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REVIEW ARTICLE

Perioperative Indications for Gabapentinoids in Pediatrics: A Narrative Review

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Abstract

In recent years, there has been increased interest in using gabapentinoids (gabapentin and pregabalin) as part of multimodal medication plans or enhanced recovery after surgery protocols to mitigate several perioperative clinical challenges. Outcomes explored in the context of using gabapentinoids perioperatively in children are variable and include acute complications of pain, anxiety, nausea and vomiting, and emergence agitation, as well as the long-term postoperative outcome of chronic postsurgical pain. This narrative review describes the current literature regarding perioperative use of gabapentinoids in pediatric patients and aims to describe the role of gabapentinoids in the perioperative setting for each specific indication.

Key Points

Perioperative administration of gabapentinoids has demonstrated benefit in pain outcomes and other postsurgical clinical challenges in pediatric patients, with acceptable side effect profiles.

Due to variability of study designs and outcomes investigated, the current literature cannot support a robust recommendation for a single preoperative dose or a combined approach of preoperative and postoperative dosing of gabapentinoids.

Enhanced recovery after surgery protocols for major surgical interventions in children currently incorporate gabapentinoids in multimodal pain management plans; nevertheless, these drugs' distinct contribution cannot be separated from that of other components of the multimodal therapy plans.

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1 Introduction

The perioperative period can pose clinical challenges in pediatric patients, including prevention and control of pain, anxiety, nausea and vomiting, and emergence agitation. Gabapentinoids (gabapentin and pregabalin) have emerged as agents that may mitigate some of these challenges.

Although gabapentinoids were originally approved for treatment of seizures, they have since gained indications for pain conditions in adults, including postherpetic neuralgia, neuropathic pain associated with diabetes, fibromyalgia, and neuropathic pain associated with spinal cord injury. Both gabapentin and pregabalin are approved for use in children, but the indications are limited to the treatment of seizures in this population [1, 2]. As structural analogs of γ-aminobutyric acid, gabapentinoids bind to voltage-gated calcium channels in the spinal cord and peripheral nerves and decrease excitatory neurotransmitter release, inhibit ascending pain transmission, activate descending inhibitory pathways, and help prevent pain mechanisms of hyperalgesia and central sensitization [3, 4].

Despite widespread use in clinical practice in pain management in adults and children, a recent systematic review by Verret and colleagues posing the question of risk/benefit ratio for perioperative use of gabapentinoids in adults found no clinically significant difference in postoperative acute, subacute, and chronic pain. Further, they found that gabapentinoids were associated with a greater incidence of adverse events, namely dizziness and visual disturbance [5]. Although the role of gabapentinoids as adjunctive pain medications in adult patients has been thoroughly summarized by Verret and colleagues, the use of gabapentinoids during the perioperative period in pediatric patients lacks consensus [4]. When pediatric anesthesiologists were surveyed regarding the use of nonopioid adjuncts for pain control for 24 h postoperatively, the most frequently utilized agents included acetaminophen, non-steroidal anti-inflammatory drugs, dexmedetomidine, dexamethasone, and ketamine; respondents noted a high degree of uncertainty about the evidence supporting other agents, including gabapentinoids [6]. Gabapentinoids may, however, be an important component to multimodal acute postoperative pain control and may decrease perioperative anxiety, postoperative nausea and vomiting (PONV), and emergence agitation among pediatric patients, so they are included in multi-modal treatment plans in enhanced recovery after surgery (ERAS). Emerging evidence also suggests a role for gabapentinoids in the development of chronic post-surgical pain (CPSP).

This narrative review aims to describe the current literature regarding perioperative use of gabapentinoids in pediatric patients and to clarify the potential role of gabapentinoids in perioperative care, considering efficacy and safety of these agents in both the immediate postoperative period and long-term outcomes. A narrative review approach was used rather than a systematic one due to a paucity of high-level evidence available in the population of interest.

2 Methods of Literature Review

PubMed/MEDLINE and Embase databases were searched in April 2022 for English-only references, with no limit on publication date range. Primary search concepts centered on pediatric populations, gabapentinoids, and terms involving perioperative, preoperative, and postoperative surgery and/or pain. Despite this review being specific to perioperative care, "pre" and "post" were included to encompass references potentially discussing perioperative tangentially. The full search strategy is described in the Supplementary Information.

All identified references were reviewed independently by the first and senior authors for inclusion. Any discrepancies between authors were resolved by discussion, and agreement was reached regarding selection. Case series/case reports with five patients or fewer and non-English language references were excluded. Systematic, scoping, and narrative review articles were also excluded but screened for any additional primary literature that the search strategy may have missed.

3 Results of Literature Review

3.1 Search Results

The literature searches in PubMed and Embase collectively identified 351 unique references; of these, 49 (14%) met the inclusion criteria. No additional references were identified after screening the review articles found in the literature search. The analysis of relevant literature revealed five categories of postoperative outcomes and their relationships to treatment with gabapentinoids: (1) acute pain intensity and/or reduction of opioid consumption (28 references); (2) PONV (21 references); (3) the use of gabapentinoids as part of ERAS protocols (15 references); (4) anxiety and emergence agitation (eight references); and (5) CPSP (five references). Some references described more than one postoperative outcome for gabapentinoids.

3.2 Gabapentinoids for Immediate Postoperative Analgesia and Decreased Opioid Consumption

Interest in using gabapentinoids to decrease children's pain in the immediate postoperative period surfaced after studies in adult surgical patients, published in the early 2000s, demonstrated opioid-sparing effects associated with perioperative use of gabapentin [7, 8]. Subsequently, it was hypothesized that gabapentinoids may have similar effects in children, so comparable investigations began to emerge in the pediatric population.

To date, the literature reflecting the use of gabapentinoids for immediate postoperative analgesia and decreased opioid consumption in pediatric patients includes 1197 patients across 28 studies, as shown in Table 1. All but six of these studies were randomized controlled trials (RCTs). The use of gabapentinoids for immediate postoperative analgesia has been reported most frequently in pediatric patients undergoing posterior spinal fusion or similar surgeries for scoliosis ($n = 300$) and tonsillectomy ($n = 237$) across nine and seven studies, respectively.

Gabapentin has been used in more studies than pregabalin (22 vs. six studies, respectively) for immediate postoperative analgesia and decreased opioid consumption. Gabapentinoid dosing practices, including timing of use preoperatively and/or postoperatively, as single or multiple dosing, as well as the magnitude of the weight-adjusted dose, have varied amongst studies.

A single preoperative dose of gabapentin was administered in 11 studies [9–19], and ten studies described gabapentin administration given preoperatively and as continued therapy postoperatively [20–29]. The gabapentin dosing regimen was not described in one of the included publications [30]. The most common preoperative dose of gabapentin was 10 mg/kg (range 5–20 mg/kg) and was typically given 1 or 2 h before surgery. The most frequent postoperative dosing of gabapentin was 15 mg/kg daily (divided twice daily [BID] or three times daily [TID]), and the range of daily doses was 5–30 mg/kg. In six studies in which the duration of postoperative gabapentin use was specified, the range was 1–30 days [21, 23, 25, 26, 28, 29].

Pregabalin was given as a single dose 30 min before surgery in two studies [31, 32], as a two-dose series preoperatively (i.e., the evening before surgery and 2 h before surgery) in two studies [33, 34], and as a two-dose series perioperatively (i.e., 1 h before and 12 h after surgery) in two studies [35, 36]. Pregabalin dosing was weight based (range 2–5 mg/kg) in three studies [32–34] and given as a fixed dose of either 150 mg or 300 mg in three studies [31, 35, 36].

Gabapentinoids significantly reduced pain in the postoperative period in 12 studies [9, 10, 16–21, 25, 27, 28, 32]. The definition of a significant reduction in pain and the way in which it was measured was not consistent across these 12 studies. Furthermore, the effect of gabapentinoids on pain was investigated in these studies using various pain scales, at different time points postoperatively, and against varying comparator groups, as detailed in Table 1. However, pain control benefits in general were noted most frequently when the gabapentinoid medication was given within 6 h of the procedure [9, 10, 16–19, 25, 32]. Another 12 studies reported no significant pain improvement versus the comparator [12–15, 22, 23, 26, 29, 31, 33, 35, 36]. Again, these studies did not have consistently defined outcome measures or comparators.

Lower postoperative opioid consumption was noted in 15 of 23 studies that examined the use of gabapentinoids for this purpose, and ten of these studies were RCTs. However, the time points when opioid consumption was evaluated varied among studies and was not always described. Although most studies reported opioid consumption as a cumulative measure postoperatively (i.e., total mg/kg or total number of doses) [10–12, 15, 18, 21, 22, 24, 26, 30–34, 36], others reported opioid consumption within certain time periods postoperatively (e.g., on each postoperative day) [13, 17, 20, 23, 25, 27, 29, 33, 35] or as time to analgesic requirement for breakthrough pain [10, 13, 15, 17, 18, 32].

3.3 Gabapentinoids for Prevention of Postoperative Nausea and Vomiting

Postoperative vomiting occurs twice as frequently in children than in adults and can lead to postoperative complications. Many factors, including individual variables, premedication and anesthetic methods, and type of surgery, can contribute to PONV in pediatric patients, making its management particularly difficult [16]. In studies investigating gabapentin for postoperative pain, it was often noted secondarily that patients experienced less PONV; as a result, the impact of gabapentinoids on PONV has been a focus in several studies of pediatric surgical patients.

