Prognostic factors of chronic postsurgical pain in children and adolescents: a systematic review and meta-analysis

Rosenbloom BN, Frederiksen SD, Wang V, et al
Regional Anesthesia & Pain Medicine 2025;50:144-152.

The aim of this systematic review and meta-analysis was to update the previous 2017 review with newly published studies, to demonstrate which pre-operative prognostic factors are associated with paediatric chronic postsurgical pain (CPSP). This is an important topic due to the high prevalence of CPSP (>20%) in children undergoing major surgery.

Eligible studies were peer-reviewed articles published in English that included children aged 6 to 18 years who underwent major surgery under general or regional anaesthesia, which compared children who developed CPSP with those who did not. Children with cancer or neurological disabilities were excluded. Only longitudinal studies reporting presurgical risk factors and postoperative pain outcomes assessed 3–12 months after surgery were included.
A structured search was conducted across three major databases using predefined criteria. From an initial 4871 records, 15 studies met the inclusion criteria. Study selection and exclusion were detailed in a PRISMA flow diagram. Most included studies focused on adolescents undergoing spinal surgery, reflecting a limited patient population.

Risk of bias was assessed using the QUIPS tool, with results ranging from low to moderate. Evidence quality was evaluated using the GRADE approach, with overall certainty rated as moderate, downgraded due to study limitations and inconsistency. Meta-analysis was conducted using appropriate methodology for the four prognostic factors with sufficient data.

Most studies reported at least one significant factor associated with CPSP, including child pain intensity, psychological variables, caregiver influences, and surgical duration. However, meta-analysis only demonstrated that presurgical pain intensity was significantly associated with CPSP (OR = 0.540; 95% CI = 0.184–0.894). Potentially important factors such as sex, mood, and sleep were highlighted as a priority for future research.
This paper highlights the importance of the assessment of pre-operative pain intensity, as a risk factor of CPSP, within perioperative paediatric care and pain management.

Reviewed by Dr Charlotte Leahy

Bronchial Blocker Versus Endobronchial Intubation in Young Children Undergoing One-Lung Ventilation: A Multicenter Retrospective Cohort Study

McLaughlin CS, Samant A, Saha AK et al.
Anesthesia & Analgesia 2025; 140(2): 326-333

This retrospective cohort study aimed to evaluate the prevalence of moderate and severe airway complications in paediatric patients undergoing one-lung ventilation, comparing the use of bronchial blocker with endobronchial intubation. This multi-centre study included children aged 2 months to 3 years, ASA 4 or lower, undergoing one-lung ventilation, from July 2004 to July 2022. Methodology included manual chart review for covariates, and of the free-text and airway notes to evaluate complications. Objective data from anaesthetic machines and monitors were not interrogated. The study instead relied on clinician-entered contemporaneous notes, which may be incomplete or subject to reporting bias. Airway complications were predefined and grouped as either “moderate” or “critical”.

While Multicenter Perioperative Outcomes Group (MPOG) is a large multicentre database, the initial query identified a relatively small number of eligible cases which met the inclusion criteria (n=727, across 21 centres). The paper provides a diagram of the flow of cases and exclusion criteria; 704 were available for analysis, with bronchial blocker usage in 260 cases (36.9%) and endobronchial intubation in 444 cases (63.1%).

The chosen statistical methods were generally appropriate; however, the exclusion of missing data could have introduced bias. Propensity score matching (PSM) addressed the imbalance in group sizes and demographics and produced 243 matched cases for each cohort.

The overall results showed that 12.0% of cases had at least 1 airway complication (95% CI, 9.5%–14.3%). 65 cases (9.2%) experienced a total of 74 moderate airway complications, and 33 cases (4.7%) experienced a total of 42 critical airway complications. The most common airway complication overall was the loss of one-lung isolation secondary to dislodgement of the bronchial blocker or endotracheal tube. Endobronchial intubation was associated with a higher incidence of critical airway complication, compared with bronchial blockers; this difference was only statistically significant in the unadjusted analysis. There was no significant difference in moderate airway complications between the two cohorts. Longer OLV duration and younger age were also associated with increased complication rates.

