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ORIGINAL RESEARCH

Role of Preoperative Single Dose of Pregabalin for Attenuating Postoperative Pain and Analgesic Consumption in Patients Undergoing Laparoscopic Abdominal Surgeries

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ABSTRACT

Background and Aim: Preemptive analgesia is an anti-nociceptive treatment that prevents establishment of altered processing of afferent input, which amplifies postoperative pain.Gabapentinoids are anti-convulsants with membrane stabilizing and anti-nociceptive effects. This study was designed to evaluate the role of preoperative single dose of Pregabalin for attenuating postoperative pain and analgesic consumption in patients undergoing laparoscopic abdominal surgeries. **Material and Methods:** This study was conducted in 100 ASA grade I, II patients in the age group of 18-60 years undergoing elective laparoscopic surgeries under general anaesthesia. Patients were randomized and divided into 2 groups of 50 patients each. Group A was given capsule Pregabalin 150 mg orally 1 hour before surgery. Group B was given tab B complex orally 1 hour before surgery. Postoperative pain intensity was measured by Visual analogue scale at 1,2,4,6,8,12 and 24 hours after the surgery. Intraoperative Hemodynamic Monitoring was done**. Results:** The timing of first rescue analgesic postoperatively in Pregabalin group was 350.40± 72.08min compared to placebo group which was 171.60± 68.58 min. Consumption of Tramadol in Pregabalin group was 116.48± 42.13 mg and in placebo group, it was 174.10 ± 44.99 mg. **Conclusion:** Oral pregabalin significantly decreases incidence of pain postoperatively. It also decreases total tramadol consumption in comparison to placebo group in laparoscopic abdominal surgeries.

Key words: Laparoscopic surgery, Pain, Pregabalin, Tramadol

INTRODUCTION

Preemptive analgesia is an anti-nociceptive treatment that prevents establishment of altered processing of afferent input, which amplifies postoperative pain[1].Postoperative pain is one of the factors that prevents early discharge from PACU, as multiple mechanisms are involved in postoperative pain, usually a single drug or modality is not effective in preventing it, so multimodal analgesia regime is usually practiced for control of postoperative pain. Various pharmacological agents and techniques like local infiltration, epidural analgesia, nonsteroidal anti-inflammatory drugs, opioids, Gabapentin, Pregabalin, alpha-2 agonist, cox-2 inhibitors are used to produce analgesia[2].Gabapentinoids are anti-convulsants with membrane stabilizing and anti-nociceptive effects. These drugs bind to the presynaptic a2–d subunit voltage-dependent calcium channel. The anti-nociceptive effect is believed to be related to the reduction of the Ca^{2+} influx at presynaptic terminals in hyperexcited neurons, which may lead to the reduction of the release of several excitatory neurotransmitters, including glutamate, norepinephrine, substance P, and calcitonin gene-related peptide. Thus, Gabapentinoids appear to reduce the hyperexcitability of dorsal horn neurons that is induced by tissue damage. Evidence supporting the postoperative analgesic efficacy of Pregabalin is limited to randomized controlled trials in patients undergoing dental surgery, spinal fusion

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surgery, laparoscopic hysterectomy and day-case gynecological laparoscopic surgery[3].

Few of these trials have investigated the role of preoperative single-dose administration of Pregabalin in attenuating postoperative pain after laparoscopic abdominal surgeries. The present study was therefore designed to evaluate the role of preoperative single dose of Pregabalin for attenuating postoperative pain and analgesic consumption in patients undergoing laparoscopic abdominal surgeries.

MATERIAL AND METHODS

This prospective, randomized, comparative clinical study was conducted in a tertiary care teaching institute from 2023-2024 after obtaining approval from the Institutional Ethics Committee (Ref No-66/2023 dated- 26/12/2023). Written and informed consent was obtained from patients aged 18-60 years of both genders with ASA Risk I-II scheduled for elective laparoscopic surgery for the study. Patients having ASA grade III and IV patients who were allergic to pregabalin and patients with hypertension, uncontrolled diabetes mellitus, systemic infection, history of malignancy, history of alcohol or drug abuse were excluded. All preoperative assessment of the patient including history, general examination, systemic examination with all required investigations was done a day before the procedure. Patient was kept nil per oral for 8 hours before surgery.