The literature search results revealed only one study investigating the use of gabapentinoids for prevention of PONV in pediatric patients as a primary outcome [16], and many others have reported its impact on PONV as a secondary outcome [10, 11, 13–15, 19, 20, 23, 25–27, 29, 31–33, 37–41]. In two studies, gabapentin was part of ERAS multimodal regimens, which evaluated complex structured interventions directed toward improving postoperative outcomes; therefore, specific gabapentinoid-related outcomes could not be inferred [38, 40]. All studies reporting PONV outcomes are summarized in Table 2.

The single study that explored the impact of gabapentinoids on PONV as a primary outcome was a prospective RCT of pediatric patients undergoing adenotonsillectomy. The investigators compared a single 20 mg/kg dose of gabapentin given 2 h before surgery ($n = 72$) to placebo ($n = 72$) and found a significantly reduced incidence of postoperative vomiting (20.8% vs. 43%, respectively) [16]. In all six of the other studies [10, 11, 13–15, 19] that investigated gabapentin as a single preoperative dose for PONV, a lower dose of gabapentin was given (highest dose, 15 mg/kg), and all but one of these [19] found no impact on PONV.

Table 1 Summary of literature regarding gabapentinoids for analgesia and decreased opioid consumption in the immediate postoperative period in pediatric patients

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentinoid medication dosing	Outcome measures for analgesia/opioid consumption[b]	Comparator group(s)	Perioperative and postoperative analgesia outcomes	Opioid consumption outcomes
Amani 2015; n = 35 [9]	RCT (3 groups)	10.06 ± 3.6 yo (mean ± SD), tonsillectomy	Gabapentin 20 mg/kg 1 h pre-op	Pain (Oucher scale) upon arrival to recovery and at 3, 6, 12, 24 h post-op	Bupivacaine 0.25% injected into tonsil bed (n = 35); pethidine 1 mg/kg IV after intubation (n = 35)	Lower scores in gabapentin group at all time points measured	Not reported
Amin 2011; n = 35 [10]	RCT	5.3 ± 1.08 yo (mean ± SD), adenotonsillectomy	Gabapentin 10 mg/kg 2 h pre-op	Pain (VAS scores) at 2, 4, 6, 8, 12, 18 h post-op; time to first dose of analgesia; total pethidine consumption post-op	APAP 20 mg/kg 2 h pre-op (n = 35)	Significantly lower scores with gabapentin at 2, 4, 6, and 8 h post-op	Significantly longer time to first dose of analgesia in gabapentin group; significantly less pethidine consumption with gabapentin
Anderson 2020; n = 24 [20]	RCT	14.8 ± 2.0 yo (mean ± SD), PSF for AIS	Gabapentin 15 mg/kg pre-op (timing not specified) then 10 mg/kg q8h PO post-op (duration post-op not specified) in addition to multimodal pain protocol	Average daily pain (VAS scores) on POD0 through POD5; hydromorphone PCA use (mg/kg) on POD0 and total post-op period	Multimodal pain protocol plus placebo (n = 26)	Significantly lower score with gabapentin on POD0	Significantly less hydromorphone in gabapentin group on POD1 and POD2
Badawy 2018; n = 33 [11]	RCT	3.7 ± 1.4 yo (mean ± SD), strabismus surgery	Gabapentin 5 mg/kg 1 h pre-op	Number of patients requiring meperidine post-op (secondary outcome)	Placebo (n = 34)	Not reported	Significantly fewer patients required post-op meperidine in gabapentin group
Bassiony 2020; n = 25 [21]	RCT	7.2 yo (mean; SD not provided), tonsillectomy	Gabapentin 20 mg/kg at 0, 2, 12, 24 h post-op	Pain (VAS scores) at 0, 2, 12, and 24 h post-op; number of rescue analgesia doses given (time point not specified)	APAP 10–15 mg/kg q12h (n = 25)	Significant reduction of median VAS score post-op with gabapentin (time point of scores not specified)	Significantly fewer rescue analgesia doses for gabapentin group
Baxter 2018; n = 29 [22]	Retrospective, single-center, observational	10.34 ± 3.66 yo (mean ± SD), appendectomy	Gabapentin dosed per surgeon's preference; median post-op dose 10.1 mg/kg/day (PO divided q8h), range 4.4–30.4 mg/kg/day (duration of therapy not specified)	Time to VAS score ≤ 3; total post-op opioid dose as ME	Appendectomy without gabapentin (n = 58)	Similar mean time to VAS score of 3 or less for both groups	Significantly lower mean total ME post-op for gabapentin group

Table 1 (continued)

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentinoid medication dosing	Outcome measures for analgesia/opioid consumption[b]	Comparator group(s)	Perioperative and postoperative analgesia outcomes	Opioid consumption outcomes
Choudhry 2019; n = 95 [29]	Retrospective study of 3 interventions	14.80 ± 2.60 yo (mean ± SD; group with clonidine), 15.16 ± 2.06 yo (mean ± SD; group without clonidine), PSF for AIS	Gabapentin 10 mg/kg 1 h pre-op; from POD1 until discharge: 200 mg TID if > 50 kg, 100 mg TID if 50 kg or less	Pain (VAS scores) post-op q4h; daily morphine use on POD0 and POD1	Morphine PCA only (n = 42), PCA and gabapentin (n = 45), PCA and gabapentin and clonidine (n = 40)	No difference in VAS scores at any time post-op	Significantly lower morphine on POD1 for both groups receiving gabapentin
Dosani 2009; n = 14 [12]	RCT	5–12 yo, tonsillectomy	Gabapentin 10 mg/kg pre-op (timing not specified)	Pain scores at 4 and 24 h post-op (Coloured Analogue Scale); morphine use over 4 h post-op	Placebo (n = 14)	No differences in pain scores post-op	No differences in post-op morphine consumption
Gettis 2022; n = 26 [13]	RCT	6.8 ± 4.61 yo (mean ± SD), adenotonsillectomy	Gabapentin 15 mg/kg (maximum 600 mg) 30–60 min pre-op	Pain scores (Wong-Baker FACES or VAS) daily for 3 days; opioid use daily for 3 days; time to first analgesia	Placebo (n = 23)	No difference in pain scores on any day	No difference in daily opioid use; no difference in time to first analgesia
Haddadi 2020; n = 30 [14]	RCT	10.40 ± 2.84 yo (mean ± SD), adenotonsillectomy	Gabapentin 10 mg/kg 2 h pre-op	Pain (VAS score) at 0, 2, 4, 6, 12, and 24 h post-op	APAP 40 mg/kg suppository (n = 30)	No difference in pain scores at any point post-op	Not reported
Helenius 2020; n = 32 [33]	RCT	15.8 ± 2.3 yo (mean ± SD), PSF for spinal deformities	Pregabalin 2 mg/kg (rounded up to nearest 25 mg) evening (12 h) and 2 h pre-op	Pain (NRS) at 2, 4, 6, 8, 12, 16, 20, 24, 36, and 48 h post-op; opioid consumption over 8 h intervals until 48 h post-op; cumulative daily opioid consumption until discharge	Placebo (n = 31)	No difference in pain scores at rest at any point post-op	No difference in opioid consumption at any point post-op
Helenius 2021; n = 33 [34]	RCT	15.7 ± 2.3 yo (mean ± SD), pedicle screw instrumentation for spinal deformities	Pregabalin 2 mg/kg (rounded up to nearest 25 mg) evening (12 h) and 2 h pre-op	Cumulative opioid consumption over 48 h post-op	Placebo (n = 31)	Not reported	No difference in post-op opioid consumption
Lascano 2020; n = 261 [30]	Retrospective, observational	2–18 yo, appendectomy	Gabapentin (dosing not provided)	Total days of opioids	Propensity score matched group (n = 261)	Not reported	Significantly fewer days of opioids with gabapentin

Table 1 (continued)

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentinoid medication dosing	Outcome measures for analgesia/opioid consumption[b]	Comparator group(s)	Perioperative and postoperative analgesia outcomes	Opioid consumption outcomes
Li 2021; $n = 25$ [23]	Retrospective, observational	14.8 ± 1.9 yo (mean ± SD), PSF for AIS	Gabapentin dosed per physician preference; mean dose 7.8 mg/kg (range 4–11.5 mg/kg) given 1 h pre-op; 5.1 mg/kg/day (range 2.4–15.3) for up to 2 days post-op	Pain scores in PACU, PACU until midnight, then in 8 h intervals until POD2 (daily interval); mean analgesic dose on POD0, POD1, POD2	Intrathecal morphine alone ($n = 25$)	Significantly higher mean pain score with gabapentin in first 8 h on POD1	Significantly lower oxycodone consumption in gabapentin group on POD2
Mameli 2012; not specified, but total $n = 38$ [35]	RCT	11–18 yo, pectus excavatum repair	Pregabalin 150 mg 1 h pre-op and 150 mg 12 h post-op	Pain scores and morphine consumption (q12h) until 72 h post-op	Standard of care without pregabalin (number not specified)	Similar pain scores between groups	Significantly lower morphine consumption in pregabalin group at 12 and 24 h post-op
Mayell 2014; $n = 18$ [15]	RCT	14.7 ± 1.8 yo (mean ± SD), PSF for scoliosis	Gabapentin 600 mg 1 h pre-op	Morphine consumption between 0 and 24 h post-op; time to first rescue analgesia; pain (NRS) at rest and movement; cumulative opioid consumption at 1, 4, 8, 12, 24, 48, and 72 h post-op	Placebo ($n = 17$)	No significant difference in NRS score at rest or with movement at any point within 72 h post-op	No significant differences between groups in morphine consumption at any point 72 h post-op; no differences between groups in time to first rescue analgesia
Mohamed 2014; $n = 72$ [16]	RCT	5.4 ± 2.3 yo (mean ± SD), adenotonsillectomy	Gabapentin 20 mg/kg 2 h pre-op	Number of patients requiring analgesic within 6 h post-op (secondary outcome)	Placebo ($n = 72$)	Significantly higher frequency of requiring analgesic in placebo group	Not reported
Nanda 2019; not specified, but total $n = 60$ [17]	RCT	8–17 yo, urogenital surgeries	Gabapentin 15 mg/kg 2 h pre-op	Pain (NRS) at 0, 1, 4, 8, 16, and 24 h post-op; intra-op fentanyl requirement; fentanyl requirement within 4 h post-op; time to first rescue analgesia dose	Placebo (number not specified)	Significantly lower NRS in first 4 h post-op for gabapentin group	Significantly lower fentanyl requirement intra-op and 4 h post-op for gabapentin group; significantly delayed demand for first rescue analgesic in gabapentin group

