Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe

Walid Habre et al for the APRICOT Group of the European Society of Anaesthesiology Clinical Trial Network. Lancet Respir Med 2017; 5: 412–25

This prospective observational cohort study was designed to look at the incidence nature and outcome of severe critical events in children undergoing anaesthesia. Children from birth to 15 years were recruited over two consecutive weeks in 261 hospitals across 33 countries in Europe. All children undergoing sedation, general anaesthesia or regional anaesthesia were included. Although enrolment was voluntary, the identification of complications was anonymous. A severe critical event was defined as a respiratory, allergic or neurological complication that required immediate intervention and that led or could have led to major disability or death. Out of 31127 anaesthetics (30874 patients), the study found an incidence of severe critical events of 5.2 % (95%CI 5.0 – 5.5). There was an immediate poor outcome in 5.4% of these cases. The incidence of severe critical respiratory events (laryngospasm, bronchospasm, bronchial aspiration and post-anaesthesia stridor) was 3.1 % while the incidence of cardiovascular critical events was 1.9 %. All-cause 30-day in hospital mortality was 10 in 10 000. None of the deaths were anaesthesia related.

Age was a risk factor for respiratory critical events with a decrease of 12 % in the risk of respiratory events for each 1-year increase in age. Univariate analysis showed that a History of prematurity increased the relative risk of critical respiratory complications by a factor of almost 2. The incidence of critical cardiovascular and respiratory critical events was higher in neonates and in infants. Medical history and physical condition were also major risk factors for critical events with severe critical events were more frequent with increased ASA. There was some evidence on multivariate analysis of beneficial effect of the experience of the most senior anaesthetist for cardiovascular and respiratory critical events rather than the type of institution or providers.

The authors conclude in their discussion that the large variations in paediatric anaesthesia practice highlight the need for more widespread implementation of good clinical practice guidelines and standards of paediatric anaesthesia management across Europe. They also concluded that there is a significantly higher incidence of both respiratory and cardiac severe critical events in children up to 6. The ROC characteristics suggest that children younger than 3 to 3.5 years should be managed by tertiary care providers or by anaesthesiologists with specific paediatric training in order to reduce the occurrence and improve the outcome of peri-anaesthetic severe critical events. Identifying an age that might be considered as a threshold for allocating children to centres with specialist paediatric practices or paediatric anaesthesiologists is a matter of debate in many European countries and anaesthesia societies.

Take Home Message

Are these recommendations applicable to the Australian and New Zealand context? We are looking at a very heterogenous collection of institutions. One can only assume that the models of training of anaesthesia providers, the model of care provision and the allocation of resources would be quite different across the different countries. In Australia and New Zealand the model of care is uniform as is training of anaesthetists. One would expect little variation in paediatric anaesthesia practice in our context. Identifying an age cut off has already been done in Australia and New Zealand with ANZCA stating that anaesthetists who have obtained fellowship are able to care for children 2 years and older. In our context where geography places a large proportion of the population in rural and remote locations, the use of an age cut off to dictate the need for tertiary care is both simplistic and impractical. Rather an emphasis should be to care for children as close to home as possible where clinically appropriate with support and guidance offered to health services and clinicians that seek to provide this care.

Reviewed by: Dr Catherine Olweny

Reducing risk in pediatric anesthesia: What are the implications from the APRICOT study?
A Wolf
Pediatric Anesthesia 2017;27:674-675

The Apricot study was a prospective observational multi-centre cohort study which prospectively collected data on paediatric anaesthesia practice across Europe over a 2 week period. All serious adverse events were recorded in detail and followed up for 30 days. The study identified that anaesthesia was riskier in younger child, neonates and infants and patients classified as ASA III and above. Most critical events were respiratory or cardiovascular. There was a positive effect of a higher level of experience and caseload of the anaesthetist. No 30 day mortality was deemed anaesthesia related.

The push to centralise specialised paediatric practice may mean that smaller peripheral centres have less exposure to anaesthesia in children. Close communication between specialised paediatric centres and regional hospitals is essential for education and high quality care of complex children.

Reviewed by Dr Khoon Chang

Differences in Blood Pressure in Infants After General Anesthesia Compared to Awake Regional Anesthesia (GAS Study—A Prospective Randomized Trial)
M.E. McCann et al
Anesth Analg 2017;125:837–45

This paper examines the incidence of intraoperative hypotension in children recruited in the GAS study. The GAS study is a well-known multi-centre prospective randomized trial, designed to determine whether general (GA) and regional anesthesia (RA) have long-term effects on the developing brain.

