

# COMPARISON BETWEEN TAB. CLONIDINE AND TAB. LABETALOL AS ORAL PREMEDICATION IN ATTENUATION OF HAEMODYNAMIC CHANGES DURING LAPAROSCOPIC SURGERY: A RANDOMISED DOUBLE BLIND STUDY

Saroj Patta<sup>1</sup>, Pradeep Kumar Karem<sup>2</sup>, Krishna Chaitanya Bevara<sup>3</sup>, A. Satyanarayana<sup>4</sup>

<sup>1</sup>Associate Professor, Department of Anaesthesiology, Andhra Medical College, Visakhapatnam.

<sup>2</sup>Senior Resident, Department of Anaesthesiology, Andhra Medical College, Visakhapatnam.

<sup>3</sup>Senior Resident, Department of Anaesthesiology, Andhra Medical College, Visakhapatnam.

<sup>4</sup>Professor and HOD, Department of Anaesthesiology, Andhra Medical College, Visakhapatnam.

## ABSTRACT

### BACKGROUND AND AIMS

To study and compare Labetalol and Clonidine as premedication to attenuate haemodynamic changes to Laparoscopy through oral route, as it is safe method of administration and easy to prescribe.

### METHODS

In a prospective, comparative randomised study, 60 adult patients of both sexes of ASA Grade I and II were divided randomly into 2 groups of 30 each, Group L and Group C. Group L were given Tab. Labetalol 200mg orally 60-90 minutes before induction. Group C were given Tab. Clonidine 300µg orally 60-90 minutes before induction. We compared the degree of attenuation of haemodynamic changes during laparoscopic surgeries.

### RESULTS

Oral Clonidine has better control on the rise in heart rate and mean arterial pressure (MAP) during laryngoscopy for laparoscopy compared to oral Labetalol.

### CONCLUSION

We conclude that oral Clonidine showed better attenuation of haemodynamic changes than oral Labetalol.

### KEY WORDS

Clonidine, Labetalol, Laryngoscopy, Laparoscopy.

**HOW TO CITE THIS ARTICLE:** Patta S, Karem PK, Bevara KC et al. Comparison between tab. clonidine and tab. labetalol as oral premedication in attenuation of haemodynamic changes during laparoscopic surgery: a randomised double blind study. J. Evid. Based Med. Healthc. 2016; 3(16), 606-613. DOI: 10.18410/jebmh/2016/139

**INTRODUCTION:** With the advancements in the field of anaesthesia and surgery minimally invasive procedure using endoscopy gained importance. Laparoscopy is a minimally invasive procedure with several benefits of decreased hospital stay,<sup>1</sup> decreased analgesic requirements<sup>2</sup> and decreased stress response.<sup>3</sup> Increased intra-abdominal pressure has disadvantages of alterations in cardiopulmonary physiology, complications like surgical emphysema,<sup>4</sup> pneumothorax<sup>5</sup> or pneumopericardium,<sup>6</sup> endo-bronchial intubation,<sup>7</sup> air embolism,<sup>8</sup> and post-operative complications like shoulder pain,<sup>9</sup> nausea and vomiting etc. Increased intra-abdominal pressure increases the pressure on inferior vena cava reducing preload and cardiac output. Increased intra-abdominal vascular resistance along with release of arginine, vasopressin due to stimulation of peritoneal receptors increase systemic vascular resistance leading to rise in mean arterial

pressures.<sup>10</sup> Respiratory complications include CO<sub>2</sub> subcutaneous emphysema, pneumothorax, endobronchial intubation, and gas embolism.<sup>11</sup> Several non-pharmacological and pharmacological methods are used to prevent the hemodynamic changes to laparoscopy but with their individual disadvantages. Labetalol is a combined alpha- and beta-adrenoceptor blocking agent for oral and intravenous use in the treatment of hypertension. Clonidine is an  $\alpha_2$  agonist and exerts central sympatholytic properties.<sup>12</sup> Premedication with Clonidine blunts the stress response to surgical stimuli and reduces narcotic and anaesthetic doses. We decided to study and compare Labetalol and Clonidine as a premedication to attenuate hemodynamic changes to laparoscopy through oral route as it is a safe method of administration, easy to prescribe and is cost effective.

### AIM OF THE STUDY: The aim of our study is:

1. To compare the attenuation of haemodynamic changes during laparoscopic surgery by premedication with Oral Clonidine hydrochloride (300µg) versus Oral Labetalol (200mg).

Submission 26-01-2016, Peer Review 12-02-2016,

Acceptance 20-02-2016, Published 24-02-2016.

Corresponding Author:

Dr. Saroj Patta,

# 10-4-18, Asilmetta, A. U. Post,

Visakhapatnam-530003.

E-mail: saroj\_patta@yahoo.com

DOI: 10.18410/jebmh/2016/139

- To evaluate a hypothesis, which drug has better haemodynamic control comparing HEART RATE, MEAN ARTERIAL BLOOD PRESSURE and sedation scores at predetermined intervals of time.

**MATERIALS AND METHODS:** After approval from hospital ethical committee, a prospective randomised comparative study was conducted on adult patients undergoing laparoscopic surgeries.

This study was conducted on 60 adult patients of both sex divided randomly to two groups of 30 each.

Group - L patients were given Tab Labetalol 200mg per oral 60-90min before induction.

Group - C patients were given Tab Clonidine 300µg per oral 60-90min before induction.

