Pediatric Airway Management in COVID-19 Patients: Consensus Guidelines from the Society for Pediatric Anesthesia's Pediatric Difficult Intubation Collaborative and the Canadian Pediatric Anesthesia Society

Matava C, Kovatsis P, Lee J et al. *Anesthesia and Analgesia*. July 2020; 131 (1): 61-73

Methods

The Paediatric Difficult Intubation Collaborative (PeDI-C) consisting of 44 anaesthesiologists from North America hosted a virtual consensus meeting in March 2020 to produce best practice guidelines on aerosol generating procedures (AGPs) during the COVID-19 pandemic. In addition, a literature search was performed identifying 30 articles relevant to paediatric AGPs and are referenced in the guideline.

PeDI-C Key Recommendations:

1. *Simulation training* should be relevant to the location and healthcare service being provided e.g. peri-operative staff training for intubation and extubation in full personal protective equipment to minimize virus transmission. Clear and carefully planned local *cognitive aids* may improve workflow and patient safety.
2. *Clinical care:* Routine pre-medication administration to children to reduce anxiety and crying. Parental presence at induction is not recommended. Intravenous induction of anaesthesia is preferable but if performing an inhalational induction use the lowest flow possible with a tight facemask seal. Ideally use a videolaryngoscope and neuromuscular blockade to site a cuffed endotracheal tube by a senior anaesthesiologist. However, a laryngeal mask with a good seal is acceptable. PeDI-C outline advanced airway approaches in a difficult airway setting. Consider an extubation technique which minimizes coughing and use in line closed suction if possible.
3. *Staff safety:* Appropriate risk assessment of staff with potential exposure to COVID 19 cases should be performed. Personal protective equipment should be available with training provided in donning and doffing. Essential staff only present during AGPs.

Conclusion

PeDI-C consensus guidelines are based on expert led opinion and aim to promote clinical care provided whilst reducing risk of COVID-19 transmission to healthcare staff.

Reviewed by Dr Kira Achaibar

Multisystem Inflammatory Syndrome in U.S. Children and Adolescents

Feldstein L, Rose E, Horwitz J.P et al. *New England Journal Medicine* July 2020;383:334-46.

Methods

The Overcoming COVID-19 study reports a mixture of prospective and retrospective observational data on cases of multi-system inflammatory syndrome (MIS-C) in children from March to May 2020 across 53 paediatric centres in the USA. The criteria for inclusion were serious illness requiring hospital admission, fever lasting 24 hours, laboratory evidence of inflammation, multi-system organ involvement, positive SARS CoV-2 PCR or antibody test and epidemiological tracing to a COVID-19 positive person within a month.

Results

The authors report on 186 cases of MIS-C during the study period of which 70% tested positive for COVID-19 by PCR or antibody testing and 30% demonstrated contact with a COVID-19 person. The median interval from symptom onset of COVID 19 to MIS-C was 25 days. Demographic data suggests a median age of 8.3 years old, male predominance and 73% pre-morbidly healthy children.

The majority of children with MIS-C developed four or more organ system involvement including: gastrointestinal (92%), cardiac (80%) of which 48% required vasoactive support, haematological (76%), cutaneous (74%) and respiratory (70%). Whilst 80% of children were cared for on the intensive care unit, far fewer required invasive ventilation (20%) or ECMO (4%). The median hospital stay reported was 7 days and mortality (2%).

Discussion

Feldstein et al suggest a strong temporal relationship between confirmed COVID 19 infection and the inflammatory syndrome described but causality cannot be inferred. Younger MIS-C patients <5 years old (40%) demonstrated some features of Kawasaki disease. However, myocardial dysfunction requiring vasoactive drugs was more common in MIS-C (50%) compared to Kawasaki disease (5%). Multiple laboratory inflammatory markers were elevated in MIS-C and patients were often treated with immunomodulation therapies including intravenous immunoglobulin and steroids.

Limitations

This case series is based on wide ranging inclusion criteria hence not all the inflammatory cases presented may be secondary to COVID 19. Establishing accurate onset of COVID 19 infection and accounting for false positive tests was not possible due to some retrospective data collection.

