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Original Article

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Impact of timing of preoperative gabapentin administration on postoperative somnolence

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Abstract

Context: Enhanced Recovery After Surgery (ERAS) is a multimodal protocol aimed to improve quality of postoperative recovery, minimize complications, and optimize overall self-regulation. Preoperative gabapentin decreases postoperative pain but can be associated with prolonged postoperative somnolence and respiratory depression risk. Although it is known that gabapentin affects the postoperative course, it is unclear if the timing of preoperative administration affects this finding.

Objectives: This study aims to assess the optimal preoperative timing for gabapentin administration in patients undergoing gynecologic surgery to minimize postoperative somnolence risk.

Methods: A retrospective cohort study evaluated patients who underwent major gynecologic surgery and received preoperative gabapentin. Patients were grouped based on timing from gabapentin administration to surgical incision (<4 h group vs. ≥4 h group). Preoperative, intraoperative, and postoperative data were abstracted and compared. Univariate associations between the timing of gabapentin administration and the patient and surgical characteristics and outcomes were tested utilizing two-sample equal-variance t-tests, linear model ANOVA, or Fisher's exact tests. Associations between the timing of gabapentin administration and the time until the Richmond Agitation Sedation Scale (RASS) score of 0 were modeled utilizing linear regression, adjusted for age, initial postoperative anesthesia care unit (PACU), RASS score, and postoperative narcotics.

Results: Each group contained 127 patients. Demographics were similar except for age (<4 h group mean=44.2 years; ≥4 h group mean=40.5 years; p=0.021), chronic pain (<4 h group=17.6%; ≥4 h group=43.3%; p<0.001), and surgical indication (<4 h group=pelvic pain [29.1%]; ≥4 h group=pelvic pain [51.2%]; p=0.007). The <4 h group had a similar postoperative narcotic administration (<4 h group mean morphine milligram equivalents [MME]=3.667; ≥4 h group mean MME=4.833; p=0.185). The minutes from surgical closure until the patient received a RASS score of 0 and initial PACU pain score (Visual Analogue Scale [VAS]) were similar. The initial PACU oxygen administration volume, hours from surgical closure until the patient transitioned to room air, and initial PACU respiratory rate were similar. The PACU duration, admission secondary to somnolence, and initial PACU Glasgow Coma Scale (GCS) score showed no difference. Postoperative nausea/vomiting was decreased in the ≥4 h group (<4 h group=24.4%; ≥4 h group=13.4%; p-value=0.036), and urinary retention (<4 h group=14.2%; ≥4 h group=5.5%; p-value=0.033) was decreased in the ≥4 h group.

Conclusions: The timing of gabapentin administration less than or more than 4 h preoperatively in patients ≥18 years does not significantly affect postoperative somnolence or respiratory depression. Further, it does not have a significant effect on GCS scores or VAS scores.

Keywords: ERAS; gabapentin; hysterectomy; respiratory depression; somnolence.

Enhanced Recovery After Surgery (ERAS) is a multimodal protocol aimed to improve the quality of postoperative recovery and minimize complications [1]. The effectiveness of ERAS protocols have been assessed through analyzing patients' average length of stay and complications postoperatively [1]. ERAS supports the tenets of osteopathic medicine, including the promotion of self-regulation and self-healing, through preemptive management and optimization of anticipated intraoperative and postoperative physiologic changes [2]. The treatment employed in ERAS

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supports the interrelationship between all aspects of the body unit. Elements of ERAS protocols include, but are not limited to, patient education, patient optimization prior to admission, timing of oral intake of fluids and solids, nausea/vomiting prophylaxis, multimodal analgesia, and day of surgery ambulation [3–5].

