Original Research Paper

Volume - 13 | Issue - 03 | March - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

# HEMODYNAMIC RESPONSE TO ORAL PREGABALIN AS PREMEDICATION IN LAPAROSCOPIC CHOLECYSTECTOMY AT TERTIARY CARE CENTER : AN OBSERVATIONAL STUDY.

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## ABSTRACT

**Introduction** Laparoscopic surgeries are a boon for the surgeons as it reduces tissue trauma, post-operative morbidity, hospital stay and thereby reduced healthcare costs. Phillipe Mouret, introduced Laparoscopic surgery in 1987(1), which started a new era of minimally invasive surgery. However, it was not possible to perform laparoscopic procedure unless proper anesthetic technique was developed to combat the additional hemodynamic stress of pneumoperitoneum with co2 insufflation and patient's position (2,3). Direct laryngoscopy and pneumoperitoneum during laparoscopy are associated with increase in heart rate and blood pressure. Many pharmacological methods were evaluated to attenuate adverse hemodynamic responses. Most common practice is use of benzodiazepines to decrease pre-operative anxiety but it does not have any positive effect on post-operative outcome. In the present study oral pregabalin was used as premedication to evaluate its efficacy in maintaining hemodynamic stability during laryngoscopy and laparoscopic pneumoperitoneum. Use of pregabalinoids as a pre medicant helps in blunting adverse hemodynamic response during laryngoscopy and laparoscopy (4,5). Pregabalinoids, which include pregabalin (PG), are a new class of drugs which binds to α –δ protein subunit of voltage-gated calcium channels and inhibits the release of excitatory neurotransmitters in the central and peripheral nervous system (6). This study was designed to know the effectiveness of pregabalin as a premedication on the arterial pressor response to laryngoscopy and on hemodynamic variables. **AIMS AND OBJECTIVES**

**Aim:** "To study hemodynamic response to oral pregabalin as pre medication in laparoscopic cholecystectomy at tertiary care centre."

**Objectives:**

1.To study the hemodynamic response to tablet pregabalin during laryngoscopic endotracheal intubation and during surgery in patients undergoing laparoscopic cholecystectomy.

2. To study the immediate post-operative complications of Tablet Pregabalin in study participant

**MATERIALAND METHODS**

This prospective comparative study was conducted in the Department of Anesthesiology in tertiary health care center attached to Medical College, from August 2019 to December 2021. A total number of 75 patients scheduled for laparoscopic surgery in the age group of 18 to 60 years belonging to ASA grade 1 and 2 were included in the study. Written informed consent was obtained. After preliminary screening, the patients posted for laparoscopic cholecystectomy were thoroughly examined clinically one day before operation for pre-anesthetic evaluation. Routine investigations such as blood hemoglobin, serum urea and creatinine levels, blood sugar, serum electrolytes, liver function tests, HBsAg, urine analysis, X-ray chest (PA view), electrocardiography and cardiological evaluation reports were reviewed and recorded. SCALE TO BE USED (vital parameters to be monitored):

- Heart Rate, Blood Pressure Monitoring, Spo2
- ASA Grading (46)

The purpose and procedure of the study was explained. Patients were selected based on inclusion and exclusion criteria.

**Results and conclusions:** Pregabalin 150mg proved to be an effective drug in blunting the hemodynamic stress response to laryngoscopy and pneumoperitoneum though it is not statistically proven. The heart rate, systolic blood pressure, diastolic blood pressure, MAP are the parameters used to determine hemodynamic response to oral Pregabalin as a premedication. Bradycardia, nausea/vomiting, dizziness and headache were the common post-operative side-effects observed in few cases.

## KEYWORDS :

## INTRODUCTION:

Laparoscopic surgeries are a boon for the surgeons as it reduced tissue trauma, post-operative morbidity, hospital stay and thereby reduced healthcare costs. Phillipe Mouret, introduced laparoscopic surgery in 1987(1), which started a new era of minimally invasive surgery. However, it was not possible to perform laparoscopic procedure unless proper anesthetic technique was developed to combat the additional hemodynamic stress of pneumoperitoneum with co2 insufflation and patient's position (2,3).