**Inclusion Criteria:** ASA grades I and II, both males and females, adult patients aged 25-60 yrs. with scheduled laparoscopic cholecystectomy surgeries.

**Exclusion Criteria:** Patients not fulfilling eligibility criteria, lack of patient consent, drug dependence, anticipated difficult airway, body mass index (BMI) >25, diabetic and hypertensive patients, history of cardiopulmonary disease, psychiatric illness, therapy with α2 adrenergic agonists, β blockers, methyl dopa, MAO inhibitors, tricyclic antidepressants and benzodiazepines.

During pre anaesthetic assessment, a detailed history and examination of each patient was carried out to optimize them prior to surgery.

Before administration of oral premedication with tab Clonidine and tab Labetalol, each patients base line heart rate, mean systemic arterial blood pressure, pulse oximetry and end tidal carbon dioxide levels were measured. In addition sedation level is assessed by Ramsay sedation scale shown in Table-I. All measurements were repeated before induction.

1	Patient anxious, agitated or impatient
2	Patient co-operative, oriented and calm
3	Patient only responds to verbal commands
4	Patient that demonstrates a brisk response to the glabellar tap test or auditory stimulus
5	Patient that demonstrates a sluggish response to the glabellar tap test or auditory stimulus
6	Patient that does not respond to glabellar tap or auditory stimulus
<b>Table 1: Ramsay sedation scale</b>	

In the operating room, monitoring for heart rate, mean arterial systemic blood pressure, end tidal carbon dioxide levels, peripheral oxygen saturation and sedation scores were noted just before inducing the patient.

After pre-oxygenation, anaesthesia was induced with sleeping dose of 2.5% thiopentone sodium followed by succinylcholine 2mg/kg body weight to facilitate tracheal intubation and trachea is intubated with an appropriate sized cuffed, disposable endotracheal tube. Lungs were

mechanically ventilated with O<sub>2</sub> – N<sub>2</sub>O (50-50), sevoflurane (1-2%), vecuronium bromide 0.1mg/kg bolus followed by 1 mg intermittently for neuromuscular blockade. Tidal volume and ventilator frequency were adjusted to maintain normocapnea (EtCO<sub>2</sub>40±5 mmHg). Analgesia is provided by intravenous fentanyl (1µg/kg body weight).

Pneumoperitoneum was created by insufflation of CO<sub>2</sub> through 12-mm trocar at a rate of 2L/min. necessary change in minute ventilation was done to maintain normocapnea. The mean arterial blood pressure was maintained at 20% above or below the pre-operative value by adjusting the concentration of sevoflurane. Operation table was tilted to about 15° reverse Trendelenburg. Intra-abdominal pressure was not allowed to exceed 15mmhg.

Throughout the study period all the parameters selected (HR, MAP, SpO<sub>2</sub>, EtCO<sub>2</sub>) were recorded at specified timings. In case of severe hemodynamic fluctuations, medial intervention other than adjustment of sevoflurane was applied. For bradycardia (HR< 60 bpm) atropine 0.6mg I.V was administered. Hypotension (MABP < 60mmhg) was managed by fluid challenge and/or I.V mephentermine 6mg bolus.

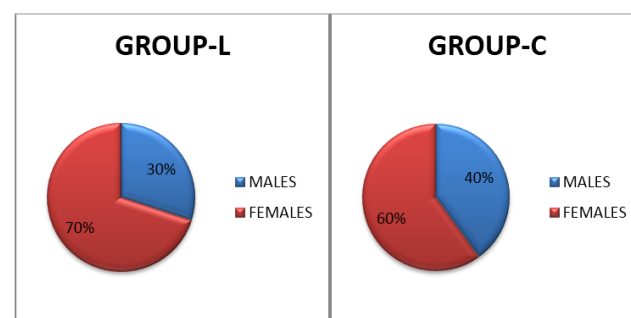
Hypertension (MABP >110mmhg) was treated with injection nitroglycerine 0.5-5 µg/kg/min I.V.

Sevoflurane was discontinued after the last skin suture and residual neuromuscular block was antagonised with appropriate doses of neostigmine (0.05 mg/kg) and glycopyrrolate (0.01mg/kg). The extubation was performed when respiration was spontaneous and adequate.

**RESULTS AND ANALYSIS:** Sixty ASA I and II grade patients were randomly allocated to receive oral Clonidine 300µg [Group – C] and oral Labetalol 200mg [Group – L] as pre-medication 60-90 min before elective laparoscopic cholecystectomy.

In group – L (n=30) the age group ranged from 30 – 52 yrs. and the mean age with standard deviation is 38.20±7.02 and sex distribution is 9 males: 21 females and the mean weight is 64.6±3.05 kgs. (range 61 – 70 kgs.).

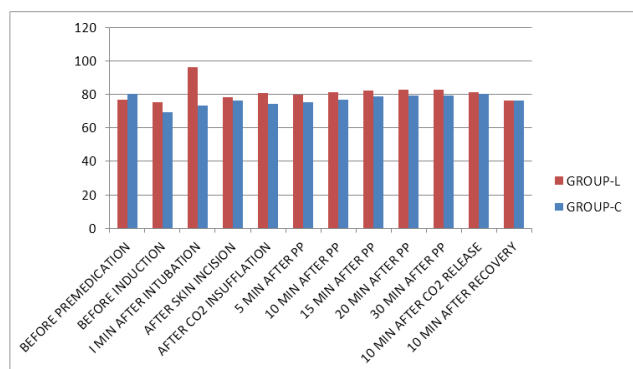
In group – C (n=30) the age group ranged from 28 – 55 yrs. and the mean age with standard deviation is 39.33 ± 8.62 and sex distribution is 12 males: 18 females and the mean weight is 64.8±4.35 kgs (range 58 – 72 kgs).



