

## Update on Pediatric Anesthesia

The objective of this presentation is to provide a brief overview of noteworthy pediatric anesthesia literature that were published in 2016. While it is nearly impossible to cover all pediatric anesthesia literature published in 2016, I will focus my attention on the following topics:

- Neurotoxicity concerns
- Pediatric traumatic brain injury guidelines
- Opioid poisoning in children and adolescents
- Screening for pediatric OSA

Additional articles of interest are listed at the end of this document.

### Neurotoxicity Concerns

Pediatric neurotoxicity continues to be a hotly debated topic in pediatric anesthesia. The results of two major clinical trials – GAS study and PANDA study were published in 2016.

### **Neurodevelopmental outcomes at 2 years of age after general anesthesia and awake-regional anesthesia in infancy (GAS): an international multicentre, randomized controlled trial.**

Davidson AJ, et al. Lancet 2016;387:239-50.

- The GAS trial is an ongoing international, multicentre, randomized controlled trial comparing neurocognitive outcomes following randomization to either awake-regional anesthesia or to sevoflurane-based general anesthesia in children younger than 60 weeks, but born at more than 26 weeks gestation who required inguinal hernia repair.
- The primary outcome of the trial is Wechsler Preschool and Primary Scale of Intelligence third edition (WPPSI-III) full scale IQ at 5 years. The secondary outcome is the composite cognitive score of the Bayley Scales of Infant and Toddler Development III at age 2 years.
- The initial 2-year follow up results were published in January 2016. Data were evaluated from 238 children treated with awake-regional anesthesia and 294 children were administered general anesthesia. The median duration of sevoflurane GA was 54 minutes.
- There was no difference in Bayley III development scores between the two study arms. The authors concluded that sevoflurane GA of less than one hour does not appear to increase the risk of adverse neurodevelopmental outcomes at age 2 years compared to awake-regional anesthesia. The GAS study still needs to be completed to evaluate the primary WPPSI-III IQ outcome measure at age 5 years.

### **Association between a single general anesthesia exposure before age 36 months and neurocognitive outcomes in later childhood.** Sun LS, et al. JAMA 2016;315: 2312-20.

- The Pediatric Anesthesia Neurodevelopment Assessment (PANDA) study is a sibling matched cohort study that examined if a single general anesthesia exposure for inguinal hernia repair in otherwise healthy children younger than 3 years of age was associated with impaired neurocognitive development and abnormal behavior in later childhood- 8-15 yrs.

- 105 sibling pairs were examined. The exposed sibling received general anesthesia using volatile agents with a mean duration of 84 minutes and 17 children were anesthetized for more than 2 hours.
- There was no statistically significant difference in IQ scores in later childhood. Also, there was no statistically significant difference in secondary outcomes including memory, attention, visuospatial function, executive function, language, motor and processing speed.

### **FDA Drug Safety Communications**

On December 14<sup>th</sup>, 2016, the United States Food and Drug Administration (FDA) released a Drug Safety Communication warning that “repeated or lengthy (more than 3 hours) use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children’s brains”. They also required warnings to be added to the labels of general anesthetic and sedation drugs. The complete FDA statement can be found at:

<http://www.fda.gov/Drugs/DrugSafety/ucm532356.htm>

### **Pediatric Traumatic Brain Injury Guidelines**

Guidelines for the acute medical management of severe traumatic brain injury (TBI) in infants, children and adolescents were updated in 2012. The following review article summarizes the anesthetic considerations in the management of abusive head trauma, using the pediatric TBI guidelines.

### **Anesthesiologist’s role in treating abusive head trauma**

Lee JK, Brady KM, Deutsch N. Anesth Analg 2016;122:1971-82.

