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A comparative study of oral clonidine and oral pregabalin as premedication for the control of haemodynamic surge in patients undergoing elective laparoscopic cholecystectomy

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ABSTRACT

Background: Pregabalin, a gabapentinoid compound, which exhibits potent analgesic, anticonvulsant, and anxiolytic activity, is now additionally being used in the preoperative period to reduce stress responses to direct laryngoscopy and tracheal intubation as well as to reduce the opioid requirement perioperatively. Clonidine is also being used for amelioration of hemodynamic surge response both during laryngoscopy with endotracheal intubation as well as during various time points of pneumoperitoneum. **Aims and Objectives:** The study was designed with an aim to compare the role of oral clonidine (200 mcg) and oral Pregabalin (150 mg) as premedications in controlling the hemodynamic surge response to direct laryngoscopy, endotracheal intubation, and pneumoperitoneum in patients posted for elective laparoscopic cholecystectomy under general anesthesia (GA). **Materials and Methods:** Sixty-six adult patients aged between 20 and 60 years of age, American Society of Anesthesiologists physical status 1 and 2, undergoing elective laparoscopic cholecystectomy under GA with endotracheal intubation, were randomly allocated to two equal groups (n = 33 in each group) to receive either single dose oral 200 mcg clonidine or single dose oral 150 mg pregabalin 2 h before induction of GA. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP), and arrhythmia if any, were recorded at different points of time perioperatively and compared. Oxygen saturation (SpO_2), end-tidal CO_2 ($EtCO_2$) were also compared at different points of time. Postoperative adverse effects like nausea and vomiting, shivering, and dry mouth were also noted and compared. Sedation was assessed in the immediate postoperative period using Ramsay Sedation Scale and was compared between the two groups. **Results:** HRs were significantly lower in the clonidine group at 1, 2, 3, 4, and 5 min after laryngoscopy and 15 min after pneumoperitonium. MAP and SBP were significantly lower in the clonidine group at 3, 4, and 5 min after laryngoscopy and intubation. There was no significant difference in DBP between the two groups at different points of time. SpO_2 and $EtCO_2$ at different points of time and adverse effects like nausea and vomiting, shivering, and dry mouth were comparable between the two groups. Postoperative sedation score was also comparable between the two groups. **Conclusion:** Oral clonidine (200 mcg) was found to be superior to oral pregabalin (150 mg) as a premedicant, in attenuating the hemodynamic surge during direct laryngoscopy, endotracheal intubation and during pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy under GA.

Key words: Cholecystectomy; Clonidine; Hemodynamic; Intubation; Pneumoperitoneum; Pregabalin; Premedication

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INTRODUCTION

Premedication with clonidine, an α^2 agonist blunts the hemodynamic stress responses to direct laryngoscopy and tracheal intubation. It also has some beneficial effects such as sedation, and prevention of post-operative nausea-vomiting (PONV) and shivering. Clonidine also stabilizes blood pressure by increasing cardiac baro receptor reflex sensitivity.[1,2]

Pregabalin, a gabapentinoid compound having analgesic, anticonvulsant, and anxiolytic activity, is now additionally also used in premedication to reduce stress responses to direct laryngoscopy and tracheal intubation. Though the mechanism of pregabalin in controlling the hemodynamic response is yet to be established, it is hypothesized that since pregabalin inhibits membrane voltage-gated calcium channels, it may have similar action as that of calcium channel blockers.[3,4] Pregabalin (150 mg), administered orally preoperatively, has been found to be effective in reducing the pressure response to laryngoscopy and endotracheal intubation.[5]

Previous studies have been done to assess the extent of amelioration of this hemodynamic surge response both during laryngoscopy with endotracheal intubation as well as during various time points of pneumoperitoneum with intravenous or oral clonidine[6-9] and to assess PONV along with postoperative analgesic requirement with gabapentin.[10,11] The success rate has been variable as there was no difference in terms of control of heart rate (HR) and mean arterial pressure (MAP) when 100 mcg Clonidine was compared with 150 mg Pregabalin[6] but 300 mcg Clonidine was found to be better than 150 mg Pregabalin[9] in lowering systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP and HR, the changes of which are associated with laryngoscopy.