ERAS protocols have narcotic-sparing effects by implementing multimodal analgesia with the incorporation of preemptive analgesia, systemic medications, and regional and neuraxial analgesia [4]. Acetaminophen, gabapentinoids, and nonsteroidal anti-inflammatory drugs are examples of non-narcotic drugs administered preoperatively to decrease narcotic consumption [3]. Specifically, preoperative gabapentin has shown to have narcotic-sparing effects and decreases postoperative pain in patients undergoing major gynecologic surgery [6–11]. Furthermore, patients who underwent minimally invasive gynecologic surgery who were administered gabapentin were found to have earlier ambulation, higher patient satisfaction, and earlier discharge from the hospital [11–13].

Gabapentin is an anticonvulsant that binds calcium-dependent ion channels with antinociceptive and antihyperalgesic properties [9]. Specifically, gabapentin is utilized for chronic pain syndromes, such as neuropathic pain, and for seizure control [9, 10, 14]. Side effects include dizziness, diplopia, and ataxia [4]. When utilized perioperatively, it has also been associated with increased postoperative somnolence [9, 15] and respiratory depression [16]. Specifically, some ERAS protocols have discontinued the use of gabapentin in their protocols due to the Food and Drug Administration warning of respiratory depression from gabapentinoids, specifically when taken with central nervous system depressants and for geriatric patients or patients with renal impairments [17]. Gabapentin alone does not cause respiratory depression; however, in combination with opioids and specific patient characteristics, there is some evidence of respiratory depression [16]. Because of this potential interaction leading to adverse outcomes, some ERAS protocols have suspended the use of gabapentin.

Although it is known that gabapentin affects the postoperative course, it is unclear if the timing of preoperative administration affects this finding. The peak plasma concentration of gabapentin is known to occur approximately 2–3 h after administration [18]. This study aims to assess the optimal preoperative timing for gabapentin administration in patients undergoing gynecologic surgery to minimize the risk of prolonged postoperative somnolence. The primary outcome was measured by the time from surgical closure to a Richmond Agitation Sedation Scale (RASS) score of 0. Secondary outcomes included the postoperative anesthesia care unit (PACU) stay duration, unplanned admission, and endpoints related to sedation, respiration, and pain.

Methods

After obtaining approval from the Mayo Clinic Institutional Review Board (IRB number: 20-003782), a retrospective cohort chart review was completed. The electronic health records (EHRs) of patients ≥18 years old who received preoperative gabapentin and underwent major gynecologic surgery (benign, oncologic, and urogynecologic procedures) between March 2018 and November 2020 were identified. Major gynecologic surgery was defined as a surgical procedure that required entrance into the peritoneal cavity (laparotomy, laparoscopy, and robotic and vaginal surgeries). Patients were grouped based on the timing from gabapentin administration to surgical incision (less than 4 h vs. four or more hours). Medical, surgical, and anesthesia records were reviewed. Preoperative, intraoperative, and postoperative data were abstracted and compared.

The demographic data abstracted included age, weight, height, menopause status, race/ethnicity, chronic narcotic use, chronic gabapentin use, and chronic pain status. Race/ethnicity was self-designated by patients utilizing the hospital-predetermined classifications of: American Indian or Alaska Native; Asian; Black or African American; Hispanic or Latino; Native Hawaiian or Other Pacific Islander; White; or Other. Race/ethnicity were assessed solely to describe the patient demographics in this study. The surgical data abstracted included surgical indication, surgical approach, procedure performed, time of first incision, time of closure, surgical duration, and estimated blood loss. The time of the gabapentin administration was recorded. Per institutional ERAS protocol, patients aged 18–59 were given 600 mg of gabapentin, and patients aged 60 years and older received 300 mg of gabapentin. Preoperative, intraoperative, and postoperative narcotic consumption were abstracted. Narcotic administration was converted to IV morphine milligram equivalents (MME) [19]. The PACU data abstracted included variables that were utilized collectively as surrogate markers of somnolence. These included vital signs, RASS scores, oxygen administration, Glasgow Coma Scale (GCS) scores, unplanned hospital admission, dizziness, nausea/vomiting, urinary retention, and duration of PACU stay. Postoperative nausea and vomiting were recorded if they were subjectively reported in the patient's medical record.

