Effect of Gabapentin on Postoperative Pain, Nausea, Vomiting and Requirement of Analgesia in First 24 Hours in Patients Undergoing Laparoscopic Cholecystectomy Under General Anaesthesia - A Randomized Double Blind Placebo Controlled Study

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ABSTRACT

Introduction: Postoperative pain, nausea, and vomiting are frequent and unpleasant adverse effects associated with anaesthesia and surgery. Objective of the study was to evaluate the effect of oral gabapentin on postoperative pain, nausea, vomiting and requirement of analgesia in first 24hours (hrs) in patients undergoing laparoscopic cholecystectomy.

Materials and Methods: A total of 60 patients posted for laparoscopic cholecystectomy were included in this randomized double-blind placebo-controlled study. Patients were divided randomly into two groups (Group A and Group B) of 30 patients (n=30) each with the help of computer generated random number table. Group A patients received two doses of 300 mg gabapentin: first dose evening before surgery and second dose 2hrs before induction. Group B patients received matching placebo tablets of same size and shape as gabapentin tablets. All patients were observed for (pain measured by visual analogueue scale, VAS), nausea, vomiting, need of opioids and antiemetics in first 24hours postoperatively. In addition, Pulse Rate (PR), Non-Invasive blood pressure (NIBP); systolic blood pressure (SBP) and diastolic blood pressure (DBP) were analyzed pre and postoperatively.

Results: Both groups were comparable with respect to demographic profile ($p>0.05$). Change in PR and NIBP between the two groups were insignificant ($p>0.05$). Pain score in gabapentin group at 1,6,12 and 24hours (hrs) postoperatively was significantly less than placebo group ($p<0.001$).

Conclusion: Administration of gabapentin evening before surgery and 2 hours before induction significantly decreased the incidence of postoperative pain, nausea, and vomiting.

Keywords: Laparoscopic cholecystectomy, gabapentin, postoperative pain, nausea, vomiting.

INTRODUCTION

After laparoscopic cholecystectomy under general anaesthesia pain, nausea, and vomiting are the common complications which present a vexing challenge to anaesthesiologist. These symptoms have been reported in as many as 42%–72% of patients after laparoscopic cholecystectomy.[1] The etiology of postoperative nausea and vomiting (PONV) is complex and is multifactorial. Although there are multiple definitions of pain, most experts agree that it is primarily a sensory experience.[2] There are two major components that contribute to postoperative pain, inflammatory and neuropathic pain. Both of these states share many common features and can be mitigated either jointly or separately.[3] Opioids are the most popular analgesic agents used for the prophylaxis and treatment of postoperative pain. So, researches 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 as opiods have many side effects.[4] The other drugs currently used for treatment and prevention of PONV are prokinetics, dopaminegic antagonist, 5HT3 antagonists, butyrophenones, anticholinergics, phenothiazines, antihistaminics, benzamides and steroids alone or in combination with other antiemetics.[5–10]

Gabapentin is an analogue of gamma aminobutyric acid and generally used as an antiepileptic agent.[11] It is used for neuropathic pain, diabetic neuropathy, postherpetic pain, and reflex sympathetic dystrophy.[11–13] It is an analgesic drug that can be affect directly by interaction with nociceptors in the central nervous system. Although the exact mode of its actionis 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.[14] Gabap-

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entin is also effective in reducing the nausea and vomiting, which are induced by chemotherapy.[15] There is evidence that tachykinin activity is a part of pathogenesis of chemotherapy induced emesis. Tachykinin neurotransmitter activity changes in response to gabapentin, which may be the possible mechanism. Therefore, the effects of tachykinin may be the mechanism leading to nausea reduction after surgery and chemotherapy.[15]

MATERIALS AND METHODS

This double-blind placebo-controlled study was conducted in the Departments of anaesthesia and critical care in Rohilkhand Medical College and Hospital, Bareilly. After approval from Institutional Ethical Committee, and written informed consent, total 60 patients were selected. The patients with uncontrolled diabetes mellitus, renal or liver diseases, concomitant diseases with nausea and vomiting, use of antiemetics in the 24hours before surgery, pregnancy, breast feeding, antidepressant use, and conversion from laparoscopic cholecystectomy to open cholecystectomy were excluded from the study. The primary outcome was the incidence of pain after laparoscopic cholecystectomy. The secondary outcome was the effect of gabapentin on postoperative nausea and vomiting. Patients were randomly divided into two groups using computer generated random number table. Group A patients received tablet gabapentin 300mg in the evening before surgery and 300mg, 2hrs before induction. Group B patients received a matching placebo (tablet) of same size and shape as gabapentin tablet. All patients were induced with general anesthesia by using inj. Propofol (2mg/kg) and inj. Vecuronium bromide (0.1mg/kg). No analgesia or antiemetic was administered preoperatively.

