Effect of oral gabapentin premedication on hemodynamic parameters and postoperative pain in patients of laparoscopic cholecystectomy: A randomized double-blind controlled study

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Abstract

Background and Aims: Carbon dioxide (CO_2) pneumoperitoneum created during laparoscopic cholecystectomy causes adverse hemodynamic changes such as rise in arterial pressure. The aim of this study was to assess the effect of oral gabapentin premedication on hemodynamic parameters in addition to postoperative nausea and vomiting (PONV) and pain in patients of laparoscopic cholecystectomy conducted under general anesthesia.

Material and Methods: Randomly selected 60 American Society of Anesthesiologists (ASA) class I patients scheduled for laparoscopic cholecystectomy were premedicated with either gabapentin 1200 mg (Group GB) or placebo (Group PL) 2 h prior to induction of anesthesia. Anesthesia was induced with fentanyl, propofol, and vecuronium; and maintained with oxygen (33%), nitrous oxide (66%), and isoflurane (1%) with controlled ventilation. Hemodynamic parameters were recorded at various time intervals intraoperatively and during pneumoperitoneum every 10 min till 50 min. Postoperatively visual analog score (VAS) for pain, incidence of PONV, and sedation score were recorded for 6 h. The collected data were analyzed statistically by using repeated measures analysis of variance (ANOVA), Student's t test, Chi-square test, and Mann–Whitney U test.

Results: Changes in mean BP, systolic BP, and diastolic BP from prepneumoperitoneum values were significantly less in group GB during pneumoperitoneum ($P < 0.05$) with no significant change in HR in both groups (>0.05). VAS score was significantly lower in group GB. The duration of analgesia and PONV free period were significantly higher in group GB ($P < 0.01$).

Conclusion: Oral gabapentin premedication may be used to control hemodynamic parameters during pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

Keywords: Gabapentin, hemodynamics, postoperative nausea and vomiting, postoperative pain

Introduction

During laparoscopic cholecystectomy, carbon dioxide (CO_2) pneumoperitoneum is created which causes adverse hemodynamic changes such as rise in arterial pressure, systemic vascular resistance, and reduction in cardiac output.[1,2] Release of catechoalamines and vasopressin during pneumoperitoneum are attributed to these hemodynamic responses.[3] These hemodynamic changes are well tolerated by American Society of Anesthesiologists (ASA) class I patients but may be detrimental in the patients having compromised cardiovascular system (with poor reserve).[4] Various agents such as clonidine,[3] nitroglycerine,[4] esmolol,[5] nicardipine,[6] and magnesium[7] have been used to control these changes intraoperatively with their limitations. Recently

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gabapentin, a newer antiepileptic drug, has been used to attenuate the hemodynamic response to laryngoscopy and tracheal intubation[8-11] and has been reported in a study to provide hemodynamic stability during laparoscopic cholecystectomy.[12] Although the exact mechanism of action of gabapentin is not known, it appears to have its effect on presynaptic voltage-dependent calcium channels.[13]

Postoperative pain, nausea, and vomiting are also the common complications occurring after laparoscopic cholecystectomy. Gabapentin has been used effectively for reduction of pain, nausea, and vomiting after laparoscopic cholecystectomy in various clinical trials.[14-19]

Thus, this study was designed as a double-blind placebo controlled trial to assess the effects of 1200 mg of oral gabapentin premedication on hemodynamic parameters and postoperative pain, nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

Material and Methods

This study was conducted as randomized double blinded controlled trial after getting approval from the institutional review board and written informed consent was obtained from each patient willing to participate in the study. Sixty ASA grade I patients aged between 18 and 60 years of either sex and scheduled for laparoscopic cholecystectomy under general anesthesia were included in the study. Patients with systemic diseases such as hypertension, ischemic heart disease, and diabetes mellitus and those on drug therapy such as diuretic, β-blocker, calcium channel blocker, analgesic, antiemetic, or gabapentin were excluded from the study. The selected patients were allocated either to group GB or PL group as per computer generated random number tables contained in sealed envelopes. Thirty patients of group GB were premedicated with capsule gabapentin 1200 mg orally, whereas 30 patients of PL group were premedicated with identical capsules containing glucose powder as placebo, orally 2 h prior to induction of anesthesia. To ensure double blinding, the capsule was prepared and administered by a researcher who was not involved in data collection.