A sample size of 254 patients with 127 patients in each group was estimated to provide power of 80% or greater, assuming a mean somnolence recovery time of 90 min in the more than or equal to 4 h gabapentin group, 150 min in the less than 4 h gabapentin group, a standard deviation of 150 min, and a significance level of 5%. This sample size allowed for a missing data rate of 10%. Patients were identified starting in March 2018 and continued until 127 patients were reached in each group. Patients were excluded if they did not have both a gynecologic surgery and preoperative gabapentin administration.

The data were analyzed to determine if there was a difference in patient-oriented outcomes among individuals taking gabapentin within 4 h of surgery or more than 4 h of surgery. This cutoff was based on the typical time intervals with patients self-administering gabapentin at home vs. receiving gabapentin in the preoperative unit. Associations were tested utilizing two-sample equal-variance t-tests or

linear model ANOVA for continuous variables, or Fisher's exact tests for categorical variables. Associations between the time from taking gabapentin to the time of first incision and the time until RASS score of 0 were modeled utilizing linear regression, adjusting for age, initial PACU RASS score, and postoperative narcotics (MME). Statistical analysis was performed utilizing R version 4.0.3.

Results

A total of 254 patients were included. Gabapentin was administered less than 4 h prior to skin incision for 127 patients (50.0%) (<4 h group) and four or more hours in 127 patients (50.0%) (≥4 h group). Demographics were similar between the groups with the exception of age (<4 h group mean=44.2; ≥4 h group=mean 40.5; p=0.021), chronic pain (<4 h group=17.6%, n=22; ≥4 h group=43.3%, n=55; p<0.001), and surgical indication (<4 h group=pelvic pain [29.1%, n=37]; ≥4 h group=pelvic pain (51.2%, n=65); p=0.007). Surgical approach was minimally invasive in 78.0% (n=99) of patients in <4 h group and 88.2% (n=112) of patients in ≥4 h group. Hysterectomy was the most frequent procedure performed (<4 h group=50.4%, n=64; ≥4 h group=49.6%, n=63), followed by excision of endometriosis (<4 h group=27.6%, n=35; ≥4 h group=55.1%, n=70). Details of demographics and surgical characteristics are summarized in Table 1.

Narcotic administration preoperatively (p=0.111) and intraoperatively (p=0.237), and postoperatively (p=0.185) were similar between the two groups. Oxycodone and hydromorphone were administered less frequently in the <4 h group (31.5%, n=40 and 29.9%, n=38, respectively) than in the ≥4 h group (48.8%, n=62 and 44.9%, n=57) (p=0.007 and 0.019 respectively). Preoperative, intraoperative, and postoperative medications are outlined in Table 2.

The minutes from surgical closure until the time the patient received a RASS score of 0 (<4 h group mean [SD] =163.5 [117.9] min, ≥4 h group mean [SD]=143.9 [100.4] min, p=0.168) and initial PACU pain score (VAS) were similar for both groups (p=0.245). The initial PACU oxygen administration volume (p=0.678), hours from surgical closure until the patient transitioned to room air (p=0.679), and initial PACU respiratory rate (p=0.913) were similar between the two groups. The mean PACU stay duration did not show a statistical difference with the less than 4 h group duration of stay of 250.1 min compared to 240.1 min in the more than 4 h group (p=0.449). Unplanned admission secondary to excessive somnolence was uncommon in both groups, with one instance (0.8%) in the less than 4 h group and two instances (1.6%) in the more than 4 h group (p=1.00). The initial PACU GCS score (p=0.473) showed no statistically significant difference between the two groups. Postoperative dizziness had no significant difference between the two groups; however, postoperative nausea/vomiting (<4 h group=24.4%, n=31; ≥4 h group=13.4%, n=17; p=0.036) and urinary retention (<4 h group=14.2%, n=18; ≥4 h group=5.5%, n=7; p=0.033) were both decreased in the 4 h or more group. Table 3 compares the postoperative clinical outcomes by time of taking gabapentin to time of first incision.