The PR, SBP and DBP were measured preoperatively before induction and postoperatively after 1, 6, 12, and 24hrs in both the groups. Measurement of pain was done by using visual analogue scale, "VAS" (0-No pain, 10-Worst possible pain) in both the groups. Injection ondansetron and butorphenol were used as rescue antiemetic and analgesic medications, respectively, on as-and-when required basis postoperatively. The average number of analgesics and antiemetics used in first postoperative day i.e. for 24hours were calculated in both the groups.

Variables	Group A (n=30)	Group B (n=30)	*p*-value
Age (years)	36±5.05	37±5.95	0.78
Durationof surgery (minutes)	68±9.65	61±7.89	0.15
Duration of Anesthesia (minutes)	119±10.03	117±9.89	0.74

Table-1: Demographic profile

STATISTICAL ANALYSIS

Statistical analysis was done by using paired and unpaired *t*-test. *P*-value <0.05 was considered as statistically significant and $p<0.001$ was considered as statistically highly significant.

RESULTS

A total of 60 patients were included in the study. All values were calculated in mean±SD. The mean age of patients receiving gabapentin (group A) was 36.0±5.05 years and in the placebo group (group B) was 37.0±5.95 years [Table.1]. The mean preoperative PR in groups A and group B was 80.5±2.54/minutes (min) and 84.7±3.19/min, respectively ($p>0.05$). The mean postoperative PR after 1, 6, 12, and 24hrs in gabapentin group (group A) was 87.7±2.91/min, 89.54±2.75/min, 82.4±1.94/min and 80.8±1.76/min, respectively, and in placebo group was 88.45±2.09/min, 85.2±1.97/min, 89.8±2.08/min, and 83.78±1.98/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 132.3±5.26 and 128.25±4.59 mmHg, ($p>0.05$). The postoperative SBP after 1, 6, 12, and 24hrs in gabapentin group was 129.7±3.54, 131.21±2.94,

Parameters	Time of measurment				
	Preoperative	Postoperative			
		1hr	6hrs	12hrs	24hrs
PR/minute					
Group A	80.5±2.54	87.7±2.91	89.54±2.75	82.4±1.94	80.8±1.76
Group B	84.7±3.19	88.45±2.09	85.2±1.97	89.8±2.08	83.78±1.98
p-value	>0.05	>0.05	>0.05	>0.05	>0.05
SBP mmHg					
Group A	132.3±5.26	129.7±3.54	131.21±2.94	129.57±2.83	130.53±3.65
Group B	128.25±4.59	127.8±2.91	129.6±3.76	129.41±1.89	127.81±3.73
p-value	>0.05	>0.05	>0.05	>0.05	>0.05
DBP mmHg					
Group A	79.32±1.23	82.43±1.19	79.85±2.84	86.09±1.69	86.29±2.69
Group B	77.82±2.434	84.9±2.76	86.37±2.58	87.26±1.97	83.72±2.22
p-value	>0.05	>0.05	>0.05	>0.05	>0.05

Table-2: Change in Pulse Rate (PR) and Non-InvasiveBlood Pressure (NIBP)

129.57±2.83, and 130.53±3.65 mmHg, respectively, and in placebo group was 127.8±2.91, 129.6±3.76, 129.41±1.89 and 127.81±3.73 mmHg, respectively. The preoperative DBP in group A and group B was 79.32±1.23 and 77.82±2.43mmHg, (p>0.05). The postoperative DBP after 1, 6, 12, and 24hrs in gabapentin group was 82.43±1.19, 79.85±2.84, 86.09±1.69, and 86.29±2.69 mmHg and in placebo group was 84.9±2.76, 86.37±2.58, 87.26±1.97, and 83.72±2.22 mmHg respectively. Intergroup SBP and DBP comparison was insignificant (p>0.05) [Table. 2].

Pain score was measured in both the groups using visual analogue scale (VAS), at 1,6,12 and 24hrs on first postoperative day. Pain score in gabapentin group and placebo group at 1,6,12 and 24hrs on first postoperative day was 6.12±1.05, 4.18±1.68, 2.49±1.03 and 0.36±0.45 and in placebo group were 8.17±1.25, 6.18±1.89, 4.17±1.09 and 1.37±0.95 respectively. Intergroup comparison was highly significant (p<0.001) [Table.3 figure.1]. Number of patients complaining vomiting were less in gabapentin group in comparison to placebo group (p<0.001) [Table. 4].