Take Home Message:
Feldstein and colleagues outline the life-threatening presentation and course of multi-system inflammatory syndrome and current treatment strategies being administered in US children.

Reviewed by Dr Kira Achaibar

A Retrospective Analysis of Neuromuscular Blocking Drug Use and Ventilation Technique on Complications in the Pediatric Difficult Intubation Registry Using Propensity Score Matching

Garcia-Marcinkiewicz AG, Adams HD, Gurnaney H, et al. *Anaesthesia and Analgesia* 2020; 131(2):469-479.

The primary aim of this study was to compare the incidence of peri-intubation complications in paediatric patients with anticipated difficult intubation, depending on whether they were managed with spontaneous ventilation or with controlled ventilation.

Methods
This is a retrospective observational study using data from the Pediatric Difficult Intubation Registry - a national US database which collects data on airway management of children with difficult intubation. Data was compiled on ventilation techniques and complications which were categorized severe (e.g. cardiac arrest, death, aspiration) or non-severe (e.g. hypoxia, laryngospasm, bronchospasm), as well as potential confounders such as age, ASA classification, presence of a syndrome and operator experience. In addition to directly comparing incidence of complications between ventilation groups, statistical analysis was performed to account for the effect of potential confounders.

Results
1289 encounters were included – 507 spontaneous ventilation, 453 controlled ventilation with neuromuscular blocking drug (NMBD) and 329 controlled without NMBD. There was no difference in severe complications between the ventilation groups however there was a statistically significant increase in non-severe complications in the spontaneous group (22.5% vs 13.3% in controlled with NMBD and 13.4% in controlled without NMBD). When potential confounders of age, weight, sex, first attempt airway device, clinician type and ASA classification were accounted for, the elevated risk in the spontaneous group remained (OR 1.85). This association was eliminated when the presence of operator-identified airway reactivity (laryngospasm, bronchospasm or coughing) was included in the model.

Conclusions

In this study, managing anticipated difficult paediatric intubation with spontaneous ventilation was associated with a higher incidence of non-severe complications. This was independent of many confounders but not independent of the presence of airway reactivity. This suggests a lighter plane of anaesthesia in the spontaneous ventilation group could contribute, as controlled ventilation generally requires deeper anaesthesia to achieve. Therefore, the authors conclude, whatever technique adequate depth of anaesthesia is vitally important.

Reviewed by Dr Katherine Brooks

Impact of clear fluid fasting on pulmonary aspiration in children undergoing general anesthesia: Results of the German prospective multicenter observational (NiKs) study

Beck CE, Rudolph D, Mahn C, et al. *Pediatric Anesthesia* 2020; 30: 892-899.

The primary aim of this study was to determine whether shorter fasting times for clear fluids or light meals (cereal, toast, dairy products) has an impact on the incidence of regurgitation or pulmonary aspiration under general anaesthesia. Secondarily they intended to assess the effect of age, ASA classification, induction method, airway management, emergency vs elective case and surgical procedure.

Methods

Data collection was carried out in 15 centres in Germany and the Netherlands on a standardised form. Data was collected on demographics, real fasting times - for large and light meals, breastmilk, formula milk and clear fluids - anaesthetic technique, surgical procedure and occurrence of regurgitation or aspiration. Target adverse events were regurgitation, suspected pulmonary aspiration (clinical) and confirmed pulmonary aspiration (bronchoscopic or radiological).

Results

12093 children were included in the study which exceeded the planned 10000 and the sample size needed to demonstrate non-inferiority. Overall rate of regurgitation was 0.26%, suspected aspiration 0.08% and confirmed aspiration 0.03%. There was no significant difference in the rates of these between the 1, 2 and 4 hour clear fluid fasting groups and 1 hour clear fluids fasting was non-inferior to 2 hours. There was an association with higher adverse events in those fasting from clear fluids for less than 1 hour, but this did not remain on multivariate analysis. Age 1-3 years and emergent procedures increased the incidence of adverse events (OR 2.7 and 2.8) but the

other factors from the secondary aim did not. The number of patients with shorter fasting times than recommended for light meals was inadequate.