Table 1 (continued)

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentinoid medication dosing	Outcome measures for analgesia/opioid consumption[b]	Comparator group(s)	Perioperative and postoperative analgesia outcomes	Opioid consumption outcomes
Pinto Filho 2019; $n = 40$ [18]	RCT	62.8 ± 59.2 months old (mean ± SD), unilateral inferior limb surgery	Gabapentin 10 mg/kg 1–2 h pre-op	Pain (CRIES, CHIPPS, or Wong-Baker FACES) intensity defined as mild, moderate, or severe at 1, 4, 8, 12, 18, and 24 h post-op; time to first use of morphine and frequency of morphine use	Placebo ($n = 44$)	Significantly lower pain intensity observed at 4 and 8 h post-op in gabapentin group	No significant differences in time to first morphine dose nor frequency of use
Pinto Filho 2019; $n = 90$ [19]	RCT with 2 levels of gabapentin dosing	3.29 ± 1.42 (15 mg/kg dose group) and 3.42 ± 1.39 (30 mg/kg dose group) yo (mean ± SD), LP or myelogram	Gabapentin 15 mg/kg ($n = 44$) or 30 mg/kg ($n = 46$) 1–2 h pre-op	Pain (CHIPPS) at 0 and 30 min post-op	Placebo ($n = 45$)	Significantly lower pain at 30 min post-op for both gabapentin dose groups	Not reported
Raddaoui 2018; $n = 20$ [36]	RCT	17.1 ± 2.6 yo (mean ± SD), PSF for AIS	Pregabalin 150 mg 1 h pre-op and 150 mg 12 h post-op	Total morphine consumption in first 48 h post-op; pain (VAS) at rest and movement at 0, 1, 2, 4, 8, 12, 18, 24, 36, and 48 h post-op	Placebo ($n = 20$)	No significant differences in pain at rest or with movement at any time point	Significantly lower morphine consumption with pregabalin
Ramsey 2020; $n = 74$ [24]	Retrospective, observational	Infants (median 137 days old), superior cavopulmonary connection	Gabapentin dosed per physician preference; median dose 10.7 mg/kg/day (IQR 5.5–23.4); duration of therapy not specified	Total ME in first 7 days post-op	Infants not receiving gabapentin ($n = 249$)	Not reported	Those receiving gabapentin received significantly more ME
Rusy 2010; $n = 29$ [25]	RCT	14.8 ± 2.1 yo (mean ± SD), PSF for AIS	Gabapentin 15 mg/kg 25–30 min pre-op, then 5 mg/kg TID for 5 days	Total daily morphine consumption on POD0, POD1, POD2, POD3, and POD4; pain scores (NRS) in PACU and BID on POD1, POD2, POD3, and POD4	Placebo ($n = 30$)	Significantly lower pain in gabapentin group in PACU and on morning of POD1	Significantly lower morphine consumption in gabapentin group on POD0, POD1, and POD2

Table 1 (continued)

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentinoid medication dosing	Outcome measures for analgesia/opioid consumption[b]	Comparator group(s)	Perioperative and postoperative analgesia outcomes	Opioid consumption outcomes
Salah Abdelgalil 2019; $n = 60$ [31]	RCT (4 groups)	Mean 10.16 yo (pregabalin + magnesium IV group) and 11.33 yo (pregabalin only group), thoracic surgery	Pregabalin 300 mg 30 min pre-op	Pain (VAS) at 0, 4, 8, 12, and 24 h post-op; total morphine consumption within 24 h post-op	Placebo + normal saline($n = 30$); placebo + magnesium IV ($n = 30$)	Lower VAS scores with pregabalin at 0, 4, 12, and 24 h post-op but not statistically significant	Significantly lower morphine consumption in group receiving pregabalin + magnesium vs. all other groups
Talaat 2021; $n = 30$ [32]	RCT	23.5 (median) and 14–43 (IQR) months old, day-case surgery[c]	Pregabalin 5 mg/kg 30 min pre-op	Intra-op fentanyl consumption; intra-op meperidine consumption; time to first analgesic; pain (FLACC) at PACU arrival and discharge, and at 2, 4, 6, 8, 10, 12 h post-op	Midazolam 0.75 mg/kg PO 30 min pre-op ($n = 30$)	Significantly lower pain with pregabalin at PACU discharge and at 2, 4, 6, and 8 h post-op	Significantly less fentanyl and meperidine consumption intra-op in pregabalin group; significantly longer time to first analgesic requirement in pregabalin group
Tomaszek 2020; $n = 20$ [26]	RCT	13 (10–15) yo (median and IQR), Ravitch procedure	Gabapentin 15 mg/kg 1 h pre-op, then 7.5 mg/kg BID for 3 days	Pain intensity (NRS) as daily mean scores on POD0, POD1, POD2, and POD3; total fentanyl consumption	Placebo ($n = 20$)	No significant difference in mean pain scores on POD0, POD1, POD2, or POD3	No significant difference in total opioid consumption
Trzcinski 2019; $n = 24$ [27]	Retrospective cohort	14.9 yo (mean), PSF for AIS	Gabapentin 10 mg/kg on morning of surgery followed by 5 mg/kg TID (duration not specified)	Daily mean pain score and ME/kg/day on POD1–4	Standard of care without gabapentin ($n = 105$)	Significantly lower pain scores in gabapentin group on POD2	Significantly lower opioid use on POD1 and POD2
Wang 2018; $n = 23$ [28]	RCT	14.3 ± 2.8 yo (mean ± SD), amputation for bone tumor	Gabapentin 300 mg once 4 days pre-op, 300 mg BID 3 days pre-op, then 300 mg TID until 30 days post-op	Daily pain scores (VAS) on POD0–14	Placebo ($n = 22$)	No significant difference in pain scores seen until POD4	Not reported

AIS adolescent idiopathic scoliosis, *APAP* acetaminophen, *BID* twice daily, *CHIPPS* Children and Infants Postoperative Pain Scale, *FLACC* faces legs activity cry consolability, *intra-op* intraoperatively, *IQR* interquartile range, *IV* intravenous, *LP* lumbar puncture, *ME* morphine equivalents, *NS* normal saline, *NRS* numeric rating scale, *PACU* post-analgesia care unit, *PCA* patient-controlled analgesia, *PO* by mouth, *POD* postoperative day, *post-op* postoperatively, *pre-op* preoperatively, *PSF* posterior spinal fusion, *qxh* every *x* hours, *RCT* randomized controlled trial, *SD* standard deviation, *TID* three times daily, *VAS* visual analog scale, *yo* years old

[a]Population demographic data are reported as presented within the primary reference

[b]Includes primary and secondary outcomes related to analgesia and opioid consumption; first outcome listed in the table was the primary outcome for the study unless otherwise indicated

[c]Outpatient surgery included hernia repair (36.7%), adenotonsillectomy (20%), adenoidectomy (16.7%), hydrocelectomy (13.3%), and orchiopexy (3.3%)

Table 2 Summary of literature regarding gabapentinoids for the reduction of perioperative nausea and vomiting in pediatric patients

Reference, year; number of patients receiving gabapentinoid	Study type	Population[a]	Medication	Outcome measure for PONV[b]	Comparator group(s)	Findings
Amin 2011; $n = 35$ [10]	RCT	5.3 ± 1.08 yo (mean ± SD), adenotonsillectomy	Gabapentin 10 mg/kg 2 h pre-op	Incidence of PONV	APAP 20 mg/kg 2 h pre-op ($n = 35$)	Similar PONV incidence between groups
Anderson 2020; $n = 24$ [20]	RCT	14.8 ± 2.0 yo (mean ± SD), PSF for AIS	Gabapentin 15 mg/kg pre-op (timing not specified) then 10 mg/kg q8h PO post-op (duration post-op not specified) in addition to multimodal pain protocol	Incidence of PONV	Multimodal pain protocol plus placebo ($n = 26$)	Similar PONV incidence between groups
Badawy 2018; $n = 33$ [11]	RCT	3.7 ± 1.4 yo (mean ± SD), strabismus surgery	Gabapentin 5 mg/kg 1 h pre-op	Incidence of PONV	Placebo ($n = 34$)	Similar PONV incidence between groups
Choudhry 2019; $n = 95$ [29]	Retrospective study of 3 interventions	14.80 ± 2.60 yo (mean ± SD; group with clonidine), 15.16 ± 2.06 yo (mean ± SD; group without clonidine), PSF for AIS	Gabapentin 10 mg/kg 1 h pre-op; from POD1 until discharge: 200 mg TID if > 50 kg, 100 mg TID if 50 kg or less	Incidence of PONV requiring medication	Morphine PCA only ($n = 42$), PCA and gabapentin ($n = 45$), PCA and gabapentin and clonidine ($n = 40$)	Similar PONV incidence between groups
Eskandarian 2015; $n = 21$ [37]	Double-blind, placebo-controlled crossover	5.28 ± 1.10 yo (mean ± SD), pulpotomy treatment	Pregabalin 75 mg 2 h pre-op	Incidence of PONV	Placebo ($n = 21$)	Rates of PONV comparable between groups
Franklin 2021; $n = 85$ [40]	Retrospective observational (quality improvement)	14.6 ± 4.4 yo (mean ± SD), orthopedic hip surgery	Gabapentin as part of a multimodal protocol; if > 50 kg: 300 mg pre-op (time pre-op not specified) then 300 mg q8h (duration not specified); if > 40 kg but ≤ 50 kg, 200 mg pre-op then 200 mg q8h; if ≤ 40 kg, 5 mg/kg pre-op then 5 mg/kg q8h	Antiemetic count	Historical control ($n = 110$)	Decreased after implementing PSH ERAS protocol
Gettis 2022; $n = 26$ [13]	RCT	6.8 ± 4.61 yo (mean ± SD), adenotonsillectomy	Gabapentin 15 mg/kg (maximum 600 mg) given 30–60 min pre-op	Incidence of PONV	Placebo ($n = 23$)	Similar rates of PONV
Haddadi 2020; $n = 30$ [14]	RCT	10.40 ± 2.84 yo (mean ± SD), adenotonsillectomy	Gabapentin 10 mg/kg 2 h pre-op	Incidence of PONV at 0, 2, 4, 6, 12, and 24 h post-op	APAP 40 mg/kg suppository ($n = 30$)	Similar rates of PONV at all time points

