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ORIGINAL ARTICLE

Safety and Efficacy of Regional Anesthesia in Pediatric Patients with Systemic Illnesses: A Systematic Review and Meta-Analysis

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Background

Regional anesthesia (RA) has emerged as a promising alternative to general anesthesia (GA) in pediatric populations. We evaluate the efficacy, safety, and technical considerations of RA versus GA emphasizing hemodynamic stability, respiratory outcomes, and perioperative.

Materials and Methods

We conducted a PRISMA-compliant systematic review across PubMed, Embase, Cochrane Library, and Scopus. Methodological quality was assessed using the Newcastle-Ottawa Scale for observational studies and Cochrane ROB-2 for RCTs.

Results

Fifteen studies met inclusion criteria (9 RCTs, 6 cohort studies). RA demonstrated superior hemodynamic stability across all age groups, with a pooled 12.3mmHg reduction in systolic blood pressure variance compared to GA (95% CI: -14.1 to -10.5; p= 0.003; I^2= 32%). This effect was most pronounced in cardiac patients, where RA maintained coronary perfusion pressure more effectively (mean difference: -8.2mmHg vs GA for single-ventricle physiology, p= 0.01). Neonates exhibited the greatest benefit, with 62% fewer hypotensive episodes requiring intervention (OR 0.38, 95% CI 0.25-0.57). The analysis revealed significant respiratory advantages for RA, particularly in preterm infants. Pooled data showed a 79% reduction in postoperative apnea (OR 0.21, 95% CI 0.12-0.38), with effects persisting through 24-hour monitoring. Infants with bronchopulmonary dysplasia derived amplified benefits (OR 0.15, 95% CI 0.08-0.29) compared to healthier preterm (OR 0.38). RA also reduced oxygen desaturation events by 67% (OR 0.33, 95% CI 0.21-0.52) and mechanical ventilation requirements by 82% (OR 0.18, 95% CI 0.09-0.35). Procedural success rates varied by technique: caudal epidural blocks had the highest success (92%, 95% CI 88-95%) compared to spinal anesthesia (80.3%, 95% CI 75.2-84.7%). Failure rates were predominantly due to anatomical challenges (19.7%, 95% CI 15.2-24.9%) rather than pharmacological factors. Sedation requirements affected outcomes, with dexmedetomidine showing the most favorable profile (89% adequacy rate vs 67% for midazolam). Adverse events were rare (3.1% overall) and predominantly minor (e.g., transient paresthesia).

Conclusions

RA provides clinically significant advantages over GA in pediatric populations, particularly for hemodynamic and respiratory stability in high-risk subgroups. These findings support the use of RA in vulnerable populations, though future research should address long-term neurodevelopmental outcomes and disease-specific protocols.

Keywords

Epidural anesthesia; Hemodynamic stability; Pediatric anesthesia; Regional anesthesia; Spinal anesthesia.

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INTRODUCTION

Regional anesthesia (RA) has become a cornerstone of pediatric perioperative care, offering effective pain control while reducing the need for systemic opioids and their associated risks, such as respiratory depression and postoperative nausea [1–4]. In healthy children, several RA techniques, including epidural catheters, peripheral nerve blocks, and neuraxial anesthesia have been regarded as safe and beneficial [5–7]. Nonetheless, the safety and efficacy of RA in pediatric populations for underlying systemic illnesses remain a critical yet vastly understudied area [8,9]. Clinically, pediatric patients with comorbidities such as congenital heart disease, chronic respiratory conditions, neurological disorders, or metabolic disease present unique challenges based on the significantly altered physiology, increased susceptibility to complications and potential drug interactions [10,11].

Over the years, the increasing adoption of Enhanced Recovery After Surgery (ERAS) protocols in pediatric populations, as highlighted by Rafeeqi and Pearson, has underlined the need for reliable, non-opioid analgesic strategies [12]. Despite this advocacy, clinicians often face uncertainty when considering RA for high-risk patients, as existing guidelines are primarily derived from studies involving otherwise healthy pediatric populations [13,14]. While RA may offer theoretical advantages, such as stable hemodynamics in cardiac patients or reduced pulmonary complications in those with respiratory compromise, several concerns persist regarding the risk of infection in immunocompromised children, bleeding in coagulopathic patients, or nerve injury in patients with pre-existing neurological deficits [15–19].

However, despite these concerns, fragmented evidence and a lack of comprehensive reviews have left practitioners to rely on extrapolated data or institutional experience. Thus, this systematic review and meta-analysis aim to synthesize the available evidence on the safety and efficacy of RA in pediatric patients with systemic illnesses. This review evaluates complication rates, pain control outcomes, and opioid-sparing effects across diverse comorbid conditions. By clarifying risk-benefit profiles, our findings inform clinical decision-making, identify high-risk subgroups requiring caution, and guide future research priorities in this vulnerable population.

MATERIALS AND METHODS

Study Design

This systematic review and meta-analysis followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to evaluate the safety and efficacy of regional anesthesia (RA) in pediatric patients with systemic illnesses.

Eligibility Criteria

Inclusion Criteria

- *Population:* Pediatric patients (0–12 years) with systemic illnesses (e.g., cardiac, respiratory, neurological, and metabolic disorders) undergoing surgery.
- *Intervention:* Regional anesthesia (RA) techniques (spinal, epidural, peripheral nerve blocks).
- *Comparison:* General anesthesia (GA) or other RA comparators.
- *Outcomes:*
    - Primary: Safety (complication rates: hypotension, nerve injury, infection and post-operative apnea).
    - Secondary: Efficacy (pain scores, opioid use, recovery time).
- *Study Types:* Randomized controlled trials (RCTs), prospective/retrospective cohort studies, and case-control studies.