On arrival to the operating room, monitoring for continuous electrocardiogram (ECG), heart rate (HR), noninvasive blood pressure (NIBP), and pulse oximetry (SpO_2) of all patients was started and continued throughout the procedure. Preoperative baseline values of HR, systolic, diastolic, and mean blood pressure (SBP, DBP, and MBP, respectively) and SpO_2 were recorded. An intravenous (IV) cannula was secured and crystalloid solution (Ringer Lactate) infusion was started through it. Anesthesia was induced with IV injections fentanyl 1.5 μg/kg, propofol 2 mg/kg, and vecuronium bromide 0.1 mg/kg. Patients were ventilated with bag and facemask for 3 min after which endotracheal intubation was performed with orotracheal cuffed tube of appropriate size by a trained anesthesiologist. Anesthesia was maintained with 33% oxygen, 66% nitrous oxide, 1% isoflurane through close circuit with controlled ventilation (IPPV) to maintain end tidal CO_2 (EtCO_2) between 35 and 40 mm Hg and top up doses of vecuronium were given using neuromuscular monitoring. Pneumoperitoneum was created by CO_2 insufflation into the peritoneal cavity and intraabdominal pressure was maintained near to 12 mm Hg throughout the laparoscopic procedure. All the patients were positioned with a head up tilt for about 15°. Intraoperatively, values of HR, SBP, DBP, MBP, and SpO_2 were recorded before induction of anesthesia (base value) and at various time intervals intraoperatively and just before pneumoperitoneum and thereafter every 10 min till 50 min of pneumoperitoneum.

Intraoperatively, SBP was maintained ±20% of base line value of respective group by titrating the delivered concentration of isoflurane by dial setting and by changing the rate of IV fluid infusion. Bradycardia, that is, HR <60 beats/min was managed with IV injection of atropine 0.6 mg. After conclusion of surgery, CO_2 from peritoneal cavity was removed and neuromuscular blockade was reversed by appropriate doses of neostigmine and glycopyrrolate and trachea was extubated. The observer of parameters and the patient participating in the study were blind to the allotted group and the nature of medication given.

Postoperatively every patient was monitored for HR, NIBP, and SpO_2. Sedation score, PONV, and visual analog score (VAS) for pain was recorded at the interval of 30 min for 2 h and thereafter every 1 h for next 4 h in all patients of both groups. Sedation was assessed by using following sedation score: 1—awake and alert; 2—sedated, responding to verbal stimulus; 3—sedated, responding to mild physical stimulus; 4—sedated, responding to moderate to strong physical stimulus and 5—not arousable.[20]

Postoperative pain was assessed by using VAS, consisted of 10 cm horizontal line with "zero" indicates as "no pain" and "10" as "worst pain." Rescue analgesia was given in the form of morphine 0.1 mg/kg IV when VAS score was 3 or more and duration of analgesia was recorded. Duration between induction of anesthesia and first rescue analgesia required was considered as duration of analgesia. All patients were also observed for appearance of any adverse effect of gabapentin such as dizziness, somnolence, fatigue, urinary retention, pruritus or headache.

Primary outcome was the change in MBP during pneumoperitoneum and secondary outcomes were the changes in other hemodynamic parameters (SBP, DBP, and HR) during pneumoperitoneum, duration of postoperative analgesia, incidence of PONV, and sedation score between two groups.

Power of the study

A *post hoc* power analysis was conducted using the software package, G*Power (Faul and Erdfelder 1992). Using the change in MBP at 50 min after creation of pneumoperitoneum as the parameter from this study, the power of our study came out to be 0.83 with 30 subjects per group and with an effect size of 0.67 with 10% chance of error with $\alpha = 0.05$, $\beta = 0.20$, and confidence interval of 95%.

