A Study of the Haemodynamic Response to Oral Clonidine as Pre–medication in Laparoscopic Surgeries

Alka Koshire[1], Rupesh Sinha[2] and Utkarsh S. Rayakar[3*]

[1]Professor, Department of Anaesthesiology at MVPS Dr. Vasantrao Pawar Medical College, Nasik; alkakoshire15@gmail.com

[2]MD Anaesthesia, Department of Anaesthesiology at MVPS Dr. Vasantrao Pawar Medical College, Nasik; rupesh_sinha7585@yahoo.co.in

[3]Senior Resident, Department of Anaesthesiology at MVPS Dr. Vasantrao Pawar Medical College, Nasik; utkarsharaykar1000@gmail.com

Abstract

Introduction: Laparoscopic surgery is a boon for surgeons as it reduces tissue trauma, post–operative morbidity, hospital stay and healthcare costs. However, it is not possible to perform a laparoscopic procedure unless a proper anaesthetic procedure is available to combat the additional haemodynamic stress of pneumoperitoneum with CO_2 insufflation and the patient's position[1,2]. Use of an alpha–2 against tablets such as clonidine helps in blunting the adverse haemodynamic response during laparoscopy[3,4]. **Aims of this study were**: To study haemodynamic response to oral clonidine tablet during endotracheal intubation in laparoscopic surgery. To study haemodynamic response to oral clonidine tablet in the intraoperative period in laparoscopic surgery. To study side–effects of clonidine. **Materials and Methods:** This prospective placebo controlled study was conducted in the Department of Anaesthesiology, in a tertiary health care centre attached to a medical college. A total of 60 patients scheduled for laparoscopic surgery in the age group of 18–60 years belonging to ASA grade 1 & 2 were included in the study. After appropriate preoperative evaluation they were divided into 2 groups. Group C (n = 30) received Tab. Clonidine 150 mcg orally. Group V (n = 30) received a placebo Vitamin tablet. After appropriate premedication, patients were given general anaesthesia. Various parameters like pulse rate, Non–Invasive Blood Pressure (NIBP) including systolic, diastolic and mean arterial pressure, $ETCO_2$ were measured pre–operatively, during intubation and at various points intraoperatively. Statistical analysis was done using statistical package for Social Sciences Ver. 18. The results was expressed in mean and standard deviation. Independent t–test was used to compare mean of the two groups. For the purpose of this study, 95% confidence limit was chosen and corresponding p–value <0.05 was taken as statistically significant. **Conclusion:** We found that pre–medication with oral clonidine provides haemodynamic stability and protection against the stress response triggered by laryngoscopy, intubation and pneumoperitoneum with CO_2 in patients undergoing laparoscopic surgery. It also was found to reduce nausea, vomiting and shivering post–operatively.

Keywords: Clonidine, Haemodynamic, Laparoscopy.

1. Introduction

Previously, the only specialty performing laparoscopy on a widespread basis was gynaecology, mostly for short, simple procedures or tubal ligations. With the advent of newer technologies laparoscopic procedures evolved as a therapeutic modality. Phillipe Mouret, introduced laparoscopic cholecystectomy in 1987[5] which started a new era of minimally invasive surgery. However laparoscopy is associated

*Author for correspondence

with certain haemodynamic changes which are undesirable.

1.1 Haemodynamic Changes during Laparoscopy

Laparoscopic surgeries are commonly carried out through trans–peritoneal or retroperitoneal approaches with insufflations of CO_2 and in some cases with another inert gases like helium or argon. Haemodynamic changes in laparoscopy are a result of the combined effect of pneumoperitoneum, patient position, anaesthetic agents and hypercapnea secondary to the absorbed CO_2[6]. These disturbances are characterized by decrease in cardiac output, increase in arterial pressure and elevation of systemic and pulmonary vascular resistance. Similarly, the procedure of endotracheal intubation also elicits a haemodynamic response, which involves activation of the adrenocortical system, release of catecholamines and increase in heart rate and blood pressure[7]. Though transitory, they may be deleterious to the patient because of the increased cardiac workload involved.