- Abusive head trauma (AHT) refers to brain injury from non-accidental, intentional or inflicted trauma and was previously known as “shaken baby syndrome”.
- AHT is the most common cause of severe traumatic brain injury (TBI) in infants and the leading cause of child abuse-related deaths. Incidence is approximately 30 cases per 100,000 infants per year (conservative estimate)
- For reasons that remain unclear, outcomes after AHT are worse than those after accidental TBI with injuries of similar severity.
- Younger patients, <1 to 2 years old are at greatest risk for AHT secondary to a large head with relatively poor cervical muscular control and lax ligaments.
- AHT must be considered in the diagnosis of all injured children, when the mechanism of injury is unclear or if the clinical history doesn’t match the injuries.
- Injury mechanisms that contribute to AHT are complex and include shaking, blunt force trauma, diffuse axonal injury, hypoxemia-ischemia, brainstem and spinal cord injuries.
- Rapid movement of the brain within the cranial vault can tear bridging vessels causing subdural hematomas and retinal hemorrhages.
- Retinal hemorrhages are associated with a higher risk of death. However, absence of retinal hemorrhages should not exclude a diagnosis of AHT and retinal hemorrhages are not diagnostic of abuse.

### **Anesthetic management**

- Rapid sequence induction and secure airway with in-line stabilization of cervical spine.
- Minimize secondary injury by preventing hypoxia, avoiding hypotension, maintaining normothermia and treating seizures.
- Hyperthermia must be strictly avoided.
- Normocarbica should be maintained with PaCO<sub>2</sub> > 30 mm Hg, particularly during first 48 hrs.
- Prophylactic hyperventilation is not recommended and should be reserved for patients with refractory intracranial hypertension. Prolonged hyperventilation induces cerebral vasoconstriction that risks cerebral ischemia.
- ICP monitoring is recommended in all children with severe TBI (GCS <9).
- Open fontanel does not protect the infant brain from intracranial hypertension during cerebral swelling.
- Maintain ICP < 20 mm Hg and CPP > 40 -50 mm Hg, with higher target CPP in older children. With increases in ICP, the lower limit of autoregulation is increased. In addition to maintaining target CPP, attempts at lowering ICP should be made concurrently.
- Treatment for intracranial hypertension should include deep general anesthesia, administration of 3% hypertonic saline (0.1-1 ml/kg/h) and decompressive craniectomy. Practice of moderate hypothermia (core temperature of 32-33C) remains controversial.
- Choice of anesthetic regimen is at discretion of anesthesiologist- TIVA vs volatile agents. No specific vasopressor has been recommended –phenylephrine, dopamine or norepinephrine
- Corticosteroids are not recommended for pediatric TBI.

### **Opioid Poisoning in Children and Adolescents**

The current public health crisis caused by prescription opioid overdose has affected both adults and children. The following two articles examined the alarming trends in hospitalization for opioid poisoning for children and how controlled substances are prescribed to pediatric outpatients.

#### **National trends in hospitalization for opioid poisoning among children and adolescents, 1997 to 2012.** Gaither JR, et al. JAMA Pediatr 2016; 170: 1195-1201.

- Trends in hospitalization following prescription opioid overdose among children and adolescents were analyzed over a 12-year period using the Kids inpatient database.
- Annual incidence of hospitalizations increased by 165% (1.4 to 3.71 per 100,000 children). The greatest change occurred in the 1-4 years' age group (205% increase). In children 10-14 years of age, the incidence of poisoning attributed to suicide increased 37% and accidental intent increased 82%.
- In adolescents aged 15-19 years, the incidence of hospitalizations increased by 176%. In addition, poisonings from heroin increased by 161% and poisonings involving methadone increased by 950%.

#### **An analysis of 34,218 pediatric outpatient controlled substance prescriptions**

George JA, et al. Anesth Analg 2016; 122: 807-13.

- Authors examined a database of >34,000 controlled substance prescriptions written for children over a 7-year period at Johns Hopkins hospital.

- Regardless of age, oxycodone (not codeine) was the most commonly prescribed opioid and it was ordered as a single agent rather than combined with acetaminophen.
- Liquid formulations were ordered for 98% of children < 6 years, 70% of children 6-12 years and 16% of children > 12 years.
- Regardless of the opioid prescribed, the amount of liquid dispensed averaged  $106 \pm 125$  mL and numbers of tablets dispensed averaged  $51 \pm 51$ . How much medicine was used at home and what happened to the leftover medications are unknown and has enormous public health implications.