Statistical analysis

The data were presented as mean with standard deviation (SD) and number with percentage. HR, MBP, SBP, and DBP were compared within and between the groups using repeated measures analysis of variance (ANOVA). The changes in MBP, SBP and DBP; duration of analgesia and PONV free period were analyzed using Student's t test. For comparison of incidence of PONV, sedation score and side effects between both the groups, Pearson Chi-square test used. VAS was analyzed using nonparametric Mann–Whitney U test. All the statistical tests were two-sided and were performed at a significance level of $\alpha = 0.05$. All statistical calculations were done using SPSS (Statistical Package for the Social Sciences) software program.

Results

All of the 60 patients recruited were randomized and analyzed. The demographic parameters and the duration of pneumoperitoneum were comparable with no statistical significant difference between two groups ($P > 0.05$) [Table 1]. The mean ± SD of MBP, SBP, DBP, and HR in both groups recorded at varying time intervals are shown in Figures 1 and 2. The changes in MBP, SBP, DBP, and HR from prepneumoperitoneum (just before pneumoperitoneum) value during pneumoperitoneum in two groups are shown in Tables 2 and 3.

In group GB, the MBP values were lower, however, statistically insignificant compared to group PL at the corresponding time during pneumoperitoneum [Figure 1]. On comparing both groups for their changes in MBP from prepneumoperitoneum value of respective group during pneumoperitoneum at the corresponding time, statistically significant difference ($P < 0.05$) was found at 20, 30, 40, and 50 min of pneumoperitoneum [Table 2]. The SBP values were lower in group GB compared to group PL at the corresponding time during pneumoperitoneum but not statistically significant [Figure 2]. On comparing the changes in SBP during pneumoperitoneum from their prepneumoperitoneum value in both groups at the corresponding time, statistically significant difference ($P < 0.05$) was found at 20, 30, and 50 min of pneumoperitoneum [Table 2].

The DBP values were lower in group GB compared to group PL at the corresponding time during pneumoperitoneum but not statistically significant except at just before and

Table 1: Demographic profile of patients of both groups with *P*

	Group GB (*n*=30)	Group PL (*n*=30)	*P*
Age (years) (mean±SD)	35.9±10.7	35.3±11.2	0.887 (NS)
Body wt. (kg) (mean±SD)	56.5±9.6	55.6±11.2	0.474 (NS)
Male:female ratio	3:27	3:27	1.00 (NS)
Total duration of pneumoperitoneum (min)	62.6±14.6	67.6±14.9	0.932 (NS)

P>0.05=NS (not significant)
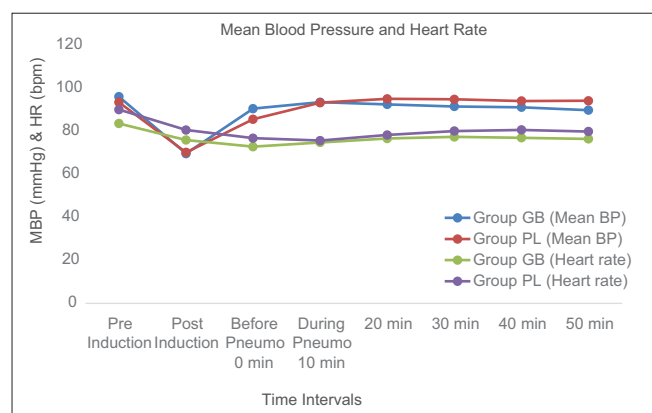
Figure 1: Mean blood pressure (mm Hg) and heart rate (beats per min) at various time intervals in both groups (pneumo–pneumoperitoneum)
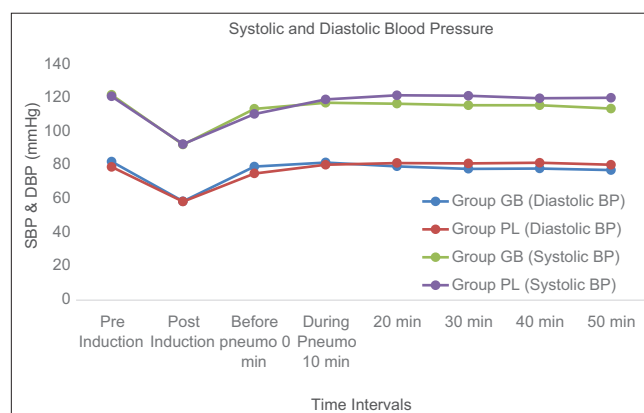
Figure 2: Systolic and diastolic blood pressure (mm Hg) at various time intervals in both groups (pneumo–pneumoperitoneum)

