Oral Pregabalin vs Oral Hormone in An Exceedingly Attenuation of Hemodyanamic Response to Laryngoscopy Insertion, Extubation in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Background: Premedication in the form of vasodilators, adreno receptor blockers, calcium channel blockers and opioids were used earlier to attenuate these responses, with variable results. This study will be conducted to evaluate & compare efficacy of oral pregabalin & oral melatonin in attenuation of haemodynamic responses during laryngoscopy, intubation & extubation in laparoscopic cholecystectomy. Subjects and Methods: This is a Prospective randomized double blind comparative study done on 60 Patients undergoing laparoscopic cholecystectomy in Department of Anesthesiology, Saraswathi Institute of Medical Sciences, Anwarpur, Hapur, Uttar Pradesh, India. All patients were explained about the anaesthesia technique and written informed consent taken. Group P - (30 patients) oral pregabalin 150mg, 120 min before surgery and Group M- (30 patients) oral melatonin tablets 6 mg (two tablets of 3 mg), 120 min before surgery. Pre-anaesthetic evaluation was done a day prior. Patients to be kept NPO 8 hours prior to surgery. Results: Our study showed that the mean age of patients was 36.50±12.01 years in group P and 34.70±14.82 years in group M, but statistically non-significant (P=0.6073). The heart rate, SBP, DBP & Mean arterial pressure was statistical non-significant. The complications occurred more in group P as compare to group M. The bradycardia, headache was more common complications in both groups. Conclusion: We concluded that both the drugs can be used as an effective premedicant to attenuate the sympathetic response to laryngoscopy and tracheal intubation without much side effects and the added advantage of intraoperative and postoperative analgesia.

Keywords: Morphine, Oral Pregabalin, Endotracheal Intubation, Pre-Anaesthetic Evaluation.

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Introduction

Laryngoscopy and endotracheal intubation during general anesthesia are associated with various cardiovascular changes such as hypertension, tachycardia, dysrythmias and increased circulating catecholamines. The effect although is transient, from 30 seconds after intubation to upto 10 minutes. It occurs because of adrenergic response which leads to stimulation of the cardio-accelerator fibres. Endotracheal intubation is well tolerated by normotensive patients, but even transient stimulation has been associated with increased morbidity and mortality in patients with pre-eclampsia, recent myocardial infarction, hypertension, and cerebro-vascular pathology such as aneurysms, tumors, or raised intracranial pressure. Laparoscopy is a technique for visualization of the internal organs of abdomen or pelvis with an aid of camera using small incisions for ports which became very popular in early 1990s because less postoperative complications and pain were noted as compared to open cholecystectomy.

Pregabalin, a gabapentinoid compound appears to produce an inhibitory modulation of neuronal excitability particularly in neocortex, amygdala and hippocampus of CNS. Pineal hormone melatonin (N-acetyl-5-methoxytrypt-tamine) is an endogenous sleep regulating hormone that can be used as premedication, regulation of circadian rhythms, as sedative, analgesic, anti-inflammatory, and antioxidant. Various studies have been performed to study efficacy of drugs on attenuating haemodynamic responses to laryngoscopy. By far no study has been done to compare oral pregabalin & oral melatonin. This study will be conducted to evaluate & compare efficacy of oral pregabalin & oral melatonin in attenuation of haemodynamic responses during laryngoscopy, intubation & extubation in laparoscopic cholecystectomy.
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Inclusion Criteria
• Sixty ASA grade I and II patients,
• Age between 18-65 years,
• Under going laparoscopic cholecystectomy