Recently oral clonidine has been found to have properties which blunt the undesirable haemodynamic changes associated with laparoscopy and intubation[8,9]. Clonidine has been utilized as a preoperative medication providing anxiolysis, sedation, analgesia, haemodynamic stability, anti–sialogogue and anti–emetic effect. It blunts the stress response to surgical stimuli and the narcotic and anaesthetic doses are also reduced. In addition, clonidine increases cardiac baroreceptor reflex sensitivity to increase in blood pressure and thus stabilizes it.

This study has been undertaken to elucidate the role of oral clonidine in blunting the adverse haemodynamic responses during endotracheal intubation and laparoscopy.

2. Material and Methods

A total of 60 patients scheduled for laparoscopic surgery in the age group of 18–60 years belonging to ASA grade 1 or 2 were included in this study. Written informed consent was obtained from every patient.

After preliminary screening, the patients were thoroughly examined clinically one day prior to the surgery as a part of the pre–anaesthetic evaluation. Routine investigations such as blood haemoglobin, serum urea and creatinine, blood sugar, serum electrolytes, liver function tests, urine analysis, chest X–ray, ECG and cardiological evaluation reports were reviewed. Resting blood pressure and heart rate were recorded to serve as a baseline value. The patients were selected based on certain inclusion and exclusion criteria.

2.1 Inclusion Criteria

1. Age between 18 to 60 years.
2. ASA (American Society of Anaesthesiolgists) Grade 1 & 2.
3. Written informed consent.

2.2 Exclusion Criteria

1. ASA (American Society of Anaesthesiolgists) Grade 3 & 4.
2. Pregnant and lactating females.
3. Patients with any cardiac disease.
4. Patients with any respiratory disease.
5. Neurological and psychiatric illnesses.
6. Uncontrolled hypertension.

Patients were then divided into two groups according to the premedication they received.

Group C (n=30) received Tab. Clonidine 150 mcg orally.

Group V (n=30) received a placebo Vitamin tablet.

2.3 Pre–operative Preparations

All patients were kept fasting overnight after 10 pm. On the day of the surgery, patients received the study drug or placebo in the pre–operative room around 60–90 minutes prior to surgery administered with a sip of water. On arrival in the operation theatre, monitoring was started and baseline readings were taken.

2.4 Pre–medication

All patients were premedicated with Inj. Glycopyrrolate 0.2 mg IV and Inj. Ondansetron 4 mg IV.

2.5 Induction, Intubation and Maintenance

After pre–oxygenating the patients with 100% oxygen for 5 minutes, induction was performed using Inj. Propofol 1–2 mg/kg body weight IV. Laryngoscopy and endotracheal intubation with an appropriately sized cuffed tube was facilitated by Inj. Succinylcholine 1.5–2 mg/

kg body weight IV. Anaesthesia was maintained with Nitrous Oxide (50%), Oxygen (50%) and Isoflurane. Intraoperatively muscle relaxant used was Inj. Vecuronium bromide 0.08–0.10 mg/kg. Intraoperatively the following vital parameters were monitored and recorded:

a. Heart rate (Pulse Rate).
b. Non–Invasive BP (NIBP) including systolic, diastolic and mean arterial pressure.
c. $ETCO_2$.

Pneumoperitoneum was created by insufflations of CO_2 and the operating table was tilted by about 15° in Trendelenburg or Reverse–Trendelenburg position as the surgeon required. Intra–abdominal pressure was not allowed to exceed 15 cm H_2O throughout the procedure. After pneumoperitoneum, necessary changes to the ventilator settings were made to maintain normocapnea. The above mentioned parameters were recorded at the following points in time:

1. Before premedication.
2. Before induction.
3. During intubation.
4. After intubation.
5. Before pneumoperitoneum.
6. 15 minutes after pneumoperitoneum.
7. 30 minutes after pneumoperitoneum.
8. At the release of pneumoperitoneum.
9. Extubation.
10. 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 IV and Inj. Glycopyrrolate 8 mcg/kg IV. Patient was then extubated and transferred to the recovery room. Patients were observed for any complications during this period such as hypotension, apnea, bradycardia, coughing, nausea, vomiting or shivering.