**Figure 1**

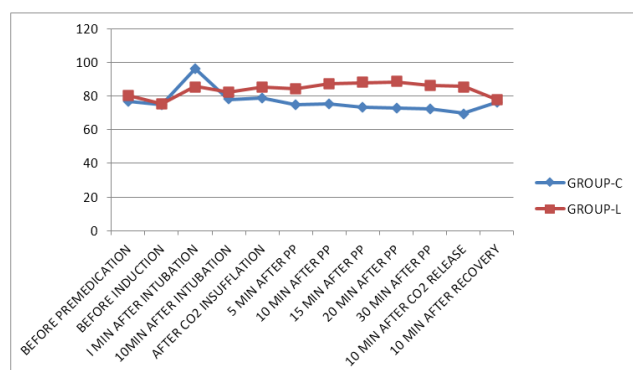
Patients received oral premedication 60-90 min before surgery and vital parameters of heart rate, mean arterial blood pressure were recorded before giving premedication using L&T planet 55 multichannel monitor.

Heart rate before oral premedication in Group – L ranged from 62 – 96 beats per min with a mean $\pm$ SD of 76.73 $\pm$ 9.94 and in Group – C ranged from 63-92 beats per min with a mean $\pm$ SD of 80.33 $\pm$ 8.40. There is no statistical significance;  $p = 0.13$  in between the two groups.



**Figure 2: Changes in heart rate at various specified timings in two groups**

**Heart Rate Variability:** After arrival into the operation theatre heart rates were again recorded just before induction. In group – L heart rates ranged from 65-86 beats per min with a mean $\pm$ SD of 75.13 $\pm$ 6.99 and is compared with group – C in which heart rate ranged from 54 – 84 beats per min with a mean $\pm$ SD of 69.30 $\pm$ 7.58.



**Figure 3: Changes in heart rate at various specified timings in two groups**

There is statistically significant decrease in heart rate in group – C when compared to group– L ( $p=0.003$ ).

One minute after intubation the heart rate in the group – L ranged from 78 – 117 beats per min with a mean $\pm$ SD 96.40  $\pm$  13.41 and in group – C ranged from 44 – 90 beats per min with a mean $\pm$ SD of 73.23 $\pm$ 18.35. A high statistical significance ( $p = 0.0001$ ) is noted in between the groups.

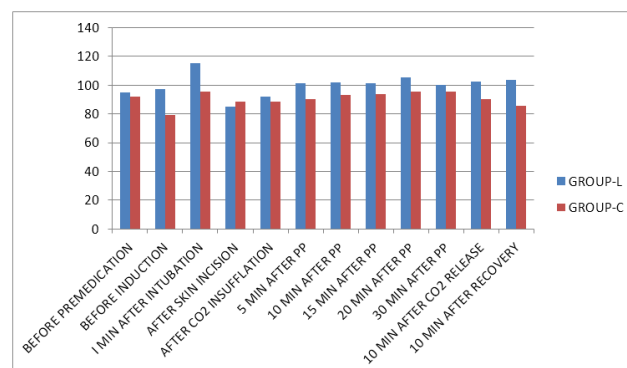
Ten minutes after intubation the heart rates in both the groups reached nearing the baseline values before induction. In group – L, heart rates ranged from 63-90 beats per min with a mean $\pm$ SD of 78.13 $\pm$ 7.51 and in group – C heart rates ranged from 67-91 beats per min with a mean $\pm$ SD of 76.50 $\pm$ 5.57. There is no statistically significant difference ( $p= 0.34$ ) noted in between the groups.

Heart rate was recorded after CO<sub>2</sub> insufflation and mean  $\pm$  SD is 80.93 $\pm$ 5.25 vs 74.30 $\pm$ 4.97(Group – L vs. Group – C) ( $p=0.001$ ), 5min after insufflation and mean $\pm$ SD is 80.00 $\pm$ 8.95 vs. 75.53 $\pm$ 5.69 (Group – L vs. Group – C) ( $p=0.02$ ), 10min after insufflation and mean $\pm$ SD is 81.40 $\pm$ 8.18 vs. 76.70 $\pm$ 5.19 (Group – L vs. Group – C) ( $p=0.01$ ), 15min after insufflation and mean $\pm$ SD is 82.53 $\pm$ 8.68 vs 78.73 $\pm$ 5.01 (Group – L vs. Group – C) ( $p=0.04$ ), 20min after insufflation and mean  $\pm$  SD is 82.87  $\pm$ 8.14 vs. 79.30 $\pm$ 4.82 (Group – L vs. Group – C) ( $p=0.04$ ), 30min after insufflation and mean $\pm$ SD is 82.97 $\pm$ 8.46 vs 79.47 $\pm$ 3.98 (Group – L vs. Group – C) ( $p=0.04$ ) and were found statistically significant in Group – C when compared to Group – L.