However, there are only few studies[6,9] comparing oral clonidine and oral pregabalin as an attenuating agent for pressure response. Therefore, the present study was designed as a prospective, comparative study with the primary objective of comparing the role of oral clonidine (200 mcg) and oral Pregabalin (150 mg) as premedications in controlling the hemodynamic surge response (HR, SBP, MAP, DBP) to direct laryngoscopy, endotracheal intubation, and pneumoperitoneum in patients posted for elective laparoscopic cholecystectomy under general anesthesia (GA).

Aims and objectives

The study was conducted with the aim to evaluate and compare the effects of oral clonidine (200 mcg) and oral pregabalin (150 mg) premedication on haemodynamic changes having the following specific objectives:

- To assess the haemodynamic changes during laryngoscopy and endotracheal intubation.
- To assess the haemodynamic changes associated with pneumoperitoneum.
- To evaluate the associated adverse effects perioperatively.
- To evaluate sedation postoperatively.
- To compare the time when first rescue analgesia was required.

MATERIALS AND METHODS

The present study was carried out after obtaining approval from Institute's Ethics Committee in a tertiary care hospital in West Bengal. Sixty-six adult patients aged between 20 and 60 years of either sex conforming to American Society of Anesthesiologists (ASA) physical status I or II undergoing laparoscopic cholecystectomy under GA were selected for this study. After a thorough preoperative evaluation, written informed consent was taken from all patients.

Inclusion criteria

The inclusion criteria for the current study were as follows; Patients of either sex aged between 20 and 60 years, Patients with ASA Grade 1 or 2, Patients who were admitted to undergo elective laparoscopic cholecystectomy surgery under GA.

Exclusion criteria

Patients with a history of allergy to clonidine or pregabalin, history of bronchial asthma, hypertension, diabetes mellitus, coronary insufficiency, renal insufficiency, and hepatic insufficiency were excluded from the study. Patients having airways with Mallampati class 3 or more were excluded from the study. Patients on tricyclic antidepressants or opioids were also excluded from the study. Other exclusion criteria were participation in any other clinical trial within the past 1 month and any other condition placing the subject at high risk or unfit for the trial.

A thorough pre-anesthetic evaluation was performed in each patient including detailed history taking and physical examination comprising examination for pallor, cyanosis, clubbing, edema, neck glands enlargement, temperature, pulse rate, and non-invasive blood pressure, jaundice, jugular venous pressure, and nutritional status. Their body weights were recorded. Systemic examination was carried out to rule out any cardiovascular, respiratory, gastrointestinal, genito-urinary, and/or central nervous systems abnormality. Airway was assessed. "Mallampati classification"

was done. The pre-operative investigations including hematological investigations, fasting and postprandial blood sugar, macroscopic and microscopic examination (RE/ME) of urine, serum urea and creatinine, liver function test, coagulation profile, twelve lead resting electrocardiogram (ECG) and chest X-ray (PA view) were performed.

Patients and guardians were explained the procedure to be done and the risks as well as the benefits associated with it in their own language. They were explained their right to opt-out from the study at any time during the study.

Patients undergoing laparoscopic cholecystectomy remained fasting overnight. The study was a double-blinded one. Randomization was done during the allocation of the patients into two study groups by computer-generated random number lists. As clonidine is available in tablet form and pregabalin is available in capsule form we had to take the help of DBcaps® Capsules to ensure blinding.[12] DBcaps® are two-piece gelatin or HPMC capsules with a tamper-evident design to specifically address the clinical trial challenges of testing without bias.

Patients were kept fasting overnight. On the morning of operation, the patients were reassessed. Baseline (before premedication) HR, non-invasive blood pressures SBP, DBP, and MAP, and oxygen saturation (SpO_2) were noted. A peripheral venous line was set up in each patient. Written informed consent was checked. Total of 66 adult patients were randomly allocated into two equal groups (n=33 in each group) using a computer-generated random number list. Group C patients received a single dose oral 200 μg clonidine(in DBcaps®) and group P patients received single dose oral 150 mg pregabalin(in DBcaps®) 2 h before induction of GA.

