



Pre-operative fasting in children. A guideline from the European Society of Anaesthesiology and Intensive Care.

Frykholm P, Disma N, Andersson H et al. Eur J Anaesthesiol. 2022; 39:4–25

Traditional pre-operative fasting recommendations often translate to excessive starvation times in children, with associated adverse consequences for physiology and well-being. Combined with the rarity of clinically significant pulmonary aspiration, many institutions now favour a more liberal policy. Indeed, since 2018 the APAGBI has advocated a 1h fasting window for clear fluids prior to elective surgery.

This comprehensive review from the ESAIC employs a detailed and robust methodology to provide a series of graded recommendations and suggestions to help guide clinician decision making and allow institutions to develop appropriate protocols. As well as clear fluids, the impact of different food and milk types, presence of co-morbidities, medications and prematurity, and the role of gastric ultrasound are analysed. A detailed literature search resulted in 28,000 articles screened for inclusion, of which 125 were ultimately analysed. Articles were assessed for risk of bias according to Cochrane guidelines, and GRADE definitions used to assess methodological quality. Following this, a three-stage Delphi process was used to produce 26 recommendations and suggestions, with expert panel members from a number of international paediatric anaesthesia societies.

The recommendations and suggestions are divided into the categories of:

- Clear fluid fasting
- Semi-solids and solids
- Co-morbidities, medications and prematurity
- Gastric ultrasound
- Post-operative fasting

The associated evidence base is clearly detailed both in text and tabular form and provides a comprehensive reference for clinicians.

The fasting recommendation of 6h for solids, 4h for formula and non-human milk, 3h for breast milk and 1h for clear fluids is just the tip of the iceberg of the detailed discussion presented. Several areas for future research are highlighted, including what actually constitutes a 'light breakfast', what the emerging role of pre-operative gastric ultrasound is, and the need for large observational studies to provide big-data in a field where randomised controlled trials are often unfeasible.

Reviewed by Dr. Matthew Sinnott

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Intraoperative Hypotension and Acute Kidney Injury after Non-cardiac Surgery in Infants and Children: A Retrospective Cohort Analysis

Schacham NY, Chhabada S, Efunne PN, Pu X, Liu L, Yang D, Raza PC, Szmuk P, Sessler DI.
Anesthesiology 2022; 136:93–103

While age and sex specific normograms for paediatric blood pressure ranges exist, there is no consensus definition for intra-operative hypotension, nor are there known thresholds for harm. In adults, there is a clear association between intra-operative hypotension and the development of post-operative AKI. This cohort study aimed to assess the impact of both absolute and relative blood pressure reduction on the odds of AKI development in paediatric patients (≥ 37 weeks and < 18 years) undergoing non-cardiac surgery under general anaesthesia, of duration ≥ 60 minutes.

A total of 4,506 patients were included in the analysis, with an incidence of AKI (according to KDIGO criteria) of 11% (7.6% stage 1, 2.6% stage 2, and 0.9% stage 3). This likely over-represents AKI rates as healthy patients undergoing day surgery and patients not requiring post-operative creatinine measurement would presumably lower it. Similarly, the increased AKI risk observed in younger patients may reflect a measurement bias as the difficulty of blood sampling in younger patients means only the sickest patients may have had post-operative samples taken.

In contrast with adults, neither absolute nor relative hypotension were found to be associated with risk of AKI. While the total sample size was lower than initially predicted, the power of the study was still 0.9 so this conclusion is unlikely to be a false negative. The authors postulate that paediatric autoregulation may be more robust than that of adults, in part due to the relative rarity of acquired disease states including chronic arterial hypertension, generalised atherosclerosis and type 2 diabetes mellitus. The authors conclude that while hypotension may result in other end organ dysfunction, and presumably there *is* a blood pressure at which renal injury will occur, hypotension should not be the primary concern of clinicians attempting to reduce AKI incidence in paediatric surgical patients.

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The Association Between Race and Adverse Postoperative Outcomes in Children With Congenital Heart Disease Undergoing Non-cardiac Surgery

Nasr V, Staffa S, DiNardo J, et al. *Anaesthesia and Analgesia* 2022; 134: 357-68

Background

An improvement in multidisciplinary services for children with congenital heart disease (CHD) has led to improved outcomes and an increase in children with CHD presenting for non-cardiac surgery. Studies looking at outcomes in low risk paediatric populations have shown poorer perioperative outcomes in Black children. This study addresses this issue in the higher risk CHD cohort.