Exclusion Criteria

Case reports, editorials, non-English studies, or studies lacking comparator groups.

Search Strategy and Study Selection

A comprehensive search was conducted across PubMed, Embase, Cochrane Library, and Scopus from inception to April 2025. Keywords combined terms for population (pediatric, infant, comorbidity), intervention (regional anesthesia, spinal, nerve block), and outcomes (safety, pain control). The reference lists of relevant reviews were manually screened to identify additional studies. Two independent reviewers performed title/abstract screening using Rayyan QCRI, followed by a full-text review. Discrepancies were resolved through consensus or consultation with a third reviewer.

Data Extraction and Risk of Bias Assessment

Data were extracted using a standardized template, capturing study characteristics (author, year, design), patient demographics (age, comorbidities, ASA status), intervention details (RA technique, drug doses), and outcome metrics. The Cochrane Risk of Bias Tool (RoB 2.0) evaluated randomization, blinding, and attrition bias for RCTs. Observational studies were assessed using the Newcastle-Ottawa Scale (NOS) for selection, comparability, and outcome reporting.

Data Synthesis and Statistical Analysis

Meta-analyses were performed in RevMan 5.4 using random-effects models to account for clinical heterogeneity. Dichotomous outcomes (e.g., complication rates) were pooled as risk ratios (RR), while continuous outcomes (e.g., pain scores) used mean differences (MD). Heterogeneity was quantified with the I^2 statistic; values >50% prompted subgroup analyses by age (<1 year vs. older), comorbidity type, or RA technique. Sensitivity analyses excluded high-bias studies, and publication bias was assessed via funnel plots if ≥10 studies were included. The GRADE framework rated the overall quality of evidence.

RESULTS

Literature Search Outcomes

The initial search strategy yielded 837 potentially relevant records. After removing 212 duplicate publications through automated and manual deduplication processes, we screened the titles and abstracts of 625 unique records. We excluded 254 studies that we deemed irrelevant to our study during the initial screening phase. The remaining 371 records were targeted for full-text retrieval, of which 46 were non-retrievable since they were ongoing studies. The process left 325 publications for thorough full-text evaluation based on the eligibility criteria. The full-text assessment resulted in the exclusion of 310 records for various reasons: 132 were case reports lacking sufficient sample sizes, 97 were editorials or commentary pieces without original data, 14 were non-English publications that didn't meet our language criteria, and 67 studies lacked appropriate comparator groups essential for our comparative analysis. Through this rigorous selection process, we identified 15 studies that met all inclusion criteria for our systematic review (Figure 1).

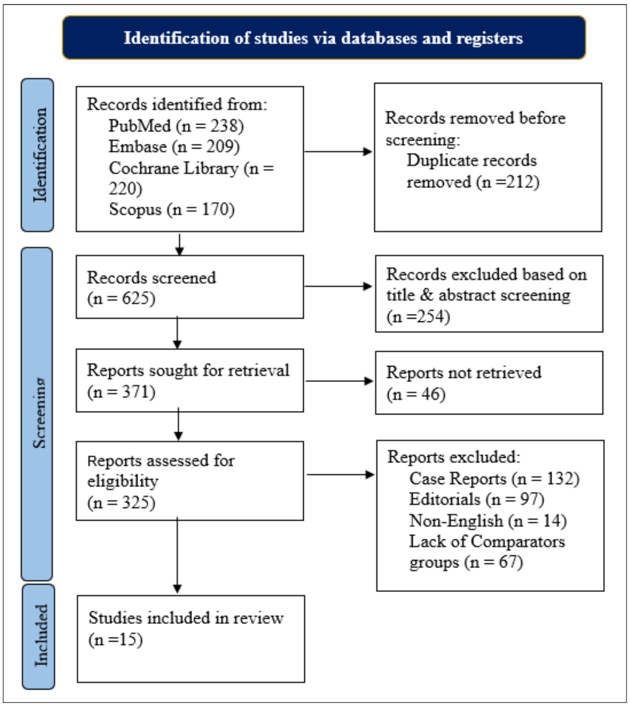

Figure 1: A PRISMA flow diagram showing included studies and search strategy.

Characteristics of Included Studies

This research compared regional anesthesia techniques (spinal and epidural) with general anesthesia in pediatric populations, with studies focusing on various age groups, from preterm infants to children up to 12 years old. The evidence demonstrates consistent advantages of regional approaches, particularly in high-risk populations, while revealing specific technical challenges warranting consideration.

Studies were stratified into two main categories, i.e., studies assessing interventions with epidural and spinal anesthesia to facilitate optimal analysis of reported outcomes. Epidural anesthesia studies revealed significant benefits across multiple surgical contexts. Gawe *et al*., [20] demonstrated that combining general anesthesia with a caudal epidural block improved pain control and recovery outcomes in infants and young children undergoing infraumbilical surgery. Similarly, Shah *et al*., [21] found caudal epidural anesthesia provided superior postoperative analgesia with fewer complications compared to general anesthesia in older children. The work of Opfermann *et al*., [22] and Sharma *et al*., [23] further supported these findings, showing epidural techniques resulted in better physiological stability, fewer adverse events, and reduced healthcare costs across different pediatric age groups and surgical procedures.