Table 2 (continued)

Reference, year; number of patients receiving gabapentinoid	Study type	Population[a]	Medication	Outcome measure for PONV[b]	Comparator group(s)	Findings
Helenius 2020; $n = 32$ [33]	RCT	15.8 ± 2.3 yo (mean ± SD), PSF for spinal deformities	Pregabalin 2 mg/kg (rounded up to nearest 25 mg) evening pre-op (12 h) and 2 h before anesthesia	Incidence of PONV over 8 h intervals until 48 h post-op	Placebo ($n = 31$)	Similar rates of PONV between groups at all time points
Li 2021; $n = 25$ [23]	Retrospective, observational	14.8 ± 1.9 yo (mean ± SD), PSF for AIS	Gabapentin dosed per physician preference; mean dose 7.8 mg/kg (range 4–11.5 mg/kg) given 1 h pre-op; 5.1 mg/kg/day (range 2.4-15.3) for up to 2 days post-op	Incidence of PONV	Intrathecal morphine alone ($n = 25$)	Significantly less PONV with gabapentin
Mangat 2020; $n = 33$ [38]	Retrospective	Median 16 (IQR 14–17) yo, Pectus excavatum repair	Gabapentin as part of a multimodal regimen; if under 12 yo or < 40 kg: 15 mg/kg pre-op (time pre-op not specified) then 5 mg/kg TID × 7 days post-discharge; if at least 12 yo and 40–59 kg 600 mg pre-op followed by 200 mg TID; if 12 yo or older and 60 kg or more 900 mg pre-op followed by 300 mg TID	Incidence of PONV	Before implementation of multimodal regimen containing gabapentin ($n = 17$)	Rates of PONV comparable between groups
Marouf 2018; $n = 30$ [39]	RCT	6.9 ± 1.68 yo (mean ± SD), adenotonsillectomy	Pregabalin 1.5 mg/kg 30 min pre-op	Incidence of PONV	Placebo ($n = 30$)	Significantly less PONV with pregabalin
Mayell 2014; $n = 18$ [15]	RCT	14.7 ± 1.8 yo (mean ± SD), PSF for scoliosis	Gabapentin 600 mg 1 h pre-op	Incidence of PONV within 72 h post-op	Placebo ($n = 17$)	Rates of PONV comparable between groups
Mohamed 2014; $n = 72$ [16]	RCT	5.4 ± 2.3 yo (mean ± SD), adenotonsillectomy	Gabapentin 20 mg/kg 2 h pre-op	Number of patients experiencing PONV within 6 h post-op (primary outcome)	Placebo ($n = 72$)	Significantly less PONV with gabapentin
Pinto Filho 2019; $n = 90$ [19]	RCT	3.29 ± 1.42 (15 mg/kg dose group) and 3.42 ± 1.39 (30 mg/kg dose group) yo (mean ± SD), LP or myelogram	Gabapentin 15 mg/kg ($n = 44$) or 30 mg/kg ($n = 46$) 1–2 h pre-op	Incidence of PONV within 48 h post-op	Placebo ($n = 45$)	Lower PONV incidence in gabapentin 30 mg/kg group

Table 2 (continued)

Reference, year; number of patients receiving gabapentinoid	Study type	Population[a]	Medication	Outcome measure for PONV[b]	Comparator group(s)	Findings
Raddaoui 2018; $n = 20$ [36]	RCT	17.1 ± 2.6 yo (mean ± SD), PSF for AIS	Pregabalin 150 mg 1 h pre-op and 150 mg 12 h post-op	Incidence of PONV within 48 h post-op	Placebo ($n = 20$)	Rates of PONV comparable between groups
Rusy 2010; $n = 29$ [25]	RCT	14.8 ± 2.1 yo (mean ± SD), PSF for AIS	Gabapentin 15 mg/kg 25–30 min pre-op, then 5 mg/kg TID for 5 days	Number of ondansetron doses given	Placebo ($n = 30$)	Number of ondansetron doses given comparable between groups
Salah Abdelgalil 2019; $n = 60$ [31]	RCT (4 groups)	Mean 10.16 yo (pregabalin + magnesium IV group) and 11.33 yo (pregabalin only group), thoracic surgery	Pregabalin 300 mg 30 min pre-op	Incidence of PONV requiring antiemetic 24 h post-op	Placebo + normal saline ($n = 30$); placebo + magnesium IV ($n = 30$)	Significantly lower incidence of PONV in both groups receiving pregabalin
Talaat 2021; $n = 30$ [32]	RCT	23.5 (median) and 14–43 (IQR) months old, day-case surgery [c]	Pregabalin 5 mg/kg 30 min pre-op	Incidence of PONV	Midazolam 0.75 mg/kg PO 30 min pre-op ($n = 30$)	No significant difference in PONV incidence between groups
Tomaszek 2020; $n = 20$ [26]	RCT	13 (10–15) yo (median and IQR), Ravitch procedure	Gabapentin 15 mg/kg 1 h pre-op, 7.5 mg/kg BID for 3 days	Incidence of PONV; doses of ondansetron given	Placebo ($n = 20$)	Rates of PONV comparable between groups, but significantly fewer doses of ondansetron given in gabapentin group
Trzcinski 2019; $n = 24$ [27]	Retrospective cohort	14.9 yo (mean), PSF for AIS	Gabapentin 10 mg/kg on morning of surgery followed by 5 mg/kg TID (duration not specified)	Incidence of PONV	Standard of care without gabapentin ($n = 105$)	Rates of PONV comparable between groups

AIS adolescent idiopathic scoliosis, *APAP* acetaminophen, *BID* twice daily, *ERAS* enhanced recovery after surgery, *IQR* interquartile range, *IV* intravenous, *NS* normal saline, *LP* lumbar puncture, *PCA* patient-controlled analgesia, *PO* by mouth, *POD* postoperative day, *PONV* postoperative nausea and vomiting, *post-op* postoperatively, *pre-op* preoperatively, *PSF* posterior spinal fusion, *PSH* perioperative surgical home, *qxh* every *x* hours, *RCT* randomized controlled trial, *SD* standard deviation, *TID* three times daily, *yo* years old

[a]Population data are reported as presented within the primary reference

[b]All PONV outcomes were secondary outcome measures except where indicated otherwise

[c]Outpatient surgery included hernia repair (36.7%), adenotonsillectomy (20%), adenoidectomy (16.7%), hydrocelectomy (13.3%), orchiopexy (3.3%)

3.4 Perioperative Use of Gabapentinoids in ERAS Protocols

ERAS protocols have emerged as evidence-based processes to improve perioperative care. The premise of ERAS protocols is that no single element will improve outcomes of surgery, so a multimodal approach combining all elements of perioperative surgical care is necessary. This approach requires coordinated efforts of a team from multiple disciplines, including surgery, anesthesia, nursing, and pharmacy. Some of the improved perioperative outcomes reported as resulting from ERAS protocols include shorter lengths of stay and reduced hospital admissions, highlighting its additional advantage within value-based care [41].

Opioid-sparing analgesia is one of the key goals of ERAS protocols. Given the benefits observed with regards to reduced opioid consumption and improved postoperative pain control, gabapentinoids have been included as an element of many ERAS protocols in adults and children. Our literature search revealed 15 unique references, all published since 2016, that included collectively more than 650 pediatric patients who received gabapentinoids as part of an ERAS protocol (Table 3). All included studies utilized gabapentin (not pregabalin). All but one [44] of the published studies were observational in design, with four prospective studies [42, 45, 46, 49] and 10 retrospective studies [38, 40, 43, 47, 48, 50–54]. These study designs are directly reflective of the quality improvement aim of ERAS protocols. Similarly, ERAS being a multimodal approach lends itself to impact many different outcome areas; our literature search found that these studies encompassed a variety of outcomes, including pain control, opioid consumption, PONV, chronic pain, length of stay, procedure time, and others.