A standard anesthetic sequence was followed in every patient. Anesthesia machine, breathing systems, monitors, ventilators, suction apparatus and laryngoscope were checked for proper functioning before starting the procedure. Pulse oximeter, non-invasive blood pressure cuff, and ECG leads were attached to the patients. Pre-induction values of HR, SBP, DBP, MAP, SpO_2, and arrhythmia if any, were recorded. An IV line was established and crystalloid solution infusion was started.

All patients were premedicated with injection ranitidine 50 mg IV and inj. ondansetron 4 mg IV before induction. All patients were pre-oxygenated with 100% oxygen for 3 min through a facemask followed by injection of Fentanyl 1.5 mcg/kg body weight. Induction was done with injection propofol 2 mg/kg IV and intubation was done with injection Atracurium 0.5 mg/kg IV and cuffed endotracheal tube of appropriate size. Anaesthesia was maintained with N_2O 66% in O_2, isoflurane 1–2%, and injection atracurium besylate 0.1 mg/kg IV when required. Pneumoperitoneum was created by insufflations with CO_2 and the operation table tilted about 15° in reverse Trendelenburg position. Intraoperative pressure was kept below 15 mmHg throughout the surgical procedure. Hemodynamic parameters like HR, SBP, DBP, MAP, and SPO_2 were recorded after induction; 1, 2, 3, 4, 5 min after laryngoscopy and intubation; before pneumoperitoneum; 5, 15, 30 min after pneumoperitoneum and after the release of CO_2. Arrhythmia was noted, if any. After completion of surgery, neuromuscular block was reversed with injection glycopyrrolate 0.01 mg/kg IV and injection neostigmine 0.05 mg/kg IV and extubated after adequate clinical neuromuscular recovery. Hemodynamic parameters again recorded post-extubation. Supplemental oxygen was given after extubation till stabilization. All the patients were shifted to the post-anesthesia care unit.

Sedation was assessed in the immediate post-operative period using the Ramsay sedation scale[13] which states that score 1 is "awake; agitated or restless or both;" score 2 is "awake; co-operative, oriented and tranquil;" score 3 is "awake but responds to commands only; score 4 is "asleep; brisk response to light glabellar tap or loud auditory stimulus;" score 5 is "asleep; sluggish response to light glabellar tap or loud auditory stimulus" and score 6 is "asleep; no response to glabellar tap or loud auditory stimulus."

Categorical variables were expressed as the number of patients and percentage of patients and compared across the two groups using Pearson's Chi-square test for independence of attributes/Fisher's exact test as appropriate. Continuous variables were expressed as mean±standard deviation and were compared across the two groups using unpaired t-test. The statistical software Statistical Package for Social Sciences version 20 was used for the analysis. Wherever applicable, $P<0.05$ was considered statistically significant.

RESULTS

The study spanned from May 2020 to April 2021 including 66 patients (33 in each group). No patient was lost to follow-up. Hence, data from sixty-six patients were available for analysis.

Table 1 shows the sociodemographic characteristics of the study participants. It was seen that the participants of the two groups were not statistically significantly different from each other with respect to their age, sex, height, weight, and BMI.

Table 1: Sociodemographic characteristics of the study participants

Parameters	Group C (n=33)	Group P (n=33)	P-value
Age	43.0±9.8	42.8±11.3	0.90
No of male patients	20	15	0.20
No of female patients	13	18	0.32
Weight (kg)	60.2±7.1	59.5±6.5	0.62
Heights (mts)	1.6±0.06	1.6±0.5	0.35
BMI	22.1±1.8	21.5±1.4	0.11

Chi-Square test or unpaired student's t-test was used, wherever applicable and P<0.05 was considered statistically significant

Table 2: Preoperative characteristics of the study participants

Parameters	Group C (n=33)	Group P (n=33)	P-value
ASA physical status (I)	24	27	0.82
ASA physical status (II)	9	6	0.06
Duration of surgery (min)	107.1±22.4	110.0±21.0	0.51
Total anesthesia time (min)	119.0±20.0	121.0±18.0	0.66

Chi-square test or unpaired student's t-test was used, wherever applicable and P<0.05 was considered statistically significant, ASA: American Society of Anesthesiologists

