ORIGINAL RESEARCH

Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis

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Objectives: Effective postoperative pain management is crucial in the care of surgical patients. Opioids, which are commonly used in managing postoperative pain, have a potential for tolerance and addiction, along with sedating side effects. Gabapentin's use as a multimodal analgesic regimen to treat neuropathic pain has been documented as having favorable side effects. This meta-analysis examined the use of preoperative gabapentin and its impact on postoperative opioid consumption.

Materials and methods: A comprehensive literature search was conducted to identify randomized control trials that evaluated preoperative gabapentin on postoperative opioid consumption. The outcomes of interest were cumulative opioid consumption following the surgery and the incidence of vomiting, somnolence, and nausea.

Results: A total of 1,793 patients involved in 17 randomized control trials formed the final analysis for this study. Postoperative opioid consumption was reduced when using gabapentin within the initial 24 hours following surgery (standard mean difference −1.35, 95% confidence interval [CI]: −1.96 to −0.73; $P<0.001$). There was a significant reduction in morphine, fentanyl, and tramadol consumption ($P<0.05$). While a significant increase in postoperative somnolence incidence was observed (relative risk 1.30, 95% CI: 1.10–1.54, $P<0.05$), there were no significant effects on postoperative vomiting and nausea.

Conclusion: The administration of preoperative gabapentin reduced the consumption of opioids during the initial 24 hours following surgery. The reduction in postoperative opioids with preoperative gabapentin increased postoperative somnolence, but no significant differences were observed in nausea and vomiting incidences. The results from this study demonstrate that gabapentin is more beneficial in mastectomy and spinal, abdominal, and thyroid surgeries. Gabapentin is an effective analgesic adjunct, and clinicians should consider its use in multimodal treatment plans among patients undergoing elective surgery.

Keywords: gabapentin, preemptive analgesia, opioid, postoperative pain

Introduction

In the United States, ~51.4 million inpatient surgeries are performed annually and postoperative pain is experienced by as much as 75% of patients.[1–3] Effective postoperative pain management following surgery is critical. Inadequate postoperative pain management can negatively impact the patient's health, recovery, and overall experience.[4] In addition to immediate discomfort, untreated pain is associated with increased morbidity and mortality and decreased quality of life.[4] Furthermore, chronic postsurgical pain, pain that lasts 2 months and is not attributable to a preexisting medical condition, can develop.[5] While the majority of surgical patients recover and return to a functional status, some patients are more likely to develop long-term opioid use

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and chronic postsurgical pain.[6,7] Following limb amputations, breast cancer surgeries, and heart bypass surgeries, the incidence of postsurgical pain is especially high.[8]

Opioids are extremely effective in managing postsurgical pain but have been documented as having an association with somnolence, respiratory depression, hypotension and bradycardia, nausea and vomiting, pruritus, and constipation.[9] Antihistamines, which are frequently used to treat nausea and pruritus, further worsen the sedation and respiratory depression.[10] Respiratory depression has been reported to affect patients treated using analgesia pumps that are patient controlled.[11,12] Given the frequency of opioid-related complications, high patient morbidity as well as prolonged duration of hospitalization, and higher health care costs, effective methods to minimize postoperative opioid consumption is required.[13]

Multimodal analgesia techniques have been researched extensively and implemented by many institutions as standard postoperative care management.[14] By utilizing multiple medications and therapies that act by different mechanisms of actions within the central and peripheral nervous system, multimodal analgesia can provide individualized targeted patient therapy by taking into account pharmacogenetics such as single gene allelic differences and medication responses to reduce the consumption of opioids and the associated side effects.[15,16] One such drug is gabapentin that has antihyperalgesic properties. Gabapentin's antihyperalgesic effects result from its action in the dorsal root ganglia and spinal cord.[17] The safety profile of gabapentin has few associated adverse side effects.[18] Alayed et al[19] reported significant reductions in morphine consumption with the use of gabapentin (standard mean difference [SMD] −1.45, 95% confidence interval [CI]: −1.79 to −1.11; $P<0.05$) in a review including four randomized control trials (RCTs) involving 190 patients undergoing abdominal hysterectomy. A significant number of RCTs have demonstrated conflicting results in the use of preoperative gabapentin.[19] Bharti et al[20] studied gabapentin administration among patients (n=40) undergoing mastectomy (20 received gabapentin and 20 received placebo) and demonstrated a reduction in the amount of morphine required during the initial 24 hours following surgery with the use of gabapentin (2.1±2.2 mg vs 4.9±3.4 mg, $P=0.06$). Conversely, Kinney et al[21] demonstrated no significant difference in cumulative morphine consumption during the initial 24 hours following surgery (111.9 mg vs 118.1 mg, $P=0.340$) in an RCT among patients undergoing thoracotomy (n=120; 57 patients received gabapentin and 63 patients received placebo).

Given the high incidence of adverse events associated with opioid medications, this meta-analysis examined the use of preoperative gabapentin and its impact on postoperative opioid consumption and opioid use after surgery and the incidence of vomiting, somnolence, and nausea.

Materials and methods
Study selection
RCTs that evaluated preoperative gabapentin on postoperative opioid consumption were identified using PubMed, Google Scholar, and the Cochrane Central Register of Controlled Trials (1966–2016). RCTs written in English were included in this study. Only the most updated and recent report of the RCT was included in the final analysis when duplicate publications existed. The inclusion criteria of the RCTs were patients >18 years, patient undergoing inpatient surgeries (open or laparoscopic) under general anesthesia, preoperative administration of gabapentin irrespective of dose and duration before surgery (compared to a placebo), and trials reporting opioid consumption as the primary outcome. RCTs reporting only postoperative use of gabapentin or in addition to a preoperative dosing were excluded from the analysis. A combination of keywords searched included "gabapentin", "preemptive analgesia", "postoperative pain", and "opioid consumption".