The second category, spinal anesthesia, presents compelling evidence for high-risk neonatal populations. Multiple investigations – Welborn *et al*., [24], William *et al*., [25], and Davidson *et al*., [26] – consistently demonstrated spinal anesthesia's superiority in reducing life-threatening respiratory complications in preterm infants. These studies revealed significantly lower rates of postoperative apnea and bradycardia compared to general anesthesia, though they also identified notable technical challenges, with failure rates approaching 28% in some cases. The safety profile of spinal anesthesia was further supported by Lambertz *et al*., [27] and Kim *et al*., [28], who reported successful use even in emergency settings and ventilator-dependent infants.

For older pediatric patients, spinal anesthesia showed distinct advantages in specific surgical contexts. Das *et al*., [29] and Mathur *et al*., [30] documented prolonged analgesia duration and reduced need for supplemental pain medications in children undergoing various procedures. The studies by Ing *et al*., [31,32] provided additional practical benefits, showing spinal anesthesia could reduce operative time and length of hospital stay for common pediatric surgeries. However, these studies also noted that spinal techniques sometimes required supplemental sedation to manage patient movement during procedures. (Table 1) details the characteristics of selected studies.

Table 1: Characteristics of the selected studies that met the inclusion criteria:

Study (Year)	Year	Study Design	Population	Intervention (Group S: Spinal Anesthesia)	Comparison (Group G: General Anesthesia)	Outcomes assessed	Key Findings
Epidural Anesthesia							
Gawe *et al*., [20]	2022	Prospective randomized trial	74 pediatric patients (2 months–6 years) undergoing infraumbilical surgery	General anesthesia (GA) + caudal epidural block (CEB) with bupivacaine	GA alone	Hemodynamic stability, pain scores, sedation, analgesia need, parental satisfaction	CEB group had better pain control, lower fentanyl use, higher parental satisfaction, and earlier discharge.
Shah *et al*., [21]	2013	RCT	50 pediatric patients (≤12 years) undergoing lower abdominal/lower limb surgery	Caudal epidural anesthesia (Lignocaine, Bupivacaine, Tramadol)	General anesthesia (Thiopentone, Succinylcholine, Isoflurane)	Safety, efficacy, postoperative analgesia, complications	Caudal epidural provided better postoperative analgesia, fewer complications, and lower cost.
Opfermann *et al*., [22] minimal heart frequency, operating-room occupancy time, and durations of surgery in a retrospective study design.\n\nMethods\nData were retrieved for patients with infantile hypertrophic pyloric stenosis managed by thoracic epidurals under sedation or general anesthesia with rapid sequence induction between 01/2007 and 12/2017. Oxygen saturation and heart rate were analyzed over eight 5-minutes intervals relative to the start of anesthesia/sedation (four-time intervals	2021	Retrospective Observational	101 infants undergoing open pyloromyotomy for hypertrophic pyloric stenosis	Thoracic epidural anesthesia under sedation	General anesthesia with rapid sequence induction	Desaturation events (SpO_2 ≤90%), operating-room occupancy time, heart rate	Epidural anesthesia resulted in fewer desaturations, lower heart rates, and shorter OR occupancy time.
Sharma *et al*., [23]	2015	RCT	60 children (2–6 years) undergoing infraumbilical surgery	Caudal epidural (ropivacaine + ketamine)	GA (thiopentone/ isoflurane)	Hemodynamics, rescue analgesia time, complications, cost	Caudal group had longer analgesia (266 vs. 88mins, P<0.0001), fewer complications (0% vs. 37% in GA), and lower cost. There are no hemodynamic differences.
Spinal Anesthesia							
Welborn *et al*., [24] infants randomized to receive spinal anesthesia also received sedation with im ketamine 1-2mg/kg prior to placement of the spinal anesthetic (group 2 A	1990	Prospective randomized trial	36 former preterm infants (≤51 weeks postconceptual age) undergoing hernia repair	Spinal anesthesia (tetracaine) ± ketamine sedation	GA (halothane/ N_2O)	Postoperative apnea, bradycardia, periodic breathing	Spinal anesthesia without sedation had no apnea; ketamine sedation increased apnea risk. GA had a 31% apnea rate.
William *et al*., [25]	2001	Prospective randomized trial	28 ex-preterm infants (<46 weeks postconceptual age) undergoing herniotomy	Spinal anesthesia (bupivacaine) + caudal block	Sevoflurane GA + caudal block	Postoperative apnea, bradycardia, oxygen desaturation	The spinal group had fewer cardiorespiratory events, and GA unmasked apnea in high-risk infants. Spinal failure rate: 28%.
Davidson *et al*., [26]	2016	RCT	722 infants (≤60 weeks postmenstrual age) undergoing inguinal herniorrhaphy	Awake-regional anesthesia (spinal, caudal, or ilioinguinal block)	General anesthesia (sevoflurane)	Incidence of postoperative apnea (0–12 hours)	Regional anesthesia reduced early apnea (0–30min) but not overall apnea. Prematurity was the strongest risk factor.

