ESPR Young Investigator Webinar Series Session I

Wednesday, June 10 12:00-1:00 PM EDT

Moderators
Heather Brumberg, MD, MPH, FAAP, ESPR President
Jayasree Nair, MD

EDT	Abstract	Title	Presenting Author
12:00 PM		Welcome and Introductions	
12:05-12:20 PM	3386035	Dexmedetomidine compared to intermittent morphine for sedation of neonates undergoing therapeutic hypothermia; Neonatology	Dr. Eni Jano, NYU Langone, *ESPR Abbott Nutrition Trainee Young Investigator Award Recipient*
12:20-12:35 PM	3373229	Tropomyosin 1 genetically constrains in vitro hematopoiesis; Development Biology	Dr. Christopher Thom, Children's Hospital of Philadelphia, *ESPR Abbott Nutrition Trainee Young Investigator Award Recipient*
12:35-12:50 PM	3368342	Decreasing pain experienced by patients 0-6 months of age during minor procedures in the YNHCH Pediatric Emergency Department by increasing the use of oral sucrose; Quality Improvement	Dr. Angelica Garcia, Yale University School of Medicine, *SPR Travel Award to Enhance Diversity in the Research Workforce Recipient*
12:50 PM-1:00 PM		Wrap Up	

CONTROL ID: 3386035

TITLE: Dexmedetomidine compared to intermittent morphine for sedation of neonates undergoing therapeutic hypothermia

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Eni Jano

AUTHORS/INSTITUTIONS: E. Jano, A. Cosnahan, R. Angert, E.V. Wachtel, Pediatrics , NYU Langone Medical Center, New York , New York, UNITED STATES|

CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal Potpourri

ABSTRACT BODY:

Background: Therapeutic hypothermia (TH) initiated within six hours of the insult has improved outcomes in neonates with hypoxic-ischemic encephalopathy (HIE). However, TH and other procedures during cooling require appropriate analgesia and sedation to minimize loss of therapeutic benefit. There is lack of literature on a single appropriate sedative agent. Opiates can cause respiratory depression and hypotension. Dexmedetomidine has a potential role for sedation and has fewer side effects. Thus, we hypothesize that dexmedetomidine could be an alternative and safe agent for sedation during TH.

Objective: To evaluate the efficacy and safety of dexmedetomidine compared to morphine in neonates that qualified for TH at our Regional Perinatal Centers.

Design/Methods: We conducted a retrospective chart review of patients who completed TH at NYU Langone or Bellevue Hospital Center from January 2018 to December 2019. Eligible neonates either received morphine (every 4 hours) based on previous practice or continuous dexmedetomidine via new protocol (started March 2019) for sedation/analgesia. Efficacy of dexmedetomidine versus morphine was determined by total morphine dose over 72-hour period and NPASS scores. Safety outcomes evaluated include changes in hemodynamics, tolerance of enteral feeds, and changes in cerebral background activity on video EEG. T-test and chi-square test were used to compare groups.

Results: Of the 30 infants included in the study, 18 received dexmedetomidine and 12 received morphine. There were no significant differences in baseline characteristics with the exception of PPHN incidence being higher in the dexmedetomidine group ($p = 0.04$). Dexmedetomidine use resulted in lower cumulative opiate administration (0.27 vs 1.7 mg/kg, $p<0.001$) and lower NPASS scores at 6 hours of cooling initiation (Table 2). Heart rate at 30 hours and MAP at 24 hours were significantly lower in the morphine group (Graph 1). There were no differences in feeding tolerance after re-warming or cerebral background attenuation (Table 3).

Conclusion(s): Decreased total opiate use and equivalent NPASS scores in dexmedetomidine patients suggest similar efficacy with decreased opiate burden. Dexmedetomidine patients did not have significant bradycardia and had improved hemodynamics at 24-30 hours into TH, which may highlight the impact of morphine accumulation in morphine group. We conclude that dexmedetomidine is an equally efficacious sedating agent that minimizes side effects seen with opiates during TH.

DATE/TIME SUBMITTED: January 08, 2020, 09:42 PM

TABLE TITLE: Table 1: Neonatal characteristics

Table 2: Efficacy of dexmedetomidine compared to intermittent morphine

Table 3: Effect of dexmedetomidine compared to intermittent morphine on feeding and VEEG

TABLE:

Note: The PDF table below is only an approximation of the HTML content and may not match formatting exactly.