Data extraction
The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were employed for data extraction, systematic review, and meta-analysis. All RCTs were assessed for data relevant to patients undergoing elective surgery, the intervention utilized, control or placebo groups, primary outcome measures, and methods. Figure 1 details the characteristics of all published RCTS included in the final analysis. The primary outcome analyzed was opioid consumption during the initial postoperative period (24 hours), while the secondary outcomes were incidence of vomiting, somnolence, and nausea.

Statistical analysis
In all, 95% CI and relative risk (RR) were calculated for vomiting, somnolence, and nausea incidences, while 95% CI and SMDs were calculated for cumulative consumption of opioids during the initial 24 hours following surgery. A continuity correction factor of 0.5 was used to calculate RR and variance in RCTs that included zero events. RCTs in which zero events occurred in both gabapentin and control arms were not calculable and were excluded from the current study. A fixed-effect
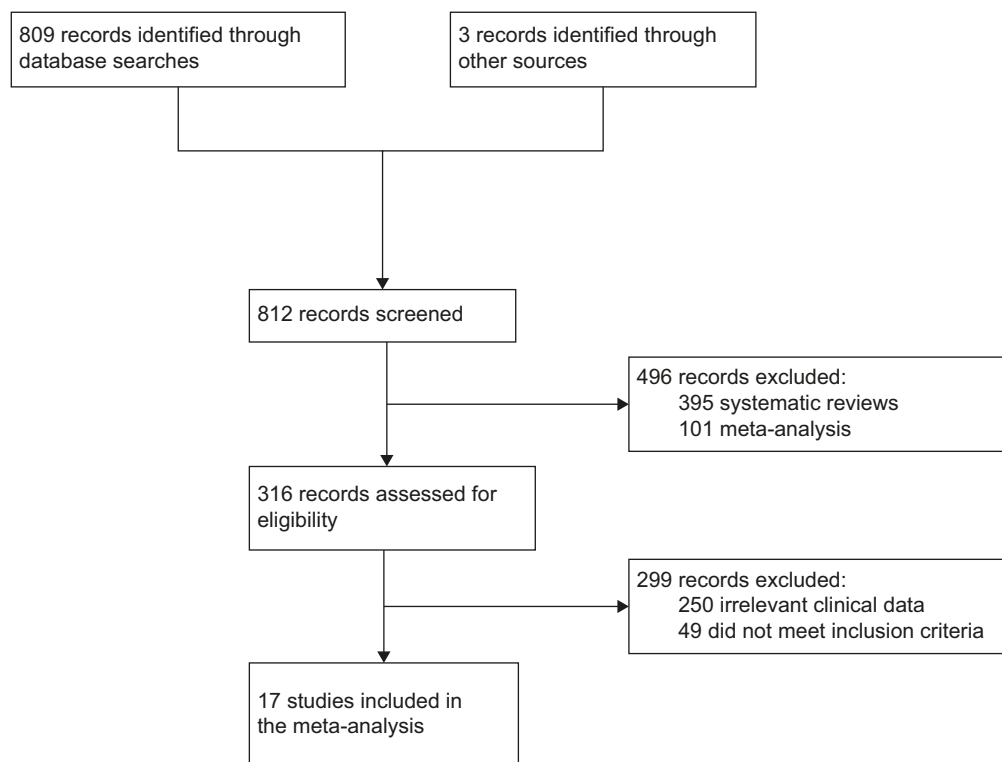
Figure 1 A CONSORT diagram detailing the study selection process.

model and a random-effects model were used following an evaluation of the heterogeneity in the included RCT. Statistical heterogeneity was assessed using the I^2 statistic and Cochran's Q statistic. While a fixed-effect model was utilized in the absence of heterogeneity, a random-effects model was used when there existed heterogeneity. Heterogeneity was assumed to be statistically significant when $I^2>50$ or $P<0.05$. A funnel plot was used to evaluate publication bias and further evaluated using Begg's and Egger's tests. A subgroup analysis was performed using opioid type (fentanyl, tramadol, or morphine), type of surgery, and dose of gabapentin administered. A two-tailed P-value of <0.05 was considered to be statistically significant. All statistical analyses for the current study were performed using the Comprehensive Meta-Analysis software Version 3 (Biostat, Englewood, NJ, USA).

Results

Table 1 details the selection process of the included RCTs. In all, 812 relevant citations were identified using the search strategy. More than half of the citations (n=496) were excluded. Of the 316 citations assessed for eligibility, an additional 299 citations were excluded based on irrelevant clinical data and failing to meet the inclusion criteria.

The final analysis included a total of 17 RCTs, involving 1,793 patients. Of the 1,793 patients, 895 received gabapentin, while the remaining 898 received a control.

Gabapentin effects on opioid consumption

Opioid consumption was reported in all 17 trials among patients in the gabapentin and control groups. Significant heterogeneity was not observed between trials (I^2=95.45, $P<0.001$). Compared to the control group, a statistically significant decrease in cumulative opioid consumption using gabapentin was observed (SMD −1.35, 95% CI: −1.96 to −0.73; $P<0.001$; Figure 2).

Subgroup analyses

The results demonstrated a statistically significant reduction in cumulative consumption of tramadol (SMD −1.57, 95% CI: −2.82 to −0.33; $P<0.05$), fentanyl (SMD −2.54, 95% CI: −3.78 to −1.31; $P<0.001$), and morphine (SMD −0.93, 95% CI: −1.41 to −0.44; $P<0.001$) using gabapentin (Figure 3).