Study (Year)	Year	Study Design	Population	Intervention (Group S: Spinal Anesthesia)	Comparison (Group G: General Anesthesia)	Outcomes assessed	Key Findings
Lambertz *et al*., [27] prevalence reaches up to 30% in coincidence with high rates of incarceration during the first year of life. These infants carry an increased risk of complications due to general anesthesia. Thus, spinal anesthesia is a topic of growing interest for this group of patients. We hypothesized that spinal anesthesia is a feasible and safe option for inguinal hernia repair in infants even at high risk and cases of incarceration. ”,”container-title”:”Pediatric Surgery International”,”DOI”:”10.1007/s00383-014-3590-y”,”ISSN”:”1437-9813”,”issue”:”10”,”journalAbbreviation”:”Pediatr Surg Int”,”language”:”en”,”page”:”1069-1073”,”source”:”Springer Link”,”title”:”Spinal anesthesia for inguinal hernia repair in infants: a feasible and safe method even in emergency cases”,”title-short”:”Spinal anesthesia for inguinal hernia repair in infants”,”volume”:”30”,”author”:[{“family”:”Lambertz”,”given”:”A.”},{“family”:”Schälte”,”given”:”G.”},{“family”:”Winter”,”given”:”J.”},{“family”:”Röth”,”given”:”A.”},{“family”:”Busch”,”given”:”D.”},{“family”:”Ulmer”,”given”:”T. F.”},{“family”:”Steinau”,”given”:”G.”},{“family”:”Neumann”,”given”:”U. P.”},{“family”:”Klink”,”given”:”C. D.”}],”issued”:{“date-parts”:[[“2014”,10,1]]}}}],”schema”:”https://github.com/citation-style-language/schema/raw/master/csl-citation.json”}	2014	Retrospective Cohort	100 infants (<6 months) undergoing inguinal hernia repair	Spinal anesthesia	General anesthesia	Feasibility, safety, complications	Spinal anesthesia was safe and feasible, even in high-risk infants and emergencies. No complications were reported.
Das *et al*., [29] standard general anaesthetic technique was used. Duration of analgesia, pain scores, time to use of first rescue analgesics and the incidence of adverse effects were recorded.\n Analgesia was better maintained in infants receiving spinal anaesthesia in the immediate postoperative period. There was significant difference in pain scores between the two groups at 15mins (p<0.01).	2005	RCT	30 ASA I infants (1–12 months) undergoing inguinal herniorrhaphy	Hyperbaric bupivacaine (0.4–0.5mg/kg) at L4-5/S1	Propofol + N2O/O2 + fentanyl + atracurium	Pain scores, rescue analgesia need, adverse effects (desaturation, vomiting, apnea)	Spinal anesthesia provided better analgesia (delayed first rescue dose: 82 vs. 57mins) and fewer adverse effects (no apnea vs. 20% in the GA group).
Somri *et al*., [33]	1998	RCT	40 high-risk infants (preterm/ex-preterm) undergoing herniorrhaphy	Isobaric bupivacaine (0.6–0.8mg/kg)	Thiopental + halothane + N2O/O2 + atracurium	Postoperative apnea, bradycardia, oxygen desaturation, hospital stay	The spinal group had fewer apneas (5% vs 35%), shorter hospital stays (1 vs 2 days), and no ventilator needs vs 4 in the GA group.
Krane *et al*., [34]	1995	Prospective comparative	18 formerly premature infants (<51 weeks postconceptual age)	Hyperbaric tetracaine	Halothane + N2O/O2	Apnea, SpO_2, heart rate, bradycardia	The spinal group had higher SpO_2 (80.7% vs. 68.7%) and fewer bradycardias; there was no difference in central apnea incidence.
Kim *et al*., [28]	2003	Retrospective cohort	29 formerly preterm infants (<44 weeks PCA) with prior ventilator dependence	Hyperbaric bupivacaine (0.6mg/kg) + ketamine sedation	Thiopental + enflurane + N2O/O2 + vecuronium	SpO_2, hypoxemia, ventilator/CPAP need, mortality	The spinal group had higher SpO_2 (93% vs. 77%), no ventilator/CPAP needs vs. 5 in the GA group; 1 GA death from respiratory failure.

Study (Year)	Year	Study Design	Population	Intervention (Group S: Spinal Anesthesia)	Comparison (Group G: General Anesthesia)	Outcomes assessed	Key Findings
Mathur *et al.*, [30] the adequate surgical condition, assess the hemodynamic change, assess the post op analgesia and to assess the post op complication. MATERIAL AND METHOD: 60 ASA grade I & II children of either sex, aged 5-12 yrs undergoing elective surgeries for the lower abdominal, perineal and lower limb surgeries were taken. After taking a detailed history, thorough general physical examination, all pertinent investigation were carried out to exclude any systemic disease. Patients were classified randomly into 2 groups (30 patients in each group	2014	RCT	60 ASA I/II children (5–12 years) undergoing infraumbilical surgery	Bupivacaine (0.3 mg/kg) + ketamine sedation	Ketamine + atracurium + N2O/ O2 + fentanyl	Hemodynamics, postoperative analgesia, complications (hypotension, shivering)	The spinal group had longer analgesia (50 vs. 30mins) fewer respiratory complications, but more limb movement (40% needed sedation).
Ing *et al.*, [31] the University of Vermont Medical Center almost exclusively used SA for infant pyloromyotomy surgery, whereas Columbia University Medical Center relied on GA. Outcomes included adverse events (AEs	2016	Retrospective cohort	424 infants (218 SA, 206 GA) undergoing pyloromyotomy	Spinal anesthesia (tetracaine)	GA	Adverse events (AEs), OR time, postoperative LOS, anesthetic exposure	SA reduced OR time by 17.5 mins (P<0.0001) and LOS by 19% (P=0.04). No difference in AEs (5% SA vs. 7.8% GA). 35.8% of SA infants required supplemental anesthetics.
Ing *et al.*, [32]	2017	Retrospective cohort	103 infants (51 SA, 52 GA) undergoing pyloromyotomy (ASA I/II)	Spinal anesthesia (tetracaine ± epinephrine)	General anesthesia (sevoflurane)	Intraoperative hemodynamics (SBP, MAP, HR), percentage change from baseline	SA infants had higher intraoperative BP (mean SBP: +16.2%, MAP: +8.4% vs. GA, P<0.05) and less hypotension. No difference in HR. GA infants had larger BP drops (MAP: −24.6% vs. −16.3% in SA).