After controlling for age, initial PACU RASS score, and postoperative narcotics use, patients took on average 0.105 min less (95% CI: 0.232 min less to 0.021 min more) to achieve a RASS score of 0 for every increase of 1 min between taking gabapentin to the time of first incision (p=0.10). However, this finding was not statistically significant. Controlling for time from taking gabapentin to time of first incision, initial PACU RASS score, and postoperative narcotics use, patients took on average 2.983 min more (95% CI: 2.675 min less to 8.640 min more) to achieve a RASS score of 0 for every five-year increase in age, although this difference was not statistically significant (p=0.30). Results for the linear regression for the outcome of time until RASS score of 0 are outlined in Table 4.

Minutes from closure until time achieved a RASS score of 0 stratified by indication of surgery showed the indication of abnormal bleeding took the greatest amount of time (median, 155). This was followed by pelvic pain (median, 134), cancer (median, 129), other (median, 128), and finally, prolapse (median, 95.50) (p=0.85). Table 5 reports the summary of time until RASS score of 0 by surgical indication.

Discussion

This retrospective chart review demonstrated that the timing of preoperative gabapentin administration as part of the ERAS protocol prior to gynecologic surgeries does not have a significant effect on postoperative somnolence, GCS scores, or pain VAS scores. Further, this study found that gabapentin does not have a significant effect on respiratory depression when given as part of the ERAS protocol for gynecologic surgeries. This finding is important in light of a recent study stating that some ERAS protocols are discontinuing the use of gabapentin due to the risk of respiratory depression [17].

This study shows that the timing of gabapentin does not affect postoperative somnolence. Previous studies have found an increased risk of sedation with preoperative gabapentin [9, 15]. It has been hypothesized that receiving gabapentin four or more hours prior to surgery would decrease the risk of postoperative sedation. However, this

Table 1: Demographics and surgical characteristics by time from taking gabapentin to time of first incision.

	<4 h (n=127)	≥4 h (n=127)	p-Value
Age, years			0.021
Mean, SD	44.2 (13.3)	40.5 (12.1)	
Median (Q1, Q3)	43.0 (35.0, 53.0)	38.0 (31.0, 47.0)	
Range	20.0–83.5	20.0–69.0	
Weight, kg			0.414
Mean, SD	75.5 (18.5)	73.6 (18.8)	
Median (Q1, Q3)	72.1 (63.1, 84.1)	68.8 (59.5, 85.5)	
Range	43.8–182.0	41.5–142.0	
Height, cm			0.050
Mean, SD	165.2 (6.3)	166.7 (6.4)	
Median (Q1, Q3)	165.0 (161.0, 170.2)	166.4 (162.7, 169.9)	
Range	152.0–181.9	149.7–184.2	
Body mass index, kg/m^2			0.122
Mean, SD	27.7 (6.7)	26.4 (6.4)	
Median (Q1, Q3)	26.2 (23.4, 31.5)	25.1 (21.7, 30.0)	
Range	16.8–66.8	14.9–49.0	
Premenopausal	86 (67.7%)	96 (75.6%)	0.210
Race/ethnicity			
American Indian or Alaska Native	0 (0.0%)	0 (0.0%)	
Asian	5 (3.9%)	7 (5.5%)	
Black or African American	8 (6.3%)	4 (3.1%)	
Hispanic or Latino	1 (0.8%)	11 (8.7%)	
Native Hawaiian or other Pacific Islander	0 (0.0%)	0 (0.0%)	
White	106 (83.5%)	101 (79.5%)	
Other	7 (5.5%)	4 (3.1%)	
Chronic narcotic use	3 (2.4%)	4 (3.2%)	0.721
Chronic pain	22 (17.6%)	55 (43.3%)	<0.001
Chronic gabapentin use	4 (3.1%)	8 (6.3%)	0.254
Surgical indication			0.007
Pelvic pain	37 (29.1%)	65 (51.2%)	
Cancer	18 (14.2%)	10 (7.9%)	
Prolapse	15 (11.8%)	8 (6.3%)	
Abnormal bleeding	23 (18.1%)	20 (15.7%)	
Other	34 (26.8%)	24 (18.9%)	
Type of procedure			<0.001
Robotic	59 (46.5%)	95 (74.8%)	
Laparoscopic	40 (31.5%)	17 (13.4%)	
Vaginal	22 (17.3%)	7 (5.5%)	
Laparotomy	6 (4.7%)	8 (6.3%)	
Procedure performed			
Hysterectomy	64 (50.4%)	63 (49.6%)	1.000
Excision of endometriosis	35 (27.6%)	70 (55.1%)	<0.001
Cancer staging	11 (8.7%)	2 (1.6%)	0.019
Ovarian cystectomy	18 (14.2%)	13 (10.2%)	0.444
Salpingectomy	59 (46.5%)	58 (45.7%)	1.000
Salpingo-oophorectomy	30 (23.6%)	17 (13.4%)	0.052
Prolapse repair	14 (11.0%)	8 (6.3%)	0.264
Other	60 (47.2%)	81 (63.8%)	0.011
Duration of procedure, h			0.043
Mean, SD	2.1 (1.3)	2.4 (1.4)	
Median (Q1, Q3)	1.8 (1.1, 2.7)	2.2 (1.5, 2.9)	
Range	0.5–8.4	0.4–9.8	
EBL, mL			0.434
Mean, SD	93.9 (199.6)	78.0 (112.7)	
Median (Q1, Q3)	50.0 (20.0, 95.0)	50.0 (20.0, 100.0)	
Range	0.0–1800.0	5.0–750.0	

