia

Purpose: Morphine has been used as the agent of choice for sedation and analgesia in newborns undergoing therapeutic hypothermia despite the risk of significant adverse effects. Dexmedetomidine is a sedative analgesic medication that works as a selective central alpha-2 adrenergic agonist. Unlike opioids, dexmedetomidine does not cause respiratory depression or decreased gastrointestinal motility. This could benefit newborns undergoing therapeutic hypothermia, as many of them require mechanical ventilation and have difficulties tolerating feeds. The purpose of this study was to evaluate if the change in the sedation agent to continuous dexmedetomidine infusion within the therapeutic hypothermia protocol affected the adverse effects.

Methods: The Institutional Review Board approved this retrospective, observational cohort study. Neonates who qualified and underwent therapeutic hypothermia at St. Louis Children's Hospital between October 2, 2018 and May 22, 2021 were included. St. Louis Children's Hospital changed their therapeutic hypothermia protocol from using continuous morphine for sedation to using continuous dexmedetomidine in October of 2020. The primary outcome was to evaluate if the change in the sedation agent to continuous dexmedetomidine infusion in the therapeutic hypothermia protocol affected the safety adverse effects of decreased respiratory drive and gastrointestinal motility. Safety was determined by evaluating the average time spent on mechanical ventilation (hours) and average time to full feeds (days). Secondary outcomes included the impact on the requirement of morphine boluses to maintain sedation and the overall length of hospital stay (days).

Results: Neonates who received dexmedetomidine for sedation while undergoing therapeutic hypothermia on average were able to reach full feeds in 7.2 days(± 2.1), while neonates who received morphine reached full feeds in 7.4 days(± 3.6). Ten patients (37%) in the dexmedetomidine group required mechanical ventilation for an average of 115.4 hours (± 69.5). Of the morphine group, 58 (54.2%) patients required mechanical ventilation for an average of 68.2 hours (± 84.6).

Conclusions: The average time needed to reach full feeds was similar between the morphine and dexmedetomidine groups. Dexmedetomidine was associated with less neonates requiring mechanical ventilation, but of those requiring ventilation, dexmedetomidine was associated with a longer average time spent on mechanical ventilation. The clinical significance of these safety adverse effects must be determined in larger, future studies.

Morphine has been used as the agent of choice for sedation and analgesia in newborns undergoing therapeutic hypothermia despite being known to pose the risk of significant adverse effects. Dexmedetomidine is a sedative analgesic medication that works as a selective central alpha-2 adrenergic agonist. Dexmedetomidine does not pose the same respiratory depression or gastrointestinal adverse effects of opioids. This could be beneficial for the newborns undergoing therapeutic hypothermia, as many of them require mechanical ventilation and have difficulties tolerating enteral feeds. The purpose of this study was to evaluate if the change in the sedation

agent to continuous dexmedetomidine infusion in the therapeutic hypothermia protocol affected the clinical or safety adverse effects.