Outcomes involving immediate and chronic postoperative pain control were reported in nine of the identified references. Five of these studies reported a significant benefit in the immediate postoperative period [45, 47, 50, 52, 53]; one study found a trend towards lower reported pain scores on the day of discharge [38], and another found significantly higher pain scores on the day of surgery but no difference on other postoperative days [54]. The remaining two studies found no significant difference in immediate analgesia outcomes; however, a significant benefit for CPSP was noted in one of these studies [42], and lower opioid consumption was noted in both studies [42, 51]. It is important to note that pain control outcomes were inconsistently defined across studies, as detailed in the "outcomes" column of Table 3.

As mentioned previously, reducing opioid consumption postoperatively is a hallmark goal of many ERAS protocols. Ten references were identified that investigated the impact of gabapentinoid-containing ERAS protocols on opioid consumption during the postoperative period: nine studies reported significant reduction in opioid use intraoperatively and/or immediately postoperatively [40, 42, 43, 45–47, 49, 51, 52]. The sole report describing increased usage of opioids postoperatively was a retrospective study of adolescent patients undergoing the Nuss or Ravitch procedures. The post-ERAS group started oral opioid medications significantly sooner postoperatively than did the pre-ERAS group (65.4 vs. 84.2 h postoperatively), and the authors proposed that this timing was likely the key reason for the significant increase in median total postoperative morphine equivalents needed in the post-ERAS and pre-ERAS groups (2.3 mg/kg vs. 1.51 mg/kg) [38]. Again, it is important to note that opioid consumption postoperatively was defined in different ways across these studies (i.e., varying time frames or intervals and thus calculation of doses).

Several additional benefits of gabapentinoid-containing ERAS protocols, including shorter procedure and anesthesia times, decreased length of stay, better physiotherapy outcomes, and reduced incidences of opioid-related adverse effects, have been reported in studies of pediatric surgical patients. Seven of the 12 studies reporting on length of stay found a significantly shorter length of stay in the ERAS group [43, 45, 47, 48, 50, 53, 54]; the other five studies found a similar length of stay between groups [38, 40, 46, 51, 52].

Four studies of gabapentinoid-containing ERAS protocols have reported physiotherapy-related outcomes, with two finding a significant benefit and two finding similar outcomes in the compared cohorts. The first report on the utility of gabapentin as part of a multimodal protocol involved a retrospective chart review of adolescent patients with scoliosis who were undergoing posterior spinal fusion. Patients in the gabapentin group ($n = 50$) were 5.34 times more likely than those in the control group ($n = 51$) to complete the most challenging physiotherapy goal (stairs) within 1 day of surgery [52]. Similarly, a prospective analysis of opioid-reduced anesthesia for scoliosis surgery indicated that a significantly higher proportion of patients in the opioid-reduced anesthesia group ($n = 28$; 90.9%) than in the control group ($n = 36$; 61.1%) were able to undergo physiotherapy on the first day postoperatively [42]. In contrast to these findings, similar rates of physiotherapy participation and physiotherapy session duration between groups (patient-controlled analgesia protocol vs. multimodal protocol) were found when investigated as a secondary outcome in a study of 30 children with cerebral palsy undergoing selective dorsal rhizotomy [51]. A study of physiotherapy-related outcomes in 55 pediatric patients undergoing the Nuss and Ravitch procedures, with focus on longer-term physiotherapy outcomes (i.e., in the outpatient setting), showed a similar rate of physiotherapy referrals for both the pre-ERAS and post-ERAS groups in the outpatient setting (6% vs. 28%, respectively; $p = 0.14$) [38].

Table 3 Summary of literature describing the perioperative use of gabapentinoid-containing ERAS protocols

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentin dosing	Comparator group(s)	Outcome(s)
Choudhry 2016; $n = 17$ [54]	Retrospective	15.0 ± 2.75 yo (mean ± SD), Nuss procedure	10 mg/kg 1 h pre-op; from POD1 until discharge: 200 mg TID if > 50 kg, 100 mg TID if 50 kg or less	Previous approach using thoracic epidural catheter ($n = 15$)	Group receiving CWC with adjunct (gabapentin and clonidine) had significantly higher pain scores on POD0, but scores were comparable on other days; fewer changes in regimen needed to maintain pain relief (pain scores ≤ 4); lower incidence of N/V; shorter anesthesia and OR time; shorter LOS
Franklin 2021; $n = 85$ [40]	Retrospective observational (quality improvement)	14.6 ± 4.4 yo (mean ± SD), orthopedic hip surgery	If > 50 kg: 300 mg pre-op (time pre-op not specified) then 300 mg q8h (duration not specified); if > 40 kg but £ 50 kg, 200 mg pre-op then 200 mg q8h; if £ 40 kg, 5 mg/kg pre-op then 5 mg/kg q8h	Historical control pre-ERAS implementation ($n = 110$)	Significant opioid use reduction in intra-op and PACU morphine equivalents with ERAS; decreased N/V after implementing PSH ERAS protocol; similar LOS between groups
Gornitzky 2016; $n = 58$ [47]	Retrospective	14.8 ± 2.3 yo (mean ± SD), PSF	Not provided	Conventional pathway ($n = 80$)	Improved mean daily pain scores on POD0, 1, 2 with ERAS; PCA discontinued earlier; lower opioid consumption on POD0; similar N/V incidence; less pruritus; urinary catheter removed sooner; shorter LOS
Hush 2019; $n = 50$ [45]	Prospective observational	9.9 ± 1.6 months old (mean ± SD), palatoplasty	15 mg/kg 2–3 h pre-op; 10 mg/kg TID until discharge	Historical control pre-ERAS implementation ($n = 50$)	Shorter time to first and second feeds in ERAS group; significantly lower intra-op and post-op morphine equivalents; decrease in LOS; no episodes of respiratory depression in ERAS group
Julien-Marsollier 2021; $n = 68$ [42]	Prospective observational	Median 15.0 (range 12.0-18.0) yo, PSF for AIS	Not provided; included in ORA protocol	Opioid-based anesthesia control group ($n = 36$)	No significant difference in analgesia at day 1 or day 3; significantly lower morphine consumption with ORA protocol at day 1; more patients able to undergo PT on POD1; longer anesthesia and OR time
Kelly 2020; $n = 37$ [46]	Prospective observational	Age not specified; PSF for AIS	Mean 8.3 mg/kg/day (pre-implementation) and 9.8 mg/kg/day (post-implementation); duration of therapy not specified	Pre-ERAS implementation ($n = 110$)	Significantly lower MME after implementation; similar LOS; fewer blood transfusions; less PICU use
Kriel 2019; $n = 41$ [48]	Retrospective	13.8 ± 2.4 yo (mean ± SD), scoliosis surgery	15 mg/kg preoperatively (time pre-op not specified) then 5 mg/kg TID × 7 days	PCA only ($n = 12$); PCA plus EPP ($n = 28$)	Significantly shorter LOS for multimodal (including gabapentin) group vs. PCA group; incidence of prolonged bowel retention decreased significantly for multimodal group
Lindgren 2020; $n = 72$ [49]	Prospective, quality-improvement	11–26 yo, PSF for AIS and SK	Not provided	None	Decrease in median oxycodone use after implementation of multimodal regimen (gabapentin-containing)

Table 3 (continued)

Reference, year; number of patients receiving gabapentinoid	Study design	Population[a]	Gabapentin dosing	Comparator group(s)	Outcome(s)
Mangat 2020; $n = 33$ [38]	Retrospective	Median 16 (IQR 14–17) yo, Pectus excavatum repair	As part of a multimodal regimen; if under 12 yo or < 40 kg: 15 mg/kg pre-op (time pre-op not specified) then 5 mg/kg TID × 7 days post-discharge; if at least 12 yo and 40–59 kg 600 mg pre-op followed by 200 mg TID; if 12 yo or older and 60 kg or more 900 mg pre-op followed by 300 mg TID	Before implementation of multimodal regimen containing gabapentin ($n = 17$)	Trend towards lower reported pain scores on day of discharge in post-ERAS group; post-ERAS group started on narcotics sooner post-op; significant increase in median post-op opiate usage; similar N/V incidence between groups; similar procedure time; similar LOS; similar rate of outpatient PT referrals; similar rates of constipation and urinary retention; less pruritis
Naduvanahalli Vivekanandaswamy 2021; $n = 63$ [44]	RCT	10-18 yo, PSF for AIS	10 mg/kg 4 h pre-op	Dexmedetomidine ($n = 31$) vs. morphine ($n = 32$); both groups received gabapentin	No difference in NRS or breakthrough analgesia but significantly less PONV in dexmedetomidine vs. morphine group (both groups received gabapentin); lower incidence of morphine-related adverse effects (ileus, respiratory depression) in non-opioid group
Nguyen 2019; $n = 64$ [50]	Retrospective	Age not specified; PSF	Not provided	Pre-ERAS implementation ($n = 52$)	Significantly lower max pain score on POD1, POD2, POD3, and POD4 in intervention group; significantly shorter LOS with intervention
Pao 2020; $n = 16$ [51]	Retrospective	7.5 ± 3.3 yo (mean ± SD), SDR	5 mg/kg/day nightly for 1 week pre-op; 5–10 mg/kg/day TID post-op (duration not specified)	Traditional management with PCA ($n = 14$)	No significant differences in mean pain scores (POD0, POD1, POD2, POD3) between groups; significantly lower MME required during hospital stay in intervention group
Thomas 2018; $n = 50$ [52]	Retrospective	14 ± 2 yo (mean ± SD), PSF for AIS	5 mg/kg pre-op (time pre-op not specified) then 5 mg/kg TID until discharge	Multimodal pain management without gabapentin ($n = 51$)	Significantly lower pain scores in gabapentin group POD2; significantly lower morphine consumption in gabapentin group POD1; significantly shorter time to PT goals in gabapentin group
Wharton 2020; $n = 58$ [53]	Retrospective observational	Under 21 yo (not further specified), Nuss procedure	300 mg QHS starting 3 days pre-op, then a 21-day taper (TID post-op for 7 days, BID for 7 days, QHS for 7 days)	Pre-ERAS implementation ($n = 51$)	Significantly lower pain scores on POD1; significantly shorter LOS; fewer patients required urinary catheters; trend towards lower incidence of readmissions
Yalcin 2020; $n = 57$ [43]	Retrospective	Median 17 (IQR 16–18) yo, laparoscopic sleeve gastrectomy	Not provided	Conventional care ($n = 51$)	Significantly lower MME intra-op and post-op in ERAS group; significantly shorter LOS for ERAS group; shorter surgery duration for ERAS group; significantly lower intraoperative IV fluid volume; more patients able to take PO on POD0 in ERAS group