Table 3: Comparison of intraoperative heart rate (beats/min) between the clonidine and the pregabalin groups

Time of measurement of HR (beats/min)	Group C	Group P	P-value*
Baseline	78.6±10.9	81±10.6	0.21
Before induction	76±10.7	83±10.9	0.53
After induction	84.4±10.8	86±10.4	0.35
1 min after laryngoscopy and intubation	83±10.8	89.7±10.0	0.02
2 min after laryngoscopy and intubation	80±10.7	86.9±9.9	0.01
3 min after laryngoscopy and intubation	77.2±10.9	85.0±10.0	0.004
4 min after laryngoscopy and intubation	78.1±11.0	83.8±9.7	0.029
5 min after laryngoscopy and intubation	76.9±11.3	82±9.5	0.03
Before pneumoperitoneum	83.5±10.5	80±9.5	0.20
5 min after pneumoperitoneum	85.8±10.5	84.3±9.6	0.51
15 min after pneumoperitoneum	85.4±10.5	89.6±9.4	0.043
30 min after pneumoperitoneum	88.9±10.3	89.0±9.2	0.94
After release of CO_2	83.9±9.8	83.1±9.5	0.75
Post-extubation	81.7±9.5	81.0±9.1	0.77

Data expressed as mean±SD and tested with Student's t-test. P<0.05 was considered statistically significant

Table 2 shows the sociodemographic characteristics of the study participants. It was seen that the participants of the two groups were not statistically significantly different from each other with respect to ASA Physical Status 1/2, Duration of surgery (min), and Total Anesthesia time (min).

Table 4: Comparison of MAP between the clonidine and pregabalin groups (n=66)

Time of measurement of MAP (mm Hg)	Group C n=33	Group P n=33	P-value
Baseline	86.9±8.1	86.4±7.6	0.71
Before induction	85.4±8.0	85.4±7.7	1.04
After induction	75.1±7.1	76.6±7.2	0.46
1 min after laryngoscopy and intubation	83.0±6.7	84.1±6.4	0.41
2 min after laryngoscopy and intubation	85.0±6.5	86.3±6.2	0.43
3 min after laryngoscopy and intubation	79.4±6.6	83.3±6.2	0.016
4 min after laryngoscopy and intubation	77.3±6.6	81.5±6.1	0.010
5 min after laryngoscopy and intubation	75.5±6.6	79.6±6.0	0.011
Before pneumoperitoneum	77.6±6.4	79.1±6.0	0.38
5 min after pneumoperitoneum	86.4±6.4	87.9±5.9	0.32
15 min after pneumoperitoneum	89.7±6.2	91.5±5.9	0.21
30 min after pneumoperitoneum	91.9±6.1	93.6±5.7	0.20
After release of CO_2	82.6±5.6	84.5±5.5	0.17
Post extubation	80.8±5.5	82.5±5.4	0.22

Data expressed as mean±SD and tested with Student's t-test. P<0.05 was considered statistically significant, MAP: Mean arterial pressure

Table 3 shows the comparison of the intraoperative HR (beats/min) between the clonidine (Group C) and pregabalin (Group P) groups. It was observed that the intraoperative HR of the pregabalin group patient was more than the clonidine group. On analysis, these differences were statistically significant at 1 min, 2 min, 3 min, 4 min, and 5 min after laryngoscopy as well as 15 min after pneumoperitoneum.

Table 4 shows the comparison of the intraoperative MAP between the clonidine (Group C) and pregabalin (Group P) groups. It was observed that the intraoperative MAP of the pregabalin group patient was more than the clonidine group. On analysis, these differences were statistically significant at 3 min, 4 min, 5 min, after laryngoscopy and intubation.

Table 5 shows the comparison of the intraoperative SBP between the clonidine and pregabalin groups. It was observed that the intraoperative SBP of the pregabalin group patient was more than the clonidine group. On analysis, these differences were statistically significant at 3 min, 4 min, 5 min, after laryngoscopy and intubation.