Table 2: Changes in mean blood pressure (MBP) and systolic blood pressure (SBP) in mm Hg in two groups during pneumoperitoneum from their prepneumoperitoneum value of respective group at varying time intervals

Time interval after creation of pneumoperitoneum	Changes in MBP		P	Changes in SBP		P
	Group GB (n=30)	Group PL (n=30)		Group GB (n=30)	Group PL (n=30)	
10 min	3.0±11.4	7.7±14.1	0.158	3.6±13.2	8.7±15.9	0.181
20 min	2.0±12.6*	9.5±12.8*	0.026*	3.1±15.9*	11.2±14.9*	0.047*
30 min	1.0±13.9*	9.3±12.8*	0.020*	2.6±15.5*	10.86±15.1*	0.041*
40 min	0.6±13.6*	8.5±12.9*	0.026*	2.1±15.7	9.4±13.6	0.061
50 min	-0.70±14.9*	8.6±12.6*	0.012*	0.1±6.2*	9.7±2.9*	0.014*

*P<0.05=sig (significant difference between the groups), *Significant difference between the groups at corresponding time interval*

Table 3: Changes in diastolic blood pressure (DBP) in mm Hg and heart rate (beats/min) in two groups during pneumoperitoneum from their prepneumoperitoneum value of respective group at varying time intervals

Time interval after creation of pneumoperitoneum	Changes in DBP		P	Changes in HR		P
	Group GB (n=30)	Group PL (n=30)		Group GB (n=30)	Group PL (n=30)	
10 min	2.5±9.8	5.2±14.5	0.401	1.9±7.6	-1.1±8.8	0.439
20 min	0.2±11.0	6.2±12.9	0.055	3.8±8.8	1.5±7.0	
30 min	-1.3±10.8*	5.9±12.7*	0.020*	4.5±9.5	3.4±7.7	
40 min	-1.1±10.7*	6.4±13.2*	0.019*	4.1±7.8	3.9±7.2	
50 min	-2.0±12.9	5.2±12.4	0.031*	3.6±8.6	3.1±8.4	

*P<0.05=sig (significant difference between the groups). *Significant difference between the groups at corresponding time interval*

Table 4: Mean±SD of VAS score for postoperative pain in two groups

Time interval	Group GB (n=30)	Group PL (n=30)	P
Postoperative ½ h	2.20±1.54	4.27±1.98	0.000 (Sig)
1 h	2.07±0.74	3.00±1.14	0.001 (Sig)
1 ½ h	2.27±1.01	2.60±0.93	0.154 (NS)
2 h	2.53±1.38	2.30±0.65	0.859 (NS)
3 h	2.07±0.64	2.17±0.46	0.639 (NS)
4 h	2.07±0.640	2.23±0.67	0.600 (NS)
5 h	2.20±0.84	2.13±0.43	0.701 (NS)
6 h	2.07±0.74	2.10±0.40	0.920 (NS)

Sig=significant difference, NS=no significant difference between groups.
P<0.01=significant

10 min after pneumoperitoneum [Figure 2]. On comparing the changes in DBP during pneumoperitoneum from their prepneumoperitoneum value in both groups at the corresponding time, statistically significant difference ($P < 0.05$) was found at 30, 40, and 50 min of pneumoperitoneum [Table 3]. During pneumoperitoneum, the HR remained significantly lower than their preinduction value at all points of time within both the groups [Figure 1]. No statistically significant difference was found in HR between both the groups at any time point during pneumoperitoneum [Table 3].