Direct laryngoscopy and pneumoperitoneum during laparoscopy are associated with increase in heart rate and blood pressure.

Many pharmacological methods were evaluated to attenuate adverse hemodynamic responses. Most common practice is use of benzodiazepines to decrease pre-operative anxiety but it does not have any positive effect on post-operative outcome.

In the present study oral pregabalin was used as premedication to evaluate its efficacy in maintaining hemodynamic stability during laryngoscopy and laparoscopic pneumoperitoneum.

Use of pregabalinoids as a pre medicant helps in blunting adverse hemodynamic response during laryngoscopy and laparoscopy (4,5).

Pregabalinoids, which include pregabalin (PG), are a new class of drugs which binds to α –δ protein subunit of voltage-gated calcium channels and inhibits the release of excitatory neurotransmitters in the central and peripheral nervous system (6).

This study was designed to know the effectiveness of pregabalin as a premedication on the arterial pressor response to laryngoscopy and on hemodynamic variables.

## AIMS AND OBJECTIVES

**Aim:**

"To study hemodynamic response to oral pregabalin as pre medication in laparoscopic cholecystectomy at tertiary care centre."

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1. To study the hemodynamic response to tablet pregabalin during laryngoscopic endotracheal
Intubation and during surgery in patients undergoing laparoscopic cholecystectomy.

2. To study the immediate post-operative complications of Tablet Pregabalin in study participant Patients were selected based on inclusion and exclusion criteria.

## INCLUSION CRITERIA:

1. Patients posted for laparoscopic cholecystectomy within the age of 18 – 60 years.

2. Patients posted for laparoscopic cholecystectomy under General Anaesthesia.
3. Patients graded under ASA Grade I & ASA Grade II.
4. Patients consenting for the above-mentioned study

**EXCLUSION CRITERIA:**
1. Patients with hepatic and renal impairment.
2. Patients with cardiovascular disorders.
3. Patients with any known drug allergies.
4. Pregnant patients.
5. Patients refusing consent.

**MATERIAL AND METHODS:**
This prospective comparative study was conducted in the Department of Anesthesiology in tertiary health care center attached to Medical College, from August 2019 to December 2021. A total number of 75 patients scheduled for laparoscopic surgery in the age group of 18 to 60 years belonging to ASA grade 1 and 2 were included in the study. Written informed consent was obtained.

After preliminary screening, the patients posted for laparoscopic cholecystectomy were thoroughly examined clinically one day before operation for pre-anesthetic evaluation. Routine investigations such as blood hemoglobin, serum urea and creatinine levels, blood sugar, serum electrolytes, liver function tests, HBsAg, urine analysis, X-ray chest (PA view), Electrocardiography and cardiological evaluation reports were reviewed and recorded.

**SCALE TO BE USED** (vital parameters to be monitored):
Heart Rate, Blood Pressure Monitoring, Spo2
ASA Grading (46)

The purpose and procedure of the study was explained.

**Pre-operative preparations:**
All the patients were kept NBM for 8 hours prior to surgery on the day of surgery patients received tab pregabalin 150 mg in the pre-operative room, around 60 minutes prior to surgery. The drug was administered with sip of water under supervision. The patient was then shifted to the operation theatre and all monitors attached and recorded.

**Pre-medication:**
All patients were premedicated with Inj. Glycopyrrolate 0.2 mg IV, Inj. Ondansetron 4 mg IV and Inj. Fentanyl 1-2 µg/ kg IV induction, intubation & maintenance:

After pre-oxygenating the patients with 100% O2 for 3 min, anesthesia was induced with Inj. Propofol 1-2 mg/kg of body weight IV. Laryngoscopy and tracheal intubation with an appropriately sized cuffed endotracheal tube was facilitated under the effect of inj. Succinylcholine 1.5-2mg/kg IV. Anesthesia was maintained with nitrous oxide 50%, with oxygen 50% and isoflurane. Ventilation was controlled with injection vecuronium bromide (0.08- 0.1mg/kg). Intra-operatively the following vital parameters were monitored and recorded:

a) Heart rate
b) Non-invasive blood pressure (NIBP) including systolic, diastolic and mean arterial pressure.
c) Oxygen saturation (Spo2)