Table 1. Baseline demographic characteristics of study and placebo group

	Group C (n=30)	Group V (n=30)	p-value
Male	6	10	>0.05
Female	24	20	>0.05
Age(years)	36.5	34.8	>0.05
Weight (kg)±SD	55.7±4.8	56.6±6.02	>0.05

3. Results

3.1 Demographic and Baseline Characteristics

Table 1 shows the baseline characteristics of the study and placebo group. It can be seen that both the study and placebo group had a comparable number of male and female patients. Most of the patients were of the middle age group. The mean weight of patients in both the groups was comparable. The differences in sex, age and weight were not statistically significant.

3.2 Preoperative Vital Parameters in Study and Placebo Group

Preoperative vital parameters in both the groups were comparable and not statistically significant as seen in Table 2.

3.3 Pulse Rate Changes in Study and Placebo Group

In our study, it was found that the pulse rate was comparatively lower in the study group as compared to the placebo group in general. There was more variation in the pulse rate in the placebo group as compared to the study group. In the study group, the mean pulse rate remained close to the baseline values. (Table 3 & Figure 1).

3.4 Mean Arterial Pressure Changes in Study and Placebo Group

In our study it was found that the MAP was in the range of 94.1 to 104.3 mmHg in the study group, whereas in the placebo group it was in the range of 94.7 to 108.8 mmHg. It was found that the MAP remained closer to the baseline values in the study group as compared to the placebo group. (Table 4 & Figure 2).

Table 2. Preoperative vital parameters in study and placebo group±SD

Vital Parameters	Group C	Group V	p-value
PR(beats/min)	79.66 ± 4.61	82.33 ± 5.17	>0.05
RR(breaths/min)	18.03 ± 1.12	18.76 ± 1.38	>0.05
SBP(mmHg)	126.13 ± 4.13	124.47 ± 5.74	>0.05
DBP(mmHg)	82.73 ± 2.25	79.86 ± 3.89	>0.05