Heart rate recordings at 10 min after Co<sub>2</sub> release with mean $\pm$ SD is 81.40 $\pm$ 7.90 vs. 80.50  $\pm$  4.62 (Group – L vs. Group – C) ( $p=0.5$ ) and at 10 min after recovery with mean  $\pm$  SD is 76.50  $\pm$  11.71 vs. 76.80  $\pm$  4.82(Group – L vs. Group – C) ( $p=0.8$ ). There is no statistical significance in between the two groups.

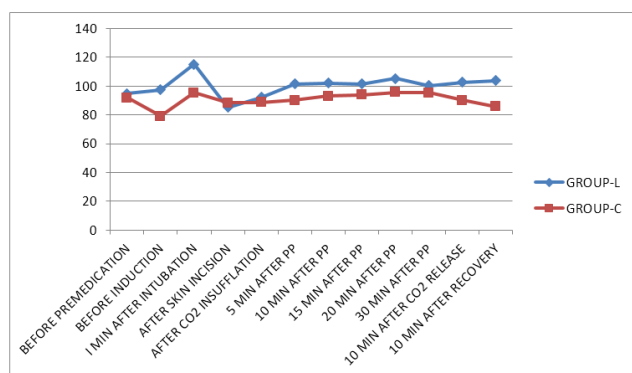
#### MEAN ARTERIAL BLOOD PRESSURE VARIABILITY:

Mean arterial blood pressure values were recorded before giving oral premedication and they ranged from 106 – 86 mmHg in group – L and ranged from 106 – 80 mmHg in group – C. Their mean  $\pm$  SD values are 94.57  $\pm$  5.88 vs 91.93  $\pm$  5.05 (Group – L vs Group – C). There is no statistical significance ( $p=0.06$ ) in premedication mean arterial pressures in between the groups.



**Figure 4: Changes in mean arterial pressures at various specified timings in two groups**

After giving premedication, mean arterial pressures were again noted before induction and they ranged from 112 – 85 mm Hg in group – L and ranged from 94 – 67 mmHg in group – C. Their mean $\pm$ SD values are 94.73 $\pm$ 8.93 vs 79.10  $\pm$  9.67 (Group – L vs Group – C). A high statistically significant difference with  $p = 0.0001$  in between the groups was observed.



**Figure 5: Changes in mean arterial pressures at various specified timings in two groups**

Mean arterial pressures noted one min after intubation ranged from 138– 97 mmHg in group – L and ranged from 112 – 84 mmHg in group – C. Their mean $\pm$ SD values are 115.00 $\pm$ 12.29 vs 95.30 $\pm$ 8.04 (Group – L vs Group– C). A high statistically significant difference with  $p = 0.0001$  in between the groups was observed.

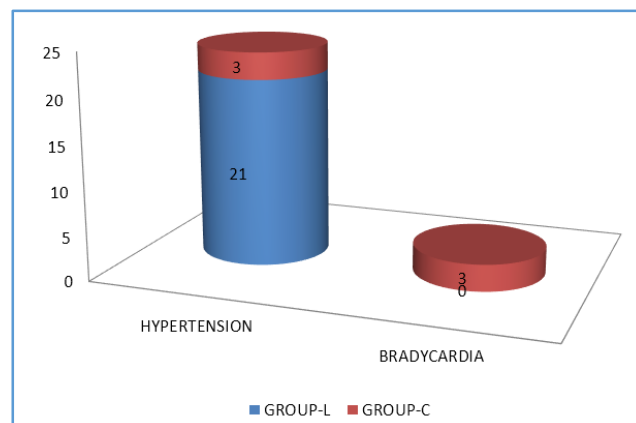
Mean arterial pressures 10 min after intubation ranged from 115 – 72 mmHg in group - L and ranged from 112 – 77 mmHg in group – C. Their mean $\pm$ SD in group – L vs group – C are 85.10 $\pm$ 11.96 vs 88.20 $\pm$ 10.58. After CO<sub>2</sub> insufflation mean arterial pressures ranged from 72 – 111 mmHg in group – L and ranged from 102 – 79 mmHg in group – C. Their mean $\pm$ SD in group – L vs group – C are 92.20 $\pm$ 12.28 vs 88.50 $\pm$ 8.69. No statistical significance is noted in between the groups 10 min after insufflation ( $p=0.2$ ) and after CO<sub>2</sub> insufflation ( $p=0.1$ ).

Mean arterial pressures recorded in group –L vs group - C at 5 min after CO<sub>2</sub> insufflation and mean  $\pm$  SD is 101.50 18.30 vs 90.00 $\pm$ 6.63 ( $p=0.002$ ), 10 min after CO<sub>2</sub> insufflation and mean $\pm$ SD is 101.90 $\pm$ 13.70 vs 93.00 $\pm$ 7.46 ( $p=0.003$ ), 15 min after CO<sub>2</sub> insufflation and mean $\pm$ SD is 101.50 $\pm$ 6.73 vs 93.70 $\pm$ 6.05 ( $p=0.0001$ ), 20 min after CO<sub>2</sub> insufflation and mean $\pm$ SD is 105.20 $\pm$ 16.99 vs 95.60 $\pm$ 8.62 ( $p=0.008$ ), 30 min after CO<sub>2</sub> insufflation and mean $\pm$ SD is 100.20 $\pm$ 9.10 vs 95.20 $\pm$ 6.85 ( $p=0.01$ ). All the variables showed statistical significance in between the groups.