A significant reduction was observed in cumulative morphine following abdominal hysterectomy (SMD −3.26, 95% CI: −4.11 to −2.41; $P<0.001$), breast cancer surgery (SMD −1.17; 95% CI: −1.63 to −0.71; $P<0.001$), cholecystectomy (SMD −2.80, 95% CI: −3.71 to −1.89; $P<0.001$), orthopedic surgeries (SMD −0.86, 95% CI: −1.54 to −0.19; $P=0.012$), spinal surgeries (SMD −2.66, 95% CI: −3.43 to −1.90; $P<0.001$), and thyroid surgeries (SMD −1.63, 95% CI: −2.16 to −1.09; $P<0.001$). A slight reduction was observed in postoperative opioid

Table 1 Characteristics of RCTs evaluating preoperative gabapentin use on postoperative opioid consumption

Author (year)	Type of surgery	Number of subjects (gabapentin/control)	Dose (mg)	Control	Type of opioid
Pandey et al (2004)[34]	Cholecystectomy	153/153	300	Placebo	Fentanyl
Pandey et al (2004)[23]	Orthopedic surgery	28/28	300	Placebo	Fentanyl
Turan et al (2004)[35]	Abdominal hysterectomy	25/25	1,200	Placebo	Tramadol
Turan et al (2004)[36]	Orthopedic surgery	25/25	1,200	Placebo	Morphine
Radhakrishnan et al (2005)[37]	Abdominal hysterectomy	30/30	800	Placebo	Morphine
Adam et al (2005)[38]	Orthopedic surgery	30/30	1,200	Placebo	Morphine
Al-Mujadi et al (2006)[39]	Thyroid surgery	37/35	1,200	Placebo	Morphine
Pandey et al (2006)[40]	Cholecystectomy	125/125	600	Placebo	Fentanyl
Montazeri et al (2007)[41]	Orthopedic surgery	35/35	300	Placebo	Morphine
Grover et al (2009)[42]	Total mastectomy	25/21	600	Placebo	Morphine
Srivastava et al (2010)[43]	Cholecystectomy	60/60	600	Placebo	Tramadol
Moore et al (2011)[22]	Cesarean section	21/23	900	Placebo	Morphine
Deniz et al (2012)[44]	Prostatectomy	25/26	900	Placebo	Tramadol
Short et al (2012)[45]	Cesarean section	42/42	300	Placebo	Morphine
Short et al (2012)[45]	Cesarean section	42/42	600	Placebo	Morphine
Kinney et al (2012)[21]	Thoracotomy	57/63	600	Placebo	Morphine
Bharti et al (2013)[20]	Mastectomy	20/20	600	Placebo	Morphine

Abbreviation: RCT, randomized control trial.
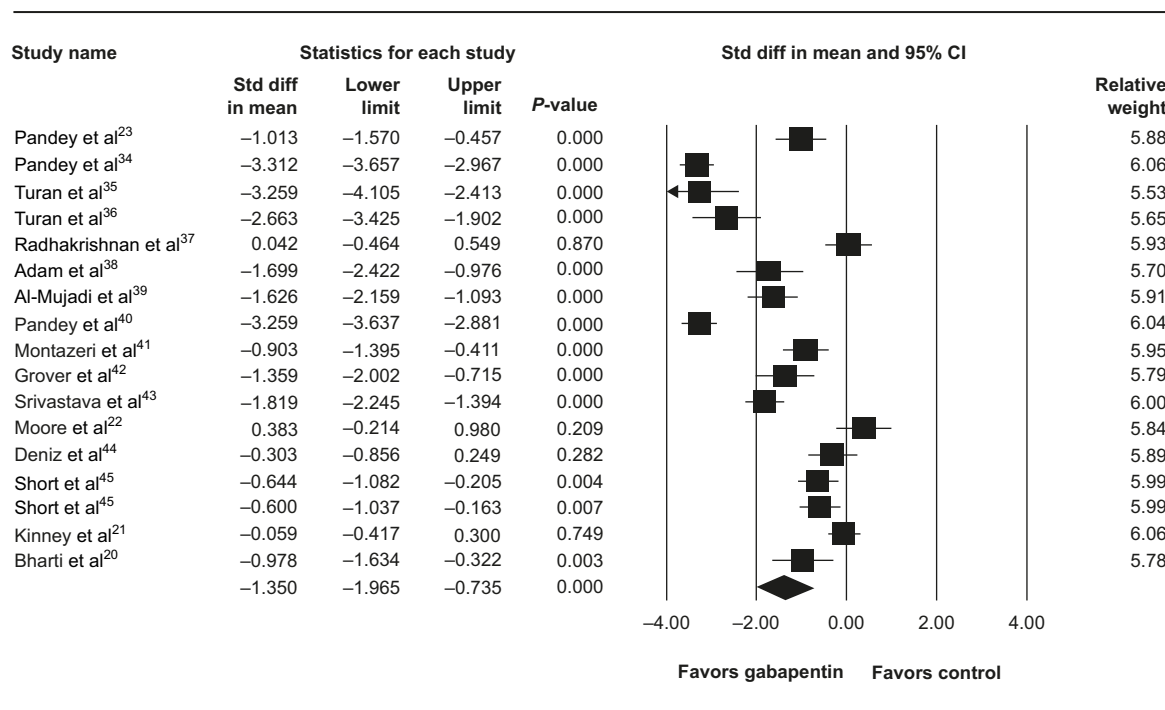
Figure 2 A forest plot evaluating the standardized difference in mean in postoperative opioid consumption with the use of gabapentin compared to control.
Abbreviations: Std diff, standard difference; CI, confidence interval.

consumption following caesarian sections (SMD −0.32, 95% CI: −0.90–0.26; P=0.279), prostatectomy (SMD −0.30, 95% CI: −0.86–0.25; P=0.282), and thoracotomy (SMD −0.06; 95% CI: −0.42–0.30; P=0.749), but failed to reach statistical significance (Figure 4).