This study addresses an important question in paediatric anaesthesia regarding the choice of OLV technique on intra-operative complications. However, it is limited by the retrospective design, potential selection bias and unknown heterogeneity in anaesthetic practice between centres/cases. The results do indicate that OLV in young children is clinically challenging, with high rates of moderate to critical airway complications. Further prospective research is needed in this area, including the effect of OLV technique on post-operative outcomes.

Reviewed by Dr Charlotte Leahy

Lidocaine vs Mometasone Furoate Around the Pediatric Tracheal Tube Cuff: Hemodynamic Stress Response and Postoperative Airway Complications: A Prospective, Randomized, Controlled Study

Ölç *AU, Yilmaz M, Saraçoğlu KT et al.*
Healthcare 2025; 13(3), 205

This single centre, prospective, randomised controlled trial aimed to assess whether agents applied topically to tracheal tube (ETT) cuffs reduce:

1) Haemodynamic stress responses to intubation and extubation (primary outcome)
2) Postoperative airway complications following intubation such as cough, sore throat, bronchospasm, hoarse voice, and shortness of breath

91 ASA I-II Children aged 3-16 undergoing elective surgery requiring tracheal intubation were randomised to 3 groups. Patients received either 10% lidocaine spray (1.5mg/kg) applied to the ETT cuff, mometasone 0.05% (1 single spray) to the cuff, or 0.9% normal saline applied to the cuff. Surgical groups included neurosurgery, ENT, general surgery, orthopaedics and plastic surgery.

Exclusion criteria included allergies to lidocaine/mometasone, surgery requiring prone position, expected difficult airway and laryngotracheal surgery.

Importantly, adenotonsillectomy and other procedures expected to cause throat pain were excluded, and any patient who had more than one attempt at intubation was excluded from the study. These may be groups which would be relevant to explore further.

Anaesthetic management was standardised across groups, and this was confirmed by statistical analysis. All patients received premedication with midazolam. All patients received fixed weight-based doses of propofol, fentanyl and rocuronium with 1mg/kg of intravenous lidocaine for induction. Anaesthesia was maintained using sevoflurane. Cuff pressures were maintained between 20-25cmH2O. Patients were extubated after return of airway reflexes and reversal of neuromuscular block and they were followed up at regular intervals for 24 hours.

Results:
There was a statistically significant reduction in post intubation diastolic and mean arterial pressures in the lidocaine group, and reduction in cough at 24 hours in the mometasone and lidocaine groups when compared to control. The lack of statistical significance in other areas is likely a marker of the smaller sample size and relatively low incidence of events such as laryngospasm.

Reviewed by Dr Rahul Bandopadhyay

Comparative evaluation of intravenous versus intranasal dexmedetomidine on emergence delirium and hemodynamics in paediatric patients undergoing adenotonsillectomy: a randomised controlled trial

Dai C, Zhao X, Li A, et al
Front Pharmacol. 2025;16:1543344

This single centre, randomised controlled trial performed at a children's hospital in China aimed to investigate if intravenous (IV) or intranasal (IN) dexmedetomidine (DEX) reduced incidence and severity of emergence delirium. Haemodynamics, time to extubation, time to awakening, length of PACU stay, and adverse events were secondary outcomes.

139 ASA I-II children 3-10 years of age for adenotonsillectomy were recruited. Exclusion criteria included BMI > 25, cardiopulmonary/liver/renal disease, developmental delay, reactive airways disease and airway abnormalities, amongst others. The sample size was just adequate to allow for power of the study.

Patients were randomised to receive either IV DEX, IN DEX, or saline. Patients in the IV DEX group received 1mcg/kg over 10 minutes, and IN saline. Patients in the IN DEX group received 2mcg/kg DEX nasally, and IV saline. Patients in the saline group received both IV and IN saline. The anaesthetic, theatre, recovery teams and investigators were blinded.

Anaesthetic management was standardised across groups with inhalational induction with 8% sevoflurane. Maintenance was with sevoflurane, propofol and remifentanil infusions, with all patients receiving neuromuscular block and dexamethasone. Patients were extubated deep and assessed at regular intervals. The Pediatric Anesthesia Emergence Delirium (PAED) score was used to assess for emergence delirium.

This study demonstrated statistically significant reductions in mean PAED score (i.e, reduction in severity and incidence of emergence delirium) in both DEX groups when compared to control. There was little difference between mean PAED score between the IV and IN DEX groups. However, the IV DEX group had lower heart rates and prolonged recovery compared to the IN DEX group.