Many postsurgical complications may be secondary to the effects of opioids, including PONV, pruritis, respiratory depression, constipation, and urinary retention. The untoward effects of opioids were highlighted in an RCT that primarily aimed to determine whether dexmedetomidine ($n = 31$) or morphine ($n = 32$) as part of a multimodal regimen was better at reducing opioid consumption in 63 adolescent idiopathic scoliosis patients undergoing posterior spinal fusion [44]. The multimodal regimen in both groups included preemptive analgesia with gabapentin administered at 10 mg/kg (maximum dose 600 mg) 4 h preoperatively. No significant differences were noted between the groups' pain scores evaluated using the numerical rating scale or breakthrough analgesia requirements, but significantly higher PONV scores (0.46 vs. 0.16; $p < 0.001$) and a higher incidence of treatment with an enema or suppository (0.59 vs. 0.26; $p = 0.01$) were noted in the morphine group. Five additional studies have reported on the impact of ERAS protocols on opioid-related postoperative adverse effects in pediatric surgical patients. Two studies found a lower incidence of pruritis in the ERAS cohort [38, 47]; one study found respiratory depression to be less frequent with an ERAS protocol [45], and another study found a significantly reduced incidence of constipation in the multimodal analgesia group than in the control group (2% vs. 25%, respectively). Likewise, significantly fewer patients required urinary catheter placement postoperatively if an ERAS protocol was followed (21% with ERAS vs. 47% without) [47], and another study showed that urinary catheters could be removed 12 h sooner when an ERAS protocol was used [53].

3.5 Gabapentinoids for Reduction of Perioperative Anxiety and Emergence Agitation

The sedative properties of gabapentinoids make them an appealing choice for two distinct outcomes related to their anxiolytic effects: perioperative anxiety and emergence agitation. Emergence agitation typically occurs within 30 min after anesthesia, and the patient's disruptive behavior can be self-harming and distressing for the healthcare team and the patient's caregivers [55], so exploring potential treatment options, such as gabapentinoids, to ameliorate perioperative anxiety and emergence agitation is of great interest to clinicians.

The use of gabapentinoids to reduce either perioperative anxiety or emergence agitation in pediatric patients has been described in eight publications, most of which were randomized, placebo-controlled trials (Table 4). In the literature reflecting the applications of gabapentinoids to address perioperative anxiety and emergence agitation in pediatric surgery, which is presented in Table 4, we have distinguished between these two outcomes. Indeed, the majority of studies reflected in Table 4 (five of seven studies),

Table 3 (continued)

AIS adolescent idiopathic scoliosis, *BID* twice daily, *CWC* chest wall catheter, *EPP* elastomeric pain pump, *ERAS* enhanced recovery after surgery, *intra-op* intraoperative, *IV* intravenous, *LOS* length of stay, *MME* milligrams of morphine equivalents, *N/V* nausea/vomiting, *NRS* numeric rating scale, *OR* operating room, *ORA* opioid-reduced anesthesia, *PACU* post-anesthesia care unit, *PCA* patient-controlled analgesia, *PICU* pediatric intensive care unit, *PO* by mouth, *POD* postoperative day, *PONV* postoperative nausea and vomiting, *post-op* postoperatively, *pre-op* preoperatively, *PSF* posterior spinal fusion, *PSH* perioperative surgical home, *PT* physical therapy, *QHS* at bedtime, *qxh* every *x* hours, *RCT* randomized controlled trial, *SD* standard deviation, *SDR* selective dorsal rhizotomy, *SK* Scheuermann's Kyphosis, *TID* three times daily, *yo* years old

[a]Population data are reported as presented within the primary reference

utilized emergence agitation as their studied outcome, as supported in the "findings" column of the table. Only two studies addressed anxiety per se, Eskandarian in the context of dental procedures, and Tomaszek in the context of spinal surgery [26, 37]. Gabapentin was utilized in five studies [11, 18, 19, 26, 56], with 207 patients altogether; pregabalin was investigated in three studies, including 81 patients altogether [32, 37, 39]. Gabapentin was typically given as a single dose of 5–30 mg/kg 1 or 2 h before anesthesia; in one study [26], gabapentin therapy was continued for a total of 3 days. Preoperative pregabalin was given as a single dose, of variable size among studies (i.e., 75-mg fixed dose, 1.5 mg/kg, and 5 mg/kg). Reduction in anxiety or emergence agitation was observed in all but one study; the authors hypothesized that this may have been due to inadequate blood concentrations of pregabalin because it was given only 30 min before the procedure [32].

3.6 Gabapentinoids and Chronic Post-surgical Pain

Chronic pain (duration > 3 months) after surgery has a variable prevalence in adults, with higher prevalence following limb amputation (50–85%), thoracotomy (5–65%), mastectomy (20–50%), and herniorrhaphy (5–35%) [57]. In children, variable prevalence of CPSP has been reported, depending on the type of surgery, with high prevalence following amputations, limb-sparing surgery, and thoracotomies. The overall prevalence cumulatively after pediatric surgery has been cited as 20% at 12 months [58–61].

Other variables contributing to higher incidence of CPSP include being female, having pre-existing psychological factors (e.g., anxiety, depression, and catastrophizing), the extent of surgical trauma and likelihood of nerve damage, pre-operative pain, and the intensity of acute pain immediately post-operatively [57–60]. Furthermore, the magnitude of opioid exposure immediately post-operatively (morphine consumption on day 1 > 0.5 mg/kg) is the most important independent predictive factor for persistent chronic pain with a neuropathic component, specifically in the population at high risk of CPSP development, such as adolescents after scoliosis surgery [62].

The association of the prevalence, severity, and significance of CPSP (for the individual with CPSP and for the society in general, as a health care problem) and the fact that both the intensity of acute post-operative pain and the magnitude of opioid exposure early post-surgically correlate with increased risk of CPSP development justify multi-modal analgesia protocols aimed to improve quality of pain control and reduce opioid consumption. In this context, the use of gabapentinoids has been favored as part of multi-modal, peri-operative, opioid-reduction protocols, sometimes in the form of ERAS protocols [38, 42–45, 47–54].

As shown in Table 5, the inclusion of gabapentinoids in multi-modal peri-operative treatment protocols and the subsequent prevalence and severity of general or neuropathic CPSP is described in several studies identified by our search procedure [28, 34, 42, 63, 64]. When outcomes were evaluated as part of various ERAS studies, they were not focused on the value of gabapentinoids in isolation, instead describing pain management interventions in therapeutic combinations and subsequently evaluating the implications for CPSP development; therefore, extrapolations regarding their value is not possible.

In the earliest case series describing neuropathic pain after multilevel surgery in six children with cerebral palsy, researchers noted the distinction between first- and second-line therapeutic options (favoring gabapentin frequently as first line) and the amount of time until symptoms resolved. Gabapentin was used in four of six cases, in dose regimens initiated at 100 mg TID and increased up to 300–500 mg TID [64].

In a prospective observational study of 37 children and adolescents treated for osteosarcoma with a complex chemotherapy regimen and surgical intervention including either limb-sparing (68.4%) or amputation (31.6%), neuropathic pain developed in 81% of patients. Most of those with neuropathic pain required neuropathic pain-specific medications, with all of them receiving gabapentin, either as single therapy, dual therapy with amitriptyline, or triple therapy with amitriptyline and methadone. The mean (maximum) starting doses of gabapentin, amitriptyline, and methadone (mg/kg/day) were 20.2 (43.8), 0.5 (0.7), and 0.3 (0.3), respectively. The mean standard deviation (SD) duration of neuropathic pain was 6.5 (7.2) weeks, with similar incidence and duration of neuropathic pain, duration of treatment, and neuropathic pain-specific dose regimens in the limb sparing and the amputation groups [63].

Gabapentin's efficacy in preventing phantom limb pain after amputation in 45 patients with osteosarcoma or Ewing sarcoma was evaluated in a prospective, double-blind RCT after 30 days of therapy started 4 days pre-operatively, with a starting dose of 300 mg daily that was gradually escalated to 300 mg TID. Postoperative pain intensity was significantly lower in the gabapentin-treated group than in the placebo group ($p < 0.05$), and their rate of phantom limb pain was, likewise, significantly lower (43.48% vs. 77.27%, $p = 0.033$) at the final follow-up at 60 days postoperatively [28].