A subgroup analysis identified that gabapentin significantly reduced total cumulative morphine consumption at 300 mg (SMD −1.48, 95% CI: −2.90 to −0.05; P=0.04),

600 mg (SMD −1.35, 95% CI: −2.41 to −0.28; P=0.01), and 1,200 mg (SMD −2.27, 95% CI: −3.02 to −1.52; P<0.001). Heterogeneity was statistically significant between groups, P<0.001 (Figure 5).

Meta-regression analyses identified a statistical association between postoperative opioid consumption and gabapentin dosage (slope 95% CI: −0.00061 [−0.00021–0.00101], P=0.00288, compared with slope =0).

Group by type of opioid	Study name	Std diff in mean	Lower limit	Upper limit	P-value	Std diff in mean and 95% CI	Relative weight
Fentanyl	Pandey et al[23]	−1.013	−1.570	−0.457	0.000		32.48
Fentanyl	Pandey et al[34]	−3.312	−3.657	−2.967	0.000		33.85
Fentanyl	Pandey et al[40]	−3.259	−3.637	−2.881	0.000		33.67
Fentanyl		−2.548	−3.783	−1.312	0.000		
Morphine	Turan et al[35]	−3.259	−4.105	−2.413	0.000		7.93
Morphine	Radhakrishnan et al[37]	0.042	−0.464	0.549	0.870		9.35
Morphine	Adam et al[38]	−1.699	−2.422	−0.976	0.000		8.47
Morphine	Al-mujadi et al[39]	−1.626	−2.159	−1.093	0.000		9.25
Morphine	Montazeri et al[41]	−0.903	−1.395	−0.411	0.000		9.40
Morphine	Grover et al[42]	−1.359	−2.002	−0.715	0.000		8.81
Morphine	Moore et al[22]	0.383	−0.214	0.980	0.209		9.00
Morphine	Short et al[45]	−0.644	−1.082	−0.205	0.004		9.59
Morphine	Short et al[45]	−0.600	−1.037	−0.163	0.007		9.60
Morphine	Kinney et al[21]	−0.059	−0.417	−0.300	0.749		9.84
Morphine	Bharti et al[20]	−0.978	−1.634	−0.322	0.003		8.76
Morphine		−0.930	−1.418	−0.441	0.000		
Tramadol	Turan et al[36]	−2.663	−3.425	−1.902	0.000		31.76
Tramadol	Srivastava et al[43]	−1.819	−2.245	−1.394	0.000		34.59
Tramadol	Deniz et al[44]	−0.303	−0.856	0.249	0.282		33.66
Tramadol		−1.577	−2.821	−0.333	0.013		
Overall		−1.199	−1.626	−0.772	0.000		

−4.00 −2.00 0.00 2.00 4.00

Favors gabapentin   Favors control

Figure 3 A forest plot evaluating the SMD in postoperative opioid consumption with the use of gabapentin compared to control: a subgroup analysis by type of opioid.
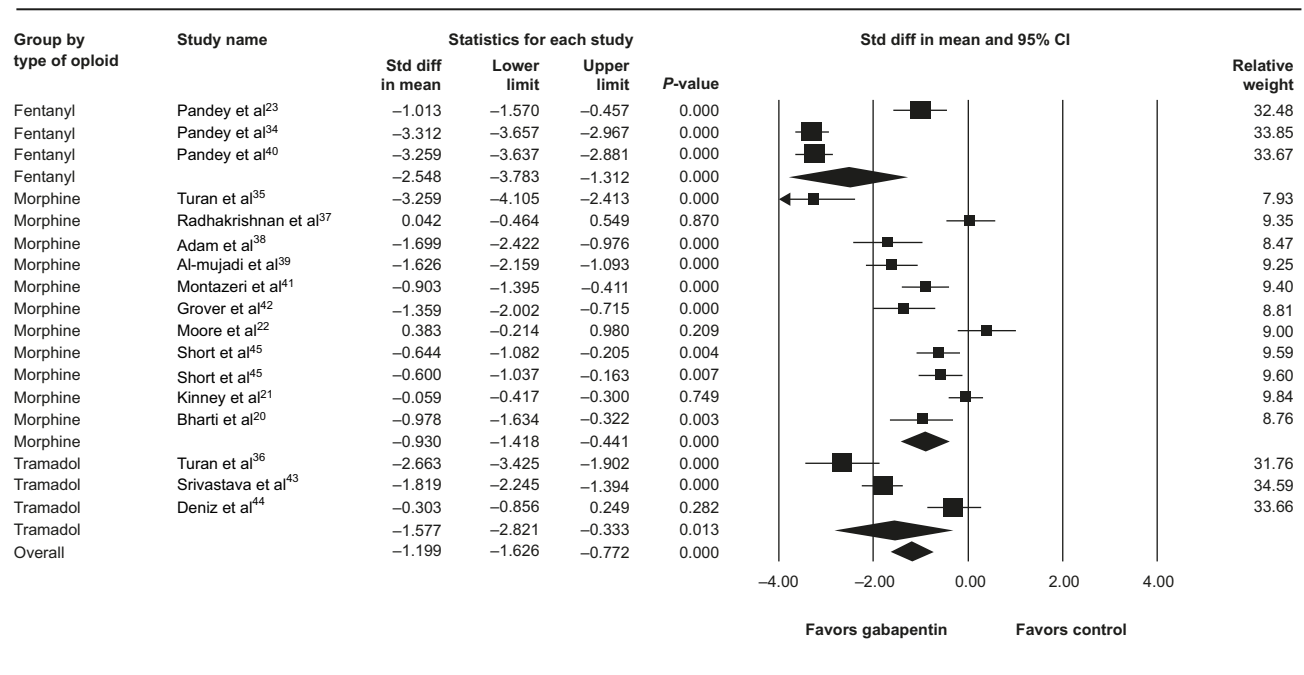**Abbreviations:** SMD, standard mean difference; Std diff, standard difference; CI, confidence interval.

