

## A Comparative Evaluation of Intravenous Clonidine on Haemodynamic Stress Response during Pneumoperitoneum in Laparoscopic Abdominal Surgeries

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### Original Research Article

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**Abstract:** Laparoscopic surgeries are gaining importance nowadays because of their benefits and less complication rate when compared with open surgical procedures. But laparoscopic procedures are not free from complications too. Pneumoperitoneum created during laparoscopic procedure leads to hemodynamic instability. So many pharmacological agents are used to subside effect of pneumoperitoneum. Clonidine is one such agent which is an  $\alpha$ -2 agonist. This randomized control study was conducted on 60 patients of ASA grade 1 and 2 after taking ethics committee approval. Group CL (n=30) clonidine is infused during the surgery and in group C (n=30) normal saline is infused. Diastolic and systolic blood pressure, mean arterial blood pressure and heart rate were measured throughout the procedure till 30 minutes after the procedure. Sedation score was also measured after the surgery. Effect of intubation and laryngoscopy induced stress response, creation of pneumoperitoneum, reversal of pneumoperitoneum and extubation was seen over heart rate, SBP, DBP and MAP in both the groups but was significantly less in the clonidine(CL) group compared to the control(C) group showing better stability of the hemodynamic vitals in the patients given clonidine intraoperatively ( $P<0.05$ ). Clonidine suppresses pneumoperitoneum induced hemodynamic instabilities in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

**Keywords:** Blood pressure, Clonidine, General anaesthesia, Heart rate, Sedation.

### INTRODUCTION

Laparoscopic approach is safe and reliable technique with several advantages over the standard open procedure[1,2]. Laparoscopic abdominal surgeries are quite common with complication rate being less than 1.5% and mortality rate less than 0.1% [3]. Because of its less cosmetic scar, less postoperative pain, decreased hospital stay and obviously less mortality, it has become the gold standard for treatment of gall bladder diseases[4].

For laparoscopic abdominal surgeries, anesthesiologists mainly emphasized on maintaining haemodynamic stability by avoiding hypertension, hypotension or tachycardia but the problem has been more complex and most of the haemodynamic instability is persistent during the duration of pneumoperitoneum (PNP) [5, 6] namely carbon dioxide (CO<sub>2</sub>) insufflations and patient positioning[7, 8].

CO<sub>2</sub> is the main gas used for insufflations in laparoscopic procedure although gases like helium and air can also be used[9,10]. The cardiopulmonary changes occur during laparoscopy. Insufflation of CO<sub>2</sub>

and increased IAP (>10 torr) produces significant alterations in haemodynamic parameters characterised by decreased cardiac output, increased arterial pressures, increased systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR)[11, 12]. Pneumoperitoneum decreases thoracopulmonary compliance by 30-50% [13].

Reduction in FRC[14] and atelectasis due to elevation of diaphragm and changes in ventilation and perfusion results from increased airway pressure[15]. Many pharmacological agents like adrenoreceptorblockers[16], beta blockers[17], Ca channel blocker, lidocaine[18], opioids[19], pregabalin[20], magnesium sulfate[21], vasodilators[22], remifentanyl[23] have been used to attenuate these responses with varying success.

Clonidine a centrally acting selective partial  $\alpha$ -2 agonist is known to induce sedation, decrease anaesthetic drug requirement and improvement in perioperative haemodynamic stability by altering blood pressure and heart rate responses to surgical

stimulation, and protection against perioperative myocardial ischemia [24,25].

### MATERIALS & METHODS

After obtaining approval from the ethics committee and well written informed consent from the patients, study was carried out on 90 patients of ASA grade I and II, aged 20-50 years, undergoing laparoscopic cholecystectomy lasting 1-3 hours requiring general anesthesia with endotracheal intubation at J.A Group of Hospitals of G.R. Medical College, Gwalior (M.P), India. Patients were allocated randomly using envelope technique in two groups of 30 each. In group C, normal saline is infused and it is a control group while in group CL, clonidine is infused during the surgery.