Methods

Retrospective analysis of children in ACS-NSQIP database with CHD between 2012-2018 was carried out. Children with race defined as White or Black were included with all other races excluded. CHD was stratified into minor, major or severe based on functional status and residual lesion. The Primary Outcome was 30 day Mortality and secondary the incidence of major postoperative complications. Black children had a higher incidence of preoperative comorbidities likely to predispose to worse outcomes so propensity score matching was used to adjust for this.

Results

55'859 children with CHD were identified (76% White and 19.4% Black). Children were well matched as a full cohort and within CHD severity groups. As a full cohort there was a significantly increased incidence of 30 day mortality, cardiac arrest, 30 day reoperation and reintubation in Black patients. In the minor CHD group rates of cardiac arrest, 30 day reoperation and thromboembolic events were significantly higher and 30 day mortality and reintubation were significantly higher in the major CHD group. There were no significant differences in primary or secondary outcomes in the severe CHD group.

Discussion

There is a significant increase in perioperative mortality and morbidity for Black children with minor and major CHD undergoing non-cardiac surgery. The mechanisms of this disparity are unclear and further studies looking at individual risk factors, attitudes within healthcare, institutional variability and healthcare access are required.

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Prophylactic progesterone prevents adverse behavioural and neurocognitive effects of neonatal anaesthesia exposure in rat

Wali B, Sayeed I, Stein DG, et al. *British Journal of Anaesthesia* 2022; 128(2): 301-310

Background

Human and animal studies show an association between neonatal anaesthesia and long-term neurocognitive issues. It is important to validate this association and find ways to protect the developing brain. Neuroinflammatory mechanisms could be causative in long-term behavioural dysfunction following anaesthesia. This study in rats aims to assess whether prophylactic treatment with progesterone attenuates the inflammatory response to anaesthesia and reduces neurocognitive harm.

Methods

127 rats divided into 4 groups, were exposed to 30% Oxygen with or without 2.5% Sevoflurane, after injection of a vehicle (2-hydroxypropyl- β -cyclodextrin) or progesterone (2mg/kg). Exposures took place on postnatal (PND) days 7, 10 and 13 for a total of 6 hours. Plasma samples taken from 49 rats immediately following the third exposure were analysed for quantities of inflammatory cytokines and chemokines. The remaining 77 rats underwent neurocognitive testing for anxiety-like behaviour, memory and spatial navigation on PND 27 + 45.

Results

Inflammatory markers: There was a significant increase in IFN- γ , IL-6 and CXCL1 in rats exposed to Sevoflurane compared to controls. Prophylactic progesterone reduced CXCL1 production but did not reduce IFN- γ and IL-6 in groups exposed to Sevoflurane.

Neurocognitive: Rats with Sevoflurane exposure showed a significant increase in anxiety-like behaviours at both PND 27 and 45. Prophylactic progesterone reduced anxiety-like behaviours in rats given Sevoflurane. Learning and memory were also significantly reduced in those exposed to Sevoflurane, this was also attenuated by progesterone.

Discussion

Repeated anaesthesia increased pro-inflammatory markers, and impaired learning, memory and behaviour in rats. Progesterone attenuates the inflammatory response and neurocognitive effects of repeated anaesthesia. These inflammatory markers could be used to assess whether mode of anaesthesia impacts neuroinflammation. The use of progesterone appears promising however, further studies are needed to establish dosing and validate results of this pre-clinical study for human trials.

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Emergence agitation in paediatric day case surgery *A randomized, single-blinded study comparing narcotrend and heart rate variability with standard monitoring*

Larsen LG, Wegger M, Le Greves S et al. *Eur J Anaesthesiol* 2022; 39: 261 – 268

Postoperative agitation is estimated to affect 10-80% of children, causing significant distress and disturbance. Whilst predisposing factors include inhalational anaesthesia and preschool age, tools available to reduce its incidence are limited.