Exclusion criteria
• Patients having compromised renal, pulmonary and cardiac status (ASA grade III or above)
• Patients with anemia, blood coagulation disorders, diabetes
• Patients with anticipated difficult intubation (mallampati grade 3 and 4)
• More than one attempts at intubation
• Patients in whom duration of laryngoscopy exceeds more than 30 secs
• Haemodynamically unstable patients (HR >120/min, HR<50/min, systolic BP > 140 mmHg, systolic BP < 90 mmHg, diastolic BP > 100 mmHg, diastolic BP <50 mmHg)
• Previous History of allergy or contraindication to anaesthetics or any drug used.
• Patient unwilling to give consent for proposed study
• Patient with any GI disturbance which hinders enteric absorption to oral medicine
• Patients on chronic neuroleptic medication and taking tricyclic antidepressants or serotonin and NE uptake inhibitor.
• Patients who took medications that would influence autonomic or cardiovascular response to laryngoscopy and intubation.
• Patient weighing >20% of ideal body weight, pregnant or breastfeeding females

Method
This study was done at Department of Anesthesiology, Saraswathi Institute of Medical Sciences, Anwarpur, Hapur, Uttar Pradesh, India. Permission from hospital ethical committee and written informed consent were obtained.

Patients were randomly divided into two groups of 30 each with the help of a chit box method. All patients were explained about the anaesthesia technique and written informed consent taken.

**Group P:** (30 patients) oral pregabalin 150mg, 120 min before surgery.

**Group M:** (30 patients) oral melatonin tablets 6 mg(two tablets of 3 mg), 120 min before surgery.

Pre-anaesthetic evaluation was done a day prior. Patients to be kept NPO 8 hours prior to surgery.

On the day of surgery, patient received in OT, confirmation of patient’s identity, fasting status, PAC and consent was done.

In the operating room standard 5 leads ECG, non-invasive blood pressure and pulse oximetry were attached and base line parameters were noted. Venous access was secured using an 18 G cannula on the dorsum of the non-dominant hand. Injection midazolam 1 mg and fentanyl 1 μg/kg were given. Pre-oxygenation was done for 3 minutes, then induction with i.v propofol 2 mg/kg. Succinylcholine were used intravenously 2mg/kg to facilitate endotracheal intubation with proper sized well- lubricated cuffed endotracheal tube. Laryngoscopy and tracheal intubation was done with appropriate sized, cuffed endotracheal tube.

Maintenance of anaesthesia with inhalation of isoflurane 1 minimum alveolar concentration; nitrous oxide: oxygen 40:60. Muscle relaxation were attained with Vecuronium bromide in the dose of 0.06–0.08 mg/kg intravenously as loading dose and one- fourth of the initial dose as maintenance doses.

After completion of the surgery, neostigmine 50μg/kg and injection glycopyrrolate 10 μg/kg were administered intravenously to reverse the residual neuromuscular blockade.

Statistical Analysis
Data are expressed as mean, intra group difference was evaluated by two way analysis of variance (ANOVA), and intergroup using t-test. P values of <0.05 were considered significant.

Results

![Figure 1: Distribution of mean age in between groups](image)

Table 1: Comparison of heart rate in different time interval in between groups

| Heart Rate                        | Melatonin group | Pregabalin group | t-value | P-value |
|-----------------------------------|-----------------|-------------------|---------|---------|
| **Baseline**                      | Mea n | SD       | Mea n | SD       |         |         |
| 85.43 | 8.08           | 87.17 | 8.91         | 0.7891 | 0.433   |
| **During laryngoscopy & Intubation** | 92.17 | 9.35 | 95.33 | 8.01       | 1.408 | 0.164   |
| 5 min.                            | 82.37 | 9.00 | 83.83 | 11.0       | 0.5627 | 0.575   |
| Before pneumoperitoneum m         | 82.83 | 8.85 | 82.83 | 9.45       | 1.244 | 0.218   |
| 30 min. after pneumoperitoneum m  | 83.77 | 5.77 | 83.70 | 9.76       | 0.0521 | 0.974   |
| After CO2 release                 | 83.37 | 7.48 | 83.47 | 9.64       | 0.4487 | 0.964   |
| After extubation                  | 88.17 | 6.48 | 89.60 | 5.58       | 0.9170 | 0.362   |

Our study showed that the mean age of patients was 36.50±12.01 years in group P and 34.70±14.82 years in group M, but statistically non-significant (P=0.6073) [Figure...
The heart rate in group M was slightly lower as compared to group P, but statistically non-significant in between groups [Table 1].

