Conservative versus liberal oxygenation targets in critically ill children (Oxy-PICU): a UK multicentre, open, parallel group, randomised clinical trial

Peters M et al. ***Lancet 2024;*** **403: 355–64 DOI: 10.1016/S0140-6736(23)01968-2**

Population	1872 children from 38 weeks corrected gestational age to <16 years receiving invasive mechanical ventilation with supplemental oxygen, admitted to a participating paediatric ICU (PICU) as an emergency with face-to-face contact with PICU or emergency transport services staff
Intervention	**Conservative oxygenation target**: SpO_2 target 88-92%
Comparison	**Liberal oxygenation target**: SpO_2 target >94%
Outcome	**Primary**: duration of organ support at 30 days following random allocation **Secondary**: mortality at PICU discharge and 30 days; duration of organ support, functional status at PICU discharge, length of PICU and acute hospital stay, incremental costs at 30 days.

Primary outcome:

- **Duration of organ support or death at 30 days was lower in the conservative group** with a probabilistic index of 0.53 (p=0.04), suggesting a higher probability for a better outcome.

Secondary outcomes:

- **Duration of invasive mechanical ventilation was shorter in the conservative group and incremental costs lower**.
- Mortality at PICU discharge and at 30 days, proportion of participants receiving non-invasive respiratory support and cardiovascular support were similar between groups. Receipt of renal and other types of organ support was low in both groups.

Further commentary:

- Authors did not detect any clinical important harm associated with lower oxygen targets.
- **Strengths**: inclusion of 15/28 UK PICUs increases representation and generalisability. Appropriately powered. Wide case-mix.
- **Weaknesses**: atypical case-mix with fewer lower respiratory tract infections (lockdown during COVID-19), exclusion of those with congenital cardiac disease and acute encephalopathy due to lack of clinical equipoise regarding oxygen targets, lack of clinician blinding due to pragmatic approach, patients in conservative group spending large proportion of time above conservative target due to lack of need for supplemental oxygen.

Reviewed by Dr Edmund Chan

The MAGIC trial: a pragmatic, multicentre, parallel, noninferiority, randomised trial of melatonin versus midazolam in the premedication of anxious children attending for elective surgery under general anaesthesia

Bolt R et al. *BJA 2024*; 132 (1): 76-85 DOI: 10.1016/j.bja.2023.10.011

Population	110 ASA 1-2 anxious children between 3-14 years undergoing day-case elective surgery under a general anaesthetic
Intervention	Melantonin 0.5mgKg^{-1}
Comparison	Midazolam 0.5mgKg^{-1}
Outcome	Primary: modified Yale Preoperative Anxiety Scale – Short Form (mYPAS-SF) measured at start of transfer to theatre, entry into anaesthetic room, and administration of anaesthesia. Secondary: other measures to assess patient and caregiver preoperative anxiety and postoperative child recovery, including longer-term measurement of anaesthetic impact at 2 weeks post-surgery.

Primary outcome:

- The adjusted mean difference in mYPAS-SF scores showed clinical superiority of midazolam compared with melantonin in reducing preoperative anxiety.
- The calculated sample size required was 624, assuming 90% power and a noninferiority margin of 4.3 on the mYPAS scale. However, the trial was terminated early due to recruitment futility, leading to underpowering and it being prone to bias. Despite this, the magnitude of difference in mYPAS scoring between the two groups led the authors to concluding that superiority of midazolam is clinically meaningful.

Secondary outcomes:

- No difference was noted between melatonin and midazolam in terms of emergence delirium and sedation recovery.
- No difference in anaesthetic recovery time between melatonin and midazolam.
- Slightly more adverse events were noted in the midazolam arm when compared with the melatonin arm (13 v 9), but only 1 was potentially linked to midazolam (nightmares). Most of these were mild (21/34, 62%) requiring no action, and no serious adverse events were reported.
- All secondary outcomes need to be carefully interpreted due to underpowering.

Reviewed by Dr Edmund Chan

Reducing the carbon footprint of general anaesthesia: a comparison of total intravenous anaesthesia vs. a mixed anaesthetic strategy in 47,157 adult patients

Bernat et al. ***Anaesthesia 79.3 (2024):*** **309-317 DOI: 10.1111/anae.16221**

Retrospective study of two French hospitals to evaluate carbon footprint of total intravenous anaesthesia (TIVA) strategy vs a mixed strategy of both intravenous and volatile anaesthetics. The environmental impact of 41,157 general and regional anaesthetics over two years was calculated using global warming potential (GWP) and carbon dioxide equivalent (CO_2e), using patient demographics, analysis of surgery conducted and pharmacy procurement records.

