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Post-anesthesia apnea in Former Preterm and Term infants: A Protocol for Qualitative Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Society for Pediatric Anesthesia, Penn State University Department of Anesthesiology & Peri-operative Medicine.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 October 2025 and was last updated on 25 October 2025.

INTRODUCTION

Review question / Objective Our primary objectives are: 1) perform a systematic review and meta-analysis of the available English literature; 2) describe the extensive literature review we used to unify the available data; 3) identify risks factors that contribute to post-anesthesia apnea susceptibility; 4) clarify with greater specificity infants at risk for post-anesthesia apnea.

Rationale Former preterm and term infants are at increased risk for apnea after sedation or anesthesia. The increased susceptibility is attributed to immaturity of central respiratory mechanisms, respiratory musculature and sensitivity to anesthetic and sedative agents. Additionally, because of their increased oxygen consumption, former preterm and term infants are at greater risk for oxygen desaturation and associated bradycardia during apnea events. Concerns regarding the potential impact on neurodevelopmental outcomes from cardio-respiratory insults further underscore the need for improved management recommendations. Studies suggested that the “at-risk” period for post-anesthesia apnea and bradycardia may be up to 60 weeks postconceptual age (PCA) for former preterm infants, and up to 45 weeks in full-term infants. Multiple case reports, clinical studies, and systematic reviews have described risk factors contributing to post-anesthesia apnea. There are no consistent criteria across institutions regarding appropriate cut-off ages for admission, monitoring modalities, and duration of monitoring.

Condition being studied Post-operative or post-anesthesia apnea in infants after therapeutic or diagnostic procedures under anesthesia or sedation. Identify associated risk factors.

METHODS

Search strategy A systematic review is in progress in accordance with Preferred Reporting

Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and methods recommended in the Agency for Healthcare Research and Quality Methods Guide for Effectiveness and Comparative Effectiveness Reviews using a pre-defined protocol. We used a combination of keywords and Medical Subject Headings (MeSH) with the major search terms: apnea, bradycardia, premature infants, anesthesia, and post operative care. Comprehensive searches include – Medline (1966-2025), Embase (1947-2017), the Cochrane Library (1992- 2017), the Cochrane Neonatal Review Group (CNRG) Web of Science (1900-2017), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1981-2017). We are examining published and unpublished research from the following sources: Clinical Trials.gov, the World Health Organization International Clinical Trials Registry Platform, the Agency for Healthcare Research and Quality, the International Standard Randomized Controlled Trial Number registry, the Health Services Research Projects in Progress, the European Union Clinical Trials Register, the Society for Pediatric Sedation, the Pediatric Regional Anesthesia Network, the Pediatric Sedation Consortium, and the Wake-up Safe Patient Safety Organization. We are reviewing all papers included in our final analysis for possible additional references. Citations are stored and managed in EndNote (Clarivate Analytics, Philadelphia, PA); duplicate records are removed.

Participant or population Infants (age <12 months) undergoing diagnostic or therapeutic procedures under sedation or anesthesia.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Case reports, case series, clinical studies and clinical trials published in English.

Eligibility criteria Inclusion criteria are manuscripts with infants <12 months of age who underwent diagnostic or therapeutic procedures under general anesthesia (with or without regional analgesia), neuraxial (spinal/caudal) anesthesia, or sedation, with a specific focus on reports of apnea and/or bradycardia and/or oxygen desaturation following sedation or anesthesia.

Information sources Medline (1966-2025), Embase (1947-2017), the Cochrane Library (1992-2017), the Cochrane Neonatal Review Group (CNRG) Web of Science (1900- 2017), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1981-2017). We also examined published and unpublished research from the following sources: Clinical Trials.gov, the World Health Organization International Clinical Trials Registry Platform, the Agency for Healthcare Research and Quality, the International Standard Randomized Controlled Trial Number registry, the Health Services Research Projects in Progress, the European Union Clinical Trials Register, the Society for Pediatric Sedation, the Pediatric Regional Anesthesia Network, the Pediatric Sedation Consortium, and the Wake-up Safe Patient Safety Organization.

Main outcome(s) Data analysis is not completed.

Data management Data Extraction Form on Microsoft Excel.

Quality assessment / Risk of bias analysis Data extraction will be done in two phases: a practical review and a methodological review. In the practical review, the title and abstract of each of the articles retrieved were reviewed independently for inclusion by a team of two reviewers. Disagreements will be resolved by a third person for the articles selected for full review. Citations rejected at the second phase will be recorded with reasons for rejection. In the full-text review, inclusion/exclusion criteria will be applied again, yielding the articles eligible for methodological review. Grading of the manuscripts will be based on the American Academy of Pediatrics policy statement on classifying recommendations as follows:

A. Well-designed, randomized controlled trials or diagnostic studies on relevant population

B. RCTs or diagnostic studies with minor limitations, overwhelmingly consistent evidence from observational studies

C. Observational studies (case control and cohort design)

D. Expert opinion, case reports, reasoning from first principles

X. Exceptional situations where validating studies cannot be performed and there is clear preponderance of benefit or harm.

Strategy of data synthesis A narrative synthesis was first conducted to describe study characteristics and intervention components. We will apply a random-effects meta-regression analysis in the form of a generalized linear mixed-effects model with a binomial outcome of the proportion of children with a post-anesthesia apnea event in each study. Point estimates with 95% confidence intervals will be reported.

Heterogeneity will be assessed using the I^2 statistic.

Subgroup analysis A subgroup analysis of inguinal hernia and genito-urological studies will be performed.

Sensitivity analysis No sensitivity analysis is planned.

Language restriction English language publications.

Country(ies) involved United States.

Keywords apnea. anesthesia, infants.

Dissemination plans We plan to publish the article in a major journal in the field of Anesthesiology.

Contributions of each author

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