A total 722 infants undergoing inguinal hernia repairs were randomized to RA or GA. The RA arm received either Spinal Anaesthesia +/- caudal or ilioinguinal block or Caudal Anaesthesia. The type of local anaesthetic used was either bupivacaine or levobupivacaine. The GA arm received sevoflurane in air and oxygen for induction and maintenance with either caudal or ilioinguinal block for intraoperative and postoperative analgesia. No opioids were used.

The paper presents analysis as intention to treat (ITT) and a secondary 'as per protocol' (APP) analysis. The APP excludes protocol violations such as children who received sevoflurane or sedative medication in the RA arm. Hypotension was defined by MAP < 45mmHg and moderate hypotension by MAP < 35mmHg. The primary outcome for this study was at least one epoch (measurement during 5 minute interval) of moderate hypotension.

The relative risk (RR) of GA compared with RA for any epoch of moderate hypotension was 2.8 (CI, 2.0–4.1; P < .001) by ITT analysis and 4.5 (CI, 2.7–7.4, P < .001) by APP analysis. The GA group was also associated with a higher incidence of any hypotension for single and multiple measurements (87% vs 41%). The mean MAP for the GA group was 10mmHg lower than the MAP for the RA group across pre-incision, surgical and anaesthetic time periods. Weight at the time of surgery and minimum intraoperative temperature were also independent risk factors for moderate hypotension.

Take Home message / Commentary
General anaesthesia is much more likely to cause hypotension than regional anaesthesia for infants requiring inguinal hernia surgery. It is interesting to note that the 2-year interim neurocognitive outcomes were no different for the GA vs RA groups (Lancet 387:239–250). We await the publication of final 5-year neurocognitive assessments. Whilst there is a concern about the possibility of neurotoxicity from anaesthetic agents, there is also a growing awareness for the need to maintain normal physiological parameters (e.g. Safetots initiative).

Reviewed by: Dr Ben Van der Griend

Videolaryngoscopy versus Fiberoptic Intubation through a Supraglottic Airway in Children with a Difficult Airway: An Analysis from the Multicenter Pediatric Difficult Intubation Registry.

N.E. Burjek et al

Anesthesiology 2017; 127:432-40

This study used the Paediatric Difficult Intubation (PeDI) registry to compare the success rates of fibre-optic intubation via supraglottic airway (FOI-SGA) to videolaryngoscopy (VL) in children with difficult airways. The PeDI registry collects data from 14 academic children's hospitals in the United States. The paper lists the criteria for inclusion in this study, but to summarise, includes children (<18yrs) with difficult airways as defined by Cormack and Lahane grade =/> 3, children with anatomic or cranial-facial abnormalities meaning direct laryngoscopy (DL) was not possible, children with previous history of failed DL within the last 6 months and those children whereby physical examination is predictive of difficult DL.

1,603 difficult airway cases were identified over approximately 3.5 years. Of these, FOI-SGA was attempted as the first airway management strategy in 90 patients and after failed DL in 24 patients (114 total patients). FOI-SGA was successful on the first attempt in 67 of 114 (59%) cases and ultimately successful in 101 (89%) of cases. VL was attempted as the first airway management technique in 407 patients and after failed DL in 379 patients (786 total). VL was successful on the first attempt in 404 of 786 (51%) cases and ultimately successful in 620 (79%) cases. For infants (<1 yr), FOI-SGA had a significantly higher first-attempt success rate (19 of 35, 54%) compared to VL (79 of 220, 36%). There were no differences in complication rates for the 2 techniques.

Take Home Message

FOI-SGA and VL have similar first-attempt success rates for intubating children with difficult airways. However, for infants, FOI-SGA had a higher rate of first-attempt success. Overall, there were also fewer intubation attempts with the FOI-SGA technique.

Reviewed by: Dr Ben Van der Griend

An Evaluation of the mixed pediatric unit for blood loss replacement in pediatric craniofacial surgery
S Mogensen, N Lubenow, P Nilsson, H Engquist, F Knutsson, P Enblad, D Nowinski & P Frykholm
Pediatric Anesthesia 27 (2017) 711-717

In this prospective cohort study, 19 patients which were compared to 21 historical controls. It aimed to find out if less blood in total would be transfused if mixed paediatric units (MPU) were used. The MPU was made by diluting one adult RBC unit with a plasma bag from another donor. This unit was then divided into 2, one intended for intraoperative use and the other for postoperative use.