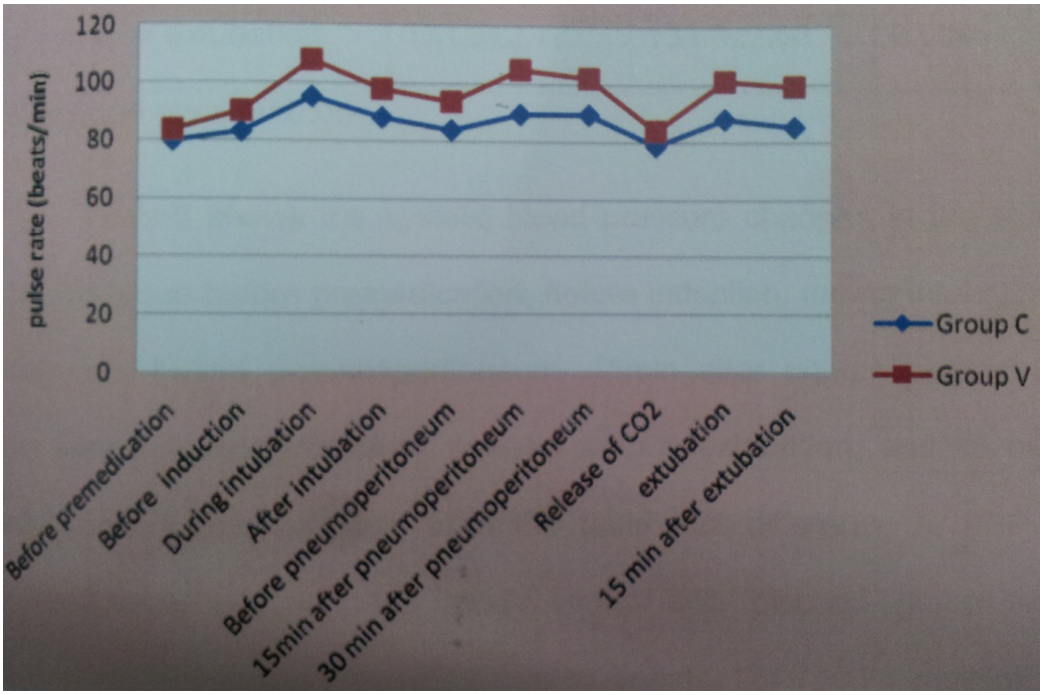

Figure 1. Pulse rate changes in study and placebo groups.

Table 3. Pulse rate changes in study and placebo groups±SD

Pulse Rate (beats/min)	Group C	Group V	p–value
Before premedication	79.7 ± 4.61	83.3 ± 5.17	>0.05
Before induction	83.0 ± 4.47	89.7 ± 4.97	0.01
During intubation	95.0 ± 4.12	107.8 ± 4.76	0.000
After intubation	88.2 ± 4.04	98.0 ± 6.29	0.000
Before pneumoperitoneum	84.0 ± 3.69	93.7 ± 5.85	0.000
15 minutes after pneumoperitoneum	89.5 ± 3.31	105.0 ± 4.12	0.000
30 minutes after pneumoperitoneum	89.2 ± 4.22	101.8 ± 3.72	0.000
At the release of pneumoperitoneum	78.8 ± 3.22	83.7 ± 5.19	0.000
Extubation	88.0 ±3.12	101.2 ± 4.71	0.000
15 minutes after extubation	85.0 ± 2.89	99.3 ± 4.74	0.000

3.5 $ETCO_2$ Changes in Study and Control Group

$ETCO_2$ changes were found to be not statistically significant according to our study (Table 5).

4. Discussion and Conclusion

Unwarranted fear and anxiety which hinders the patient in facing the operation with calmness and confidence, has led to the search for an ideal premedicant. A search has been constantly on for mitigating this response by employing many agents among which clonidine has been one of the drugs to come under a lot of scrutiny in the recent years.

Clonidine gained our approval for this study because of the added advantages it offered like its efficacy in mitigating the sympathetic response to laryngoscopy and intubation, its effect on reducing anxiety, its ability to reduce overall anaesthetic requirement and its property of potentiating post–operative analgesia.

Following conclusions were drawn from this study:

1. Clonidine attenuated the reflex tachycardia and hypertensive response to laryngoscopy and intubation significantly when compared to the placebo.
2. Clonidine reduces the increase in Mean Arterial Pressure in response to pneumoperitoneum.
3. There were significantly more episodes of hypertension in the placebo group whereas the clonidine group showed a more stable peri–operative haemodynamic status.

Table 4. Mean arterial pressure changes in study and placebo group±SD

Mean Arterial Pressure (mmHg)	Group C	Group V	p-value
Before premedication	97.2 ± 2.44	94.7±3.94	>0.05
Before induction	101.3 ± 2.66	96.3 ± 4.14	0.000
During intubation	104.3 ± 1.85	107.8 ± 2.3	0.000
After intubation	101.6 ± 2.03	105.3 ± 2.09	0.000
Before pneumoperitoneum	98.7 ± 1.98	101.9 ± 2.03	0.000
15 minutes after pneumoperitoneum	102.6 ± 1.79	108.8 ± 2.81	0.000
30 minutes after pneumoperitoneum	101.7 ± 3.37	106.7 ± 2.52	0.000
At the release of pneumoperitoneum	94.1 ± 2.73	95.3 ± 3.23	0.000
Extubation	101.5 ± 2.14	107.7 ± 2.12	0.000
15 minutes after extubation	99.2 ± 2.03	105.3 ± 2.1	0.000