Pneumoperitoneum was created by insufflation of carbon dioxide and operation table was tilted about reverse Trendelenburg position. Intra-abdominal pressure (IAP) was not allowed to exceed 15 cm of H20 throughout the surgical procedure. After pneumoperitoneum, necessary changes in ventilator settings (tidal volume and respiratory rate) were made to maintain normocapnia. Rise of MAP (greater than 20% of baseline) was treated with Inj. Nitroglycerine by an infusion pump. The dose was titrated to maintain the MAP within 20% of baseline. Fall of MAP (greater than 20% of baseline) was treated with an Inj. Ephedrine 5 mg IV bolus as and when necessary. Fall in HR less than 50 beats per minute was treated with Inj. Atropine 0.6 mg and repeated if necessary. Systemic arterial pressure including the systolic, diastolic, MAP, pulse rate and SpO2 were recorded at the following points of time –

1. Before pre-medication (oral pregabalin 150mg)
2. Before induction
3. During intubation
4. After intubation
5. Before pneumoperitoneum.
6. 15 minutes after pneumoperitoneum.
7. 30 minutes after pneumoperitoneum.
8. 45 minutes after pneumoperitoneum
9. 60 minutes after pneumoperitoneum
10. Release of Co2
11. Extubation
12. 15 minutes after extubation

At the end of the operative procedure, residual effect of the muscle relaxant was reversed by Inj. neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 8 µg/kg intravenously. Patient was extubated and transferred to recovery room. Patients was observed for any complications during this period for hypotension, apnea, bradycardia, coughing, headache, nausea, vomiting and shivering.

**STATISTICAL ANALYSIS**
All the data was noted in pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Quantitative data was represented using mean +/- standard deviation. Analysis of the quantitative data was done using paired t test. A p value <0.05 was taken as level of significance. Results were graphically represented and were deemed necessary.

SPSS version 21 was used for most analysis. Microsoft excel 2019 was used for graphical representation

**OBSERVATIONS & RESULTS**
**Table no 1: Age distribution amongst study population**

| AGE GROUP | FREQUENCY | PERCENT |
|---|---|---|
| 18 to 30 years | 21 | 28 |
| 31 to 40 years | 14 | 18.67 |
| 41 to 50 years | 25 | 33.33 |
| 51 to 60 years | 15 | 20 |
| TOTAL | 75 | 100.00 |

As seen in the above table, most of the study population belongs to the age group of 41 to 50 years (33.33%) followed by 18 to 30 years (28%), 51-60 years (20%) and 31-40 years (18.67%).

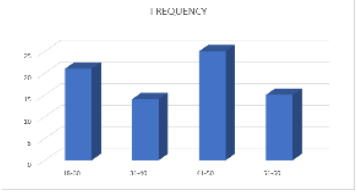



**Table no 2: Gender distribution amongst study population:**

| GENDER | FREQUENCY | PERCENT |
|---|---|---|
| Female | 28 | 37 |
| Male | 47 | 63 |
| TOTAL | 75 | 100 |

As seen in the above table, there was male predominance (63%) amongst study population as compared to Female population (37%).

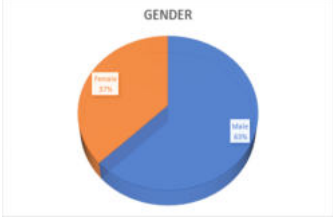



**Table no 3: ASA status amongst study population**

| ASA | FREQUENCY | PERCENT |
|---|---|---|
| ASA I | 43 | 56.7 |
| ASA II | 32 | 43.3 |
| TOTAL | 75 | 100.0 |

As seen in the above table, most of the study population had ASA grade I status (56.7%) and ASA grade II status (43.3%).