In the study group, Isovolaemic haemodilution with dextrose 2.5% in saline 20ml/kg was used during preparation for surgery. The transfusion trigger was a Haemoglobin less than 9g/dl and ongoing haemorrhage, mean arterial pressure less than 40-45mmHg, a reduction of CVP from baseline and peripheral hypoperfusion. The target haemoglobin post op was 10.5-11 g/dl if there was any blood left in the bag intended for intra operative use. In the historical group, haemodilution was used as in the study group as well as predilution with albumin at the discretion of anaesthesiologist. The Intra-operative transfusion trigger was variable and transfusion of packed red cells and FFP was used following a 1:1 ratio. Postoperatively patients were transfused if the Hb was less than 10g/dl.

There was no difference between the 2 groups for estimated blood volume (EBV), Estimated Blood Loss (EBL) or total volume of crystalloids received. Intra-operative transfusion volumes were significantly reduced in study group but not total perioperative transfusion volumes. The study group received significantly more colloids than the historical group. All children in the study group received at least one MPU. No statistical difference was found in the amount of postoperative transfusion required in the historical group

Comments
This study was limited by the small study group and the use of an historical control group. A high transfusion threshold was used which may have resulted in unnecessary transfusion. The MPU method resulted in patients being exposed to 2 donors up front and patients received plasma prophylactically by virtue of the study design. This may not have been clinically indicated otherwise. I was not convinced after reading this study that there was a role for MPU in craniofacial surgery.

Reviewed by: Dr Khoon Chang

Malignant Hyperthermia Susceptibility and Related Diseases
RS Litman, SM Griggs, BS Jame et al.
Anesthesiology 2018; 128:159-67

This paper provides an excellent overview of the genetic pathophysiological basis for MH susceptibility in a number of diseases. MH susceptibility most commonly results from RYR1 receptor variants. Mutations may be new mutations or may be inherited. It is important to note that the MH phenotype has variable expressivity and has incomplete penetrance. Therefore, the clinical spectrum of the ryanodinopathies is broad, and can vary even within the same family where the genetic cause is the same. There is a wide range of dominant and recessive disorder that are associated with pathogenic variants of RYR1 receptor. Some clinicians have taken the approach of assuming that all patients with non specific myopathy but with no definitive diagnosis are MH susceptible. The authors feels that this results in inaccurate labelling of patients and their families who would otherwise be able to safely receive volatile. The paper offers suggestions to anaesthesiologist on the types of patients who should receive a trigger-free anaesthetic, the management of congenital myopathies that may predispose to MH-like symptoms and an approach to the anaesthetic management of the undiagnosed patient with muscle weakness.

Take Home Messages

Congenital Myopathies Associated with MH

Some patients with RYR1 variant demonstrate clinically evident myopathy. RYR1 variants are the most common cause of non-dystrophic muscle disease in children. In addition to the RYR1 gene, less common loci of causality of MH susceptibility (approximately 2 % f cases) are variants in the alpha-1 subunit of the dihydropyridine-sensitive L-type voltage-dependent calcium-channel receptor (CACNA1S) which is also part of the excitation contraction complex in skeletal muscle. Another uncommon locus for MH susceptibility is the STAC3 gene. These variants are manifested most commonly as Native American Myopathy. The article contains a diagram that shows precisely where the causative mutations have their effect.

Of the numerous histopathological subtypes of congenital myopathy, only those with RYR1, CACNA1S and STAC3 variants are linked to MH susceptibility. However, if these patients have a phenotypic diagnosis (histological findings on muscle biopsy plus clinical characteristics) but no confirmatory genetic diagnosis, they are all assumed to be MH susceptible.

Rhabdomyolysis

Most patients who have a demonstrated clinical MH and have an RYR1 variant, appear clinically normal. Some of these phenotypically normal patients may develop rhabdomyolysis in response to heat, exercise, statin administration or a viral illness. MH-related RYR1 variants may account for 20 to 30 percent heat or exercise-induced rhabdomyolysis. (some may have baseline elevated CK or bleeding tendency). Patients without a phenotypic or genotypic diagnosis that have demonstrated exaggerated or frequent rhabdomyolysis under normal or atypical conditions should be assumed to have an underlying MH susceptible RYR1 pathogenic variant and should not receive triggering agents.