Table 5. $ETCO_2$ changes in study and control group±SD

$ETCO_2$ (mmHg)	Group C	Group V	p-value*
Before premedication	31.3 ± 1.08	31.5 ± 1.61	0.351
Before induction	32.3 ± 1.76	32.7 ± 2.44	0.856
During intubation	34.9 ± 1.20	35.2 ± 1.47	0.445
After intubation	35.2 ± 1.35	35.5 ± 1.52	0.249
Before pneumoperitoneum	35.5 ± 1.38	36.3 ± 1.24	0.017
15 minutes after pneumoperitoneum	36.0 ± 1.65	36.2 ± 1.80	0.710
30 minutes after pneumoperitoneum	35.1 ± 1.85	35.1 ± 1.68	0.942
At the release of pneumoperitoneum	33.7 ± 1.27	33.7 ± 1.52	0.927
Extubation	37.6 ± 1.16	37.9 ± 1.24	0.243
15 minutes after extubation	32.1 ± 1.25	31.9 ± 1.20	0.530

*p-value <0.05 is significant.

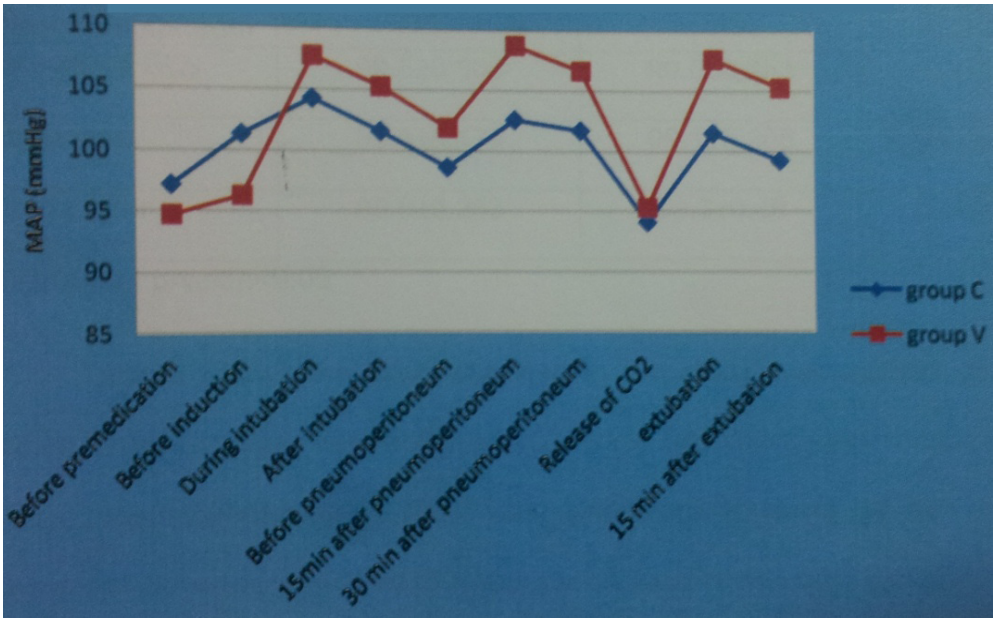

Figure 2. Mean arterial pressure changes in study and placebo group.

4. Clonidine effectively decreased the incidence of nausea, vomiting and shivering post–operatively.

In conclusion, pre–medication with oral clonidine provides protection against stress response triggered by laryngoscopy, intubation and pneumoperitoneum with CO_2 in patients undergoing laparoscopic surgeries. Clonidine also proved to be a better agent for attenuation of pressor response to laryngoscopy and intubation. It also reduces nausea, vomiting and shivering post–operatively. Thus oral clonidine as a pre–medicant can be beneficial for patients undergoing laparoscopic surgeries (Table 6).

Table 6. Perioperative adverse events in study and placebo groups

Complication	Group C n(%)	Group V n(%)
Hypertension	–	7(23)
Hypotension	2(6)	–
Bradycardia	2(6)	–
Vomiting	–	4(13.3)
Shivering	1(3.3)	6(20)

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