SD, standard deviation.

Table 2: Preoperative, intraoperative, and postoperative medications by time from taking gabapentin to time of first incision.

	<4 h (n=127)	≥4 h (n=127)	p-Value
Preoperative narcotics, MME			0.111
Mean, SD	0.220 (0.778)	0.424 (1.207)	
Median (Q1, Q3)	0.025 (0.013, 0.025)	0.025 (0.016, 0.025)	
Range	0.000–4.025	0.000–7.525	
Narcotic meds: dilaudid	0 (0.0%)	0 (0.0%)	
Narcotic meds: oxycodone	0 (0.0%)	1 (0.8%)	1.000
Narcotic meds: hydrocodone	0 (0.0%)	0 (0.0%)	
Narcotic meds: morphine	1 (0.8%)	0 (0.0%)	1.000
Narcotic meds: fentanyl	122 (96.1%)	122 (96.1%)	1.000
Narcotic meds: hydromorphone	8 (6.3%)	15 (11.8%)	0.189
Narcotic meds: oxymorphone	0 (0.0%)	0 (0.0%)	
Narcotic meds: tramadol	0 (0.0%)	0 (0.0%)	
Intraoperative narcotics, MME			0.237
Mean, SD	0.695 (1.393)	0.901 (1.376)	
Median (Q1, Q3)	0.013 (0.000, 0.025)	0.013 (0.000, 2.000)	
Range	0.000–6.400	0.000–4.025	
Narcotic meds: dilaudid	0 (0.0%)	0 (0.0%)	
Narcotic meds: oxycodone	0 (0.0%)	0 (0.0%)	
Narcotic meds: hydrocodone	0 (0.0%)	0 (0.0%)	
Narcotic meds: morphine	0 (0.0%)	0 (0.0%)	
Narcotic meds: fentanyl	68 (53.5%)	52 (40.9%)	0.059
Narcotic meds: hydromorphone	31 (24.4%)	47 (37.0%)	0.041
Narcotic meds: oxymorphone	0 (0.0%)	0 (0.0%)	
Narcotic meds: tramadol	0 (0.0%)	0 (0.0%)	
Postoperative narcotics, MME			0.185
Mean, SD	3.667 (8.054)	4.833 (5.726)	
Median (Q1, Q3)	0.019 (0.006, 7.506)	4.006 (0.006, 8.306)	
Range	0.000–78.206	0.000–46.606	
Narcotic meds: dilaudid	0 (0.0%)	0 (0.0%)	
Narcotic meds: oxycodone	40 (31.5%)	62 (48.8%)	0.007
Narcotic meds: hydrocodone	1 (0.8%)	0 (0.0%)	1.000
Narcotic meds: morphine	2 (1.6%)	0 (0.0%)	0.498
Narcotic meds: fentanyl	97 (76.4%)	96 (75.6%)	1.000
Narcotic meds: hydromorphone	38 (29.9%)	57 (44.9%)	0.019
Narcotic meds: oxymorphone	0 (0.0%)	0 (0.0%)	
Narcotic meds: tramadol	1 (0.8%)	1 (0.8%)	1.000