PROCEDURE

Patients from the group A received Pregabalin capsule one hour before the surgery. Group B received placebo (Tab B complex orally) one hour before the surgery according to computer generated randomization. An intravenous line with proper size was secured and hydration was started with appropriate intravenous fluid. In the operative room, monitors were attached and basal vitals were noted. Perioperative monitoring includes ECG, SPO_2, $EtCO_2$, NIBP. All patients were premedicated with Inj.Glycopyrrolate 4µg/kg, Inj. Fentanyl 2µg/kg and Inj. Ondansetron 0.15mg/kg IV. Patients were pre-oxygenated with 100% oxygen via bains circuit with fresh gas flow of 8L/min. for 3-5 min. Induction was achieved with Inj.Propofol 2.5-3.5mg/kg and Inj. Succinylcholine 2mg/kg IV to facilitate endotracheal intubation. Once airway was established, lungs were mechanically ventilated with Volume - controlled ventilation. 50% O_2 with 50% air with sevoflurane traces 1.5 – 2 % and Inj. Atracurium besylate 0.5mg/kg loading dose with maintenance dose of 0.1mg/kg. All patients were mechanically ventilated with tidal volume of 6-8 ml/kg body weight and frequency of 12 cycles per minute using ventilator. Ventilation parameters were adjusted to maintain $EtCO_2$ 30-35 mmHg. Patient was monitored for: ECG, NIBP, SPO_2, $EtCO_2$ Inj. PCM 15mg/kg was administered intravenously at the time of closure to all the patients in group A and group B. After the completion of surgery, neuromuscular blockade was reversed with Inj. Glycopyrrolate 8 µg/kg and Inj. Neostigmine 50 µg/kg. After thorough suctioning tube was removed with the return of consciousness, adequate muscle power and airway reflexes. Patients were transferred to the recovery then they were transferred to the ward. Postoperative pain intensity was measured by Visual analogue scale at 1,2,4,6,8,12 and 24 hours after the surgery. This VAS score was observed by anaesthesia resident who was not aware of type of medication received by the patient.

Sample size was calculated on the basis of ClinCalc software. A Total of 100 Participants which were divided into two groups comprising of 50 participants each in this study At the end of study, the data collected was analyzed using statistical software package SPSS 16.0. Data was analyzed using chi-square test for categorical data and for comparing two independent study groups, unpaired student ‘t’ test was used. The results were expressed in terms of mean and standard deviation. P value of less than 0.05 is considered to be statistically significant.

RESULTS

In this study, hundred patients posted for Laparoscopic cholecystectomy of ASA I & II were allocated randomly into two groups in equal number of 50 each. Group A(Pregabalin) received capsule Pregabalin 150 mg orally and Group B(Placebo)received tablet B complex 60 minutes prior to anaesthesia. There is no statistically significant difference among both the groups regarding age, height, weight (Figure 1)

There was no significant difference in heart rate during induction as p value is >0.05. Highest heart rate in Group A was seen at 10 min after induction while highest heart rate in Group B was seen at 120 min after induction. There was no statistically significant attenuation of heart rate in Group A(Pregabalin) group but it remained stabilized in comparison to Group B(Placebo) group(Table 1). Systolic, diastolic and mean arterial pressures were not significant during induction. After 10,30 and 60 minutes of induction, the attenuation of mean arterial blood pressure in Group A(Pregabalin) group was statistically significant as compared to group B(placebo) group. Systolic, diastolic and mean arterial pressure were comparable at 90 and 120 minutes after induction as p value >0.05 between both groups but remained stabilized to base levels in Group A (Pregabalin) group (Table 2,3,4) It was found that time interval between providing general anaesthesia and administration of first dose of tramadol was 350.40 ± 72.08 minutes in group A and 171.60 ± 68.58 minutes in group B. In group A patient’s average dose of tramadol required is 116.48 ± 42.13 mg and in group B, the dosage required is 174.10 ± 44.90mg (Table 5) The mean VAS scores during postoperative period of 1,2,4,6,8,12 and 24 hours in group A patients were 2.30,2.54,2.98,3.34,2.76,2.76

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and 2.12 respectively. The mean VAS scores during postoperative period of 1,2,4,6,8,12 and 24 hours in group B patients were 2.70,3.04,3.50,3.74,3.16,3.26 and 2.32 respectively. (Table 6)

