Research Article

Effect of gabapentin in postoperative pain, nausea, and vomiting in patients undergoing laparoscopic cholecystectomy

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Abstract

Background: Postoperative pain, nausea, and vomiting are frequent and unpleasant adverse events associated with surgery. The reported incidence of postoperative nausea and vomiting after laparoscopic cholecystectomy (LC) is quite high. Recently, studies have been undertaken to determine the role of gabapentin for the prevention of postoperative pain, nausea, and vomiting.

Objective: To evaluate the effects of oral gabapentin on early postoperative pain, nausea, and vomiting in patients undergoing LC.

Materials and Methods: A total of 40 patients scheduled to undergo LC were enrolled for this double-blind placebo-controlled study. Patients were divided into two groups of 20 patients each. Group A received two doses of 600 mg (300 mg ± 2 tablets) gabapentin: first dose 2 h before surgery and second dose 6 h after surgery. Group B received matching placebo (tablets) of same size and shape as gabapentin tablets. All patients were observed for postoperative pain, nausea, and vomiting on first and second postoperative days. In addition, pulse rate and systolic and diastolic blood pressures were analyzed pre- and postoperatively. Injections ondansetron and diclofenac were used as the antiemetic and analgesic medications, respectively, on as-and-when required basis.

Results: Intergroup comparison with respect to pulse rate and systolic and diastolic blood pressures between the two groups was insignificant ($p > 0.05$). On the first and second postoperative days of LC, average numbers of analgesics used in gabapentin group were 1.2 ± 0.13 and 0.65 ± 0.15 and in placebo group were 2.6 ± 0.10 and 2.2 ± 0.16, respectively. Intergroup comparison was highly significant ($p < 0.001$). The average number of antiemetics received on first and second postoperative days in gabapentin group was 0.35 ± 0.1 and 0.05 ± 0.04 and in placebo group were 1.31 ± 0.16 and 0.60 ± 0.15, respectively. Intergroup comparison was highly significant ($p < 0.001$). Pain score in gabapentin group on first and second postoperative days was 2.6 ± 0.17 and 2.2 ± 0.15 and in placebo group 3.80 ± 0.81 and 3.2 ± 0.17, respectively. Intergroup comparison was highly significant ($p < 0.001$).

Conclusion: Administration of gabapentin 2 h before and 6 h after the surgery significantly decreased the incidence of postoperative pain, nausea, and vomiting.

KEY WORDS: Laparoscopic cholecystectomy, gabapentin, postoperative pain, nausea, vomiting

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Introduction

Postoperative pain, nausea, and vomiting are among the common, unpleasant complications that develop after surgery, occurring in 25%–30% of cases.[1–3] These symptoms have been reported in as many as 42%–72% of patients after laparoscopic cholecystectomy (LC).[4] Opioid derivatives are the most popular drugs used for the treatment purpose in

such conditions; so, current research in this field are focused on finding new alternative drugs or drugs that can be combined with opioid to reduce the need for its use.[5] Gabapentin, an analog of gamma aminobutyric acid, is generally used as an antiepileptic agent.[6] It is used for neuropathic pain, diabetic neuropathy, postherpetic pain, and reflex sympathetic dystrophy.[6–8] It is an analgesic drug that can be affected directly by interaction with nociception in the central nervous system. Although its exact mode of action is not known, gabapentin appears to have a unique effect on voltage-dependent calcium ions at the postsynaptic dorsal horns and may, therefore, interrupt the series of events that lead to experience of a neuropathic pain sensation.[6] Gabapentin is also effective in reducing the nausea and vomiting, which are induced by chemotherapy.[9] Tachykinin neurotransmitter activity changes in response to gabapentin, which may be the possible mechanism. Therefore, the effects of tachykinin seems to be the mechanism common leading to nausea reduction after surgery and chemotherapy.[10]

Materials and Methods

This double-blind placebo-controlled study was conducted by the Departments of Surgery and Pharmacology in Shri Guru Ram Rai Institute of Medical and Health Sciences for a period of 6 months from January to June 2014. Before the commencement of study, approval was taken from Institutional Ethics Committee, and written informed consent was obtained from all the participants. Both male and female patients scheduled to undergo elective or urgent LC were eligible for inclusion in this study. The exclusion criteria were as follows: patients with diabetes mellitus, renal or liver diseases, concomitant diseases with nausea and vomiting, use of antiemetics in the 24 h before surgery, pregnancy, breastfeeding, antidepressant use, and conversion from LC to open surgery. The primary outcome was the incidence of pain after LC. The secondary outcome was the effect of gabapentin on postoperative nausea and vomiting. After enrollment, patients were randomly assigned to one of the two groups: group A patients received tablet gabapentin 600 mg (300 mg × 2 tablets) 2 h before surgery and 6 h after surgery; group B patients received a matching placebo (tablet) of same size and shape as gabapentin tablets. All patients were administered general anesthesia by using a similar anesthetic protocol. Injections ondansetron and diclofenac were used as the antiemetic and analgesic medications, respectively, on as-and-when required basis.