10 min after CO<sub>2</sub> release mean $\pm$ SD of mean arterial pressure in group – L vs group – C are 102.60 $\pm$ 8.11 vs 90.20 $\pm$ 6.23 and 10 min after recovery mean $\pm$ SD of mean arterial pressure in group – L vs group – C are 103.60 $\pm$ 7.95 vs 85.70 $\pm$ 4.96. Both the variables showed high statistical significance ( $p=0.0001$ ).

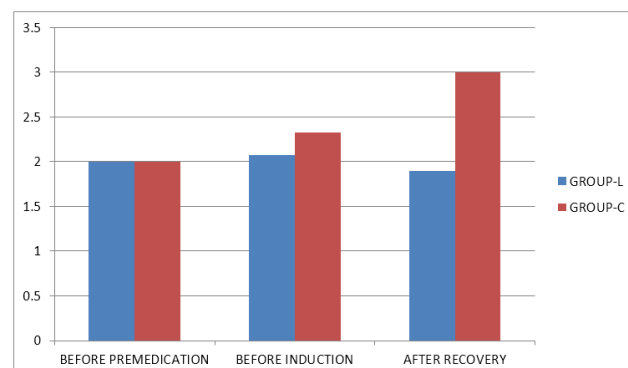
**ADVERSE EFFECTS:** 21 patients in group – L had raised mean arterial pressures > 110 mmHg and required Nitroglycerine 0.5 – 5  $\mu$ g/kg/min when compared to 3 patients of group – C.

3 patients of group – C had bradycardia (heart rate < 60 beats/ min) and required I.V atropine 0.5mg when compared to group – L patients.



**Figure 6: Adverse effects of both groups**

**SEDATION SCORES:** Sedation scores were recorded before premedication, before induction and 10 min after recovery. Significance in sedation scores were evaluated by Mann-Whitney test. Mean $\pm$ SD sedation scores preoperative (2 vs 2), before induction (2.07 $\pm$ 0.25 vs 2.33 $\pm$ 0.47) and post operatively (1.90 $\pm$ 0.30 vs 3.00 $\pm$ 0.91) were assessed between the groups (Group – L vs Group – C). There is no statistical significance in premedication sedation scores in between the groups. Sedation scores before induction ( $p=0.009$ ) and scores 10 min after recovery ( $p=0.0001$ ) which are highly significant in group – C compared to group – L.



**Figure 7: Sedation scores in between groups**

**DISCUSSION:** Laparoscopic surgery became a corner stone in the treatment of many surgical procedures like cholecystectomy, appendectomy, hernia repair, varicocoele ligation, nephrectomy, hysterectomy and several of gynaecological diagnostic and therapeutic procedures. This opened a sub speciality in anaesthesia for laparoscopy. Laparoscopic anaesthesia aims at optimising conditions for laparoscopy and attenuating several systemic changes that occur in laparoscopic surgery. Utmost importance is given to the hemodynamic changes induced during laparoscopic anaesthesia and surgery. Even though laparoscopy became popular as early as 19<sup>th</sup> century, studies for minimising adverse effects for laparoscopy began towards the end of 19<sup>th</sup> century.

The use of Dexmedetomidine, an  $\alpha_2$  agonist in attenuating hemodynamic response to laparoscopy was studied in 1992.<sup>13</sup> Since then many studies were conducted

on several pharmacological agents which are beneficial in attenuating hemodynamic changes  $\alpha$ -2 agonists like Clonidine and Dexmedetomidine are the novel drugs that came into medical practice and are used in anaesthetic practice for sedation, to decrease requirement of anaesthetic drugs and also to control hemodynamic changes during surgical and anaesthetic stress. Jean L Joris (1998) studied the effect of intravenous Clonidine on hemodynamic changes and their endocrine correlates during laparoscopy and concluded that Clonidine premedication before pneumoperitoneum reduces catecholamine release and attenuates hemodynamic changes to laparoscopy.<sup>14</sup> 60 ASA grade I and II patients including both males and females posted for elective laparoscopic cholecystectomy were studied with 30 patients in each group. Our study recorded 33 female patients out of sixty subjects in the study, reiterating the clinical data of female preponderance in cholelithiasis. Shiv K Sarin and Vir S Negi in 1995 emphasised the similar finding in their study of prevalence of first degree female relatives of cholelithiasis.<sup>15</sup>

Oral premedication was given 60-90 min before surgery and the vital parameters like heart rate, mean arterial pressure and sedation scores were recorded before premedication and at predetermined times during intra-operative period.

Heart rates between the two groups before premedication were comparable and there is no statistically significant change in the heart rates between the groups. There is no change in heart rate between premedication and before induction in group -L, as Labetalol does not alter heart rate.

Joseph S. Bernstein et al<sup>16</sup> 1989 studied the effect of two intravenous doses of labetalol (0.25 and 0.75 mg/kg) with placebo in partial attenuation of hemodynamic responses to rapid sequence induction and intubation. They found that there is significant rise in heart rate in all the three groups. But there is significantly lower increase of peak heart rates in Labetalol group when compared to placebo (33 $\pm$ 2 and 27 $\pm$ 3 vs 44 $\pm$ 7 beats/minute). In the present similar increase in heart rate 1 min after intubation was found in both the groups, but the peak rise in heart rate is more in group - L when compared to group - C (96.40 $\pm$  13.41 vs 73.23 $\pm$ 18.35 beats per min). The similar findings of increased heart rate were found in the study by Chung KS et al 1992, where he reported a rise in heart rate after intubation within the group.<sup>17</sup> But there is significant rise in placebo group when compared to Labetalol group.