The average number of analgesics required on first postoperative day in gabapentin group and placebo group were 1.21±0.23 and 4.01±1.15 respectively; the comparison between the two groups was highly significant (p<0.001). The average number of antiemetics required on first postoperative day in gabapentin group and placebo group was 1.19±0.27 and 3.97±1.02 respectively. Intergroup comparison was highly significant (p < 0.001) [Table. 5].

Time after surgery (hours)	Group A (n=30)	Group B (n=30)	*p*-value
1	6.12±1.05	8.17±1.25	<0.001
6	4.18±1.65	6.18±1.89	<0.001
12	2.49±1.03	4.17±1.09	<0.001
24	0.36±0.45	1.37±0.95	<0.001

Table-3: Intensity of pain

Time after surgery (hours)	Group A (n=30)	Group B (n=30)	*p*-value
1	6	18	<0.001
6	2	12	<0.001
12	3	6	<0.001
24	0	1	<0.001

Table-4: Number of patients complaining vomiting

	Group A (n=30)	Group B (n=30)	*p* value
Rescue analgesia	1.21±0.23	4.01±1.15	<0.001
Rescue antiemetic	1.19 ± 0.27	3.97 ± 1.02	<0.001

Table-5: Requirement of number of analgesia and antiemetic

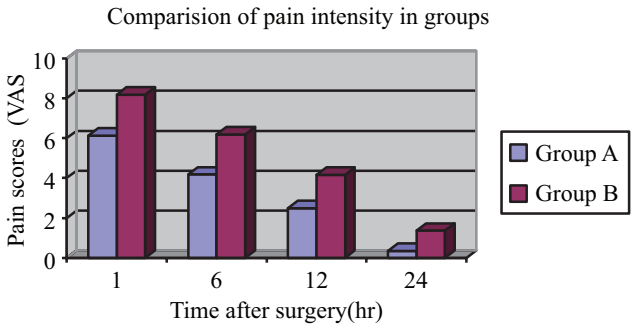

Figure-1: Comparison of pain scores (VAS) between two groups

DISCUSSION

Prevention and treatment of postoperative pain, nausea and vomiting are major challenges to anaesthesiologists in the post anaesthesia care unit (PACU). The present study was conducted to compare the effectsof oral gabapentin with placebo on postoperative pain, nausea, and vomiting in patients undergoing laparoscopic cholecystectomy. The mean age of patients in gabapentin and placebo group was 36±5.05 and 37±5.95 years respectively, which were comparable with previous studies by Soroush*et al.*[16] and Behdad*et al.*[17] Vital signs such as PR, SBP,and DBP were assessed preoperatively and during first 24hrs after surgery at 1, 6, 12, and 24 hours. There was no significant difference between the two groups with respect to PR, SBP, and DBP. This is also observed by Behdad *et al.*[17] proving that gabapentin did not alter pulse rate and blood pressure significantly at given doses. Pain score was significantly reduced on first postoperative day in the gabapentin group when compared with the placebo group. Our findings were consistent with the previous studies by Behdad *et al.*,[17] Mohammadi *et al.*,[18] Montazeri *et al.*[19] and Dirks *et al.*[20] But it was not in accordance with the study by Bartholdy *et al.*[21] where gabapentin had no effect on postoperative pain which can be due to ineffectiveness of gabapentin at low does.

Prescribing gabapentin evening before surgery and before induction resulted in decrease in average number of analgesics and antiemetics when compared with the placebo group in first 24hours postoperatively. This has been seen in previous studies by Soroush *et al.*,[16] Pandey *et al.*[22] and Khademi *et al.*[23] where gabapentin significantly reduced the incidence of postoperative nausea and vomiting and decreased the administration of antiemetics.

Like our study Rosarius *et al.*[24] used gabapentin 1200 mg orally, preoperatively to prevent postoperative pain after vaginal hysterectomy and noticed significant decrease in postoperative pain, nausea and vomiting.Turan *et al.*[25] also studied the use of oral gabapentin given preoperatively in patients of spinal surgery noticed significant reduction in incidence of nausea and vomiting compared to placebo.

Furthermore Bashir *et al*. and Sharma *et al*. also reveals that gabapentin may prove to be effective in prevention of postoperative pain, nausea and vomiting.[26-27]

CONCLUSION

The use of gabapentin evening before surgery and 2hours before induction reduced the administration of postoperative

analgesics and antiemetics. However, additional studies are required to evaluate the magnitude of effect of gabapentin on postoperative pain, nausea, and vomiting.

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