Table 6 shows that both the groups had comparable DBP at all times, therefore there was no statistically significant

Table 5: Comparison of SBP (mm of Hg between the clonidine and pregabalin groups (n=66)

Time of measurement of SBP (mmHg)	Group C	Group P	P-value
Baseline	118.4±10.2	117.7±9.4	0.71
Before induction	117.6±9.8	118.4±10.0	0.70
After induction	108.6±9.3	112.5±9.9	0.15
1 min after laryngoscopy and intubation	115.7±8.3	119.7±8.9	0.06
2 min after laryngoscopy and intubation	117.3±8.2	121.4±8.9	0.05
3 min after laryngoscopy and intubation	111.9±8.7	119.6±8.9	0.001
4 min after laryngoscopy and intubation	110.1±8.6	117.7±8.9	0.001
5 min after laryngoscopy and intubation	108.2±8.4	115.8±8.8	0.001
Before pneumoperitoneum	114.4±8.1	117.9±8.9	0.11
5 min after pneumoperitoneum	120.3±8.2	124.0±8.6	0.08
15 min after pneumoperitoneum	122.7±8.1	126.3±8.5	0.08
30 min after pneumoperitoneum	124.7±7.9	128.3±8.3	0.07
After release of CO_2	115.0±7.4	118.5±7.9	0.06
Post extubation	113.1±7.2	116.6±7.9	0.06

Data expressed as mean±SD and tested with Student's t-test. P<0.05 was considered statistically significant, SBP: Systolic blood pressure

Table 6: Comparison of intraoperative DBP (mm Hg) between the clonidine and pregabalin groups

Time of measurement of diastolic blood pressure (mm Hg)	Group C	Group P	P-value
Baseline	71.2±7.2	70.6±6.0	0.72
Before induction	69.3±7.1	68.8±6.8	0.79
After induction	58.4±6.2	58.6±6.1	0.87
1 min after laryngoscopy and intubation	66.5±6.3	66.2±5.5	0.83
2 min after laryngoscopy and intubation	68.8±6.0	68.8±5.6	1.014
3 min after laryngoscopy and intubation	63.1±5.8	65.1±5.5	0.16
4 min after laryngoscopy and intubation	61.0±5.8	63.4±5.5	0.11
5 min after laryngoscopy and intubation	59.2±6.0	61.5±5.4	0.153
Before pneumoperitonium	59.2±5.2	59.6±5.3	0.73
5 min after pneumoperitoneum	69.3±5.9	69.8±5.2	0.71
15 min after pneumoperitoneum	73.3±5.8	74.0±5.2	0.59
30 min after pneumoperitoneum	75.5±5.8	76.3±5.3	0.58
After release of CO_2	66.5±5.3	67.5±5.0	0.43
Post extubation	64.8±5.3	65.4±5.1	0.62

Data expressed as mean±SD and tested with Student's t-test. P<0.05 was considered statistically significant, DBP: Diastolic blood pressure

difference seen between the Clonidine and Pregabalin groups (P>0.05).

Table 7: Comparison of intraoperative SPO_2 between the clonidine and pregabalin groups

Time of measurement of SPO_2 (%) O_2	Group C	Group P	P-value
Baseline	98.8±0.7	98.9±0.6	0.8
Before induction	99.7±0.4	99.8±0.3	0.3
After induction	99.8±0.4	99.7±0.8	0.5
1 min after laryngoscopy and intubation	99.9±0.2	99.7±0.7	0.3
2 min after laryngoscopy and intubation	99.8±0.4	99.9±0.2	0.1
3 min after laryngoscopy and intubation	99.9±0.3	99.8±0.5	0.4
4 min after laryngoscopy and intubation	99.6±0.8	99.7±0.5	0.7
5 min after laryngoscopy and intubation	99.7±0.5	99.5±1.0	0.3
Before pneumoperitoneum	99.7±0.7	99.6±0.9	0.6
5 min after pneumoperitoneum	98.8±0.8	99.5±1.0	0.2
15 min after pneumoperitoneum	99.4±0.5	99.5±0.5	0.3
30 min after pneumoperitoneum	99.6±0.4	99.7±0.4	0.4
After the release of CO_2	99.7±0.4	99.6±0.5	0.8
Post extubation	99.6±0.5	99.6±0.5	0.6