In the present study there is significant increase in heart rates in group - L throughout the study period when compared to group - C. Clonidine on the other hand had better control of heart rate after intubation when compared to Labetalol even though it could not completely attenuate the pressor response to laryngoscopy (a rise in heart rate from 69.30 $\pm$ 7.58 to 73.23 $\pm$ 18.35 beats per min). U. A. Carabine et al 1991 studied and compared the effects of intravenous Clonidine with placebo given 15 min before induction.<sup>18</sup> He reported that Clonidine attenuated the pressor response to intubation well when compared to

placebo. He also emphasised that both the doses of Clonidine could not completely attenuate either heart rate or blood pressure.

H. Talebi<sup>19</sup> et al 2010 studied the effects of oral Clonidine (200 $\mu$ g) premedication on haemodynamic response to laryngoscopy and tracheal intubation. He concluded that Clonidine has better control on heart rate and blood pressure variability during laryngoscopy and intubation when compared with that in the placebo group. This is proved in the current study that oral premedication with Clonidine (300 $\mu$ g) in comparison with Labetalol (200mg).

Malek J et al 1999 conducted a study on attenuating hemodynamic responses to intubation by oral, intramuscular and intravenous Clonidine.<sup>20</sup> They found that both oral and parenteral administration of Clonidine decreased stress response to intubation. They also concluded that parenteral administration of Clonidine is much more effective in attenuating stress response to laryngoscopy. This difference may be due to early systemic availability of Clonidine which resulted in better hemodynamic control. In another study where he compared oral and intramuscular Clonidine, they observed the same difference between oral and intramuscular Clonidine in attenuation of hemodynamic changes during laparoscopy.

Tanmoy Roy et al 2011, compared oral and intravenous medications of Clonidine and concluded that intravenous Clonidine has better hemodynamic stability during laparoscopic anaesthesia.<sup>21</sup>

In the present study heart rates 10 min after intubation returned nearly to baseline values. In group - L the mean change from intubation value is 96.40 $\pm$ 13.41 to 78.13 $\pm$ 7.51 and in group - C the mean change from intubation value is 73.23 $\pm$ 18.35 to 76.50 $\pm$ 5.57. There is no significant change in heart rate values ( $p=0.34$ ) in both the groups.

Heart rates in the present study increased throughout the study period in both the groups but are statistically non-significant in between the two groups. But the increase in heart rate in group - L is significant when compared to group - C throughout the study period.

Dhiraj Bhandari et al 2012 compared oral Clonidine premedication in laparoscopic surgery and the increase in heart rate is significant in placebo group when compared to the Clonidine group.<sup>22</sup> They concluded that Clonidine offered better heart rate control during intubation and insufflation periods.

Kumkum Gupta et al 2011 conducted a study comparing oral pregabalin, Clonidine and placebo for attenuation of hemodynamic responses to laparoscopic cholecystectomy.<sup>23</sup> They concluded that there is significant decrease in heart rates in pregabalin and Clonidine groups when compared to placebo group. Out of pregabalin and Clonidine groups Clonidine has better control of heart rate after intubation and during pneumoperitoneum.

J MacPherson et al 1997, conducted study on premedication with oral Labetalol and oral Clonidine and they found that Clonidine group patients had lower heart rate intraoperatively.<sup>24</sup> In our study also we found lower

heart rates in Clonidine group when compared to Labetalol group.

In the present study 3 patients (10%) of group – C developed bradycardia (heart rate <60 beats per min) when compared to group – L. This similar finding of bradycardia with Clonidine is also noted in the study by Kumkum Gupta et al 2011 where they studied hemodynamic stability with oral Clonidine vs oral pregabalin. Dr Dhiraj Bhandari et al in 2012 in his study on hemodynamic stability by oral Clonidine in laparoscopic cholecystectomy also reported Clonidine induced bradycardia in one case when compared to placebo group and they recommended routine use of atropine in premedication to counter act this effect.

Laparoscopic surgery due to creation of pneumoperitoneum stimulates the release of catecholamines and vasopressin. This leads to the increase of systemic vascular resistance and thereby increase in systolic, diastolic and mean arterial blood pressure.

Jeal L. Joris et al in 1993 evaluated the hemodynamic changes during laparoscopy and found that laparoscopy significantly increases mean arterial pressure, systemic and pulmonary vascular resistance and decrease in cardiac index.<sup>25</sup>

Jeal L. Joris et al in 1998 conducted study on hemodynamic changes to laparoscopy and their endocrine correlates. They concluded that vasopressin and catecholamine release is responsible for increase in systemic vascular resistance and also emphasized the use of Clonidine for effective attenuation of hemodynamic changes.

Toshu Yotsui 2001 studied the effects of Clonidine premedication in laparoscopic surgery.<sup>26</sup> He found that Clonidine premedication only prevents sympathetic hyperactivity by decreasing epinephrine but does not prevent hypothalamo-pituitary-adrenocortical responses as seen by unaltered cortisol and ACTH levels.

In the present study mean arterial pressures before giving premedication were comparable in between the groups. For the mean arterial pressures recorded before induction there is significant difference between the two groups. Group– L versus Group – C is  $97.43 \pm 8.93$  versus  $79.10 \pm 9.67$  in group – C there is significant difference in the mean arterial pressures before premedication ( $91.93 \pm 5.05$ ) and after premedication which is recorded just before induction ( $79.10 \pm 9.67$ ). J Macpherson et al 1997 in their study on premedication using oral Labetalol and oral Clonidine obtained the similar findings of decreased mean arterial blood pressures.