MME, morphine milligram equivalents; SD, standard deviation.

study shows no significant differences in RASS scores and duration of PACU stay between the two groups. Further, both groups achieved a RASS score of 0 within 2.4–2.7 h, on average, after surgical closure. Both groups were discharged from the PACU within 4–4.17 h, on average, of surgical closure. The protocol at the study institution is to monitor patients following a hysterectomy for a minimum of 4 h in the PACU prior to discharge, indicating that, on average, patients were discharged as early as the protocol allowed. Between both groups, only three patients had an unplanned admission secondary to excessive somnolence. These findings suggest that the risk for postoperative somnolence may not be as high in patients receiving preoperative gabapentin in gynecologic surgeries as previous studies have shown [9, 15].

One study of 8,567 patients who underwent laparoscopic surgeries lasting 90 min or longer found that 15.3% of the patients had episodes of respiratory depression when receiving gabapentin preoperatively [16]. In this study, respiratory depression was evaluated through respiratory rate, liters of oxygen needed, and hours from surgical closure until the patient was transitioned to room air. This study did not find evidence of complicated respiratory depression in either group, indicating that the timing of gabapentin does not cause differences in respiration postoperatively and further illustrates that the risk of

Table 3: Main outcomes by time from taking gabapentin to time of first incision.

	<4 h (n=127)	≥4 h (n=127)	p-Value
Minutes from closure until RASS score of 0			0.168
Mean, SD	163.5 (117.9)	143.9 (100.4)	
Median (Q1, Q3)	142.5 (77.8, 205.8)	128.0 (67.5, 193.5)	
Range	11.0–743.0	8.0–708.0	
Initial PACU RASS score			0.675
Mean, SD	−1.4 (1.0)	−1.4 (1.1)	
Median (Q1, Q3)	−1.0 (−1.0, −1.0)	−1.0 (−2.0, −1.0)	
Range	−5.0–1.0	−5.0–3.0	
1 h postoperative RASS score			0.006
Mean, SD	−0.7 (0.5)	−0.6 (0.6)	
Median (Q1, Q3)	−1.0 (−1.0, 0.0)	−1.0 (−1.0, 0.0)	
Range	−2.0–0.0	−2.0–1.0	
Initial PACU pain score VAS			0.245
Mean, SD	2.6 (3.3)	3.1 (3.3)	
Median (Q1, Q3)	0.0 (0.0, 5.0)	2.0 (0.0, 6.0)	
Range	0.0–10.0	0.0–10.0	
1 h postoperative pain score			0.170
Mean, SD	3.8 (2.5)	4.2 (2.3)	
Median (Q1, Q3)	4.0 (2.0, 5.0)	4.0 (3.0, 6.0)	
Range	0.0–9.0	0.0–10.0	
Initial PACU L of O_2			0.678
Mean, SD	7.3 (2.1)	7.2 (1.8)	
Median (Q1, Q3)	8.0 (6.0, 8.0)	8.0 (6.0, 8.0)	
Range	2.0–15.0	2.0–10.0	
Initial PACU route			
Nasal cannula	10 (8.2%)	6 (4.8%)	