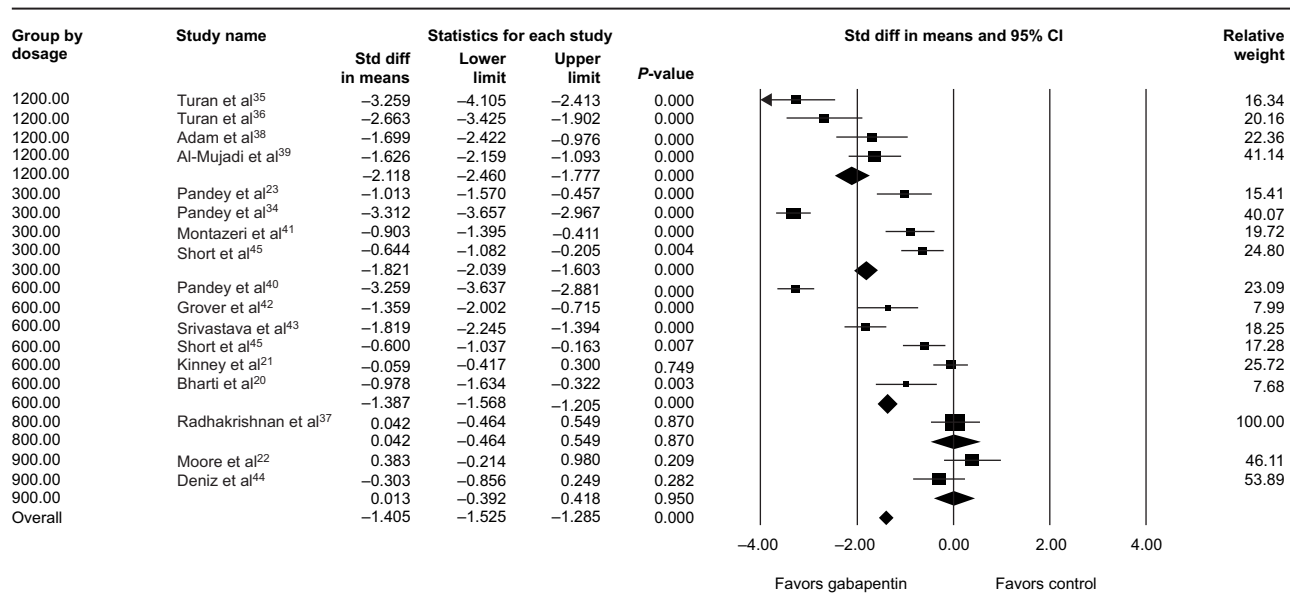| Group by type of surgery	Study name	Std diff in mean	Lower limit	Upper limit	P-value	Std diff in mean and 95% CI	Relative weight
Abdominal hysterectomy	Turan et al[35]	−3.259	−4.106	−2.413	0.000		100.00
Abdominal hysterectomy		−3.259	−4.106	−2.413	0.000		
Cesarean section	Moore et al[22]	0.383	−0.214	0.990	0.209		29.93
Cesarean section	Short et al[45]	−0.644	−1.082	−0.205	0.004		35.01
Cesarean section	Short et al[45]	−0.600	−1.037	−0.163	0.007		35.06
Cesarean section		−0.321	−0.902	0.260	0.279		
Cholecystectomy	Pandey et al[34]	−3.312	−3.657	−2.967	0.000		33.72
Cholecystectomy	Pandey et al[40]	−3.259	−3.637	−2.881	0.000		33.39
Cholecystectomy	Srivastava et al[43]	−1.819	−2.245	−1.394	0.000		32.88
Cholecystectomy		−2.803	−3.708	−1.899	0.000		
Orthopedic surgery	Pandey et al[23]	−1.013	−1.570	−0.457	0.000		25.23
Orthopedic surgery	Radhakrishnan et al[37]	0.042	−0.464	0.549	0.870		26.01
Orthopedic surgery	Adam et al[38]	−1.699	−2.422	−0.976	0.000		22.54
Orthopedic surgery	Montazeri et al[41]	−0.903	−1.395	−0.411	0.000		26.22
Orthopedic surgery		−0.864	−1.536	−0.193	0.012		
Prostatectomy	Deniz et al[44]	−0.303	−0.856	0.249	0.282		100.00
Prostatectomy		−0.303	−0.856	0.249	0.282		
Spinal surgery	Turan et al[36]	−2.663	−3.425	−1.902	0.000		100.00
Spinal surgery		−2.663	−3.425	−1.902	0.000		
Thoracotomy	Kinney et al[21]	−0.059	−0.417	0.300	0.749		100.00
Thoracotomy		−0.059	−0.417	0.300	0.749		
Thyroid surgery	Al-mujadi et al[39]	−1.626	−2.159	−1.093	0.000		100.00
Thyroid surgery		−1.626	−2.159	−1.093	0.000		
Total mastectomy	Grover et al[42]	−1.359	−2.002	−0.715	0.000		50.97
Total mastectomy	Bharti et al[20]	−0.978	−1.634	−0.322	0.003		49.03
Total mastectomy		−1.172	−1.631	−0.713	0.000		
Overall		−0.977	−1.163	−0.790	0.000		

−4.00 −2.00 0.00 2.00 4.00

Favors gabapentin   Favors control

Figure 4 A forest plot evaluating the SMD in postoperative opioid consumption with the use of gabapentin compared to control: a subgroup analysis by type of surgery.
Abbreviations: SMD, standard mean difference; Std diff, standard difference; CI, confidence interval.