Mean arterial blood pressures one minute after intubation in group – L is  $115.00 \pm 12.29$  when compared to group – C is  $95.30 \pm 8.04$ . There is significant raise in mean arterial blood pressure in group – L when compared to group –C ( $p=0.0001$ ).

E Inada et al 1989 studied the effects of intravenous Labetalol in comparison with lidocaine in the attenuation of hemodynamic response to laryngoscopy.<sup>27</sup> Their results displayed that the rise in mean arterial pressures in all the groups were similar. Hence they concluded that Labetalol

attenuates the increase in heart rates rather than blood pressure during intubation.

Similar results were observed in a study by Chung KS et al 1992 where they studied intermediate dose of Labetalol 4mg/kg on heart rate and blood pressure during laryngoscopy. They concluded that Labetalol attenuated the tachycardia during laryngoscopy but has minimal effect on blood pressure.

Sarvesh P Singh<sup>28</sup> et al 2012 compared the efficacy of Labetalol and esmolol in attenuating haemodynamics to laryngoscopy. Their results showed an increase in mean arterial blood pressure in all the groups. They concluded that Labetalol has better control on heart rate and rate pressure product over esmolol. The better attenuation in mean arterial pressure may be due to intravenous drug administration.

The mean arterial pressures recorded 10 min after intubation and after CO<sub>2</sub> insufflation showed no significant difference in between the groups. The rise in mean arterial pressures in group –L returned to their baseline values 10 min after intubation conferring to the similar findings in the study by Sarvesh P Singh et al 2012 where the raised mean arterial pressures after intubation reached their baseline values 5min after intubation.

In the present study the mean arterial pressures recorded at 5min, 10min, 15min, 20 min, 30 min after CO<sub>2</sub> insufflation showed statistically significant difference in both the groups. Group –L recorded high mean arterial pressures at all these intervals when compared to group –C.

Kumkum Gupta et al 2011 in his study concluded that mean arterial pressures were lower when compared with pregabalin and Clonidine. M. M. Chandrashekaraiiah<sup>29</sup> et al 2011 also confirmed the similar findings of better control of mean arterial pressure in Clonidine group in laparoscopic surgery.

Shivinder Singh and Kapil Arora<sup>30</sup> studied the effect of oral Clonidine premedication on peri-operative haemodynamic response and post-operative analgesic requirement for patients undergoing laparoscopic cholecystectomy.

Mrinmoy D et al 2005<sup>31</sup> studied haemodynamic changes during laparoscopic cholecystectomy and beneficial effects of oral Clonidine premedication.

Sung CS<sup>32</sup> showed the effect of oral Clonidine premedication on perioperative hemodynamic response and post-operative analgesic requirement for patients undergoing laparoscopic cholecystectomy.

In our study hypotension is not observed in either of the groups. Hypertension is observed in 21(70%) patients in group – L compared to 3(10%) in group – C which is treated by 0.5-5µg/kg/min of nitroglycerine infusions.

Sedation scores were recorded before premedication, before induction and 10 min after recovery using Ramsey sedation score. Sedation scores in group – C were significant when compared to group – L patients.

Further the study can be improvised by including intraoperative analgesic requirement, post-operative first analgesic request, different oral dosages and by different

routes in the current study to evaluate the other beneficial effects of Clonidine during laparoscopic surgery.

**CONCLUSION:** Oral Clonidine has better control on the rise in heart rate and mean arterial pressures during laryngoscopy and laparoscopy compared to oral Labetalol.