### **Screening for Pediatric OSA**

Children with sleep disordered breathing are at an increased risk of perioperative respiratory adverse events. However screening tools to identify the patients at an increased risk are lacking. While the first article in this section evaluates a screening questionnaire, authors in the second article tried to develop a risk prediction tool.

### **STBUR questionnaire for identifying children at risk for sleep-disordered breathing and postoperative opioid-related adverse effects.**

Tait AR, et al. *Pediatr Anaesth* 2016; 26: 759-766.

- Children with symptoms of sleep disordered breathing (SDB) are at risk for perioperative respiratory adverse events (PRAE) such as airway obstruction, laryngospasm & oxygen desaturation. They are also more sensitive to the respiratory depressants effects of opioids.
- This study evaluated STBUR (Snoring, Trouble breathing, Un-Refreshed) as a screening tool to identify children at risk for SDB-associated PRAE.
- Children with  $\geq 3$  STBUR symptoms had a two-fold increased likelihood of PRAE. When these children with SDB were given the same amount of opioids, they experienced more oxygen desaturation and required more escalation of care.

### **Perioperative respiratory adverse events in pediatric ambulatory anesthesia: Development and validation of a risk prediction tool.**

Subramanyam R, et al. *Anesth Analg* 2016; 122: 1578-85.

- Authors attempted to develop and validate a risk prediction tool for the occurrence of PRAE in children undergoing ambulatory anesthesia for surgery and radiology.
- Five risk factors were identified: age  $\leq 3$  years, ASA II and III (versus ASA I), morbid obesity, pre-existing pulmonary disorder and surgery (versus radiology).
- A risk score of 0 to 3 was assigned to each variable and the final score for all risk factors ranged from 0 to 11. A cutoff score of 4 determined high risk category.

### **Miscellaneous Topics**

While not directly related to pediatric anesthesia, the following articles were chosen from pediatric literature.

**Unintentional pediatric exposures to marijuana in Colorado, 2009-2015.**

Wang GS et al. JAMA Pediatr 2016; 170 (9)

- Currently 8 U.S. states have legalized recreational marijuana use- CO, WA, CA, OR, NV, MA, AK, ME and Washington DC, while 28 states allow medical marijuana use.
- Retrospective cohort study of hospital admissions and calls to regional poison center (RPC) from 2009 to 2015, following unintentional marijuana exposure in children < 9 years.
- Between 2009 and 2015, 81 patients were evaluated at Children's Hospital Colorado(CHCO) and the Colorado RPC received 163 exposure cases.
- Median age of CHCO visit was 2.4 years and median age of RPC exposure was 2 years.
- Edible products were responsible for 52% of exposures. In 9% of scenarios, the product was not in a child resistant container.
- Annual RPC pediatric marijuana cases increased more than 5-fold from 2009 to 2015. CHCO visits increased from 1.2 per 100,000 population 2 years prior to legalization to 2.3 per 100,000 population 2 years after legalization.
- In Colorado, child resistant packaging became mandatory in February 2015.

**Association between portable screen-based media device access or use and sleep outcomes**

Carter B, et al. Jama Pediatr 2016; 170: 1202-08.

- 72% of all children and 89% of adolescents have at least 1 device in their sleep environment
- Systematic review and meta-analysis to examine the association between portable screen-based media device access or use in the sleep environment and sleep outcomes.
- Strong association between bedtime media device use and inadequate sleep quantity (OR-2.17), poor sleep quality (OR-1.46) and excessive daytime sleepiness (OR-2.72)
- Media device presence in the bedroom (even without use) was also associated with an increased odds of detrimental sleep outcomes.
- American Academy of Sleep Medicine recommends that children 6-12 years of age should get 9-12 hours of sleep and teens 13-18 years of age should get 8-10 hours of sleep.
- American Academy of Pediatrics recommends that children do not sleep with devices in their bedroom, including TV, computers, smartphones and tablets. Also, children and adolescents should avoid using any electronic media for at least one hour before bedtime.

**Weight loss and health status 3 years after bariatric surgery in adolescents**

Inge TH, et al. N Engl J Med 2016; 374: 113-23.