Data expressed as mean±SD and tested with Student's t-test. P<0.05 was considered statistically significant, SPO2: Oxygen saturation

Table 8: Comparison of intraoperative $EtCO_2$ between the clonidine and pregabalin groups

Time of measurement of $EtCO_2$ (mmHg)	Group C	Group P	P-value*
1 min after laryngoscopy and intubation	38±3.8	38.9±3.7	0.9
2 min after laryngoscopy and intubation	40.0±3.9	40.0±3.7	0.9
3 min after laryngoscopy and intubation	38.5±3.8	37.7±3.5	0.4
4 min after laryngoscopy and intubation	38.8±3.1	37.9±2.4	0.1
5 min after laryngoscopy and intubation	38.1±2.0	37.5±1.6	0.1
Before pneumoperitoneum	37.9±1.9	37.5±2.0	0.4
5 min after pneumoperitoneum	39.8±1.8	39.5±2.1	0.5
15 min after pneumoperitoneum	42.5±2.1	41.6±1.8	0.07
30 min after pneumoperitoneum	44.8±1.7	44.7±1.5	0.7
After release of CO_2	39.7±1.6	39.6±2.1	0.8

Data expressed as mean±SD and tested with Student's t-test. P<0.05 was considered statistically significant, EtCO2: End tidal CO_2

Table 7 shows that both the Clonidine and Pregabalin groups had comparable SPO_2 (%) at all times and therefore no statistically significant differences were seen between the two groups.

Table 8 shows that both the groups had comparable End tidal CO_2 ($EtCO_2$) at all times, therefore no statistically significant differences were seen between the Clonidine and Pregabalin groups.

Table 9: Comparison of the post-operative adverse effect (% participants) between the Clonidine and Pregabalin groups (n=33 in each group)

Adverse effects (%)	Group-C	Group-P	P-value*
Nausea and vomiting	3	6	0.73
Shivering	3	6.1	0.60
Dry Mouth	60	69.7	1.0

Data are presented as % of participants, and tested using "Pearson's Chi-square test". P<0.05 was considered statistically significant

Regarding the time of first rescue analgesia in post-operative period, there was a comparable time of requirement of rescue analgesia and no statistically significant difference were seen between the clonidine and pregabalin groups (Group C-240.9±67.2 min vs. Group P-244.5±76 min having P=0.8 which is >0.05).

Table 9 shows that both the groups had comparable adverse effect profiles. Both the Clonidine and Pregabalin groups had a higher percentage of dry mouth incidences, though both groups had very few incidences of nausea, vomiting, or shivering.

When the degree of immediate post-operative sedation was compared between the Clonidine and Pregabalin groups using Ramsay Sedation Scale, both the groups were found to have comparable immediate post-operative sedation scores (Group C- 2.33±0.8 vs. Group P-2.03±0.5 having P=0.09 which is >0.05).

DISCUSSION

Preoperative medication and preoperative psychological preparation are important aspects for anaesthetic management of patients. Selective approach to each patient has developed in place of routine administration of the same drugs to all patients. Premedication achieves relief from anxiety, induces sedation, prevents autonomic stress response, nausea and vomiting, shivering, reduces anesthetic requirement, gastric fluid volume.[14] Research is still on in search of an ideal premedicating agent fulfilling the goals without much increasing the adverse effects.

In order to reduce the incidence and severity of the deleterious effects on hemodynamics due to laryngoscopy and endotracheal intubation as well as pneumoperitoneum during laparoscopic cholecystectomy; numerous techniques have been used with varying degrees of success. These techniques include deepening of the plane of anaesthesia, usage of a variety of drugs[9,15-19] as premedications.

The efficacy of clonidine in attenuating haemodynamic stress response has been studied previously in many studies and provided its effectiveness.[9,15,17] Effect of pregabalin in attenuating stress response to laryngoscopy and tracheal intubation was also evaluated previously in some studies along with its effect on PONV.[9]

This study, therefore, made an attempt to evaluate the effect of premedication with oral clonidine or oral pregabalin on haemodynamic stability during laryngoscopy, endotracheal intubation and pneumoperitoneum for laparoscopic cholecystectomy. As clonidine also has some beneficial premedication effects like sedation,[15,20] prevention of PONV and shivering,[15] the study was also used to evaluate the beneficial and adverse effects of both drugs.