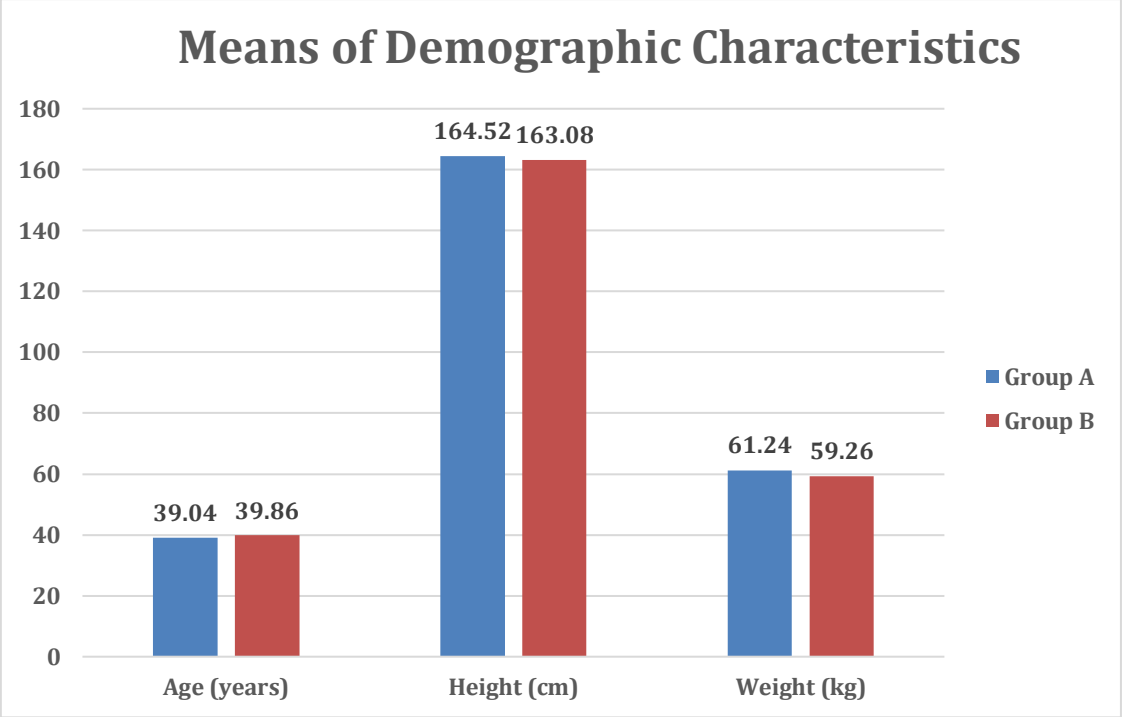

Figure 1: Demographic Details

Table 1: Intraoperative Heart Rate

HR	Group A		Group B		p Value
	Mean	SD	Mean	SD	
H.R_0	80.06	3.87	81.56	4.73	0.086
H.R_10	81.44	4.40	83.18	4.81	0.062
H.R_30	78.72	5.05	80.70	5.49	0.064
H.R_60	77.08	6.53	79.20	4.80	0.068
H.R_90	77.72	5.87	80.28	5.56	0.063
H.R_120	79.60	10.26	83.57	6.95	0.440

Table 2: Intraoperative Systolic Arterial Pressure

SBP	Group A		Group B		p Value
	Mean	SD	Mean	SD	
SBP_0	121.24	6.15	123.28	5.73	0.089
SBP_10	123.72	5.87	126.56	5.41	0.013*
SBP_30	122.08	6.88	125.28	5.52	0.012*
SBP_60	121.88	6.55	126.00	6.18	0.002*
SBP_90	123.03	7.06	126.25	7.24	0.065
SBP_120	124.40	9.32	127.14	6.62	0.562

Table 3: Intraoperative Diastolic Blood Pressure

DBP	Group A		Group B		p Value
	Mean	SD	Mean	SD	
DBP_0	74.60	4.77	75.60	4.66	0.291
DBP_10	77.32	5.09	79.24	4.31	0.045*
DBP_30	76.96	4.89	78.96	4.84	0.042*
DBP_60	75.35	5.31	78.20	4.43	0.005*
DBP_90	75.42	4.04	77.10	5.67	0.167
DBP_120	77.20	3.35	78.86	4.88	0.528

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Table 4: Intraoperative Mean Arterial Pressure

MAP	Group A		Group B		p Value
	Mean	SD	Mean	SD	
MAP_0	90.15	4.75	91.49	4.56	0.152
MAP_10	92.79	4.81	95.01	4.36	0.017*
MAP_30	92.00	5.06	94.40	4.75	0.016*
MAP_60	90.86	5.24	94.13	4.60	0.001*
MAP_90	91.29	4.58	93.48	5.40	0.074
MAP_120	92.93	2.77	94.95	3.50	0.311

Table 5: Timing and total doses of rescue analgesia needed postoperatively

Parameters	Group A		Group B		p Value
	Mean	SD	Mean	SD	
Timing of first dose	350.40	72.08	171.60	68.58	<0.0001*
Total dose of tramadol	116.48	42.13	174.10	44.99	<0.0001*

Table 6: Visual analogue scale (VAS) Score

VAS	Group A		Group B		p Value
	Mean	SD	Mean	SD	
VAS_1	2.30	0.46	2.70	0.71	0.001*
VAS_2	2.54	0.50	3.04	0.90	0.001*
VAS_4	2.98	0.68	3.50	0.84	0.001*
VAS_6	3.34	0.92	3.74	0.96	0.036*
VAS_8	2.76	0.74	3.16	0.77	0.009*
VAS_12	2.76	0.82	3.26	0.96	0.006*
VAS_24	2.12	0.33	2.32	0.47	0.016*