Conclusions

Clear fluid fasting for 1 hour instead of 2 does not increase the incidence of regurgitation or aspiration; this supports the current advice from multiple organisations including APAGBI. Age 1-3 and emergent procedures are risk factors for these adverse events.

Reviewed by Dr Katherine Brooks

Exposure to Surgery and Anesthesia in Early Childhood and Subsequent Use of Attention Deficit Hyperactivity Disorder Medications

Ing C, Ma X, Sun M, et al. *Anesth Analg* 2020;131(3):723–33.

The issue of long-term neurocognitive effects of exposure to anaesthesia in childhood is hotly debated.

Methods

This retrospective analysis of Texas and New York Medicaid data from 1999 to 2010 identified children exposed to one of four surgical procedures (pylomyotomy, inguinal hernia repair, circumcision and T&As) under 5 years of age (n= 42687) and matched them to non-exposed children (n= 213435) according to available socioeconomic and clinical data using propensity scoring. Children with more than one exposure, or exposure to surgery not listed above, were excluded. The hazard ratio (HR) of persistent ADHD medication use (>2 prescriptions) commencing over six months after exposure was calculated using Cox proportional-hazards models. Analysis of non-ADHD medication use controlled for higher overall rates of medication use in the exposed group.

Results

The authors calculated a HR of 1.37 (95% confidence interval 1.30 - 1.44) in the exposed group, indicating a 37% increased likelihood of use of ADHD medication. They also identified significant increased likelihoods of prescription of anxiolytics (HR 1.37, 95% CI 1.25- 1.51), antidepressants (HR 1.4, 95% CI 1.25- 1.58), antipsychotics (HR 1.31, 95% CI 1.2- 1.44) and mood stabilisers (HR 1.24, 95% CI 1.11- 1.4) in the exposed group. Importantly, negative control analysis indicated a small but significant increased likelihood of use of amoxicillin (HR 1.06, 95% CI 1.04- 1.07), azithromycin (HR 1.1, 95% CI 1.08-1.12) and diphenhydramine (HR 1.08, 95% CI 1.05-1.11) in the exposed group.

Discussion

Retrospective cohort studies are vulnerable to unmeasured confounders, as suggested in the negative control analysis in this study. Additionally, this study does not differentiate the possibly damaging effects of anaesthesia from those of surgery. None the less, it adds further evidence to support a vulnerability within this group of exposed children to neurocognitive diagnoses.

Reviewed by Dr Georgia Ellis

Melatonin for anaesthetic indications in paediatric patients: a systematic review

Procaccini D, Lobner K, Azamfirei R, et al. *Anaesthesia* 2020:anae.15249.

Melatonin is a hormone produced by the pineal gland in response to circadian rhythm and onset of darkness. It has hypnotic, analgesic and anticonvulsant effects. An excellent safety profile makes it an attractive drug for anaesthetic use. This systematic review examines evidence supporting its efficacy.

Methods

PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature, Web of Science and Scopus databases were searched for published studies relating to use of melatonin in anaesthesia in human paediatric populations. Studies were excluded if not in English, or relating to emergence delirium, performance of sleep EEG, or use in chronic disorders.

Results

Twenty-seven studies were included. Two studies (high GRADE rated) related to melatonin as an analgesic, its use was associated with lower pro-inflammatory cytokines and PIPP scores on NICU and a reduction in pain scores for venepuncture. Seventeen studies investigated melatonin use for sedation for MRI or ABR testing. Dosage varied and successful sedation and test completion rates were reported as 50-96% for ABR testing and 44-87% for MRI scanning. Some reported higher success rates with sleep deprivation. The single double blind RCT found no difference between time to deep sedation for MRI when melatonin was added to sedative regimens. The eight remaining studies addressed melatonin for premedication. Three high GRADE score studies found melatonin to be equal or superior to midazolam for anxiolysis. A further study found no difference for sedation and anxiety metrics compared to clonidine. Two studies looking at sedation scores found them to be worse as compared to midazolam, or no better than placebo.

Discussion

A minority of the studies included were placebo controlled and there was significant variation in methodology and research question. However, the authors conclude that melatonin may be of benefit in paediatric anaesthetic practice as an analgesic, procedural sedative, or anaesthetic adjunct.