Face mask	111 (91.0%)	118 (95.2%)	
CPAP	0 (0.0%)	0 (0.0%)	
ET tube	1 (0.8%)	0 (0.0%)	
1 h postop L of O_2			0.586
Mean, SD	2.6 (1.6)	2.5 (1.2)	
Median (Q1, Q3)	2.0 (2.0, 3.0)	2.0 (2.0, 3.0)	
Range	1.0–10.0	1.0–10.0	
1 h postoperative route			
Nasal cannula	44 (95.7%)	51 (98.1%)	
Face mask	2 (4.3%)	1 (1.9%)	
CPAP	0 (0.0%)	0 (0.0%)	
ET tube	0 (0.0%)	0 (0.0%)	
Time from closure until patient on room air, h			0.679
Mean, SD	2.4 (2.7)	2.3 (2.8)	
Median (Q1, Q3)	1.2 (0.7, 3.4)	1.4 (0.7, 2.7)	
Range	0.3–12.7	0.1–17.7	
Initial PACU respiratory rate			0.913
Mean, SD	15.5 (4.5)	15.5 (4.0)	
Median (Q1, Q3)	15.0 (12.5, 18.0)	15.5 (13.0, 17.0)	
Range	7.0–28.0	5.0–28.0	
1 h postoperative respiratory rate			0.176
Mean, SD	15.0 (4.0)	15.7 (3.4)	
Median (Q1, Q3)	15.0 (12.0, 17.0)	15.0 (13.0, 18.0)	
Range	7.0–29.0	7.0–26.0	
PACU stay duration, min			0.449
Mean, SD	250.1 (114.3)	240.1 (95.8)	
Median (Q1, Q3)	249.0 (180.5, 283.0)	243.0 (163.0, 297.0)	
Range	70.0–713.0	67.0–538.0	
Unplanned admission secondary to excessive somnolence			1.000
No	124 (99.2%)	124 (98.4%)	
Yes	1 (0.8%)	2 (1.6%)	

Table 3: (continued)

	<4 h (n=127)	≥4 h (n=127)	p-Value
Unplanned admission secondary to reason unrelated to somnolence			0.300
No	109 (87.2%)	115 (92.0%)	
Yes	16 (12.8%)	10 (8.0%)	
GCS (alertness) initial score			0.473
Mean, SD	13.9 (1.8)	13.6 (2.1)	
Median (Q1, Q3)	14.0 (14.0, 15.0)	14.0 (14.0, 15.0)	
Range	3.0–15.0	6.0–15.0	
GCS (alertness) 1 h postoperative			0.463
Mean, SD	14.8 (0.4)	14.7 (1.0)	
Median (Q1, Q3)	15.0 (15.0, 15.0)	15.0 (15.0, 15.0)	
Range	14.0–15.0	11.0–15.0	
Dizziness	9 (7.1%)	7 (5.5%)	0.797
Nausea/vomiting	31 (24.4%)	17 (13.4%)	0.036
Urinary retention	18 (14.2%)	7 (5.5%)	0.033

CPAP, continuous positive airway pressure; ET, endotracheal; GCS, glasgow coma scale; PACU, postoperative anesthesia care unit; RASS, richmond agitation sedation scale; SD, standard deviation; VAS, visual analog scale.

Table 4: Results from linear regression for the outcome of time until RASS score of 0.

	Estimate	CI lower estimate	CI upper estimate	p-Value
Time from taking gabapentin to time of first incision, min	−0.105	−0.232	0.021	0.102
Age, years	2.983	−2.675	8.640	0.300
Initial PACU RASS score:	−12.379	−26.169	1.411	0.078
Postoperative narcotics, MME	1.474	−0.507	3.455	0.144

CI, confidence interval; MME, morphine milligram equivalents; PACU, postoperative anesthesia care unit; RASS, richmond agitation sedation scale.

postoperative respiratory depression may be smaller in the gynecologic surgery population than other studies have previously shown [16, 20].