- Prospective, observational study of 242 severely obese adolescents undergoing bariatric surgery at 5 US centers. Patients underwent Roux-en-Y gastric bypass (67%), sleeve gastrectomy (28%) or adjustable gastric banding (6%). Mean baseline BMI was 53.
- At 3 years following procedure, mean weight had decreased by 27%, remission of the following comorbidities: type 2 DM in 95% of participants, abnormal kidney function in 86%, prediabetes in 76%, elevated BP in 74% and dyslipidemia in 66%.
- Adolescents have a greater potential than adults for reversal of cardio-metabolic consequences of obesity

- Risks associated with the procedure included specific micronutrient deficiencies (low ferritin, vitamin B<sub>12</sub> and vitamin A) and need for additional abdominal procedures.

### **Extra Articles That Will Not be Presented**

#### **Intramuscular fentanyl and ketorolac associated with superior pain control after pediatric bilateral myringotomy and tube placement surgery.**

Stricker PA et al. Anesth Analg 2017; 124: 245-53.

- Bilateral myringotomy and tubes (BMT) is the most common pediatric day surgical procedure. However, there is no consensus on the ideal analgesic regimen.
- Retrospective cohort study of 3669 children who underwent BMT with preoperative midazolam, mask GA, sevoflurane, oxygen and air/N<sub>2</sub>O and IM analgesics. Analgesic regimen included single agent IM fentanyl (1.5-2 mcg/kg) or IM ketorolac (1 mg/kg) and dual agent IM fentanyl and ketorolac. Multivariable analysis was performed on PACU maximum FLACC score, oxycodone administration and time to discharge readiness.
- Combination IM fentanyl and ketorolac was associated with superior PACU analgesia as measured by FLACC score and the lowest frequency of PACU oxycodone administration.
- Addition of IM fentanyl did not increase PACU emesis if dose kept < 2 mcg/kg.
- Combination of fentanyl and ketorolac has potential advantages as their pharmacokinetic profile matches pain after BMT. IM fentanyl has 7-8-minute onset of action and 1-2-hour duration. Irritation and pain from chronic otitis media are covered by ketorolac's analgesic and anti-inflammatory effects (onset in 20-25 minutes and t<sub>1/2</sub> in adults - 5.3 hours)

#### **Anesthetic management of 877 pediatric patients undergoing muscle biopsy for**

**neuromuscular disorders: a 20-year review.** Shapiro F et al. Pediatr Anaesth 2016; 26: 710-721.

- 20-year retrospective review of 877 patients undergoing muscle biopsy at Boston Children's
- Three anesthetic techniques: volatile agents ± succinylcholine, TIVA ± N<sub>2</sub>O and regional.
- No patients exhibited signs of anesthesia-induced muscle injury- MH, rhabdomyolysis, cardiac arrest or postoperative deterioration of weakness.
- Volatile agents and succinylcholine should not be used in children with specific myopathies associated with mutation of ryanodine (RyR1) receptors- King Denborough syndrome and central core myopathy.
- Anesthesia induced rhabdomyolysis is more common than MH in patients with NMD. Acute rhabdomyolysis and life threatening hyperkalemic cardiac arrest has been reported upon exposure to volatile agents and succinylcholine in patients with Duchene's muscular dystrophy and Becker's muscular dystrophy.
- Mitochondrial myopathies present specific challenges: use lactose free glucose containing normal saline for IV fluids, avoid succinylcholine, use volatile agents with caution and avoid high doses or prolonged infusions of propofol.

#### **Utility of screening questionnaire, obesity, neck circumference and sleep polysomnography to predict sleep-disordered breathing in children and adolescents**

Raman VT, et al. Pediatr Anaesth 2016; 26: 655-664.

- This study adapted questions from the pediatric Sleep Related Breathing Disorder questionnaire to develop a six-question scale and combined it with BMI and neck circumference to see if the predictive utility of OSA was enhanced.
- The six-question scale was associated with greater odds of moderate/severe OSA and attained good predictive value. The addition of BMI and neck circumference did not significantly improve predictive value.