Group by dosage	Study name	Std diff in means	Lower limit	Upper limit	P-value	Std diff in means and 95% CI	Relative weight
1200.00	Turan et al[35]	−3.259	−4.105	−2.413	0.000		16.34
1200.00	Turan et al[36]	−2.663	−3.425	−1.902	0.000		20.16
1200.00	Adam et al[38]	−1.699	−2.422	−0.976	0.000		22.36
1200.00	Al-Mujadi et al[39]	−1.626	−2.159	−1.093	0.000		41.14
1200.00		−2.118	−2.460	−1.777	0.000		
300.00	Pandey et al[23]	−1.013	−1.570	−0.457	0.000		15.41
300.00	Pandey et al[34]	−3.312	−3.657	−2.967	0.000		40.07
300.00	Montazeri et al[41]	−0.903	−1.395	−0.411	0.000		19.72
300.00	Short et al[45]	−0.644	−1.082	−0.205	0.004		24.80
300.00		−1.821	−2.039	−1.603	0.000		
600.00	Pandey et al[40]	−3.259	−3.637	−2.881	0.000		23.09
600.00	Grover et al[42]	−1.359	−2.002	−0.715	0.000		7.99
600.00	Srivastava et al[43]	−1.819	−2.245	−1.394	0.000		18.25
600.00	Short et al[45]	−0.600	−1.037	−0.163	0.007		17.28
600.00	Kinney et al[21]	−0.059	−0.417	0.300	0.749		25.72
600.00	Bharti et al[20]	−0.978	−1.634	−0.322	0.003		7.68
600.00		−1.387	−1.568	−1.205	0.000		
800.00	Radhakrishnan et al[37]	0.042	−0.464	0.549	0.870		100.00
800.00		0.042	−0.464	0.549	0.870		
900.00	Moore et al[22]	0.383	−0.214	0.980	0.209		46.11
900.00	Deniz et al[44]	−0.303	−0.856	0.249	0.282		53.89
900.00		0.013	−0.392	0.418	0.950		
Overall		−1.405	−1.525	−1.285	0.000		

−4.00   −2.00   0.00   2.00   4.00

Favors gabapentin   Favors control

Figure 5 A forest plot evaluating the SMD in postoperative opioid consumption with the use of gabapentin compared to control: a subgroup analysis by dose.
Abbreviations: SMD, standard mean difference; Std diff, standard difference; CI, confidence interval.

Effect of gabapentin on secondary outcomes

Nausea, vomiting, and somnolence incidence rates in the gabapentin and control groups were reported in ten and eleven trials, respectively. A fixed-effect model was assumed since heterogeneity was not observed between trials ($P=0.45$, $I^2=0.000$). Statistically significant differences in nausea or vomiting between the gabapentin and control groups (RR =1.08, 95% CI: 0.87–1.34, $P=0.44$ and RR =0.839, 95% CI: 0.61–1.51, $P=0.277$, respectively) were not observed in the meta-analysis (Figures 6 and 7). Eight trials reported data on the incidence of postoperative somnolence. Between trials, the results demonstrated statistically significant heterogeneity ($P=0.001$, $I^2=68.69$), and therefore, a random-effects model was assumed. Gabapentin significantly increased somnolence incidence (RR =1.304, 95% CI: 1.104–1.54, $P<0.05$; Figure 8).[22,23]

Publication bias

Egger's and Begg's tests were performed to calculate and evaluate publication bias for the primary outcome. Evidence of asymmetry was not observed on the funnel plot (Figure 9). The results demonstrated that publication bias was not statistically significant by Egger's test or Begg's test, $P=0.57$ and $P=0.53$, respectively.
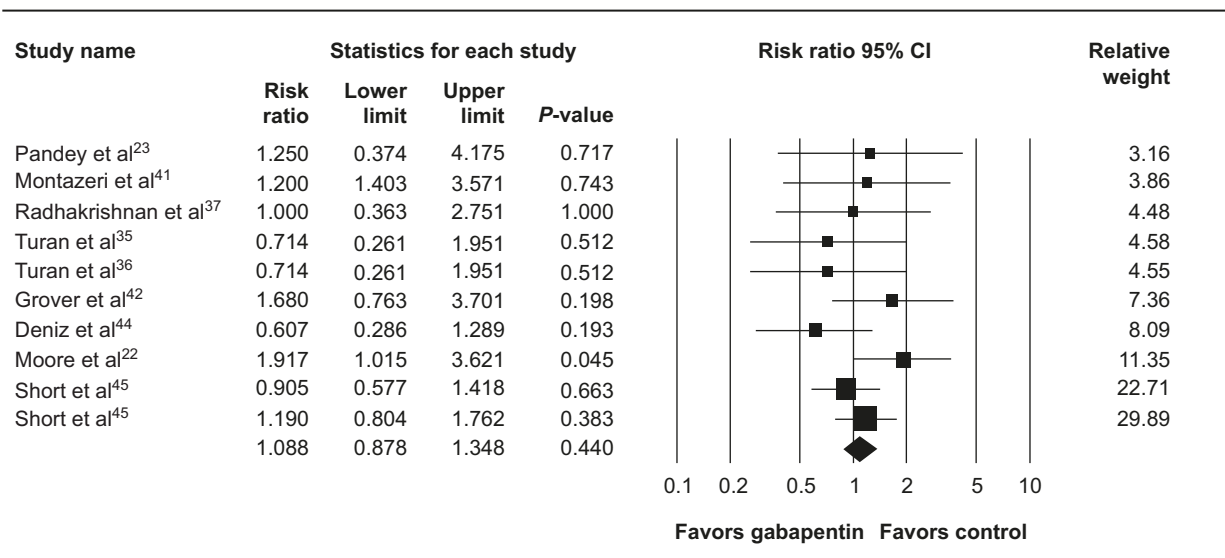
Discussion