The IN DEX group also demonstrated reduced PAED and pain scores compared to IV DEX at 6h post-surgery. The authors postulate that this could be due to the absorption profile of dexmedetomidine when given nasally.

Reviewed by Dr Rahul Bandopadhyay

Immunological factors in pediatric generalized and focal epilepsy: interplay with anti-seizure medications.

Zhang, D, Sun, H.
BMC Pediatrics. 2025;25(1):210

Paediatric epilepsy in children is presumed to have different aetiologies and different mechanisms making treatment very challenging. The most recent mechanism is thought to be neuroinflammation and release of pro-inflammatory cytokines. Immune-mediated mechanisms previously have been proposed to interact with anti-seizure medication (ASM), thus creating an opportunity to explore this field for further treatment possibilities.

A retrospective cohort study done to prove the above concept recruited 136 patients and divided them into 2 groups as ASM-Sensitive and ASM-Insensitive with each group having roughly 68 patients. Seizure control was defined as ≥ 50% reduction in seizure frequency or being seizure-free for at least 6 months on the current ASMs regimen. The inclusion criteria consisted of children aged between 3 and 14 years who demonstrated an abrupt onset of rhythmic EEG activity lasting at least 10 s with changes in amplitude, frequency or spatial distribution. The exclusion criteria did not allow children with prior anti-seizure medication usage or children with seizures resulting from hypoglycaemia or hypocalcaemia to be included in the study.

After anti-seizure medication was started, 5 ml of fasting venous blood was collected to detect the blood concentration of ASM. Further 5 ml of fasting venous blood was collected between 7:00 and 9:00 AM and analysed by ELISA to measure immunoglobulin levels. Following ASM treatment, the patients' seizure occurrence and severity were recorded. Data analysis was conducted using SPSS29.0 statistical software, Shapiro-Wilko test, Pearson and Spearman corelation analysis as necessary.

The results after analysis suggested that there existed negative correlations of IL-6, IL-1β, IL-10 levels between the ASM Sensitive and ASM Insensitive group which shows a link between immunological dysregulation and pharmacological response. This link between immune factors and response to ASMs can be envisaged for future treatment of paediatric epilepsy.

Reviewed by Dr Madhavi Gudipati

Perioperative anaphylaxis in children and first successful cisatracurium desensitization

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Pediatr Allergy Immunol. 2025; 36:e70066

Perioperative anaphylaxis (PA) results from exposure to anaesthetic drugs which can recur upon re- exposure to the allergen. This can either be IgE or non-IgE mediated. The European Academy of Allergy and Clinical Immunology (EAACI), British Society for Allergy and Clinical Immunology, and Australian and New Zealand Anaesthetic Allergy Group recommend skin testing (ST), serial serum tryptase levels, basophil activation test (BAT) and drug provocation testing (DPT) at specialized centres to address allergen drugs.

A retrospective cohort study was undertaken in Hong Kong at two tertiary paediatric centres which had immunologists, anaesthesiologists and intensivists being a part of it. Anaphylaxis was defined by the EAACI clinical criteria and R&M grading (1-4) was used to grade the degree of anaphylaxis where grade>3 was considered as severe anaphylaxis. 11 paediatric patients were referred for the study.

Allergen diagnosis by ST and BAT was done between 4 weeks to 6months after the PA event for all drugs used <2hours prior to the event. First sample of serum tryptase was obtained at zero hours followed by second sample 24hrs later in which a level of >2ng/ml was considered positive. The final confirmation was made by the immunologist based on patients' medical history and testing results.

Most of the PA events occurred during the induction followed by maintenance of anaesthesia. All the above investigations found the most common allergen to be NMBA, cis-atracurium followed by atracurium. Thus, cis-atracurium desensitisation was planned with use of 5000 and 500-fold dilutions. Cetirizine, famotidine, Montelukast along with Omalizumab, a recombinant humanized anti IgE monoclonal antibody were also administered.Statistical analysis utilised two-sided Fisher's exact test, Mann-Whitney U test and a P value <0.05 was considered significant as by software R version. Thus, NMBA desensitisation as an alternative for patients with NMBA allergy can be practised in the future.

Reviewed by Dr Madhavi Gudipat

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