**Table no 4: Systolic blood pressure at various interval amongst study population**

| SBP | MEAN | STD. DEVIATION | P VALUE |
|---|---|---|---|
| Before premedication | 119.28 | 9.9 | |
| Before induction | 120.93 | 9.4 | 0.0001 |
| During intubation | 128.29 | 10.4 | 0.0001 |
| After intubation | 124.00 | 10.3 | 0.0001 |
| Before pneumoperitoneum | 120.35 | 9.5 | 0.0001 |
| 15 min after pneumoperitoneum | 124.40 | 10.5 | 0.0001 |
| 30 min after pneumoperitoneum | 121.31 | 9.5 | 0.0001 |
| 45 min after pneumoperitoneum | 119.79 | 9.2 | 0.063 |
| 60 min after pneumoperitoneum | 120.01 | 9.7 | 0.012 |
| Release of CO2 | 121.03 | 9.7 | 0.0001 |
| Extubation | 127.49 | 10.5 | 0.0001 |
| 15 min after extubation | 121.91 | 9.01 | 0.0001 |

*Significant p-value<0.05

As seen in the above table, there was significant increase in SBP after premedication with oral pregabalin as compared to premedication level but the increase in SBP was within acceptable range. Before premedication SBP was 119mmhg which increased by 9mmhg during intubation.

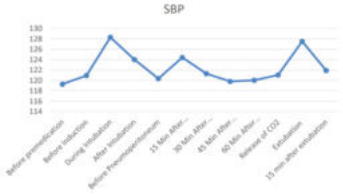



**Table no 5: Diastolic blood pressure at various interval amongst study population.**

| DBP | MEAN | STD. DEVIATION | P VALUE |
|---|---|---|---|
| Before premedication | 71.31 | 7.207 | |
| Before induction | 72.89 | 7.022 | 0.0001 |
| During intubation | 77.31 | 7.162 | 0.0001 |
| After intubation | 74.25 | 7.422 | 0.0001 |
| Before pneumoperitoneum | 72.01 | 6.863 | 0.002 |
| 15 min after pneumoperitoneum | 74.61 | 7.203 | 0.0001 |
| 30 min after pneumoperitoneum | 72.45 | 7.125 | 0.0001 |
| 45 min after pneumoperitoneum | 71.56 | 6.832 | 0.344 |
| 60 min after pneumoperitoneum | 71.27 | 7.426 | 0.898 |
| Release of CO2 | 72.73 | 7.830 | 0.0001 |
| Extubation | 76.32 | 7.249 | 0.0001 |
| 15 min after extubation | 72.81 | 7.013 | 0.0001 |

*Significant p-value<0.05

As seen in the above table, there is significant increase in DBP after premedication of oral pregabalin as compared to premedication level but the increase in DBP was within acceptable range. Before premedication DBP was 71mmhg which increased by 6mmhg during intubation.

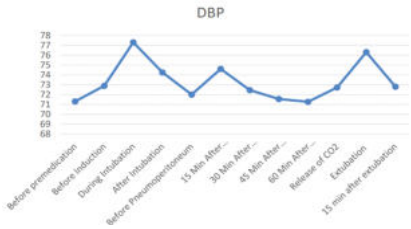



**Table no 6: Mean arterial pressure at various interval amongst study population.**

| MAP | MEAN | STD. DEVIATION | P VALUE |
|---|---|---|---|
| Before premedication | 87.32 | 7.530 | |
| Before induction | 88.96 | 7.260 | 0.0001 |
| During intubation | 94.32 | 7.673 | 0.0001 |
| After intubation | 90.89 | 7.777 | 0.0001 |
| Before pneumoperitoneum | 88.12 | 7.088 | 0.0001 |
| 15 min after pneumoperitoneum | 91.23 | 7.705 | 0.0001 |
| 30 min after pneumoperitoneum | 88.76 | 7.169 | 0.0001 |
| 45 min after pneumoperitoneum | 87.64 | 6.976 | 0.145 |
| 60 min after pneumoperitoneum | 87.48 | 7.484 | 0.509 |
| Release of CO2 | 88.88 | 7.786 | 0.0001 |
| Extubation | 93.43 | 7.687 | 0.0001 |
| 15 min after extubation | 89.17 | 7.208 | 0.0001 |

*Significant p-value<0.05

As seen in the above table, there is significant increase in MAP after premedication of oral pregabalin as compared to premedication level but the increase in MAP was within acceptable range. Before premedication MAP was 87mmhg which increased by 7mmhg during intubation.