DISCUSSION

Inflammatory, neuropathic, and visceral pain often accompany tissue injury after surgery. 80% of surgical patients have severe postoperative discomfort. Opioids are commonly used to treat post-operative pain, although they can cause respiratory depression, nausea, and vomiting. Recent pain treatment regimen proposes mixing two or more analgesics to reduce opioid use post-op.[4]

Pre-emptive analgesia prevents central sensitization from surgical incisions and inflammatory injuries.[1] Non-opioid post-operative pain killers are becoming more popular. Non-opioid pregabalin, structurally related to GABA, manages neuropathic pain[4]. Pregabalin reduces calcium influx into presynaptic terminals via binding to the alpha-2 delta subunit of presynaptic voltage gated calcium channels.[2]

All patients in our study were similar in age, height, and weight. There was no clinically meaningful demographic difference. Our study randomly assigned 100 patients to two groups. Laryngoscopy and intubation often cause tachycardia and hypertension. Shribman et al. found that laryngoscopy or tracheal intubation raises arterial blood pressure and catecholamines, but intubation significantly raises HR.[5] We found that both groups heart rates increased significantly after induction. Pregabalin did not totally reduce the HR increase following laryngoscopy and intubation but it did reduce it afterward. This is consistent with Meena et al.[6] findings that premedication did not affect HR[6].

Rastogi et al. examined how different Pregabalin premedication doses reduced the hemodynamic pressor response to airway instrumentation during general anesthesia.[7] All groups had considerably higher HR after laryngoscopy and intubation. The smallest rise occurred with 150 mg Pregabalin. Systolic, diastolic, and MAP were considerably lower in premedicated groups than placebo groups at 10, 30, and 60 mins after induction. Rastogi et al. found that oral Pregabalin premedication reduced the hemodynamic pressor response to airway instrumentation[7]. Salman et al. and Eren et al. likewise found that 150 mg of Pregabalin following laryngoscopy and intubation reduced BP and increased HR in the control group.[8,9]

This study analyzed postoperative pain using a preoperative VAS score explained to the patient. VAS was assessed at 1, 2, 4, 6, 8, 12, and 24 hours postoperatively. VAS score considerably decreased in Pregabalin group compared to placebo in immediate and late postoperative phase ($P < 0.001$). While testing a single preoperative dose of Pregabalin to reduce postoperative pain and opioid use, Agarwal et al. discovered that both static (at rest) and dynamic (on coughing) Pregabalin significantly reduced VAS score compared to placebo.[10] Simrit Kaur et al. 2023 discovered that Gabapentin and Pregabalin significantly reduced VAS scores in laparoscopic cholecystectomy patients compared to placebo.[11] R.Mishra et al. found similar results.[12] Thapa AS et al. discovered that control group mean VAS score was greater than Pregabalin group.[13]

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First rescue analgesic timing post-op was substantially higher in Pregabalin group compared to placebo. Simritkaur et al. discovered that Gabapentin and Pregabalin groups had significantly different mean times of postoperative rescue analgesia.[11] Gabapentin and Pregabalin prolong postoperative pain-free time compared to placebo. Pregabalin provided longer-lasting pain alleviation than Gabapentin. Mishra et al. found that in laparoscopic cholecystectomy patients, single oral 150 mg Pregabalin extended time for first rescue analgesic compared to placebo.[12]

Our investigation revealed that Pregabalin (116.48±42.13 mg) considerably reduced tramadol consumption compared to placebo (174.10 ± 44.99 mg), with a significant difference ($P < 0.001$). The Pregabalin and Gabapentin groups consumed much less tramadol than the placebo group, according to Simrit Kaur et al. Total tramadol intake was similar between Gabapentin and Pregabalin groups.[11] In a study by Agarwal et al., Pregabalin significantly reduced postoperative pain and total fentanyl consumption compared to placebo[10]. Our findings support Mishra et al. and Anand et al., who found that laparoscopic cholecystectomy patients taking 150 mg of Pregabalin had lower opioid usage than placebo.[12,14]

The limitation of this study were- 1) We have evaluated capsule Pregabalin in single dose of 150 mg in patients undergoing laparoscopic abdominal surgeries only. We have not studied different doses of Pregabalin in our study.2) This study was conducted only in patients undergoing Laparoscopic abdominal surgeries so we have not evaluated its role in other surgeries.3) Side effects of the Pregabalin drug were not studied

CONCLUSION

Concluding our study, a preemptive administration of oral Pregabalin 150 mg seems to be effective in attenuating the haemodynamic response to orotracheal intubation, with minimal effect on heart rate. It significantly decreases incidence of pain postoperatively. Pregabalin decreases total tramadol consumption in comparison to placebo group in laparoscopic abdominal surgeries.

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