The requirement of isoflurane was nearly 1.1% in both groups during pneumoperitoneum ($P = 0.468$). Mean ± SD of VAS score in two groups at various time points are shown in Table 4. Significant difference was found in the VAS score between the groups at postoperative 30 min and 60 min ($P < 0.01$). The mean of pain free period was 368.00 ± 123.19 min

in the group GB and 183.50 ± 110.57 min in the PL group with a significant difference ($P = 0.000$). The mean PONV free period was 258.00 ± 145.86 min in the group GB and 152.83 ± 145.09 min in the PL group with statistical significant difference ($P = 0.007$). In group GB 14 (46.66%) patients, whereas in PL group 23 (76.66%) patients required antiemetic with a significant difference between two groups ($P = 0.033$).

Majority of the patients in group GB had sedation with a score of 2, whereas in the PL group, majority of the patients were awake and alert with sedation score of 1 ($P < 0.01$). All patients were monitored in the postoperative period for any complications. In the group GB dizziness was complained by one patient, two patients complained somnolence, and one patient had urinary retention, whereas none of the patients in the PL group had any complications.

Discussion

Various agents have been tried in the past to control the hemodynamic changes occurring during pneumoperitoneum created for laparoscopic cholecystectomy.[3-7] Recently, Neogi *et al.*[12] have reported that 900 mg of oral gabapentin administered 2 h prior to induction of anesthesia attenuates the hemodynamic responses caused by CO_2 pneumoperitoneum created for laparoscopic cholecystectomy. Although the exact mechanism of action of gabapentin is not certain, it is believed that it reduces Ca^{2+} currents in dorsal horn ganglion neurons by binding to $\alpha_2\delta$ subunit of the presynaptic voltage gated calcium channels (VGCC) and thus, inhibits subsequent

release of excitatory neurotransmitters by sensory neurons.[13] In our study, gabapentin 1200 mg given 2 h prior to surgery resulted in significantly lower SBP, DBP and MBP during pneumoperitoneum with no effect on HR.

Although the MBP was increased during pneumoperitoneum in both groups, the change was significantly less in group GB as compared to PL group. Ali *et al*.,[10] Aggarwal *et al*.,[11] and Neogi *et al*.[12] also observed significantly low MBP in gabapentin group similar to our results. In this study, the changes in SBP and DBP from their just before pneumoperitoneum value were also increased significantly in the patients of PL group as compared to group GB. However, there was no significant change in HR during pneumoperitoneum in both the groups. Critchley *et al*.[2] and Joris *et al*.[3] also observed no significant change in HR during laparoscopic cholecystectomy following CO_2 pneumoperitoneum. On comparing the changes in HR from their prepneumoperitoneum value, there was no significant difference between the groups, which was in contrast to observations made by Memis *et al*.,[8] Ali *et al*.,[10] and Neogi *et al*.[12] but similar with Fassoulaki *et al*.[9] and Aggarwal *et al*.[11]

Fassoulaki *et al*.[9] studied the effect of gabapentin 1600 mg given in 4 divided doses, at 6 h intervals (starting the day before surgery) on attenuation of the pressure response in patients undergoing abdominal hysterectomy and observed that gabapentin-treated patients had significantly lower systolic and diastolic arterial pressure during the first 10 min after endotracheal intubation when compared with placebo with no effect on HR changes. In a randomized double-blind study, Memis *et al*.[8] compared the effect of oral gabapentin 400 and 800 mg with placebo, given 1 h prior to surgery and found that 800 mg of gabapentin significantly decreased mean arterial pressure and HR during first 10 min after endotracheal intubation compared with either 400 mg gabapentin or placebo. Ali *et al*.[10] also showed that oral gabapentin 1200 mg administered 2 h before surgery significantly diminished the increase in hemodynamic variables (MAP and HR) in response to intubation and this effect of gabapentin was not caused by inhibition of the catecholamine response. Aggarwal *et al*.[11] reported that gabapentin attenuates the rise in MBP but not tachycardia associated with laryngoscopy and intubation.