The mean value of SPO2 was slightly higher in group M as compared to group P. The difference was statistically significant in various time intervals in our study [Table 2]. The complications occurred more in group P as compared to group M. The bradycardia, headache were more common complications in both groups.

### Table 2: Comparison of SPO2 in different time interval in between groups

| SPO2                          | Melatonin group | Pregabalin group | t-value | P-value   |
|-------------------------------|-----------------|------------------|---------|-----------|
| **Baseline**                  | Mea n           | SD               | Mea n   | SD        |         |
|                               | 99.43           | 0.504            | 99.70   | 0.466     | 2.12     |
|                               |                 |                  |         |           | 8       | 0.0376* |
| **During laryngoscopy & Intubation** | 99.93           | 0.253            | 99.67   | 0.479     | 2.69     |
|                               |                 | 7                |         | 5         | 3        | 0.0093**|
| **5 min.**                    | 99.97           | 0.182            | 99.70   | 0.466     | 2.91     |
|                               |                 | 6                |         | 1         | 8        | 0.0500**|
| **Before pneumoperitoneum**   | 99.97           | 0.182            | 99.60   | 0.498     | 3.78     |
|                               |                 | 6                |         | 5         | 5        | 0.0004**|
| **30 min. after pneumoperitoneum** | 99.93           | 0.365            | 99.80   | 0.406     | 1.33     |
|                               |                 | 1                |         | 8         | 6        | 0.1868  |
| **After CO2 release**         | 99.93           | 0.365            | 99.73   | 0.449     | 1.89     |
|                               |                 | 7                |         | 8         | 1        | 0.0636  |
| **After extubation**          | 99.93           | 0.253            | 99.73   | 0.449     | 2.12     |
|                               |                 | 7                |         | 8         | 1        | 0.0382* |

### Table 3: Complications

| Complications | Melatonin group | Pregabalin group |
|---------------|-----------------|------------------|
| Bradycardia   | 1               | 2                |
| Headache      | 0               | 0                |
| Nausea/vomiting | 1             | 2                |
| Restlessness  | 0               | 1                |
| Arrhythmia    | 0               | 0                |
| Hypotension   | 1               | 0                |

### Discussion

Airway management is one of the core skills of the anaesthetist, either via facemask ventilation, insertion of a laryngeal mask airway, endotracheal intubation by direct or indirect (video-assisted) laryngoscopy or by use of a fibre scope. Pain relieving agents are usually administered with the concept of balanced analgesia, which involves a combination of analgesics with either synergistic or additive effects.

Various studies done by Kumkum Gupta et al (2011)\[8\] aged 35 to 52 years, Shirin Parveen et al (2016),\[9\] included aged between 20-60 years of both sexes, Bhawna Rastogi et al (2012),\[10\] aged 24-56 years. Another study done by Nadia M Bahgat et al (2016)\[11\] aged 18-60 years. No significant difference was found in age, sex in our study.

Bhawna Rastogi et al (2012),\[10\] found no significant decrease in heart rate was observed in different doses of pregabalin. Mohamed, Hosam M. et al (2013),\[12\] found no significant difference in heart rate between the different doses of melatonin. Another study done by Dhananjaya Doddaiiah et al (2017),\[13\] found that the increase in HR response to laryngoscopy and intubation was minimized by both gabapentin and pregabalin when compared with the control group (P < 0.05) at baseline and 1 min; however, there was no statistically significant difference between the two study groups (P > 0.05).

The complications occurred more in group P as compared to group M. Shirin Parveen et al (2016)\[9\] concluded that both the drugs can be used as an effective premedicant to attenuate the sympathetic response to laryngoscopy and tracheal intubation without much side effects and the added advantage of intraoperative and postoperative analgesia.

### Conclusion

We concluded that both the drugs can be used as an effective premedicant to attenuate the sympathetic response to laryngoscopy and tracheal intubation without much side effects and the added advantage of intraoperative and postoperative analgesia.

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