Table 1: Neonatal characteristics			
.	Dexmedetomidine group (n=18)	Morphine group (n=12)	p-value

BW (g), mean (SD)	3332 (533)	3410 (284)	NS
GA (weeks), mean (SD)	39.0 (1.4)	39.4 (1.4)	NS
Sex (male), mean (SD)	13 (72.2)	9 (75.0)	NS
Cesarean delivery, n (%)	9 (50.0)	7 (58.3)	NS
Apgar scores, median (range): 1 min 5 min 10 min	 2 (0-7) 4 (1-8) 4 (1-8)	 2 (1-5) 5 (3-8) 5 (3-8)	 NS NS NS
Initial blood gas: pH, mean (SD) base deficit, mean (SD)	 7.00 (0.2) 15.04 (5.2)	 6.96 (0.1) 17.10 (5.2)	 NS NS
Sarnat scores: Mild, n (%) Moderate, n (%) Severe, n (%)	 6 (33.3) 10 (55.6) 2 (11.1)	 2 (16.7) 10 (83.3) 0 (0)	 NS NS NS
Present of seizures, n (%)	6 (33.3)	4 (33.3)	NS
Brain MRI: Normal, n (%) HIE, n (%) Hemorrhage, n (%)	 13 (72.2) 4 (22.2) 1 (5.6)	 8 (66.7) 3 (25.0) 1 (8.3)	 NS NS NS
NICHD HIE Severity: Normal, n (%) Grade 1A, n (%) Grade 1B, n (%) Grade 2B, n (%)	 10 (55.6) 4 (22.2) 0 (0.0) 4 (22.2)	 8 (66.7) 1 (8.3) 2 (16.7) 1 (8.3)	 NS NS NS NS
MAS, n (%)	4 (22.2)	1 (8.3)	NS
PPHN, n (%)	5 (27.8)	0 (0)	0.046
Vasopressor use, n (%)	7 (38.9)	3 (25.0)	NS

Mortality, n (%)	1 (5.6)	1 (8.3)	NS

BW= birth weight, GA = gestational age, NICHD= The National Institute of Child Health and Human Development, HIE= Hypoxic Ischemic Encephalopathy, MAS= meconium aspiration syndrome,
PPHN= persistent pulmonary hypertension of the newborn

Table 2: Efficacy of dexmedetomidine compared to intermittent morphine

.	Dexmedetomidine Group (n=18)	Morphine Group (n=12)	p-value
NPASS scores, mean (SD):			
Baseline	0.75 (1.54)	0.25 (0.87)	NS
6 hours	0 (0.0)	1.2 (1.9)	0.02
12 hours	0.4 (1.22)	0.2 (0.6)	NS
24 hours	0.27 (0.96)	0 (0.0)	NS
48 hours	0.13 (0.50)	0 (0.0)	NS
72 hours	0.06 (0.24)	0 (0.0)	NS
Total morphine dose (mg/kg), mean (SD)	0.27 (0.23)	1.70 (0.27)	<0.01

NPASS = neonatal pain, agitation and sedation scale

Table 3: Effect of dexmedetomidine compared to intermittent morphine on feeding and VEEG

.	Dexmedetomidine Group (n=18)	Morphine Group (n=12)	p-value
Days to full feeds, mean (SD)	3.67 (1.08)	3.18 (0.87)	NS
VEEG Cerebral			
Background:	7 (38.9)	6 (50.0)	NS
Continuous, n (%)	2 (11.1)	4 (33.3)	NS
Attenuated, n (%)	4 (22.2)	1 (8.3)	NS
Discontinuous, n (%)	3 (16.7)	0 (0.0)	NS
	1 (5.6)	1 (8.3)	NS
Burst suppression, n (%)	1 (5.6)	0 (0.0)	NS
Low voltage, n (%)			
Flat, n (%)			

VEEG=video electroencephalogram

TABLE FOOTER: BW= birth weight, GA = gestational age, NICHD= The National Institute of Child Health and Human Development, HIE= Hypoxic Ischemic Encephalopathy, MAS= meconium aspiration syndrome, PPHN= persistent pulmonary hypertension of the newborn

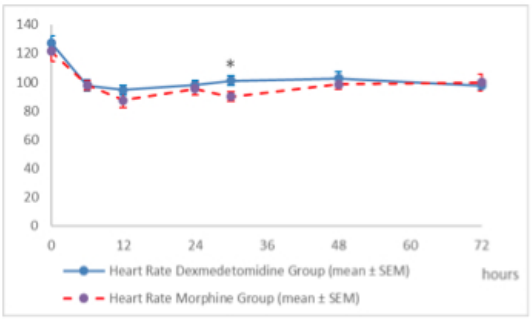
NPASS = neonatal pain, agitation and sedation scale