In this study, the VAS score was significantly low in group GB ($P = 0.000$) during 1 h of postoperative period and after that there was no significant difference between two groups. Patients of group GB had significantly prolonged postoperative analgesia and PONV free period as compared to PL group. Pandey *et al*.[14] conducted study on 459 patients and observed that 300 mg gabapentin in comparison to tramadol or placebo, given 2 h prior surgery, significantly decreased postoperative pain and requirement of rescue analgesic in the patients of laparoscopic cholecystectomy. Dirks *et al*.[15] also conducted a randomized, double-blind, placebo controlled study and concluded that a single dose of 1200 mg oral gabapentin was effective to reduce postoperative morphine consumption in patients of radical mastectomy without significant side effects. Eidy *et al*.[16] compared 800 mg gabapentin with 150 mg pregabalin and placebo 1 h before surgery and concluded that a single dose of gabapentin and pregabalin decreased postoperative pain, nausea and vomiting.

In this study, it was observed that in PL group 23 patients (76.66%), whereas in group GB only 14 patients (46.66%) required antiemetic with a significant difference between two groups ($P = 0.033$) and results were consistent with the results of studies done by many workers in different trials. Pandey *et al*.[17] used 600 mg gabapentin or matching placebo 2 h before surgery and observed PONV was significantly lower in gabapentin group as compared to placebo group (37.8% vs. 60%, respectively). Bashir *et al*.[18] concluded that a single dose of oral gabapentin 600 mg 2 h before surgery, whereas Soroosh *et al*.[19] reported that 600 mg gabapentin given 2 h before surgery and 6 h after surgery significantly decreases the incidence of PONV and the requirement for postoperative antiemetic treatment following laparoscopic cholecystectomy. Majority of patients of group GB had sedation score 2 and they all were arousable, whereas in placebo group majority of patients had sedation score 1. Gabapentin is also associated with some tolerable side effects. Ramsay reported somnolence (20%), dizziness (18%), ataxia (13%) and fatigue (11%) in patients receiving gabapentin.[21] In this study, in group GB dizziness was present in only 1 patient, urinary retention in another 1 and only 2 patients complained somnolence, whereas none of the patients in PL group had any complications.

Drawback of this study was that levels of catecholamines in blood were not estimated at any point of time and invasive hemodynamic monitoring was not done. Hence, further study in relation to these limitations is advised. The role of gabapentin as a premedicant for hemodynamic stability has not been extensively studied and the most appropriate dose of gabapentin is also not very clear. The decrease in MBP with gabapentin premedication as shown in our study is definitely useful for anesthesiologist when managing patients belonging to ASA class II or III posted for laparoscopic cholecystectomy.

Hence, on the basis of the results and observations of this study it can be concluded that oral gabapentin 1200 mg administered 2 h before surgery may be used to control the changes in hemodynamic parameters occurring during CO_2

pneumoperitoneum with significant prolongation of pain and PONV free period in patients undergoing laparoscopic cholecystectomy under general anesthesia.

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Conflicts of interest
There are no conflicts of interest.