Reviewed by Dr Georgia Ellis

Incidence of and Factors Associated with Prolonged and Persistent Postoperative Opioid Use in Children 0-18 Years of Age

Ward A, De Sousa E, Miller D, et al. *Anesthesia & Analgesia* 2020;131(4):1237-48

Opioid-naïve children, exposed peri-operatively, are at risk of prolonged opioid use with associated negative health consequences. Paediatric mortality from prescription and illicit opioid use has increased approximately 300% since 1999, with studies quoting rates of prolonged use ranging from 4-15%.

Methods

This was a large retrospective review of all eligible children, opioid-naïve, undergoing a surgical procedure in the US from 2002-2017 who filled an opioid prescription in the 30 days pre and 14 days post-operatively. A control group of children who did not undergo surgery was selected as a comparison. The primary end point was estimation of the percentage of surgical and non-surgical patients with Prolonged Opioid Use after surgery (POUS) and Persistent Postoperative Opioid Use (PPOU). Secondary aims were to identify factors associated with POUS.

Results

There was a higher proportion of POUS in surgical vs non-surgical patients in all age groups. ENT procedures in the <2's was associated with POUS, while in the older age groups a mix of ENT, general, and orthopaedic procedures were associated with POUS. Other associations were age (generally older), history of substance abuse or chronic pain and female gender. The prevalence of POUS in the control group was <1% in <12's and approximately 2% in the 12-18, both lower than the surgical group. These results are consistent with other studies.

Take home message

- Children exposed to opioids for the first time in the perioperative period are at risk of prolonged opioid use
- This risk increases with increasing age, especially in adolescents

- Certain procedures are more positively associated with POUS than others
- Identifying these patients can lead to a more tailored approach to analgesia, especially opioid-sparing techniques
- Appropriate follow-up should be implemented to assess complications

Reviewed by Dr Stephen Meneely

Association between preoperative hemoglobin levels after iron supplementation and perioperative blood transfusion requirements in children undergoing scoliosis surgery

Switzer T, Naraine N, Chamlati R et al. *Pediatric Anaesthesia* 2020;30:1077-1082

The prevalence of anaemia in children undergoing posterior spinal fusion (PSF) is reported at 14%. Anaemia and peri-operative blood transfusion are associated with morbidity and mortality.

Methods

This was a retrospective review of patients undergoing PSF between 2013 and 2017 at The Hospital for Sick Children, Toronto. All children <18 who attended the Patient Blood Management (PBM) clinic and received oral iron were included. Those without a preoperative Hb or those who had a transfusion <72 hours pre surgery were excluded. The primary end point was the association between preoperative Hb levels and perioperative exposure to red blood cells (RBC's) in patients treated with iron.

Results

382 patients were included, median age 15, 76% female and 69% had idiopathic scoliosis. 49% received an allogeneic RBC transfusion during their hospital stay with 46% receiving an intraoperative transfusion. The higher dose (6mg/kg) was not protective against transfusion compared to 2mg/kg. Risk factors for intraoperative transfusion included non-idiopathic scoliosis, Cobb angle and number of vertebrae fused. Patients with Hb >130 g/L were significantly less likely to receive a transfusion than those <130g/L. No association was found between dose or duration of therapy and transfusion requirements. Females had significantly lower Hb and ferritin but this was not associated with increased transfusion requirements.

Conclusion

The transfusion rate of 49% in this study is less than the 67% quoted in a large north American database, indicating efficacy of PBM clinics. This can lead to reduced morbidity and shorter hospital stays, particularly relevant to higher-risk patients.

Potential issues with this study are the inability to measure compliance with therapy, not measuring the starting Hb/ferritin level, and not standardising the treatment, all of which could introduce bias to the results.

Take home message

The role of PBM programs are to promote blood conservation by identifying at risk patients and using multi-modal strategies to improve outcomes.

Anaemia is common in patients having PSF and is associated with worse outcomes. Identifying these patients and initiating early iron therapy can reduce perioperative adverse events including needing transfusions. Optimal dose and duration of therapy has not been established.

Reviewed by Dr Stephen Meneely

Edited by Dr Christa Morrison