This study found that the adverse outcomes of nausea and vomiting may be decreased when gabapentin is given more than 4 h prior to surgery. Other studies have found the incidence of postoperative nausea and vomiting to be decreased in patients receiving gabapentin [9, 21, 22]. A meta-analysis found a 40% relative risk reduction in postoperative nausea and vomiting in patients who received preoperative gabapentin [22]. This may be attributed to the innate anti-emetic effects [20] of gabapentin and the longer time for gabapentin to be distributed throughout the body. Gabapentin decreases nausea and vomiting symptoms by regulating efferent and afferent neural pathways involved in their production. It is increasingly being utilized in ERAS protocols and for chronic nausea [23]. Furthermore, this study found that incidents of urinary retention may be decreased when gabapentin is given more than 4 h preoperatively. A meta-analysis of 827 patients found that urinary retention was decreased in patients who received gabapentin

Table 5: Summary of time until RASS score of 0 by indication.

	Pelvic pain (n=102)	Cancer (n=28)	Prolapse (n=23)	Abnormal bleeding (n=44)	Other (n=58)	Total (n=255)	p-Value
Minutes from closure until time achieved a RASS score of 0							0.845
Mean, SD	159.88 (124.53)	138.40 (78.59)	144.95 (116.93)	161.80 (92.74)	146.18 (104.30)	153.47 (109.48)	
Median (Q1, Q3)	134.00 (78.75, 208.25)	129.00 (82.00, 193.00)	95.50 (63.50, 186.00)	155.00 (75.00, 216.00)	128.00 (74.00, 168.00)	133.50 (74.00, 203.50)	
Range	8.00–743.00	30.00–360.00	11.00–415.00	18.00–370.00	23.00–525.00	8.00–743.00	

RASS, richmond agitation sedation scale; SD, standard deviation.

preoperatively compared to those who did not, with a 0.57 relative risk [24]. With this understanding and based on the results of this study, the optimal timing of gabapentin administration for nausea, vomiting, and urinary retention is more than 4 h prior to the start of surgery.

Research implications

This research study indicates that the risk of postoperative somnolence and respiratory depression may be low in gynecologic surgery patients and that the timing of administration of gabapentin has a minimal effect on postoperative outcomes with the exception of nausea, vomiting, and urinary retention. This study supports the osteopathic theory that the body is a unit and that all systems are interrelated. Optimizing a patient's preoperative milieu will promote postoperative recovery through support of self-healing and self-regulation. Further research can be conducted to study the optimal timing of gabapentin administration relative to the surgical indication, the procedure performed, and whether the individual patients have a chronic pain history.

Strengths and limitations

This is the first study to analyze the effects of the timing of preoperative gabapentin administration on postoperative clinical outcomes in gynecologic surgeries. This study analyzed all major gynecologic procedures, indications, and types of procedure, enabling generalizability in gynecologic surgery as a whole.

This study has limitations that should be considered, including the inherent bias of a retrospective study design. This study relied upon perioperative staff to monitor and record patient outcomes, meaning that this is prone to misclassification error and general variability in how different staff members assess patient outcomes. However, because this limitation effects all patients equally in the study, the main outcomes can still be compared across the two groups. This bias is further decreased because the study was conducted at a single institution with standard training and education of perioperative staff. Further, in the 4 h or more group, the patients reported the reported time of gabapentin administration because they took gabapentin prior to arrival for surgery. This could be limited by the recall bias of the patients. Additionally, the results are undoubtedly impacted by confounding variables that would be better accounted for with future prospective, randomized controlled trials.

Conclusions

Administration of gabapentin less than 4 h or greater than 4 h preoperatively does not significantly affect postoperative somnolence or respiratory depression. Those who took gabapentin four or more hours prior to surgery had significantly less adverse outcomes of nausea/vomiting and urinary retention as compared to those who took it within 4 h of surgery.

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