Adequate postoperative pain management is a crucial component in surgical patient care. Effective postoperative pain management not only improves the patient's level of comfort and satisfaction but also is associated with earlier mobilization, fewer cardiopulmonary complications, reduced risk of thromboembolism, earlier return of bowel function, faster recovery, and reduced hospital costs.[4,24,25] Traditionally, opioid analgesics that act on mechanisms associated with pain perception have been used in managing postoperative pain. While opioid medications, including morphine, hydromorphone, fentanyl, and meperidine, are very effective analgesics, they are also associated with numerous adverse side effects that include somnolence, respiratory depression, cardiac instability including hypotension and bradycardia, and nausea, vomiting, pruritus, and constipation.[13]
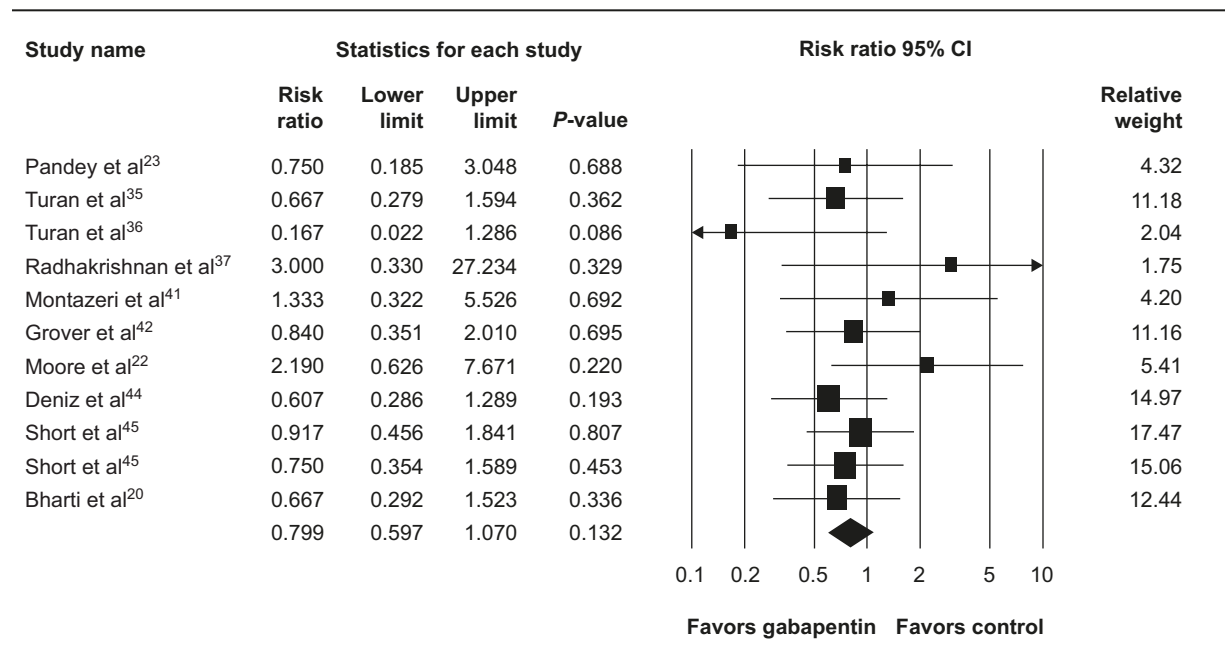
Multimodal pain management aims for additive or synergistic effects by utilizing analgesic medications of various classes that have differing pharmacologic mechanisms of actions in the nervous system.[26] By combining multiple drugs from different classes, multimodal pain management regimens aim to provide adequate pain management, while reducing the amount of required postoperative opioid use and its associated adverse effects.

Gabapentin is commonly indicated in the treatment of seizures.[27] Gabapentin, which acts on the nociceptive processes involved in central sensitization, has been shown to reduce hypersensitivity associated with nerve injury (hyperalgesia) and postoperative pain and inflammation in animal models.[28] Interestingly, gabapentin's antiemetic effects were first recognized when studies involving breast

Study name	Statistics for each study				Risk ratio 95% CI	Relative weight
	Risk ratio	Lower limit	Upper limit	P-value		
Pandey et al[23]	1.250	0.374	4.175	0.717		3.16
Montazeri et al[41]	1.200	1.403	3.571	0.743		3.86
Radhakrishnan et al[37]	1.000	0.363	2.751	1.000		4.48
Turan et al[35]	0.714	0.261	1.951	0.512		4.58
Turan et al[36]	0.714	0.261	1.951	0.512		4.55
Grover et al[42]	1.680	0.763	3.701	0.198		7.36
Deniz et al[44]	0.607	0.286	1.289	0.193		8.09
Moore et al[22]	1.917	1.015	3.621	0.045		11.35
Short et al[45]	0.905	0.577	1.418	0.663		22.71
Short et al[45]	1.190	0.804	1.762	0.383		29.89
	1.088	0.878	1.348	0.440		

0.1   0.2   0.5   1   2   5   10

Favors gabapentin   Favors control

Figure 6 A forest plot evaluating the RR of the incidence of nausea with the use of gabapentin compared to control.
Abbreviations: RR, relative risk; CI, confidence interval.