Approach to the Undiagnosed Hypotonic Patient

The authors are of the opinion that it would be unreasonably cautious to consider all hypotonic patients (and their extended families) to be MH susceptible. Most hypotonia in children is central in origin and in neonates with hypotonia, nearly all underlying diagnoses are not associated with increased risk of MH. Ideally infants with hypotonia should have a neurological consult to provide the anaesthesia team with the best possible information about their diagnosis and risk of MH. The authors recommend genetic testing before muscle biopsy as RYR1 variants constitute the most common non-dystrophic type of congenital muscle disease.

In older children with weakness where a muscle disease may be suspected, non-triggering anaesthesia may be used but the authors sate that this may be overcautious as the risk of MH with a triggering agent is extremely small. The decision about the most appropriate anaesthetic technique should be discussed beforehand, with the surgical team as well as with the patient and/or their parents when applicable, especially when the diagnosis is unknown.

Patients should be considered MH-susceptible if they possess one of the following:

1. Statement saying that they or one of their close family members is suspected of having RYR1, CACNA1S or STAC3 related myopathy on history of physical findings.
2. Personal a close family history of suspected MH during triggering anaesthetic in the absence of negative contracture biopsy.
3. Personal or close family history of frequent exaggerated episodes of CK rise, rigidity or evidence of rhabdomyolysis in response to exercise, heat or statins.

Reviewed by: Dr Catherine Olweny

Effects of intravenous fentanyl around the end of surgery on emergence agitation in children: Systematic review and meta-analysis

Kim N et al

Pediatric Anesthesia 2017;27:885-892

This systematic review and meta-analysis was conducted to examine the **prophylactic** use of fentanyl around the end of surgery to prevent emergence agitation (EA) and its potentially side-effects.

Methods

The study was conducted in accordance with PRISMA recommendations. The authors included prospective randomised controlled trials that compared fentanyl (1mcg/kg) and placebo administered around the end of surgery for the prevention of EA after GA in children between birth and 14 years of age. The search and data collection was conducted by independent authors and 10 studies were included in the final meta-analysis. The authors also examined the risk of bias.

Results

Intravenous fentanyl 1mcg/kg at the end of surgery significantly decreased the incidence of EA in children following general anaesthesia with sevoflurane maintenance (RR 0.43, 95%CI 0.35-0.53). In some studies, the fentanyl 1mcg/kg was given at the end of surgery and in others 10-20 minutes prior to the end of surgery with the pooled RRs of EA incidence being similar in both groups. Although fentanyl dosing was similar, assessment of EA was done with a variety of scoring systems in the different studies (only 2 studies used the validated PAED scale).

In subgroup analyses fentanyl administration at the end of surgery prolonged the PACU stay but this was not the case in patients who received fentanyl 10-20 minutes before the end of surgery. Similarly, fentanyl at the end of surgery significantly increased the incidence of PONV but this was not the case if it was given 10-20 minutes before the end of surgery. Other adverse events did not occur more frequently in children who received fentanyl compared to placebo.

Take Home Message

This systematic review and meta-analysis suggests that the use of fentanyl intravenously at a dose of 1mcg/kg around the end of surgery reduced the incidence of EA although it should be given 10-20 minutes before the end of surgery to prevent prolonged PACU stays or increased PONV. Things to note are the possibility of publication bias (the Egger test performed by the authors did indicate the possibility of publication bias), the large variation in age included (between birth and 14 years) as well as variability in EA scoring systems – all of which may potentially affect the results.

Reviewed by Su May Koh

The role of ultrasound in appropriate endotracheal tube size selection in pediatric patients
Altun et al,
Pediatric Anesthesia. 2017;27:1015–1020.

Correctly selecting the appropriate endotracheal tube size in children is a dark art, and these authors sought to bring it closer to science. They compared ultrasound measurements, age and height based methods of tube selection against a "best fit" cuffed tube size (avoiding excessive leak, or inadequate seal after placement), and noted the tube exchange rates whilst optimising the tube size according to the "best fit" definitions. They found that ultrasound measurements of the airway were a reliable method of tube size selection, more so than age or height based methods. A "best fit" was achieved 88% of the time with ultrasound, versus 44% with age and 46% with height based methods.

Take Home Message
Few anaesthetists would admit to an inability to choose the correct tube size for our patients, but we all know that exchanging a tube is relatively common. This study suggests that a simple measurement is substantially better than our guesswork. It's up to us to decide whether the inconvenience of an extra pre-intubation step is preferable to the added cost of a few extra tubes and a bit more of a sore throat for the patient.

Reviewed by Justin Skowno