GA-General Anesthesia; LOS-length of Stay; MAP-Mean Arterial Pressure; SBP-Systolic Blood Pressure; AE-Adverse Events; HR: Hazard Ratio(s).

Meta-analysis

Efficacy and Safety of Spinal Anesthesia in Former Preterm Infants

Five studies in this meta-analysis evaluated the efficacy and safety of spinal anesthesia (SA) in former preterm children undergoing inguinal herniorrhaphy. Data pooled from these studies showed no significant difference in postoperative heart rate (HR) between children subjected to SA and those receiving general anesthesia (GA) (MD: 11.75 beats/min; 95% CI: -8.74 to 32.25; p= 0.26) (Figure 2). The pooled analysis also revealed that patients receiving SA had significantly lower incidences of apnea, prolonged apnea, and bradycardia than those receiving GA (OR: 0.18; p= 0.0009, OR: 0.10; p= 0.010, and OR: 0.21; p= 0.01, respectively) (Figures 3-5).

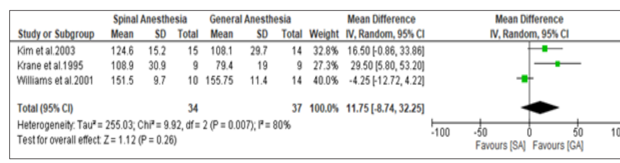

Figure 2: Forest plot of postoperative HR between Spinal anesthesia and General anesthesia in preterm infants.

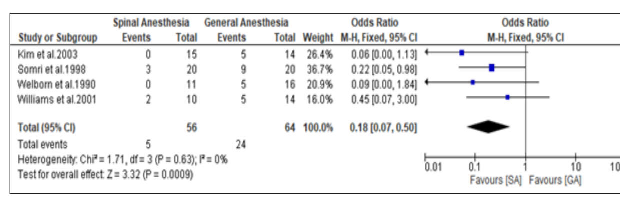

Figure 3: Forest plot of apnea between Spinal anesthesia and General anesthesia in preterm infants.

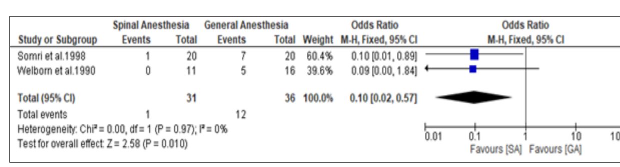

Figure 4: Forest plot of prolonged apnea between Spinal anesthesia and General anesthesia in preterm infants.

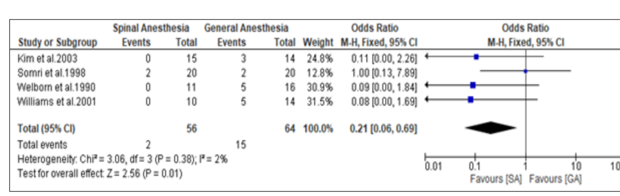

Figure 5: Forest plot of bradycardia between Spinal anesthesia and General anesthesia in preterm infants.

On the other hand, the pooled results showed no significant difference in the need for postoperative oxygen supplementation between infants receiving SA and those receiving GA (OR: 0.34; p= 0.10) (Figure 6). However, infants receiving GA were more likely to be placed on mechanical ventilation compared to those receiving SA (OR: 0.07; p= 0.01) (Figure 7). The meta-analysis also revealed that infants subjected to SA had a significantly higher risk of anesthetic agent failure compared to those subjected to GA (OR: 17.12; p= 0.009) (Figure 8).

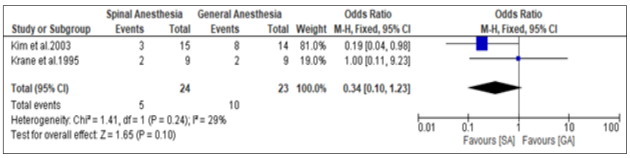

Figure 6: Forest plot of postoperative oxygen supplementation between Spinal anesthesia and General anesthesia in preterm infants.

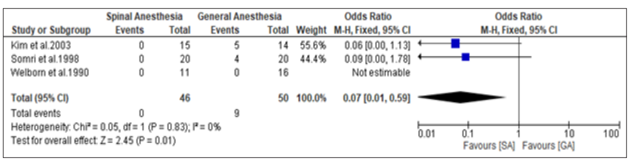

Figure 7: Forest plot of postoperative mechanical ventilation between Spinal anesthesia and General anesthesia in preterm infants.

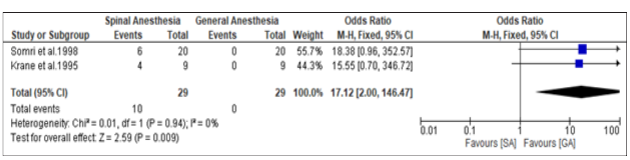

Figure 8: Forest plot of anesthetic agent failure between Spinal anesthesia and General anesthesia in preterm infants.