Study name	Statistics for each study				Risk ratio 95% CI	Relative weight
	Risk ratio	Lower limit	Upper limit	P-value		
Pandey et al[23]	0.750	0.185	3.048	0.688		4.32
Turan et al[35]	0.667	0.279	1.594	0.362		11.18
Turan et al[36]	0.167	0.022	1.286	0.086		2.04
Radhakrishnan et al[37]	3.000	0.330	27.234	0.329		1.75
Montazeri et al[41]	1.333	0.322	5.526	0.692		4.20
Grover et al[42]	0.840	0.351	2.010	0.695		11.16
Moore et al[22]	2.190	0.626	7.671	0.220		5.41
Deniz et al[44]	0.607	0.286	1.289	0.193		14.97
Short et al[45]	0.917	0.456	1.841	0.807		17.47
Short et al[45]	0.750	0.354	1.589	0.453		15.06
Bharti et al[20]	0.667	0.292	1.523	0.336		12.44
	0.799	0.597	1.070	0.132		

0.1   0.2   0.5   1   2   5   10

Favors gabapentin   Favors control

Figure 7 A forest plot evaluating the RR of the incidence of vomiting with the use of gabapentin compared to control.
Abbreviations: RR, relative risk; CI, confidence interval.

cancer patients demonstrated a significant reduction in chemotherapy-induced nausea with the use of gabapentin.[29] Gabapentin's antiemetic effects are likely attributable to the reduced tachykinin neurotransmission and the direct reduction in postoperative opioid consumption.[29,30]

The results demonstrated a statistically significant reduction in the postoperative cumulative consumption of fentanyl, morphine, and tramadol during the initial 24 hours following surgery with the administration of preoperative

gabapentin. Significant reductions in postoperative opioid consumption were observed following abdominal hysterectomy, breast cancer surgery, cholecystectomy, orthopedic surgeries, spinal surgeries, and thyroid surgeries. Although not significant, a small reduction in postoperative opioid consumption was observed following caesarian sections, prostatectomy, and thoracotomy. There was no significant differences observed in vomiting and nausea incidences with the use of gabapentin; however, a recent meta-analysis by

Study name	Statistics for each study				Risk ratio and 95% CI	Relative weight
	Risk ratio	Lower limit	Upper limit	P-value		
Pandey et al[23]	10.400	4.271	25.323	0.000		11.45
Turan et al[35]	3.000	0.128	70.296	0.495		1.60
Turan et al[36]	2.000	0.194	20.671	0.561		2.76
Radhakrishnan et al[37]	1.000	0.066	15.260	1.000		2.09
Pandey et al[40]	2.000	0.373	10.722	0.418		4.84
Srivastava et al[43]	1.750	0.793	3.862	0.166		12.88
Moore et al[22]	1.340	1.042	1.724	0.023		22.48
Short et al[45]	1.080	0.772	1.512	0.654		21.10
Short et al[45]	1.000	0.703	1.423	1.000		20.80
	1.636	1.084	2.471	0.019		

0.01   0.1   1   10   100

Favors gabapentin   Favors control

Figure 8 A forest plot evaluating the RR of the incidence of somnolence with the use of gabapentin compared to control.
Abbreviations: RR, relative risk; CI, confidence interval.
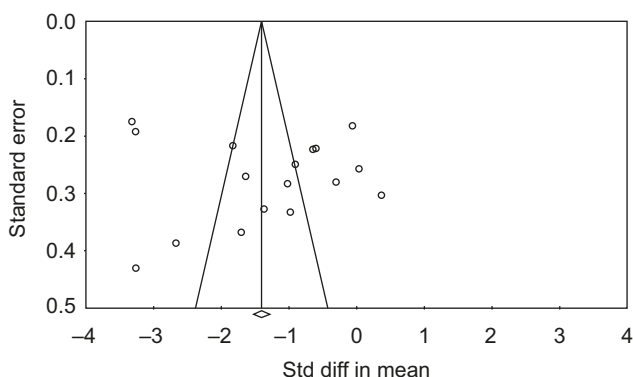
Figure 9 A funnel plot assessing publication bias (analyzing the effect of preoperative gabapentin administration on opioid consumption within the first 24 hours postoperatively).
Abbreviation: Std diff, standard difference.

Grant et al[31] evaluating the use of preoperative gabapentin on postoperative nausea and vomiting reported statistically significant reductions in postoperative nausea (RR =0.76, 95% CI: 0.67–0.85, $P<0.0001$; 42 studies involving 2,349 patients) and vomiting (RR =0.67, 95% CI: 0.56–0.80, $P<0.0001$; 36 studies involving 2,024 patients). In all the trials, gabapentin was administered preoperatively as a single oral dose or two divided doses 2–24 hours before surgery at a dose ranging from 300 mg to 1,200 mg. This study also identified an association between cumulative gabapentin dose and reduction in morphine consumption. The higher the dose of gabapentin, the greater the reduction in morphine consumption.

Gabapentin has been documented with minimal side effects and is considered a safe and tolerable medication.[32] The side effects of gabapentin are limited to somnolence, confusion, ataxia, dizziness, nausea, and weight gain.[33] Nausea and vomiting incidence rates were similar, despite having a reduction in overall opioid consumption and presumed antiemetic property of gabapentin. The findings from the current study demonstrated a slight increase in the incidence of somnolence.

This study contains several limitations. The first is the different opioid and dosage used. Three studies utilized fentanyl and three utilized tramadol, which were converted to their equivalent morphine dose for analysis. Second, details regarding the more common opioid side effects were rarely reported, with the exception of postoperative nausea and vomiting. Additional research is warranted to examine optimal gabapentin dose and frequency regimen to determine the presence of beneficial or resistant interactions between certain opioids and adjuvant gabapentin therapy. Furthermore, the small sample size of most included RCTs (<50 patients per study) presented challenges to generalize conclusions and speculate the impact of gabapentin on rare complications such as respiratory depression.

Conclusion

Preoperative adjunct gabapentin administration significantly reduces opioid consumption within the initial 24 hours following surgery, with similar incidence rates of side effects. The greatest reduction was observed in gynecologic and breast cancers, cholecystectomy, and orthopedic and thyroid surgeries. The observed reduction in postoperative opioid consumption with preoperative gabapentin supports the notion of incorporating gabapentin in the multimodal analgesic treatment plans for postoperative pain management among patients undergoing elective surgery.

Disclosure

The authors report no conflicts of interest in this work.

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