References

1. Mc Laughlin JG, Scheeres DE, Dean RJ, Bonnell BW. The adverse haemodynamic effects of laparoscopic cholecystectomy. Surg Endosc 1995;9:121-4.
2. Critchley LA, Critchley JA, Gin T. Haemodynamic changes in patients undergoing laparoscopic cholecystectomy: Measurement by transthoracic bioimpedance. Br J Anaesth 1993;70:681-83.
3. Joris JL, Chiche JD, Canivet JM, Jacquet NJ, Legros JJY, Lamy ML. Hemodynamic changes induced by laparoscopy and their endocrine correlates: Effects of clonidine. J Am Coll Cardiol 1998;32:1389-96.
4. Hein HAT, Joshi GP, Ramsay MAE, Fox LG, Gawey BJ, Hellman CL, *et al.* Hemodynamic changes during laparoscopic cholecystectomy in patient with severe cardiac disease. J Clin Anesth 1997;9:261-5.
5. Koivusalo AM, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J, *et al.* Effects of esmolol on haemodynamic response to CO_2 pneumoperitoneum for laparoscopic surgery. Acta Anaesthesiol Scand 1998;42:510-7.
6. Joris JL, Hamoir EE, Hartstein GM, Meurisse MR, Hubert BM, Charlier CJ, *et al.* Hemodynamic changes and catecholamine release during laparoscopic adrenalectomy for pheochromocytoma. Anesth Analg 1999;88:16-21.
7. Puri GD, Marudhachalam KS, Chari P, Suri RK. The effect of magnesium sulphate on hemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with coronary artery disease. Anesth Analg 1998;87:808-11.
8. Memis D, Turan A, Karamanliouglu B, Seker S, Ture M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol 2006;23:686-90.
9. Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressor response to direct laryngoscopy and tracheal intubation. Br J Anaesth 2006;96:769-73.
10. Ali AR, Gohary ME, Ashmawi SE, Kerdawy HME, Essa HH. Efficacy of preoperative oral gabapentin in attenuation of neuro-endocrine response to laryngoscopy and tracheal intubation. J Med Sci 2009;9:24-9.
11. Aggarwal S, Baduni N, Jain A. Attenuation of pressor response to laryngoscopy and intubation—a comparative study between two doses of gabapentin in patients undergoing laparoscopic cholecystectomy. Anaesth Pain Intensive Care 2015;19:33-6.
12. Neogi M, Basak S, Ghosh D, Mukherjee S, Dawn S, Bhattarjee DP. A randomized double blind placebo controlled clinical study on the effects of gabapentin premedication on hemodynamic stability during laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol 2012;28:456-9.
13. Sarantopoulos C, McCallum B, Kwok WM, Hogan Q. Gabapentin decreases membrane calcium currents in injured as well as in control mammalian primary afferent neurons. Reg Anesth Pain Med 2002;27:47-57.
14. Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. Can J Anaesth 2004;51:358-63.
15. Dirks J, Fredensborg BB. A randomized study of the effects of single-dose gabapentin versus placebo on postoperative pain and morphine consumption after mastectomy. Anesthesiology 2002;97:560-4.
16. Eidy M, Fazel MR, Abdolrahimzadeh H, Moravveji AR, Kochaki E, Mohammadzadeh M. Effects of pregabalin and gabapentin on postoperative pain and opioid consumption after laparoscopic cholecystectomy. Korean J Anaesthesiol 2017;70:434-8.
17. Pandey CK, Priye S, Ambesh SP, Singh S, Singh U, Singh PK. Prophylactic gabapentin for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: A randomized, double-blind, placebo-controlled study. J Postgrad Med 2006;52:97-100.
18. Bashir F, Mohd K, Qazi S, Hashia AM. A randomized, double blind, placebo controlled study evaluating preventive role of gabapentin for PONV in patients undergoing laparascopic cholecystectomy. JK Science 2009;11:190-3.
19. Soroosh A, Masoomi H, Khorgami Z, Marashi SM, Mofid R. Effect of prophylactic gabapentin on postoperative nausea and vomiting after laparoscopic cholecystectomy: A randomized controlled trial. J Minim Invasive Surg Sci 2012;1:17-20.
20. Culebras X, Gessel EV, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. Anesth Analg 2001;92:199-204.
21. Ramsay RE. Gabapentin toxicity. In: Levy RH, Mattson RH, Meldrum BS, editors. Antiepileptic Drugs, 4th edn. New York: Raven Press; 1995. p. 857-60.