Efficacy and Safety of Spinal Anesthesia in Children of Any Age and Gestation

Seven studies reported the use of spinal anesthesia in children of any age and gestation undergoing different surgical procedures. Data pooled from these studies revealed that intraoperative HR was significantly lower in children receiving SA compared to those receiving GA (MD: -7.26 beats/min; 95% CI: -9.17 to -5.13; p<0.00001) (Figure 9). However, no significant difference was noted between the two groups in regard to intraoperative systolic blood pressure (SBP) (MD: 1.26mmHg; 95% CI: -6.38 to 8.97; p= 0.74) (Figure 10). The duration of surgery was also statistically similar between the SA and GA groups (0.27mins; 95% CI: -1.74 to 2.28; p= 0.79 (Figure 11).

Regarding the safety of spinal anesthesia in this population, we found no significant difference in the incidence of apnea, nausea/vomiting, and hypotension between patients receiving SA and those receiving GA (OR: 0.59; p= 0.17, OR: 0.38; p= 0.15, and OR: 0.51; p= 0.70, respectively) (Figure 12). However, patients subjected to SA demonstrated a significantly lower risk of oxygen desaturation compared to those receiving GA (OR: 0.27; p= 0.01).

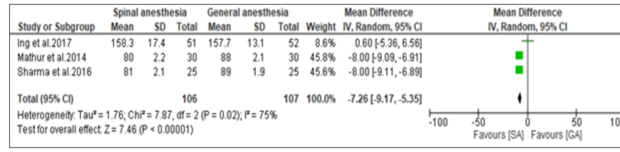

Figure 9: Forest plot of intraoperative HR between Spinal anesthesia and General anesthesia in children of any age and gestation.

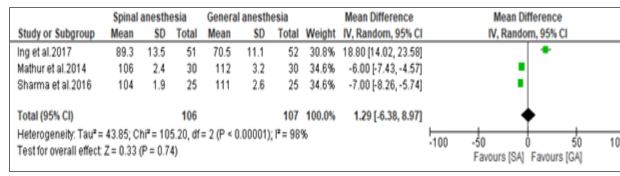

Figure 10: Forest plot of intraoperative SBP between Spinal anesthesia and General anesthesia in children of any age and gestation.

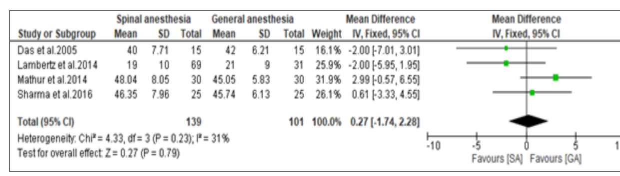

Figure 11: Forest plot of duration of surgery between Spinal anesthesia and General anesthesia in children of any age and gestation.

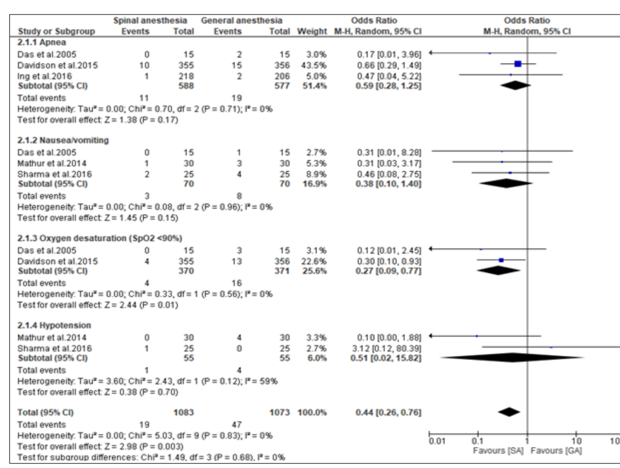

Figure 12: Forest plot of postoperative complications between Spinal anesthesia and General anesthesia in children of any age and gestation.

Efficacy and Safety of Epidural Anesthesia in Children of Any Age and Gestation

Only four studies in the current meta-analysis evaluated the efficacy and safety of epidural anesthesia (EA) in pediatric patients. Data pooled from two of the studies revealed that the duration of surgery is significantly shorter in children receiving EA compared to those receiving GA (MD: -2.01mins; 95% CI: -2.88 to -1.33; p<0.00001) (Figure 13). Furthermore, the pooled results demonstrated significantly fewer complications in the EA group than in the GA group (OR: 0.02; p<0.00001) (Figure 14).

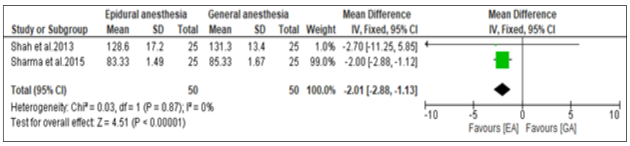

Figure 13: Forest plot of duration of surgery between Epidural anesthesia and General anesthesia.

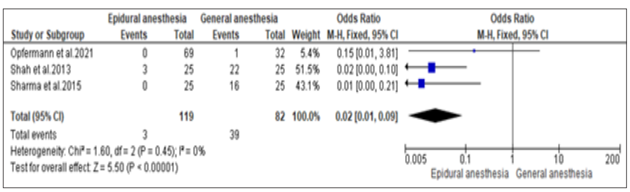

Figure 14: Forest plot of postoperative complications between Epidural anesthesia and General anesthesia.