**Current landscape of US pediatric anesthesiologists: Demographic characteristics and geographic distribution.** Muffly MK, et al. *Anesth Analg* 2016; 123: 179-85.

- The authors tried to create a comprehensive database of pediatric anesthesiologists in the US. 4048 pediatric anesthesiologists were identified in the US, representing 8.8% of the physician anesthesiology workforce. Approximately 2/3<sup>rd</sup> of them were sub-speciality board certified in pediatric anesthesiology.
- There was substantial heterogeneity in the geographic distribution of pediatric anesthesiologists by state, with urban clustering.

**Use of neuraxial catheters for postoperative analgesia in neonates: A multicenter safety analysis from the pediatric regional anesthesia network.**

Long JB, et al. *Anesth Analg* 2016; 122: 1965-70.

- This study examined the safety of neuraxial catheters in neonates across multiple institutions in the pediatric regional anesthesia network (PRAN).
- Overall incidence of complications was 13.3%- catheter malfunction, catheter contamination and vascular puncture. There were no long-term complications.
- A potentially toxic local anesthetic dose was used in 31% of neonates, especially when bupivacaine was used for postoperative infusion.

**Neurotoxicity, general anesthesia in young children and a survey of current pediatric anesthesia practices at US teaching institutions.**

Ward CG, et al. *Pediatr Anaesth* 2016; 26: 60-65.

- Anesthesia related neurotoxicity is currently a hotly debated topic
- Survey of how academic pediatric anesthesia departments in the US have responded to the issue of anesthesia related neurotoxicity.
- There is no consistent approach to disseminate information to faculty and trainees. 91% of respondents discussed the issue only if the parents asked. 95% of respondents had these discussions with the parents on the day of surgery.
- Only a minority of respondents discuss a safe age cutoff and an age of 3 years as a safe cutoff was used in 19 of 45 programs.
- There is a lack of consensus regarding what constitutes a truly elective procedure.

**Perioperative outcomes and management in pediatric complex cranial vault reconstruction**

Stricker PA, et al. *Anesthesiology* 2017; 126: 00-00

- A multicenter study from the pediatric craniofacial collaborative group that includes 31 institutions in the US.

- 1223 cases were analyzed. 95% of children  $\leq$  24 months of age and 79% of children  $>$  24 months of age received at least one transfusion. There were no deaths.
- Notable complications included cardiac arrest, postoperative seizures, unplanned postoperative mechanical ventilation, large volume transfusion and unplanned second surgeries.
- Utilization of blood conservation techniques was highly variable.

**Anesthesiologist- and system-related risk factors for risk-adjusted pediatric anesthesia-related cardiac arrest.** Zgleszewski SE, et al. *Anesth Analg* 2016; 122:482-9.

- Anesthesia related cardiac arrest (ARCA) is more common in children than adults and two identified risk factors are children  $<$ 1 year of age and ASA status  $\geq$  3.
- Authors analyzed  $>$  300,000 anesthetics at Boston Children's hospital over a 12-year period and identified 72 ARCAs (2.6 per 10,000 anesthetics)
- Risk of ARCA was higher in cardiac patients and when anesthesiologist performed  $<$  150 anesthetics per year or spent  $<$ 30% of annual days delivering anesthetics.

**Lignocaine topicalization of the pediatric airway** (review article)

Roberts MH, Gildersleve CD. *Pediatr Anesth* 2016; 26:337-344.

- Topicalization of the pediatric airway prior to intubation or open airway procedures is a common practice. While there is some evidence that it may reduce perioperative respiratory adverse events such as coughing and laryngospasm, other studies contradict this. Current evidence cannot support its routine use in all children.
- Both topical and intravenous lidocaine attenuate bronchial hyper-reactivity caused by drugs like histamine that increase bronchial tone.
- Current evidence supports a maximum dose of 4 mg/kg
- Topical lidocaine has a fast onset of action. Airway instrumentation can be achieved 1.5-2 minutes after topicalization.
- There is currently insufficient evidence to make formal recommendations on withholding oral intake following topicalization. The author's practice is to withhold oral intake for 1 hour post topicalization.