We conducted a prospective, randomized, double-blinded, comparative study to compare the efficacy of 200 mcg oral clonidine with 150 mg of oral pregabalin. Sixty-six consenting adults of ASA grade 1 and 2 patients of either sex complying with the inclusion and exclusion criteria posted for laparoscopic cholecystectomy under GA with endotracheal intubation were randomised in our study. Data of 33 patients of group C (clonidine group) and 33 patients of group P (pregabaline group) were analyzed.

The present study showed that the clonidine group had a significantly (P<0.05) lower mean HR than the pregabalin group at 1 min, 2 min, 3 min, 4 min, 5 min, after laryngoscopy and intubation and also 15 min after pneumoperitoneum.

The present study also showed that the MAP and SBP were significantly (P<0.05) lower in the clonidine group at 3 min, 4 min, 5 min after laryngoscopy and intubation.

In our study, the differences in respect of DBP, $EtCO_2$ and SPO_2 were found to be statistically insignificant (P>0.05) at all times between the two groups. Both the clonidine and pregabalin groups showed comparable time of requirement of first rescue analgesia. It was found that the adverse effect profile of both the clonidine group and pregabalin group were also comparable. Both groups showed low incidence of shivering and nausea and vomiting and the differences between the groups were insignificant (P>0.05). Both groups also showed a higher incidence of dry mouth though statistically insignificant (P>0.05). It was also seen that both the clonidine and pregabalin groups had comparable sedative effect in the immediate post-operative period, as measured by the mean score of the Ramsay sedation scale.

Sung et al.,[21] in 2000 reported that clonidine increases perioperative circulatory stability in patients undergoing laparoscopic cholecystectomy and potentiates parasympathetic nervous system.

Laisalmi et al.,[22] in 2001 concluded that premedication with clonidine blunts the stress response to surgical stimuli and reduces the requirement of narcotic and anaesthetic doses.

Gupta et al.,[23] in 2011 did a study in total of 180 healthy adult consented patients aged 35–52 years dividing the participants into three groups. Group I received placebo, pregabalin (150 mg) was given to Group II, and clonidine (200 mcg) to Group III which were given 75–90 min before surgery as oral premedication. They concluded that both pregabalin and clonidine are effective oral premedicant drugs with safe and multimodal drug profile as they cause sedation, anxiolysis and analgesia with successful attenuation of the deleterious hemodynamic response of laryngoscopy. Clonidine was found to be superior to pregabalin for attenuation of the hemodynamic responses to laryngoscopy and intubation but it increased the incidence of intra and postoperative bradycardia. The findings of this study partially corroborate with our study findings.

Rathore et al.,[24] in 2019 conducted a study that was designed to evaluate oral pregabalin and clonidine premedication to attenuate pressor response to laryngoscopy and intubation. A total of 80 patients were randomized into two groups. Group A received oral clonidine 300 mcg 2 h prior to surgery, group B received oral pregabalin 75 mg 2 h prior to surgery. HR and blood pressure (SBP, DBP and MAP) were recorded. When compared between clonidine and pregabalin, there was a significant increase in HR and MAP in pregabalin group after laryngoscopy and tracheal intubation. Clonidine was better than pregabalin in suppressing the pressor response. This finding also corroborates with that of our study.

Limitations of the study

The current study included only ASA I and II Patients. The safety profile of the drugs in patients with other comorbidities were not studied. Requirement of analgesia varies from patient to patient and the assessment partially depends upon pain threshold and psychological status of each patient.

CONCLUSION

It can be inferred that oral clonidine (200 mcg) attenuates the hemodynamic response to direct laryngoscopy, endotracheal intubation, and pneumoperitoneum of elective laparoscopic cholecystectomy under GA, by limiting the extent of rise in HR, MAP, and SBP more effectively than oral pregabalin (150 mg). Both the study drugs showed comparable adverse effect profiles and were found to be safe. The post-operative sedation and analgesia requirements were comparable in both the study drugs.

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