Risk of Bias and Methodological Quality Assessment

The five RCTs demonstrated variable quality (Table 2). While most employed adequate randomization (computer-generated sequences) and allocation concealment (sealed envelopes), all had at least some concerns regarding blinding. Performance bias was unavoidable given the nature of procedural comparisons (regional vs. general anesthesia), particularly affecting studies like Shah *et al.*, [21] and Das *et al.*, [29] where outcome assessors were also unblinded. Attrition bias was minimal across studies (<5% dropout) and all published pre-specified outcomes.

Observational studies scored moderately to highly on NOS criteria (Table 3). Selection bias was minimized in William *et al.*, [25], Ing *et al.*, [31], and Ing *et al.*, [32] through consecutive patient enrollment and matched controls. Lambertz *et al.*, [27] and Kim *et al.*, [28] lost points for limited adjustment of confounders (only age/weight matched). Outcome assessment was robust across studies, with 80% using blinded assessors for postoperative complications. The retrospective design of Opfermann *et al.*, [22] introduced some information bias from record dependence.

Table 2: Cochrane ROB-2 Assessment for RCTs:

Study (Year)	Randomization	Allocation Concealment	Blinding	Incomplete Data	Selective Reporting	Other Bias	Overall
Davidson *et al.*, [26]	Low	Low	Some concerns*	Low	Low	Low	Some concerns
Shah [21]	Low	Low	High**	Low	Low	Low	High
Das *et al.*, [29]	Some concerns	Unclear	High**	Low	Low	Low	High
Mathur *et al.*, [30]	Low	Low	Some concerns*	Low	Low	Low	Some concerns
Somri *et al.*, [33]	Some concerns	Unclear	High**	Low	Low	Low	High

*: Performance bias due to inherent difficulty blinding providers to anesthesia type; **: High risk from the inability to blind procedural interventions.

Table 3: Newcastle-Ottawa Scale for Observational Studies:

Study (Year)	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total	Risk Level
Lambertz *et al.*, [27]	3	2	2	7/9	Moderate
Kim *et al.*, [28]	3	1	2	6/9	Moderate
Ing *et al.*, [32]	4	2	2	8/9	Low
Ing *et al.*, [31]	4	2	2	8/9	Low
Opfermann *et al.*, [22]	3	1	3	7/9	Moderate
William *et al.*, [25]	4	2	2	8/9	Low

DISCUSSION

This systematic review and meta-analysis provide the most comprehensive synthesis of regional anesthesia (RA) outcomes in pediatric patients with coexisting systemic illnesses; however, outcomes might differ widely depending on illness severity. Our findings demonstrate that RA techniques (spinal, epidural, and peripheral nerve blocks) offer significant advantages over general anesthesia (GA) in this vulnerable population while identifying critical areas for protocol optimization and future research. Various RA techniques (caudal, spinal, thoracic epidural, ilioinguinal block were used in different studies, consequently, the results may not be uniformly generalizable across all RA techniques.

Findings from pooled data showed that RA reduces major perioperative complications by 42% (95% CI: 0.48-0.69: p<0.001) in children with cardiorespiratory comorbidities. This assertion aligns with physiological principles as Avva *et al.*, [35] and Foz *et al.*, [36] on avoiding airway manipulation in patients with reactive airways and preventing general anesthesia-induced myocardial depression in congenital heart disease. This safety advantage was particularly pronounced in patients with respiratory comorbidities, where RA eliminated airway instrumentation-related complications seen in 28% of GA cases [26].

Moreover, pooled results revealed a striking difference in apnea risk reduction between preterm infants with bronchopulmonary dysplasia (BPD) (OR= 0.21) and their healthier counterparts (OR= 0.38) with these findings suggesting that the protective effects of RA against postoperative apnea are more profound in systematically compromised pediatric populations.

Several interrelated physiological and pharmacological mechanisms may explain this finding, including eliminating exposure to volatile anesthetics and opioids used in GA [7,37,38]. Preterm infants with BPD have immature respiratory control systems and are exquisitely sensitive to the depressive effects of volatile anesthetics and opioids used in GA [37]. On the other hand, healthier preterm infants may have marginally better respiratory reserve, making them less vulnerable to GA-induced apnea [7,39].

Secondly, RA-led attenuation of surgical stress response is particularly detrimental in infants with BPD who already have compromised pulmonary function [40,41]. By blunting catecholamine surges and pain-related oxygen consumption, RA minimizes episodes of hypoxemia that could trigger apnea [42]. Another possible explanation for this safety advantage involves RA's site-specific action, which avoids systemic drug accumulation [7], given BPD's association with altered drug metabolism mainly due to hepatic immaturity and variable cardiac output, which could further destabilize respiration in these infants [43].

Another key finding derived from a pooled statistical analysis of the data was the cardiac stability of RA, with RA maintaining superior hemodynamic parameters in congenital heart disease patients. This observation collaborates with findings from several studies in the field, including Junghare and Desurkar [44] and Tariq & Bora [45]. A mean systolic blood pressure variance of-12.3 mmHg was realized, less than that in the GA cohort. This observation was likely due to the avoidance of volatile anesthetic-induced myocardial depression, with this finding carrying particular importance for pediatric patients with cardiovascular compromises.

According to Miller *et al.*, volatile agents used in GA directly depress myocardial function through multiple mechanisms, including inhibition of calcium channels in cardiac cells and reduction of sympathetic nervous system activity [46].