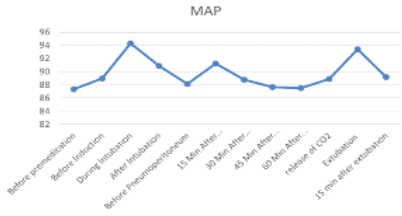



**Table no 7: Mean Heart rate at various interval amongst study population.**

| Heart Rate | Mean | Std. Deviation | P value |
|---|---|---|---|
| Before premedication | 77.84 | 8.835 | |
| Before induction | 80.09 | 8.640 | 0.0001 |
| During intubation | 82.11 | 9.274 | 0.0001 |
| After intubation | 81.91 | 9.456 | 0.0001 |
| Before pneumoperitoneum | 78.88 | 8.354 | 0.003 |
| 15 min after pneumoperitoneum | 81.59 | 9.280 | 0.0001 |
| 30 min after pneumoperitoneum | 79.07 | 8.867 | 0.001 |
| 45 min after pneumoperitoneum | 78.05 | 9.034 | 0.748 |
| 60 min after pneumoperitoneum | 77.95 | 8.590 | 0.029 |

| | | | |
|---|---|---|---|
| Release of CO2 | 78.68 | 8.847 | 0.0001 |
| Extubation | 79.55 | 9.390 | 0.0001 |
| 15 min after extubation | 80.01 | 8.270 | 0.0001 |

*Significant p-value<0.05

As seen in the above table, there is significant increase in heart rate after premedication of oral pregabalin as compared to premedication level but the increase in heart rate was within acceptable range. Before premedication HR was 77beats/minute which increased by 5beats/minute during intubation.

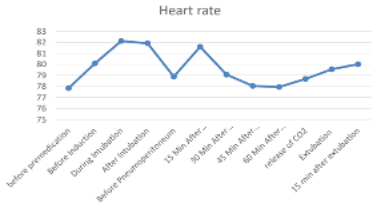



**Table no 8: SpO2 at various interval amongst study population.**

| SpO2 | Mean | Std. Deviation | P value |
|---|---|---|---|
| Before premedication | 100.00 | .000a | |
| Before induction | 100.00 | .000a | 1 |
| During intubation | 100.00 | .000a | 1 |
| After intubation | 100.00 | .000a | 1 |
| Before pneumoperitoneum | 100.00 | .000a | 1 |
| 15 min after pneumoperitoneum | 100.00 | .000a | 1 |
| 30 min after pneumoperitoneum | 100.00 | .000a | 1 |
| 45 min after pneumoperitoneum | 100.00 | .000a | 1 |
| 60 min after pneumoperitoneum | 100.00 | .000a | 1 |
| Release of CO2 | 100.00 | .000a | 1 |
| Extubation | 100.00 | .000a | 1 |
| 15 min after extubation | 100.00 | .000a | 1 |

*Significant p-value<0.05

As seen in the above table, there was no significant difference in SpO2 post medication as compared to premedication level.

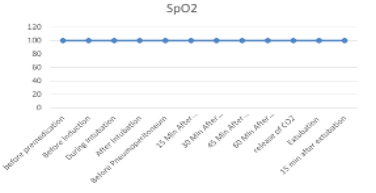



**Table no 9: Respiratory rate at various interval amongst study population.**

| Respiratory rate | Mean | Std. Deviation | P value |
|---|---|---|---|
| Before premedication | 17.03 | 1.404 | 0.000 1 |
| After premedication | 16.27 | 1.369 | |

*Significant p-value<0.05

As seen in the above table, there was significant decrease in respiratory rate post medication as compared to premedication level but the decrease in respiratory rate was within acceptable range.