Results:
Analysis of TIVA strategy (n = 25,137) and mixed strategy (n = 22,020) displayed a vastly different carbon dioxide equivalent with 2.42kg CO_2e and 48.85kg CO_2e per intervention respectively. This represents a 20-fold reduction in greenhouse gas emissions in TIVA based anaesthetics compared to a mixed propofol/volatile regimen.
Over the two year study period, plastic waste was estimated as 1627kg vs 733kg in the TIVA strategy vs the mixed strategy respectively. Propofol usage was calculated as 2,300,150mls in the TIVA arm vs 1,000,000mls in the mixed strategy. Propofol wastage was 202 mg per anaesthetic (16% of drawn up volume) in the TIVA strategy vs 79 mg per anaesthetic (14% of drawn up volume) in the mixed strategy group.

Conclusion:
Taking into consideration global warming potential, carbon emissions and plastic waste; a TIVA only anaesthetic strategy has a significantly smaller carbon footprint compared to a TIVA-volatile anaesthetic. The difference in propofol wastage is only 2% between the two anaesthetic strategies.

Reviewed by Dr Will Creasy

Noninvasive Neurally Adjusted Ventilatory Assist in Infants With Bronchiolitis: Respiratory Outcomes in a Single-Center, Retrospective Cohort, 2016–2018 patients

Lepage-Farrell et al. ***Pediatric Critical Care Medicine*** **25.3 (2024): 201-211.**
DOI: 10.1097/PCC.0000000000003407

Single centre, single arm retrospective cohort study interpreting data from 205 patients treated for bronchiolitis at a paediatric intensive care unit in Canada over two years. 64 patients (who met inclusion criteria) treated for bronchiolitis were commended on NIV-NAVA (non-invasive ventilation with neurally adjusted ventilatory assist). Change in respiratory effort, clinical parameters, ventilatory support and clinical outcome were measured. Evolution of respiratory

effort was observed using mWCAS (modified Wood Clinical Asthma Score). Data collected was compared to clinical measurements taken prior to starting NIV-NAVA.

Results:
76 of 205 (37%) were treated with NIV-NAVA during a two year study window, 64 met inclusion criteria into study.
NIV-NAVA was associated with a reduction in mWCAS ($p < 0.01$) when comparing two hours before and after starting therapy. NIV-NAVA did not cause a statistically different reduction in respiratory rate, however a statistically significant reduction in heart rate was displayed.
Six patients (9%) required intubation following NIV-NAVA failure. This rate is in keeping with conventional respiratory support failure rate in paediatric critical care.

Conclusion:
This n=64 single arm study demonstrates a statistically significant reduction in work of breathing using the mWCAS assessment tool in patients on paediatric intensive care over a two year window in Canada. Prospective studies with larger sample sizes are required to determine whether NIV-NAVA has clinical benefit as a second-tier ventilation support strategy in bronchiolitis.

Reviewed by Dr Will Creasy

Perioperative Management and Outcomes in Patients With Autism Spectrum Disorder: A Retrospective Cohort Study

O'Brien E et al. *Anesthesia & Analgesia 2024*; 138(2): 438-446;
DOI: 10.1213/ANE.0000000000006426

This retrospective, single-centre cohort study explored post-operative pain scores in children with autistic spectrum disorder (ASD) compared to those without the condition undergoing ambulatory surgery, hypothesising that ASD patients would have higher maximum PACU pain scores.

Methods:

Patients aged 3-18 years with a diagnosis of ASD undergoing ambulatory surgery at the Children's Hospital of Philadelphia were identified over a 5-year period. Data for maximum postoperative pain scores in post anaesthetic care unit (PACU) were collected.

Secondary outcomes included premedication patterns, behaviour at induction, opioid administration in PACU, incidence of vomiting, emergence delirium, and PACU length of stay.

Results:

335 patients with ASD and 11,551 non-ASD patients were identified. Inverse probability treatment weighting took into account the effect of confounding factors on the relationship between ASD and outcomes.

Maximum pain scores in PACU were not significantly higher in the ASD group compared to controls, with equivocal distribution of moderate-to-severe pain scores between groups.

There was no significant difference in the administration of preoperative premedication to both groups; however, ASD patients were more likely to receive ketamine.

Regarding the induction process, ASD patients were more likely to have parental and child life specialist (CLS) presence at induction, and their induction was less likely to be a smooth process.

Post-operatively, there were no significant differences regarding opioid administration, incidence of vomiting, and length of stay in PACU.