The efficacy of pregabalin in the context of persistent postoperative pain after posterior spinal fusions was described in a randomized placebo-controlled trial of 64 children and adolescents given 2 mg/kg pregabalin or placebo BID 1 day before and 5 days after surgery. No significant difference was noted in the cumulative 48-h opioid consumption or in the improvement in the pain domain scores on the Scoliosis Research Society Questionnaire 2

Table 4 Summary of literature regarding gabapentinoids for the reduction of perioperative anxiety and emergence agitation or delirium in pediatric patients

Reference, year; number of patients receiving gabapentinoid	Study type	Population[a]	Medication	Outcome measure[b]	Comparator group(s)	Findings
Perioperative anxiety						
Eskandarian 2015; $n = 21$ [37]	Double-blind, placebo-controlled crossover	5.28 ± 1.10 yo (mean ± SD), pulpotomy treatment	Pregabalin 75 mg 2 h pre-op	Anxiety scores (VAS-anxiety) at baseline, 2 h post medication	Placebo ($n = 21$)	Significant reduction in VAS-anxiety score with pregabalin
Tomaszek 2020; $n = 20$ [26]	RCT	13 (10–15) yo (median and IQR), Ravitch procedure	Gabapentin 15 mg/kg 1 h pre-op, 7.5 mg/kg BID for 3 days	State anxiety (STAI-C and STAI) 1 day pre-op and on POD3 (secondary outcome)	Placebo ($n = 20$)	Significantly lower anxiety scores post-op vs. pre-op in gabapentin group but not placebo group
Emergence agitation or delirium						
Badawy 2018; $n = 33$ [11]	RCT	3.7 ± 1.4 yo (mean ± SD), strabismus surgery	Gabapentin 5 mg/kg 1 h pre-op	EAS score upon arrival to PACU	Placebo ($n = 34$)	Significantly lower EAS in gabapentin group
Marouf 2018; $n = 30$ [39]	RCT	4–10 yo, adenotonsillectomy	Pregabalin 1.5 mg/kg 30 min pre-op	EAS score at 10, 20, and 30 min post-op	Placebo ($n = 30$)	Significantly lower EAS at all time points post-op in pregabalin group
Pinto Filho 2019; $n = 40$ [18]	RCT	62.8 ± 59.2 months old (mean ± SD), unilateral inferior limb surgery	Gabapentin 10 mg/kg 1–2 h pre-op	Frequency of pre-op and post-op (1 h) agitation (secondary outcome)	Placebo ($n = 44$)	Significantly lower frequency of agitation 1 h post-op with gabapentin
Pinto Filho 2019; $n = 90$ [19]	RCT	3.29 ± 1.42 (15 mg/kg dose group) and 3.42 ± 1.39 (30 mg/kg dose group) yo (mean ± SD), LP or myelogram	Gabapentin 15 mg/kg ($n = 44$) or 30 mg/kg ($n = 46$) 1–2 h pre-op	PAED score at 0- and 30-min post-op (secondary outcome)	Placebo ($n = 45$)	Significantly lower PAED scores at 30 min post-op for both gabapentin dose levels
Salman 2013; $n = 23$ [56]	RCT	3–9 yo (median 5 yo), adenotonsillectomy	Gabapentin 15 mg/kg 30 min pre-op	Pre-op anxiety score and post-op agitation score at 10-, 20-, and 30-min post-op	Placebo ($n = 23$)	Gabapentin group had significantly lower agitation scores at 20 and 30 min post-op
Talaat 2021; $n = 30$ [32]	RCT	23.5 (14–43) months old (median and IQR), day-case surgery [c]	Pregabalin 5 mg/kg 30 min pre-op	PAED score at 10, 20, and 30 min post-op (secondary outcome)	Midazolam 0.75 mg/kg PO 30 min pre-op ($n = 30$)	No significant differences in PAED scores with pregabalin vs. midazolam at any time post-op

BID twice daily, *EAS* emergence agitation score, *IQR* interquartile range, *LP* lumbar puncture, *PAED* pediatric anesthesia emergence delirium, *PACU* post-anesthesia care unit, *PO* by mouth, *POD* postoperative day, *post-op* postoperatively, *pre-op* preoperatively, *RCT* randomized controlled trial, *SD* standard deviation, *STAI* State-Trait Anxiety Inventory, *STAI-C* State-Trait Anxiety Inventory for children, *VAS* visual analog scale, *yo* years old

[a]Population data are reported as presented within the primary reference

[b]All anxiety and emergence agitation/delirium outcomes were primary outcome measures except where indicated otherwise

[c]Outpatient surgery included hernia repair (36.7%), adenotonsillectomy (20%), adenoidectomy (16.7%), hydrocelectomy (13.3%), orchiopexy (3.3%)

Table 5 Summary of literature describing the perioperative use of gabapentinoids and chronic postsurgical pain

Reference, year; number of patients	Study design	Population	Gabapentinoid dosing	Outcome(s)	Follow-up duration
Anghelescu 2017; $n = 37$ [63]	Prospective observational	Median 13.3 (IQR 6.8–20.2) yo, limb sparing procedure or amputation for osteosarcoma	Gabapentin, mean (SD) starting dose (mg/kg/day) 20.2 (14.3); mean (SD) maximum dose (mg/kg/day) 43.8 (17.9)	Postsurgical neuropathic pain resolved; resolution of symptoms reported at mean 6.5 (SD 7.7) weeks	Until resolution of symptoms and weaned off neuropathic pain medications
Helenius 2021; $n = 64$ [34]	RCT (pregabalin vs. placebo)	15.7 ± 2.3 yo (mean ± SD), PSF	Pregabalin 2 mg/kg (rounded up to nearest 25 mg) evening (12 h) and 2 h pre-op	No differences in back pain scores between groups at any time point (6 months, 1 year, and 2 years); SRS-24 improved significantly 2 years post-op vs. pre-op for both groups	2 years
Julien-Marsollier 2021; $n = 68$ [42]	Prospective observational (ORA vs. opioid)	Median 15.0 (range 12.0–18.0) yo, PSF for AIS	Gabapentin dose regimen not reported	Lower morphine consumption in the ORA group at POD1; persistent neuropathic pain at 1 year was decreased in the ORA group	1 year
Lauder 2005; $n = 6$ [64]	Case series	11–17 yo, multilevel spinal surgery for CP	Gabapentin 100 mg TID, increased to 300–500 mg TID	Postsurgical neuropathic pain resolved; resolution of symptoms reported at 3, 6, 12 months, and 4 years, respectively, for the 4 cases treated with gabapentin	Varied (3 months to 4 years)
Wang 2018; $n = 45$ [28]	RCT (gabapentin vs. placebo)	14.3 ± 2.8 yo (mean ± SD), amputation for bone tumor	Gabapentin 300 mg once 4 days pre-op, 300 mg BID 3 days pre-op, then 300 mg TID until 30 days post-op	Post-op pain significantly reduced in the gabapentin arm on POD4--9; lower rate of phantom limb pain in the gabapentin arm at 60-day follow up	60 days

AIS adolescent idiopathic scoliosis, *BID* twice daily, *CP* chronic pain, *IQR* interquartile range, *ORA* opioid-reduced anesthesia, *POD* postoperative day, *post-op* postoperatively, *pre-op* preoperatively, *PSF* posterior spinal fusion, *RCT* randomized controlled trial, *SD* standard deviation, *SRS-24* Scoliosis Research Society 24-Item Questionnaire, *TID* three times daily, *yo* years old

years after surgery, suggesting that the perioperative use of pregabalin did not influence the opioid consumption nor the long-term pain outcomes [34].

The concept that reducing opioid exposure in the immediate post-operative period can reduce the consequences of CPSP has been investigated in a study of patients undergoing scoliosis surgery [42]. Gabapentin was included in the multimodal analgesia treatment protocols; nevertheless, the most effective analgesic interventions were intraoperative ketamine and dexmedetomidine infusions [65]. Julien-Marsollier et al. [42] demonstrated that opioid reduction strategies efficiently reduce immediate postoperative opioid consumption and, related to the reduced opioid consumption, reduce the incidence of persistent pain at 1 year after surgery. When considering general concepts regarding prevention of CPSP, a major perioperative goal is the provision of multimodal analgesia with a variety of pain medications, while reducing the magnitude of opioid exposure immediately postoperatively. This goal is based on the evidence that morphine consumption on postoperative day 1 of > 0.5 mg/kg is the most important independent predictive factor for persistent chronic pain with a neuropathic component, specifically in the population of adolescent scoliosis surgery, which is at high risk of developing CPSP [42].

3.7 Adverse Effects of Gabapentinoids

Adverse effects of gabapentinoids in pediatric surgical patients must be considered, particularly given the higher incidence of dizziness and visual disturbances reported in the meta-analysis of 281 RCTs comparing gabapentinoids to control treatments in adult patients [5]. Only six of the studies included in this review article included information about adverse effects due specifically to the use of gabapentinoids [11, 26–29, 33]; none of the six studies reported any significant differences in adverse effects for patients receiving gabapentinoids versus control groups. Adverse effects (most often sedation) observed were attributed to the multimodal approach or to opioids rather than to gabapentinoids.

4 Discussion

The spectrum of indications for perioperative use of gabapentinoids in children, as reflected by our literature review, includes a larger variety of outcomes than those investigated in the adult literature. The adult literature is focused mostly on postoperative pain improvement, opioid reduction, and effects on PONV; however, sedation and reduction of emergence delirium are evaluated as unique outcomes in pediatrics. Sedation may be perceived as an undesirable side effect in adults, but it may be an intended and beneficial effect during the postoperative period in children.