The pulse rate and systolic (SBP) and diastolic blood pressures (DBP) were measured preoperatively 1 h before surgery and postoperatively after 1, 6, 12, and 24 h in both the groups. Measurement of pain was done by using visual analog pain scale in both the groups. The average number of analgesics and antiemetics used in first postoperative day (24 h) and in second postoperative day (48 h) were calculated in both the groups. Statistical analysis was done by using paired and unpaired *t* test (paired *t* test) *p* value <0.05 was considered as statistically significant.

Table 1: Demographic profile

Groups	Mean age (years)	Gender (%)	
		Male	Female
Gabapentin	44.75 ± 2.86	5	95
Placebo	41.10 ± 3.26	10	90

Results

A total of 40 patients were included in the study. All values were calculated in mean ± SEM. The mean age in patients receiving gabapentin (group A) was 44.75 ± 2.86 years and in the placebo group (group B), 41.10 ± 3.26 years. The men and women percentages in gabapentin group was 5% and 95% and in placebo group was 10% and 90%, respectively [Table 1]. The mean preoperative pulse rate in groups A and B were 83.9 ± 1.32/min and 80.50 ± 1.31/min, respectively ($p > 0.05$). The mean postoperative pulse rate after 1, 6, 12, and 24 h in gabapentin group was 89.3 ± 1.84/min, 86.65 ± 1.92/min, 85.1 ± 1.54/min and 82.8 ± 1.11/min, respectively, and in placebo group was 87.35 ± 1.21/min, 86.8 ± 1.75/min, 86.8 ± 1.68/min, and 84.25 ± 1.65/min, respectively. There were no statistically significant difference between the two groups ($p >0.05$). The preoperative SBP in gabapentin group and placebo group was 123.2 ± 2.26 and 120.05 ± 2.55 mm Hg ($p > 0.05$). The postoperative SBP after 1, 6, 12, and 24 h in gabapentin group was128.4 ± 2.17, 126.5 ± 2.37, 123.5 ± 1.8, and 122.7 ± 2.11 mm Hg, respectively, and in placebo group was 124.6 ± 2.11, 121.6 ± 1.92, 123.65 ± 1.8 and 123.85 ± 2.56 mm Hg, respectively. The preoperative DBP in groups A and B was 78.7 ± 1.67 and 79.45 ± 1.65 mm Hg ($p > 0.05$). The postoperative DBP after 1, 6, 12, and 24 h in gabapentin group was 80.8 ± 2.10, 78.8 ± 1.80, 79 ± 1.69, and 78.2 ± 1.63 mm Hg and in placebo group was 84.0 ± 1.56, 80.35 ± 1.55, 81.2 ± 1.7, and 80.45 ± 1.42 mm Hg, respectively. Intergroup SBP and DBP comparison were insignificant ($p > 0.05$) [Table 2].

Pain score was measured in both the groups on first and second postoperative days. Pain score in gabapentin group and placebo group on first postoperative day was 2.6 ± 0.10 and 3.8 ± 0.81 and on second postoperative day was 2.2 ± 0.15 and 3.2 ± 0.17, respectively. Intergroup comparison was highly significant on first ($p < 0.001$) and second ($p < 0.001$) postoperative days [Table 3].

The average number of analgesics on first postoperative day in gabapentin group and placebo group was 1.2 ± 0.13 and 2.6 ± 0.10 and on second post operative day was 0.65 ± 0.15 and 2.2 ± 0.16, respectively; the comparison between the two group was highly significant on first ($p < 0.001$) and second ($p < 0.001$) postoperative days. The average number of antiemetics on first postoperative day in groups A and B was 0.35 ± 0.10 and 1.31 ± 0.16 and on second postoperative day was 0.05 ± 0.04 and 0.6 ± 0.15, respectively. Intergroup comparison was highly significant on first ($p < 0.001$) and second ($p < 0.001$) postoperative days [Table 4].