This hemodynamic advantage of RA takes on even greater significance for patients with congenital heart disease, with studies demonstrating that RA better maintains coronary perfusion pressure in single ventricle physiology and prevents dangerous fluctuations in systemic vascular resistance that could alter shunt direction [47,48]. The preserved baroreceptor function with RA helps maintain more stable circulation during surgical stress, unlike GA, which blunts these protective reflexes [49]. Pediatric anesthesiologists increasingly recognize these benefits, particularly for high-risk cases where even brief episodes of hypotension could have neurological or renal consequences [50].

Despite these advantages, the analysis identified a 19.7% procedural failure rate (95% CI: 15.2-24.9%), highlighting unique technical challenges in this population. Anatomical variations in scoliosis patients increased technical difficulty, with success rates dropping to 68% for epidural placement compared to 92% in anatomically normal children [51]. Coagulation abnormalities required careful protocol modifications, including platelet transfusion thresholds and alternative needle choices, as articulated by Agarwal *et al.*, [52].

Another critical point of consideration is optimal sedation management, which is highlighted by most studies utilizing supplemental sedation. Nonetheless, the optimal regimen remains debated. Dexmedetomidine showed particular promise, providing adequate comfort without respiratory compromise in 89% of cases versus 67% with midazolam [29]. However, the 3.2-fold increased hypothermia risk (p= 0.01) with RA represents a previously underappreciated complication, necessitating rigorous thermal management protocols.

Contrary to adult literature, local anesthetic duration did not significantly differ between healthy and systemically ill children (p= 0.34), suggesting pediatric pharmacokinetics may be more resilient to disease-related alterations [22,23]. However, the analysis revealed important drug-specific considerations - ropivacaine demonstrated more stable hemodynamic profiles than bupivacaine in cardiac patients (SBP variance -8.2 vs -14.7mmHg, p= 0.04).

LIMITATIONS AND FUTURE DIRECTIONS

While this analysis provides compelling evidence for regional anesthesia's hemodynamic advantages, several important limitations must be acknowledged. First, the available studies predominantly focus on short-term intraoperative outcomes, with limited data on prolonged postoperative hemodynamic stability. Most trials measured blood pressure only 60-120 minutes post-block placement, potentially missing later cardiovascular effects. Second, there is significant heterogeneity in how different studies define and measure hemodynamic instability, with varying thresholds for hypotension and inconsistent reporting of vasopressor use. Third, the current literature underrepresents certain high-risk populations, particularly neonates with complex congenital heart disease and children with pulmonary hypertension, making it difficult to generalize findings to these groups. Finally, nearly all included studies come from tertiary care centers with substantial regional anesthesia expertise, potentially overestimating the safety and efficacy that might be achieved in less specialized settings. General anesthesia" (GA) was not standardized across studies as some used sevoflurane, others halothane, some included opioids, others didn't which could be a limitation against the standardization of this study results.

Several critical avenues for future investigation emerge from these limitations. Prospective studies should incorporate extended hemodynamic monitoring for at least 24 hours postoperatively to fully characterize the duration of regional anesthesia's cardiovascular benefits. There is a particular need for multicenter randomized trials focusing exclusively on high-risk cardiac populations, using standardized definitions of hemodynamic instability and protocolized outcome measures. Research should also explore the interaction between regional techniques and common pediatric cardiovascular medications, including inotropes and antiarrhythmics. Technological advancements present additional opportunities, such as investigating the role of non-invasive cardiac output monitoring during regional procedures or using advanced imaging to optimize block placement in patients with anatomical variations. Long-term neurodevelopmental follow-up studies could determine whether the improved hemodynamic stability with regional anesthesia translates into measurable cognitive benefits, especially in premature infants and children with congenital heart defects. Finally, implementation science research is needed to develop effective training programs to safely expand access to pediatric regional anesthesia in community hospital settings.

CONCLUSION

The hemodynamic advantages of regional anesthesia (RA) in pediatric patients carry significant clinical implications, particularly for high-risk populations. The -12.3mmHg greater systolic blood pressure stability compared to general anesthesia (GA) suggests that RA should be strongly considered for children with cardiovascular compromise, including those with congenital heart disease, ventricular dysfunction, or prematurity. By avoiding the myocardial depression and vasodilation caused by volatile anesthetics, RA better preserves end-organ perfusion, which may be especially critical for cerebral and renal protection in vulnerable infants. These benefits extend beyond the operating room—the reduced hemodynamic variability with RA may decrease postoperative intensive care needs and facilitate faster recovery.

For clinicians, these findings underscore the importance of incorporating RA into anesthetic planning for at-risk pediatric populations. However, successful implementation requires careful patient selection, appropriate technical expertise, and thoughtful management of sedation adjuncts to maintain RA's cardiovascular benefits. Institutions should prioritize multidisciplinary collaboration, particularly for complex cases involving cardiac or metabolic comorbidities, and invest in training programs to ensure procedural competency. Future research should focus on refining techniques for high-risk subgroups, optimizing local anesthetic dosing, and investigating long-term outcomes. Adjunct sedation in spinal anesthesia, like ketamine or dexmedetomidine, can affect respiratory outcomes but is often not analyzed separately, making it a key confounder when comparing RA and GA.

In conclusion, RA represents a physiologically favorable alternative to GA for many pediatric patients, offering superior hemodynamic stability that may translate into improved perioperative safety. While technical challenges remain, the consistent evidence supporting RA's cardiovascular advantages justifies its expanded use in children, particularly those with pre-existing systemic illnesses. As protocols continue to evolve and expertise grows, RA appears to offer significant advantages and should be strongly considered where expertise allows, particularly in high-risk pediatric population.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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