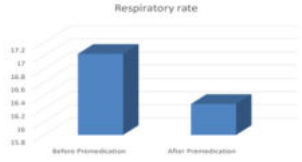
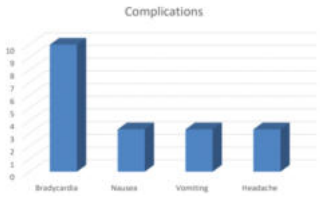



**Table no 10: Complications amongst study population**

| Complications | Frequency | Percent |
|---|---|---|
| Bradycardia | 3 | 10.0 |
| Nausea/Vomiting | 1 | 3.3 |
| Dizziness | 1 | 3.3 |
| Headache | 1 | 3.3 |

As seen in the above table, complications bradycardia, nausea/vomiting, dizziness and headache was observed in 10%, 3%,3% and 3% of study population respectively.




**DISCUSSION:**

A hazardous consequence of general anesthesia is hemodynamic pressor reaction to airway equipment (direct laryngoscopy and intubation). (47) Many pharmacological techniques, such as deepening of anesthesia, pre-treatment with vasodilators, adrenoceptor blockers, calcium channel blockers, and opioids, were performed either in the premedication or during the induction to attenuate these adverse hemodynamic responses to airway instrumentation, with mixed results. (48,49) Although several studies have shown that pregabalin is effective as a post-operative analgesic and improves patient satisfaction. No randomized controlled trial has been conducted to assess the hemodynamic pressor response to airway instrumentation. (50) Pregabalin, a gabapentin compound, is described structurally as (S)-3 aminomethyl-5-methylhexanoic acid. Pregabalin shares structural similarities with the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), but not functionally. It acts on the central nervous system by inhibiting the synthesis of the neurotransmitter glutamate, and it has analgesic, anticonvulsant and anxiolytic properties. It is also useful in suppressing the neuropathic component of acute nociceptive pain after surgery. (51) After oral treatment, it is highly absorbed and tolerated, with peak plasma concentrations occurring within 1 hour. It has a very little hepatic metabolism. It is non-narcotic and has clinically significant effect in decreasing pain and hemodynamic pressor response.

In the present study, it is observed that

1. Majority of the study population belongs to the age group of 41 to 50 years (33.33%) followed by 18 to 30 years (28%), 51-60 years (20%) and 31-40 years (18.67%). These findings were comparable to study conducted by Dhanshree Kale et al., in which most of the study population belongs to the age group of 41 to 50 years (67%). (52)

2. There is male predominance (63%) amongst study population as compared to female population (37%). These findings are comparable to study conducted by Dhanshree Kale et al., in which most of the study population were male (63%). (52)

3. Majority of the study population is from ASA grade I status (56.7%) and ASA grade II status (43.3%).

4. There is significant increase in SBP after premedication of oral pregabalin as compared to before premedication level but the increase in SBP is within acceptable range. Before premedication SBP was 119 mm Hg which increased by 9mmhg during intubation. These findings are comparable with the study conducted by Puja Thapa et al., in which SBP was significantly lower in the Pregabalin group. (53)

5. There is significant increase in DBP after premedication of oral pregabalin as compared to before premedication level but the increase in DBP is within acceptable range. Before premedication DBP was 71mmhg which increased by 6mmhg during intubation. These findings are comparable with the study conducted by Puja Thapa et al., in which they found that after premedication diastolic blood pressure was better controlled in pregabalin group. (53)

6. There is significant increase in MAP after premedication of oral pregabalin as compared to before premedication level but the increase

in MAP is within acceptable range. Before premedication MAP was 87mmhg which increased by 7mmhg during intubation. These findings are comparable with the study conducted by Puja Thapa et al., in which they found that after premedication mean arterial blood pressure was better controlled in pregabalin group. (53)

7. There is significant increase in heart rate after premedication of oral pregabalin as compared to before premedication level but the increase in heart rate is within acceptable range. Before premedication HR was 77beats/minute which increased by 5beats/minute during intubation. Similarly in the study conducted by Pravinkumaar et al., found a significant increase in heart rate of 8 bpm in pregabalin groups which received 150mg dose of pregabalin compared to the control group. (54) This is consistent with the study done by Rastogi et al. and co-workers, where they studied two different doses of pregabalin of 75mg and 150mg. (22) The results were consistent with the study by Meena et al and El-Hussiny H et al where the rise of heart rate was of shorter duration in the Pregabalin group. (55,28) In the study done by Rastogi et al, there was a significant rise in heart rate postintubation in the pregabalin group. (22)

8. There is no significant difference in SpO2 after premedication of oral pregabalin as compared to before premedication level.