VEEG=video electroencephalogram

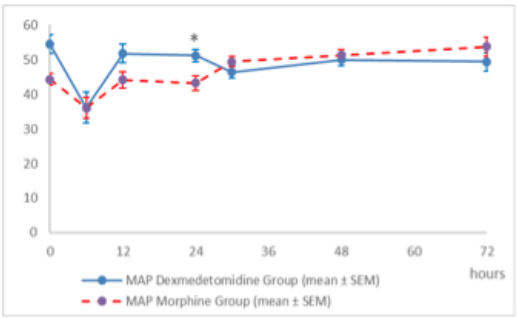
IMAGE CAPTION:

Graph 1. Changes in A. heart rate, B. mean arterial pressure (MAP), and C. respiratory rate in dexmedetomidine group compared to morphine group

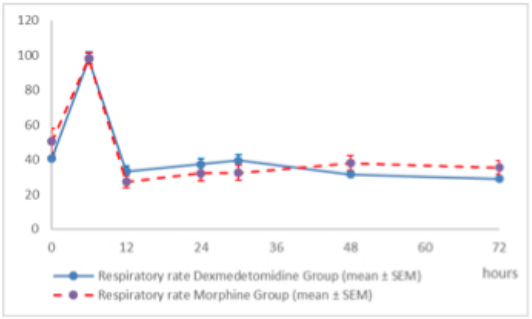
A.



B.



C.



CONTROL ID: 3373229

TITLE: Tropomyosin 1 genetically constrains in vitro hematopoiesis

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Christopher Thom

AUTHORS/INSTITUTIONS: C. Thom, C. Jobaliya, J. Maguire, A. Gagne, P. Gadue, D. French, Childrens Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|K. Lorenz, B. Voight, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

CURRENT CATEGORY: Developmental Biology/Cardiac & Pulmonary Development

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Donated platelet supplies cannot meet clinical demand, and platelet transfusions increase morbidity and mortality in preterm infants. Novel approaches are needed to increase safely transfusable platelet supplies. In vitro-derived products from cultured induced pluripotent stem cells (iPSCs) could address these clinical needs, but current methods are cost-inefficient. Genetic manipulation could enhance efficiency of in vitro hematopoiesis and megakaryopoiesis. While genome wide association studies (GWAS) have linked hundreds of DNA loci with altered human platelet traits, related genes and mechanisms that impact in vitro production are largely unknown.

Objective: To identify and validate loci and related genes that impact hematopoiesis and megakaryopoiesis.

Design/Methods: We used penalized regression (the least absolute shrinkage and selection operator, LASSO) to create a quantitative prediction model, querying which of 860 epigenetic features best discriminated 700 platelet trait GWAS loci from matched controls. We then identified high-priority loci and related genes, and validated hematopoietic impact using established induced pluripotent stem cell (iPSC) culture protocols.

Results: Our LASSO model, comprising 38 epigenetic features, specified platelet trait GWAS loci more accurately than any other computational approach (area under the receiver operating characteristic curve [AUC] = 0.80; next highest model AUC = 0.75). Our LASSO model highlighted exact genetic variants known to regulate platelet traits and function, as well as putatively functional sites and genes.

Among nominated loci was rs11071720, a common variant that decreases Tropomyosin 1 (TPM1) gene expression and increases platelet count in human cells. TPM1 regulates cytoskeletal biology in many cell types, but its role in human hematopoiesis was unknown. We created TPM1-knockout human iPSCs using CRISPR/Cas9. TPM1KO iPSCs were healthy and early hematopoietic development was normal. However, TPM1KO hematopoietic progenitor cell (HPC) was enhanced (2.4±0.3-fold increase vs controls for 3 distinct TPM1KO iPSC clones, $p<0.001$). TPM1KO HPCs produced normal megakaryocyte quantities, more than doubling megakaryocyte yield overall. TPM1KO megakaryocytes had normal morphology, gene expression patterns, and functional responses to platelet agonists, suggesting that TPM1KO platelets would also function normally.

Conclusion(s): Our findings help explain human platelet trait genetics, and identify TPM1 manipulation as a novel strategy to enhance in vitro hematopoiesis and megakaryocyte production.

DATE/TIME SUBMITTED: December 20, 2019, 03:36 PM

(no table selected)

(No Image Selected)

CONTROL ID: 3368342

TITLE: Decreasing pain experienced by patients 0-6 months of age during minor procedures in the YNHCH Pediatric Emergency Department by increasing the use of oral sucrose

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Angelica Marie Garcia

AUTHORS/INSTITUTIONS: A.M. Garcia, B.L. Emerson, Pediatrics, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|C. Alvarez, J. Douglas, Pediatric Emergency Department, YNHH, New Haven, Connecticut, UNITED STATES|S. Hurley, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

CURRENT CATEGORY: Quality Improvement/Patient Safety

CURRENT SUBCATEGORY: Hospital-based Quality Improvement: Emergency Medicine

ABSTRACT BODY:

Background: Pain is the most common adverse event during minor procedures performed in the pediatric Emergency Department. Inappropriate procedural pain management in young infants can lead to unsuccessful procedures, patient discomfort, and parental dissatisfaction. Many studies have shown that oral sucrose is associated with an overall decrease in pain responses in young infants. Oral sucrose is inexpensive, non-invasive, and easily administered.