#### REFERENCES:

- Grace PA, Quereshi A, Coleman J, et al. Reduced post-operative hospitalisation after laparoscopic cholecystectomy. *Br J Surg* 1991;78(2):160-2.
- Vallina VL, Velasco JM, McCulloch CS. Laparoscopic versus conventional appendectomy. *Ann Surg* 1993;218(5):685-692.
- Glaser F San, Gerd A Sannwald, Heinz J Buhr, et al. General stress response to conventional and laparoscopic cholecystectomy. *Ann Surg* 1995; 221(4):372-380.
- Wolf Jr JS, Monk TG, McDougall EM, et al. Extra-peritoneal approach and subcutaneous emphysema are associated with greater absorption of carbon dioxide during laparoscopic renal surgery. *J Urol* 1995;154(3):959-63.
- Whiston RJ, Eggers KA, Morris RW, et al. Tension pneumothorax during laparoscopic cholecystectomy. *Br J Surg* 1991;78(11):1325.
- Knos GB, Sung YF, Toledo A. Pneumopericardium associated with laparoscopy. *J Clin Anesth* 1991;3(1):56-59.
- Brimacombe J, Orlande H, Graham D. Endobronchial intubation during upper abdominal laparoscopic surgery in the reverse trendelenburg position. *Anesth Analg* 1997;78:607.
- Greville AC, Clements EA, Erwin DC, et al. Pulmonary air embolism during laparoscopic laser cholecystectomy. *Anaesthesia* 1991;46(2):113-114.
- Metin Berberouli, Osman Nuri Dilek, Feyzan Ercam, et al. Effect of CO<sub>2</sub> insufflation rate on the post laparoscopic shoulder pain. *Journal of laparoscopic and advanced surgical techniques* 1998;8(5):273-277.
- Walder AD, Aitkenhead AR. Role of vasopressin in the haemodynamic response to laparoscopic cholecystectomy. *Br J Anaesth* 1997;78(3):264-66.
- Wahba RW, Tessler MJ, Kleiman SJ. Acute ventilatory complications during laparoscopic upper abdominal surgery. *Can J Anaesth* 1996;43(1):77-83.
- Hayashi Y, Maze M. Alpha 2 adrenoceptor agonists and anesthesia. *Br J Anesthesia* 1993;71:108-18.
- Aho M, Scheinin M, Lehtinen AM, et al. Intramuscularly administered dexmedetomidine attenuates hemodynamic and stress hormone responses to gynecologic laparoscopy. *Anesth Analg* 1992;75(6):932-9.
- Joris JL, Chiche JD, Canivet JL, et al. Hemodynamic changes induced by laparoscopy and their endocrine correlates: Effects of clonidine. *J Am Coll Cardiol* 1998;32(5):1389-96.
- Shiv K Saren, Vir S Negi, Richa Dewan, et al. High familial prevalence of gallstones in the first-degree relatives of gallstone patients. *Hepatology* 1995;22(1):138-141.
- Joseph S Bernstein, Thomas J Ebert, David F Stowe, et al. Partial attenuation, of hemodynamic responses to rapid sequence induction and intubation with labetalol (Abstract). *Journal of Clinical Anaesthesia* 1989;1(6):444-451.
- Sam Chung K, Raymond S Sinatra, Jonathan D Halevy, et al. A comparison of fentanyl, esmolol, and their combination for blunting the haemodynamic responses during rapid-sequence induction. *Canadian Journal of Anaesthesia* 1992;39(8):774-9. (Impact Factor: 2.53). DOI: 10.1007/BF03008287.
- Carabine UA, Wright PM, Moore J. Preanaesthetic medication with Clonidine: a dose-response study. *Br J Anaesth* 1991;67(1):79-83.
- Talebi H, Nourozi A, Fateh S, et al. Effects of oral clonidine premedication on haemodynamic response to laryngoscopy and tracheal intubation: A clinical trial. *Pakistan Journal of Biological Sciences* 2010;13:1146-1150.
- Málek J, Knor J, Kurzová A, et al. Adverse hemodynamic changes during laparoscopic cholecystectomy and their possible suppression with clonidine premedication. Comparison with intravenous and intramuscular premedication. *Rozhl Chir* 1999;78(6):286-91.
- Tanmoy Roy. Attenuation of pressor response to endotracheal intubation–intravenous vs. oral clonidine. Diss. Rajiv Gandhi University of Health Sciences, 2008.
- Dhiraj Bhandari, Sucheta Tidke, Vijay Sharma, et al. Hemodynamic changes associated with laparoscopic cholecystectomy: Effect of oral clonidine premedication. *IOSR Journal of Pharmacy (IOSRPHR)* ISSN: 2250-3013, 2012;2(4):72-77.
- Kumkum Gupta, Deepak Sharma, Prashant K Gupta. Oral premedication with pregabalin or clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy: A comparative evaluation. *Saudi Journal of Anaesthesia* 2011;5(2):179-184.
- MacPherson J, Kennedy R, Gin T. Comparison of oral premedication for laparoscopic cholecystectomy: Labetalol versus clonidine. *Anaesthesia and Intensive Care* 1997;25(6):720.
- Joris JL, Noirot DP, Legrand MJ, et al. Hemodynamic changes during laparoscopic cholecystectomy. *Anesth Analg* 1993;76:1067-71.
- Toshu Yotsui. Clonidine premedication prevents sympathetic hyperactivity but does not prevent hypothalamo-pituitary-adrenocortical responses in patients undergoing laparoscopic cholecystectomy. *J Anesth* 2001;15:78-82.



27. Inada E, Cullen DJ, Nemeskal AR, et al. Effect of labetalol or lidocaine on the hemodynamic response to intubation: a controlled randomized double-blind study. *J Clin Anesth* 1989;1(3):207-13.
28. Sarvesh P Singh, Abdul Quadir, Poonam Malhotra. Comparison of esmolol and labetalol, in low doses, for attenuation of sympathomimetic response to laryngoscopy and intubation. *Saudi J Anaesth* 2010;4(3):163–168.
29. Chandrashekaraiah MM, Upadya M, Jayachandran SP, et al. Effects of clonidine premedication on hemodynamic changes during laparoscopic cholecystectomy – A randomized control study. *Applied Cardiopulmonary Pathophysiology* 2011;15: 91-98.
30. Shivinder Singh, Kapil Arora. Effect of oral clonidine premedication on perioperative haemodynamic response and post-operative analgesic requirement for patients undergoing laparoscopic cholecystectomy. *Indian J Anaesth* 2011;55(1):26-30.
31. Mrinmoy D, Manjushree R, Gauri M. Haemodynamic changes during laparoscopic cholecystectomy: Effect of oral clonidine premedication. *Indian J Anaesth* 2007;51:2005-10.
32. Sung CS, Lin SH, Chan KH, et al. Effect of oral clonidine premedication on perioperative hemodynamic response and post-operative analgesic requirement for patients undergoing laparoscopic cholecystectomy. *Acta Anaesthesiol Sin* 2000; 38(1):23-9.