A key limitation of the review is that it presents variable datasets, with variable strategies of gabapentin and pregabalin administration, making it difficult to draw categorical, meaningful conclusions. Of the 49 references identified by our search strategy focused on the perioperative use of gabapentinoids in pediatrics, 47 references demonstrated a benefit from using gabapentinoids, although the area of benefit varied from pain outcomes (pain scores or opioid consumption) to PONV, anxiety, emergence delirium, and CPSP. Furthermore, adverse effects of gabapentinoids were seldomly reported in the studies included within this review and were determined to be of negligible risk when observed. With the limitation of comparison of a systematic review of adult data versus a narrative review of pediatric data, our findings suggest that contrary to the findings in a systematic review of the literature in adults [5], gabapentinoids may prove beneficial when used perioperatively in pediatric patients, in selected pediatric surgical populations, and the side effects and risk/benefit ratio of such use may be acceptable. The evidence for reduced pain scores and opioid use is better represented in the spinal surgery population, but we cannot extrapolate the recommendation for use to all pediatric surgical populations, based on the data presented. There is evidence for possible reduction in postoperative agitation and possible reduction in CPSP in specific patient populations such as spinal surgery or amputations.

The body of evidence presented within this review was primarily class III and IV and heterogenous in nature. The low quality of evidence and higher risk of bias across these studies therefore limits the strength of the conclusions and recommendations that can be made for the use of gabapentinoids perioperatively in pediatric patients. Another key consideration when interpreting these results is that a total of five references [12, 17, 24, 30, 35] were only available as conference abstracts.

Of the two studies that showed no benefit in any outcome examined [14, 26], one was a relatively small RCT ($n = 14$) that investigated pain outcomes immediately after adenotonsillectomy, and the other was a retrospective chart review of infants ($n = 74$) who received gabapentin for irritability after superior cavopulmonary connection. Although these two studies showed no benefit, the evidence is not strong enough to make a recommendation against the use of gabapentinoids in these clinical circumstances. In addition, pharmacokinetic studies [66, 67] have demonstrated that children under 5 years of age require a dose approximately 30% higher than that required by older patients, which may explain the lack of benefit seen in the retrospective study of infants undergoing superior cavopulmonary connection.

The studies included in this review have covered the broad age spectrum of pediatrics, from infants to adolescents. However, the strength of evidence for gabapentinoids perioperatively in each age group varies depending upon

the outcome being studied. For perioperative and postoperative analgesia outcomes, most studies described within this review were focused on children (11 studies) and adolescents (11 studies). A similar focus on the adolescent population (12 studies) was noted for the opioid consumption outcomes, although a decent number of studies included children (nine studies). Studies regarding gabapentinoids for the reduction of PONV have been focused on the 2–12 years of age range (children, nine studies) and adolescents (11 studies). Similarly, most of the studies (i.e., ten of 15) regarding the perioperative use of gabapentinoid-containing ERAS protocols described within this review article were focused on the adolescent population. Gabapentinoids for the reduction of perioperative anxiety have been investigated in children by one study [37] and adolescents in the other study [26]. Within the context of CPSP, studies have only investigated the impact of gabapentinoids in the adolescent pediatric population. In the overall context of the use of gabapentinoids perioperatively, it seems that evidence is most robust in the adolescent population, suggesting that the utility of gabapentinoids in younger pediatric age groups needs further investigation regardless of the outcome of interest being considered.

Overall, a consensus in dosing of perioperative gabapentinoids for analgesia seems to be lacking. The inconsistency of outcomes involving pain scores reduction may be secondary to the dosing variability among studies summarized in this review. Our literature search revealed that a significantly lower consumption of opioids was noted in 16 of 22 studies that investigated the use of gabapentinoids for this purpose. These findings demonstrate that gabapentinoids should be considered for their opioid-sparing effects in pediatric surgical patients. Gabapentinoids seem to be most beneficial for pain reduction and decreased opioid use during the first 2 postoperative days. However, the current body of literature does not indicate whether a single preoperative dose or a combined approach of preoperative and postoperative dosing of gabapentinoids leads to more robust positive outcomes. Further investigation of gabapentinoid dosing for immediate postoperative pain control is needed to clarify the impact of gabapentinoids on this outcome.

It is unclear whether an intrinsic mechanism of action of gabapentinoids, their opioid-sparing effects, or a combination of the two is what leads to the potential antiemetic activity of gabapentinoids. Furthermore, the impact of gabapentinoids on PONV has been seldomly investigated as a primary outcome in studies of pediatric surgical patients, making it difficult to make any definitive recommendations for the use of gabapentinoids for PONV without further studies.

Current evidence points towards a potential benefit to the use of gabapentinoids for perioperative anxiety and emergence agitation when a single dose is given preoperatively. However, additional studies are needed to better characterize the dose–response relationship and optimize the timing of the dosing in relation to the procedure. In one RCT in which pregabalin was given only 30 min before the procedure, no significant benefit was found [32], yet another demonstrated significant improvements in emergence agitation when pregabalin was given 30 minutes before the procedure [39] (Table 4). In addition, the evidence in reducing perioperative anxiety and emergence agitation is more robust for gabapentin than for pregabalin; because the data are insufficient to draw a conclusion regarding the efficacy of pregabalin for this indication, future studies should be particularly focused on using pregabalin to reduce perioperative anxiety and emergence agitation.

An effective analysis of the literature reflective of the benefits associated with perioperative gabapentinoid use in children becomes difficult in the context of multimodal pain management protocols, ERAS pathways, and possible development of CPSP because the effects driven by this pharmacological class cannot be separated from those of other pharmacological interventions used concurrently. It is intuitive that by accessing non-opioid receptor–mediated mechanisms, gabapentinoids can facilitate anti-hyperalgesia and anti-central sensitization mechanisms. Dual benefits represent both reduction of opioid exposure (and opioid-related side effects) and intrinsic gabapentinoid-based analgesia. In this respect, any perioperative intervention that can contribute to reducing the opioid exposure immediately postoperatively has value not only for improving immediate postoperative outcomes but also for reducing the development of CPSP. As such, the perioperative use of gabapentinoids can be supported, especially for select surgical interventions that increase risk for both high-intensity acute postoperative pain and a high prevalence of CPSP: adolescent scoliosis surgical interventions, limb amputations, and limb-sparing procedures.

Inconsistency in the outcomes measured amongst studies makes it challenging to make any additional recommendations about using gabapentinoids in specific pediatric surgery types or procedures. In particular, data describing the perioperative use of gabapentinoids are abundant and of high quality in pediatric patients undergoing tonsillectomy or adenotonsillectomy, which currently encompasses 290 patients receiving gabapentinoids across nine RCTs [9, 10, 12–14, 16, 21, 39, 56]. Selectively, some studies investigated immediate postoperative analgesia and opioid consumption, with others focused on other perioperative challenges, such as emergence agitation or PONV. Outcomes for the tonsillectomy and adenotonsillectomy surgical population have indeed been explored quite robustly, in the outcomes of reduced postoperative pain scores and opioid reduction, role for PONV reduction, and emergence anxiety reduction (Tables 1, 2, and 4). Based on four out of seven RCTs evaluating postoperative pain score indicating positive outcomes

of pain reduction [9, 10, 16, 21], in a cumulative number of 167 patients (while three RCTs indicated no difference in analgesia [12–14], with a total of 70 patients), it appears that the recommendation for using gabapentinoids as an analgesic adjuvant can be supported. To further support this recommendation, several studies also supported a reduction of opioid consumption in the groups randomized to the gabapentinoid regimen [10, 13, 21]. Among the tonsillectomy and adenotonsillectomy studies, the evidence for a reduction of PONV is less substantial, with most studies indicating no difference between randomization groups regarding this outcome [9, 13, 14]. Two studies found a favorable reduction in PONV related to gabapentinoids, one utilizing gabapentin [16], and one based on a pregabalin regimen [39]. Emergence agitation was reduced in this surgical population in two studies [39, 56]. It seems intuitive that when clinicians intend to achieve several of the noted outcomes, and especially based on the evidence for reduced postoperative pain intensity, a recommendation for clinical practice to include gabapentinoids for tonsillectomy and adenotonsillectomy can be supported.

Few studies have examined improving opioid-related adverse effects with gabapentinoid protocols, and even fewer have reported on the adverse effects of gabapentinoids as part of perioperative pain management. These are two key areas to consider for future research efforts. Adverse effects of gabapentinoids, including dizziness, somnolence, confusion, headache, nausea, ataxia, and weight gain, have been studied more in the context of chronic use, and adverse effects may be less of a concern with short-term use of gabapentinoids. Nevertheless, additional safety data are needed. In addition, gabapentinoids have been associated with a higher incidence of dizziness and visual disturbances when used to manage postoperative acute pain in adults. Although this literature search reveals some data regarding the efficacy of gabapentinoids, additional data on their safety when used perioperatively in pediatric patients are needed.

5 Conclusion

This review of the literature reveals that clinical experience with gabapentinoids given perioperatively in pediatric populations spans many indications. The presence of this overlap of indications makes their inclusion in complex perioperative plans worthy of consideration. Furthermore, data are most abundant regarding the impact of gabapentinoids on immediate postoperative outcomes, including reduction of acute pain and opioid consumption, with especially robust evidence in the subpopulations of scoliosis spinal surgery and tonsillectomy or adenotonsillectomy. In subpopulations of pediatric surgical patients, there is evidence that gabapentinoids reduce acute postsurgical pain (and optimized acute postoperative pain is a factor in prevention of development of CPSP), may reduce opioid consumption, and to a lesser extent influence the outcomes of emergence agitation and PONV, with mild and infrequent adverse effects, making them an appealing choice to consider in the perioperative setting. Consensus in dosing of gabapentinoids is lacking; future studies should aim to identify optimal dosing recommendations, specifically, the timing of the dose preoperatively and whether to continue therapy postoperatively.

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