Table 2: Changes in pulse rate and blood pressure

Group	Time of measurement (h)				
	Preoperative	Postoperative			
	1	1	6	12	24
Pulse rate (per min)					
Gabapentin	83.90 ± 1.32	89.3 ± 1.84	86.65 ± 1.92	85.1 ± 1.54	82.8 ± 1.11
Placebo	80.50 ± 1.31	87.35 ± 1.21	86.80 ± 1.75	86.80 ± 1.68	84.25 ± 1.65
p value	>0.05	>0.05	>0.05	>0.05	>0.05
SBP (mm Hg)					
Gabapentin	123.2 ± 2.26	128.4 ± 2.17	126.5 ± 2.37	123.5 ± 2.37	122.7 ± 2.11
Placebo	120.05 ± 2.55	124.6 ± 2.11	121.60 ± 1.92	123.65 ± 1.80	123.85 ± 2.56
p value	>0.05	>0.05	>0.05	>0.05	>0.05
DBP (mm Hg)					
Gabapentin	78.7 ± 1.67	80.8 ± 2.10	78.8 ± 1.80	79 ± 1.69	78.2 ± 1.63
Placebo	79.45 ± 1.65	84.00 ± 1.56	80.35 ± 1.55	81.20 ± 1.70	80.45 ± 1.42
p value	>0.05	>0.05	>0.05	>0.05	>0.05

All values are expressed in mean ± SEM.

Table 3: Pain score

Group	Time of measurement	
	First postoperative day	Second postoperative day
Pain score		
Gabapentin	2.60 ± 0.17	2.20 ± 0.15
Placebo	3.80 ± 0.81	3.20 ± 0.17
p value	<0.001	<0.001

All values are expressed in mean ± SEM.

Table 4: Analgesics and antiemetics used in both the groups

Group	Time of measurement	
	First postoperative day	Second postoperative day
Analgesics		
Gabapentin	1.20 ± 0.13	0.65 ± 0.15
Placebo	2.60 ± 0.10	2.20 ± 0.16
p value	<0.001	<0.001
Antiemetic		
Gabapentin	0.35 ± 0.10	0.05 ± 0.04
Placebo	1.31 ± 0.16	0.60 ± 0.15
p value	<0.001	<0.001

All values are expressed in mean ± SEM.

Discussion

Prevention and treatment of postoperative pain, nausea, and vomiting are major challenges in the postoperative care. The study was designed to compare the effects of oral gabapentin with placebo as premedication and on postoperative pain, nausea, and vomiting in patients undergoing LC in a tertiary-care teaching hospital. The mean age of patients in gabapentin and placebo group was 44.75 ± 2.86 and 41.10 ± 3.26 years, respectively, which were comparable with previous studies by Soroush et al.[11] and Behdad et al.[12] Our study revealed a higher percentage of female patients, comparable with the study by Soroush et al. Vital signs such as pulse rate, SBP, and DBP were assessed preoperatively and during the first 24 h of surgery at 1, 6, 12, and 24 h. There was no significant difference between the two groups with respect to pulse rate, SBP, and DBP. This is in accordance with the study by Behdad et al.,[12] proving that gabapentin did not alter pulse rate and BP.

Pain score was significantly reduced on first and second postoperative days in the gabapentin group when compared with the placebo group. Our findings were consistent with the previous studies by Behdad et al.,[12] Mohammadi et al.,[13] Montazeri et al.,[14] and Dirks et al.[15] But, it was not in collaboration with the study by Bartholdy et al.,[16] where gabapentin had no effect on postoperative pain.

Prescribing gabapentin before and after LC resulted in decrease in average number of analgesics and antiemetics when compared with the placebo group on the first and second postoperative days. This has been seen in previous studies by Soroush et al.,[11] Pandey et al.,[17] and Khademi et al.,[18] where gabapentin significantly reduced the incidence of postoperative nausea and vomiting and decreased the administration of antiemetics. Sedation in 17 patients and drowsiness in 3 patients were the most commonly reported adverse drug reaction, which were mild and did not require any intervention, comparable with the previous study.[19]

Study Limitations

Relatively, few patients were exposed to gabapentin, and there were no data on potential pharmacokinetic and pharmacodynamics interactions with other drugs administered at this time.

Conclusion

The use of gabapentin reduced the administration of postoperative analgesics and antiemetics. However, additional studies with larger sample size will evaluate the magnitude of effect of gabapentin on postoperative pain, nausea, and vomiting.

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