This study investigated whether narcotrend EEG depth-of-anaesthesia (DOA), or heart rate variability (HRV) monitoring (to detect nociceptive stimulus and guide analgesia administration) could reduce post-operative delirium compared to standard monitoring and clinical titration. Narcotrend implements age-related algorithms with promising results in young children.

Analysis was performed on 93 children, aged 1-6 years, undergoing minor general day case surgery. Primary outcome was postoperative agitation with a Richmond Agitation-Sedation Scale score of >0. Secondary outcomes included intra-operative airway events, total intraoperative fentanyl dose, time in post-anaesthetic care unit (PACU), post-operative nausea and vomiting (PONV) and pain.

All cases were maintained at 0.9-1.1 mean alveolar concentration sevoflurane, received simple analgesia, 2-4 µg/Kg fentanyl, local anaesthetic infiltration or caudal anesthesia and standard monitoring.

Intervention groups additionally received either HRV monitoring, and additional doses of 1 µg/Kg fentanyl when the AWI threshold reached -50; or DOA monitoring, with sevoflurane adjusted to maintain an index of 40-60.

Postoperative agitation incidence varied significantly between groups ($p=0.016$; 48% standard, 30% HRV, 65% DOA). However, pairwise analysis showed **no** significant difference between the intervention groups and standard management.

The HRV group received statistically significant, but clinically modest increased total fentanyl doses (3 vs 2.56 and 2.68 µg/Kg for standard and DOA groups respectively). Baseline characteristics and secondary outcomes (including PACU duration and PONV) were comparable between groups.

This study showed that HRV monitoring led to a non-significant reduction in emergence delirium, and statistically significant increase in fentanyl dose, with no negative consequences when compared to 'standard' practice. However, the theory that inadequate intraoperative analgesia may contribute to postoperative agitation, and a role for HRV monitoring, warrants further investigation.

Reviewed by Dr. Rebecca Harris

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Peri-operative red blood cell transfusion in neonates and infants: NEonate and Children audit of Anaesthesia pRactice IN Europe (NECTARINE) A prospective European multicentre observational study

Fuchs A, Disma N, Virag K et al. *Eur J Anaesthesiol* 2022; **39**: 252-260

There is no international consensus on transfusion triggers for neonates and young infants, and the increasing physiological anaemia of the first three weeks of life complicates determining appropriate thresholds.

NECTARINE studied perioperative critical events amongst 6542 procedures performed under 60 weeks post-menstrual age across 31 countries. 447 (6.9%) required perioperative red blood cell (RBC) for anaemia and/or cardiovascular instability. This study sought to determine the transfusion triggers used in clinical practice and morbidity and mortality of those receiving RBC in their first, second and third weeks of life.

Key findings:

- There was large variability in haemoglobin concentrations triggering transfusion (7.3 – 10.9 g.dL⁻¹)
- Thresholds were surprisingly lower than existing national guidelines recommend. Median triggers were 9.6 g.dL⁻¹ (10 - 13 g.dL⁻¹ recommended), 9.6 g.dL⁻¹ (9.5 – 12.5 g.dL⁻¹ recommended) and 8 g.dL⁻¹ (8.5 – 11 g.dL⁻¹ recommended) in the first, second and third week of life respectively
- Thirty-day morbidity was 47.8% and overall mortality 11.3% in those receiving RBC, with a four-fold and five-fold increased risk of morbidity and mortality respectively compared to those who received no transfusion
- Transfusion in the second week of life was associated with highest mortality. This group also contained the highest proportion of i) young gestational age, ii) ASA 3, iii) cardiac surgery and iv) largest volume transfusion patients. It was unclear whether these characteristics reflect an intrinsic vulnerability or higher risk for poor outcome after transfusion
- Statistical analysis was unable to identify a transfusion volume threshold influencing mortality and morbidity (median transfusion volume 17.1 ml/kg)

Haemoglobin concentration is only one of many objective parameters and clinical signs that transfusion is required. Whilst the study design had several limitations for understanding this complex issue, the considerable mortality and morbidity reported following RBC transfusion highlights the critical need for further research to inform evidence-based guidelines in this unique cohort.

Reviewed by Dr. Rebecca Harris

Edited by Dr. Kira Achaibar (APAGBI Trainee Representative)

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