Evaluation of Caffeine Dosing and Monitoring for the Treatment of Apnea of Prematurity

Background:
Caffeine for the treatment of apnea of prematurity has been shown to stimulate respiratory drive and reduce the need for mechanical ventilation in preterm infants. Caffeine has a long half-life and a wide therapeutic index that allows for once daily dosing. Maintenance doses for caffeine range between 5 to 10 mg/kg/day. However, there is minimal literature to support the most efficacious starting dose within that range. Additionally, some literature suggests that caffeine can be adjusted and monitored exclusively by symptoms of apnea or toxicity such as tachycardia and/or seizures without lab monitoring. The purpose of this study is to establish an effective starting maintenance dose for caffeine and investigate if the practice of weekly caffeine blood level monitoring is necessary.

Methods:
This retrospective chart review will include approximately 100 neonatal intensive care unit patients diagnosed with apnea of prematurity who received a loading dose of caffeine prior to maintenance caffeine therapy at Mercy Hospital Springfield between January and December 2019. The primary outcome measure will be the mean value of caffeine maintenance doses across the patient's course of treatment. Secondary outcome measures include the average number of caffeine blood level draws performed per patient and the impact caffeine has on the patient's weight across the course of therapy. Baseline characteristics to be collected include gender, ethnicity, gestational age at birth and caffeine initiation, multiple or single birth and length of hospital stay. This study will exclude patients who expired prior to discharge. The study will utilize descriptive statistics.

Results:
Baseline characteristics favored singleton Caucasian males. The average gestational age was 30.6±3.1 weeks and the average length of hospital stay decreased from 7.6±4.9 weeks in 2019 to 5.7±3.1 weeks in 2020 (P=0.019). The primary outcome resulted in an overall median starting caffeine dose of 7.5 mg/kg (6-7.5), and a median ending caffeine dose of 7.5 mg/kg (7.3-8.3). The data was further evaluated by gestational age in the following categories: <28 weeks, 28-30 weeks, 31-33 weeks, and >33 weeks. The median starting caffeine dose for <28 weeks and 28-30 weeks gestational age was 6 mg/kg (6-7.5, 6-7.5), while the median starting dose for 31-33 weeks and >33 weeks gestational age was 7.5 mg/kg (6-7.5, 7.5-7.5). The median ending caffeine dose for all gestational ages was approximately 7.5 mg/kg with varying interquartile ranges. In 2019, there were 56/86 patients with caffeine troughs and a combined total of 365 blood draws (average of 6.5 blood draws per patient); while, in 2020, there were 53/71 patients with caffeine troughs and a combined total of 196 blood draws (average of 3.7 blood draws per patient) (P=0.0019). Starting caffeine doses ≤6.5 mg/kg produced an average of 2.4 dose changes per patient while starting doses of >6.5 mg/kg led to 1.3 dose changes per patient (P=0.16). Neonates on caffeine therapy gained an average of 0.12 kg/week. The cost of a caffeine blood draw and overhead is $4 at Mercy Hospital Springfield, making the total cost of blood draws for caffeine monitoring $2244 ($1460 in 2019 and $784 in 2020).

Conclusions:

We can reasonably assume the starting caffeine dose of 7.5mg/kg appears to be an appropriate maintenance dose for neonates regardless of gestational age with AOP based on the results of an overall median ending dose of 7.5mg/kg, decreased average dose changes per patient, decreased blood draws per patient and decreased average length of hospital stay. Higher starting maintenance doses were able to achieve the desired therapeutic dose faster with less blood draws collected and less adjustments made. The weight change results are consistent with other literature, implying caffeine may not statistically or clinically impact weight gain. [1,6-8,10] The cost associated with caffeine blood draws did not account for nursing time, collection supplies or risk of infection costs; thus, savings could potentially be greater. Two possible limitations for this study are Mercy Hospital Springfield's standard of practice to allow neonates to grow out of their therapeutic caffeine dose to facilitate weaning and the Mercy Hospital Springfield efforts to decrease patient length of stay in the NICU. Results of this retrospective chart review support considering the discontinuation of weekly caffeine blood level monitoring at Mercy Hospital Springfield.