Discussion:

This study demonstrated that ASD children did not have significantly higher maximum pain scores in PACU compared to non-ASD children following ambulatory surgery. This is encouraging, given ASD patients can face challenges in communicating pain scores and articulating the need for analgesia. Additionally, postoperative opioid administration, emergence delirium, emesis and length of stay were similar between cohorts.

It does highlight some important perioperative considerations for ASD patients. The induction period was often more challenging, despite a higher parental and CLS presence, and similar preoperative premedication administration to non-ASD counterparts. It suggests that there may be more subtle factors affecting preoperative anxiety levels, and reinforces the need for a tailored anaesthetic plan for the individual patient. Also, in this study, ASD severity was not taken into account which could confound results. The authors acknowledge this, and recommend the development of a severity scale for these patients in the perioperative setting.

The authors recognise limitations of this study, including the need to investigate whether outcomes are different in patients undergoing major surgery requiring hospital admission.

Reviewed by Dr Alok Chauhan

The effects of dexmedetomidine on intraoperative neurophysiologic monitoring modalities during corrective scoliosis surgery in pediatric patients: A systematic review

Alkhatip A et al. *Pediatric Anesthesia 2024*; 34(2): 112-120
DOI: https://doi.org/10.1111/pan.14795

This systematic review sought to determine whether dexmedetomidine altered motor evoked potential (MEP) amplitude or somatosensory evoked potential (SSEP) latency and amplitude at a range of doses during paediatric spinal fusion surgery.

Methods:

This systematic review was performed according to the PRISMA checklist.
There were 3 proposed review questions:

1. Does dexmedetomidine alter the amplitude of MEP?
2. What is the effect of dexmedetomidine on the amplitude and latency of SSEP?
3. Is there an association between various doses of dexmedetomidine and its effect on spinal cord monitoring?

Of the 44 studies identified, 5 were included which were a mix of randomised controlled trials (RCTs), observational cohort and case-control studies, and case series. Individual patient groups within these studies were excluded if they did not meet inclusion criteria. Risk of bias was assessed via validated tools, cross-checked with a biostatistician.

Results:

MEP Amplitude:

- 3 studies (with most concerns of bias) demonstrated:
  - After loading dose: no difference in mean MEP size
  - At 0.7µg/kg/h: 30% had an isolated decrease in MEP amplitude, within an "acceptable range".
- 2 studies (with lower risk of bias) demonstrated:
  - Significant MEP amplitude reduction

SSEP Amplitude and Latency:

- 4 studies evaluated SSEP.
- 2 reported no significant changes (although "significance" and "change" were not clearly defined)
- The other 2 studies defined SSEP evaluation more clearly, with measurements remaining within accepted thresholds.

Association between dosing and effect on spinal cord monitoring:

- Difficult to compare as range of anaesthetic agents used and MEP monitoring technique differed among studies.

- One study comparing low (to achieve 0.4ng/ml) and high (to achieve 0.8ng/ml) dosing found higher doses were associated with higher risk of MEP loss and statistically significant decrease in mean MEP.
-

Discussion:

This was a challenging systematic review due to the variation of study protocols and data acquisition (e.g. MEP monitoring). The authors highlight the risk of bias in 3 studies (related to confounding, participant selection, results reporting, lack of statistical power and more). Although a lower risk of bias, the evidence from the 2 remaining studies is limited by study design (as they were not RCTs).

The authors suggest several mechanisms for dexmedetomidine causing reduction MEP reduction. These include haemodynamic effects (due to reduced cardiac output [despite maintained systolic blood pressure] affecting spinal cord perfusion) and via beta-suppressive effects on the human cortico-muscular system; however, the role of other contributory or indeed causative intra-operative factors were not made clear during the recording of these MEP events.

The use of dexmedetomidine in adults undergoing procedures requiring neurophysiological monitoring is more common, with recent guidelines recognise its use, suggesting it can be used safely at lower doses. The authors address its use in adults, suggesting physiological differences in paediatric patients may account for the effect on neurophysiological monitoring. This is unlikely given that most paediatric patients requiring spinal deformity surgery are older, and therefore will be physiologically mature.

The impact of dexmedetomidine on intra-operative neurophysiological monitoring is a controversial topic. Although this review highlights possible detrimental effects of its use, advantages have not been mentioned; for example, its anxiolytic effect, and its anaesthetic and opiate-sparing properties. Although this systematic review does not resolve the controversy, it raises the important point that high quality data is lacking, and more robust, larger RCTs are required.

Reviewed by Dr Alok Chauhan

Edited by Dr Shivan Kanani
APAGBI Trainee Representative