Objective:

To increase oral sucrose use for pain management for common invasive procedures (PIV, lumbar punctures, urine catheterization, venipuncture) in patients 0-6 months of age from 50% to 80% in the YNHH Pediatric Emergency Department within 12 months.

Design/Methods: We initiated this project in June 2018 at an urban tertiary pediatric ED. We used the Model for Improvement (Plan-Do-Study-Act (PDSA)) methodology for this QI project. Baseline data was obtained prior to initiation of QI project, which consisted of percentage of oral sucrose use for common invasive procedures in the PED. We observed the process of ordering oral sucrose for common minor procedures, from triage to the time of the procedure. Furthermore, we identified key drivers that would lead to appropriate use of oral sucrose for this population: identification of patient needing procedure, family expectations, PED staff education, and order ease of use. (Figure 1) We conducted multiple interventions: (1) provider (attendings, fellows and nurse practitioners) education; (2) nurse education; (3) reporting at weekly management meetings; (4) resident education (5) technician education; (6) ordering process modification; (7) visual aids; and (8) EMR order set. We collected weekly data to inform PDSA cycles. (Figure 2) We utilized statistical process control for analysis.

Results: Our study demonstrated improvement in oral sucrose use for pain management for common invasive procedures in patients 0-6 months of age from 50% to 90% over the course of 12 months. (Figure 3).

Conclusion(s): We use QI methodology to identify barriers and study interventions to increase oral sucrose use in patients 0-6 months old. Our intervention led to a 40% increase in oral sucrose use in this age group. Specifically, we found a significant improvement in oral sucrose use for patients ages 4-6 months (21% to 64%).

DATE/TIME SUBMITTED: January 08, 2020, 10:51 AM

(no table selected)

IMAGE CAPTION:

Figure 1. Key Driver Diagram

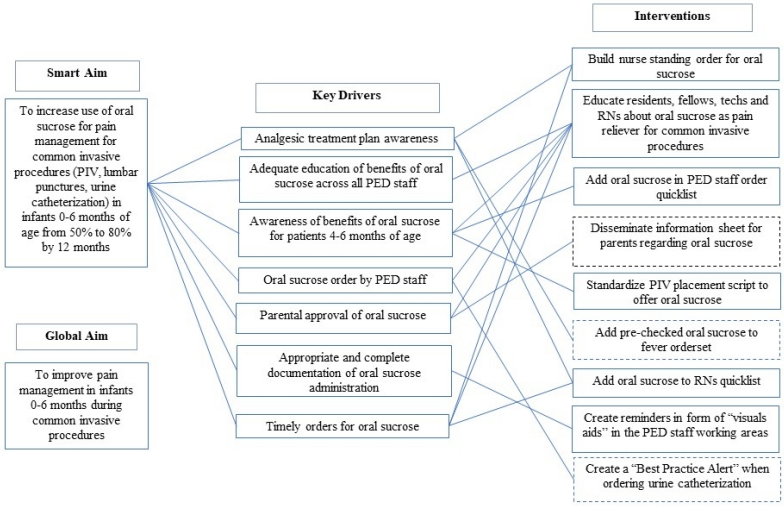


Figure 2. PDSA cycles

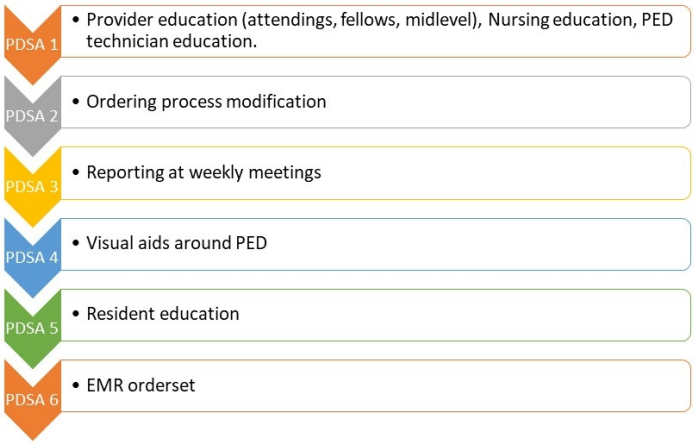


Figure 3. Statistical Process Control Chart. P-chart. The percent of oral sucrose utilized from July 2018 to July 2019 increased from 50%% to 90%. A run of eight in a row on the same side of the centerline was used to determine 'out of control signals' to shift mean.