9. There is significant decrease in respiratory rate after premedication of oral pregabalin as compared to before premedication but the decrease in respiratory rate is within acceptable range.

10. Out of the 75-study population, 3 patients were recorded with bradycardia post operatively, 1 patient complained of nausea/vomiting, 1 patient complained of dizziness and 1 complained of headache. These findings are comparable with the study conducted by Sudhir Sachdev et al., in which bradycardia and nausea/vomiting were the common side effects observed.

## SUMMARY AND CONCLUSION:

- Majority of the study population belongs to the age group of 41 to 50 years (33.33%) followed by
- 18 to 30 years (28%), 51-60 years (20%) and 31-40 years (18.67%).
- There is male predominance (63%) amongst study population as compared to female population
- (37%).
- Majority of the study population is from ASA grade I status (56.7%) and ASA grade II status
- (43.3%).
- There is significant increase in SBP after premedication of oral pregabalin as compared to before
- Premedication level but the increase in SBP is within acceptable range.
- There is significant increase in DBP after premedication of oral pregabalin as compared to before premedication level but the increase in DBP is within acceptable range.
- There is significant increase in MAP after premedication of oral pregabalin as compared to before premedication level but the increase in MAP is within acceptable range.
- There is significant increase in heart rate after premedication of oral pregabalin as compared to before premedication level but the increase in heart rate is within acceptable range.
- There is no significant difference in SpO2 after premedication of oral pregabalin as compared to before premedication level.
- There is significant decrease in respiratory rate after premedication of oral pregabalin as compared to before premedication level but the decrease in respiratory rate was within acceptable range.
- Pregabalin 150mg proved to be an effective drug in blunting the hemodynamic stress response to laryngoscopy and pneumoperitoneum though it is not statistically proven. The heart rate, systolic blood pressure, diastolic blood pressure, MAP are the parameters used to determine hemodynamic response to oral Pregabalin as a premedication. Bradycardia, nausea/vomiting, dizziness and headache were the common post-operative side-effects observed in few cases.

## REFERENCES


1. Singh S, Arora K. Effect of oral clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth. 2011;55(1):26-30.
2. Vecchio R, Mac Fayden BV, Palazzo F. History of laparoscopic surgery. PAnminerva Med. 2000; 42:87-90
3. Joshi GP. Anaesthesia for laparoscopic surgery. Can J Anesth. 2002;49(1):45-49.
4. Cunningham AJ, Brull SJ. Laparoscopic cholecystectomy: anesthetic implications. Anesth Analg. 1993 May;76(5):1120-33.
5. Milne B. Alpha-2 agonists and anesthesia. Can JAnaesth1991;38;7: 809 – 13.
6. Dworkin RH, Kirkpatrick P. Pregabalin. Nature reviews Drug discovery. 2005 Jun 1;4(6):4557.
7. Odeberg-Wernerman S. Laparoscopic surgery: effects on circulatory and respiratory physiology: an overview. Eur J Surg Suppl. 2000; 166:4–11.
8. Mandy perrin, Anthony flecher. Laparoscopic abdominal surgery. Contin Educ Anaesth Crit Care Pain (2004) 4(4): 107-110
9. Joshi GP. Complications of laparoscopy. Anesthesiol Clin North Am. 2001 Mar;19(1):89-105.
10. Sood J, Kumra VP. Anaesthesia for laparoscopic surgery. Indian J Surg 2003; 65:232-40.
11. Safran DB, Orlando R 3rd. Physiologic effects of pneumoperitoneum. Am J Surg. 1994 Feb;167(2):281-6.
12. Hirvonen EA, Poikolainen EO, Pääkkönen ME, Nuutinen LS. The adverse hemodynamic effects of anesthesia, head-up tilt, and carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy. Surg Endosc. 2000 Mar;14(3):272-7