Exclusion Criteria were: ASA grade III and above, BMI >30, patients undergoing laparoscopic to open surgery conversion intraoperatively, pneumoperitoneum

duration >90 minutes, known history of allergy or sensitivity or any other reaction to study drugs, patients with cardiopulmonary and respiratory disorders, patients with hypertension on treatment with beta-Blocker, Methyl-dopa, MAO inhibitors, tricyclic antidepressant, patients with psychiatric illness, patients with renal and hepatic dysfunction, pregnant and lactating females.

### Consent

Details of procedure were explained to all the patients during preanaesthetic assessment and an informed and written consent was obtained.

### Patients' grouping

90 patients of ASA grade I & II of either sex scheduled for abdominal surgeries under general anaesthesia were divided into 2 groups (n=30 each) randomly using envelope technique as below:

Group C (n=30)	50 ml normal saline over a period of 10 minutes after induction and before pneumoperitoneum (PNP), followed by a continuous slow infusion at the rate of 0.5 ml/kg/hr.
Group CL (n=30)	Clonidine 1.5µg/kg in 50ml normal saline over a period of 10 minutes after induction and before PNP, followed by a continuous infusion at the rate of 2 µg/kg/hr.

### Preparation of the patient

Upon arrival of the patient in the operation room, intravenous access with 18G cannula was established and 500 mL of crystalloid infusion was started. All the baseline vital parameters (HR, SBP, DBP, MAP), electrocardiography using three lead ECG were monitored. Oxygen saturation (SPO<sub>2</sub>) was monitored by using pulse oximeter. End tidal Carbon dioxide was monitored intraoperatively and kept between 25 and 30 mmHg.

### Anaesthesia procedure and recording

All the drugs were administered by a person who was not involved in the study to avoid bias. Patients were preoxygenated with 100% oxygen at appropriate flow for 3 minutes by facemask. After premedication with i.v. Inj Pentazocine 0.5mg/kg, general anesthesia was induced with i.v. Inj Thiopentone Sodium 5 mg/kg body weight. Endotracheal intubation was facilitated with i.v. Inj. Succinylcholine 1.5 mg/kg body weight and IPPV was done for 60 seconds with 100% oxygen.

Laryngoscopy was done with laryngoscope having Macintosh blade and tracheal intubation done with appropriate size of cuffed endotracheal tube. Cuff was inflated and bilateral equal air entry was checked and then tube was fixed.

General anaesthesia was maintained with nitrous oxide & oxygen (67:33) and Isoflurane (0.5-1%) with Bain's anaesthetic circuit. Loading and

intermittent dosage of non-depolarizing muscle relaxant, IV Atracurium Besylate 0.5mg/kg body weight initially followed by increment doses at 0.1mg/kg was used to maintain general anaesthesia under controlled ventilation throughout the surgical procedure. After intubation, the infusion of Clonidine (1.5µg/kg) in 50 mL normal saline or 50 mL normal saline was started 10 min before induction of pneumoperitoneum. This was followed by a continuous infusion clonidine at a rate of 2 µg/kg/hr and NS at a rate of 0.5 ml/kg/hr according to the study group.

During study period haemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded at 0 minute (B), D<sub>0</sub>, D<sub>10</sub>, BPN, APN, APN<sub>10</sub>, APN<sub>20</sub>, APN<sub>30</sub>, APN<sub>40</sub>, APN<sub>50</sub>, APN<sub>60</sub>, APN<sub>90</sub>, RPN, AR, AR<sub>15</sub>, AR<sub>30</sub>, intervals. PNP- Pneumoperitoneum, B- Basal value (0 minute), D<sub>0</sub>- Before study drug, D<sub>10</sub>- After study drug, BPN-Before pneumoperitoneum, APN- After pneumoperitoneum, RPN- Release of pneumoperitoneum, AR- After reversal.

All the study drugs were stopped once surgical procedure was done and pneumoperitoneum was released.

After surgery, patients were reversed with Inj. Glycopyrrolate 0.005mg/kg and Neostigmine 0.08mg/kg intravenously. After extubation patients were

observed for recovery time defined as time to vocalize after extubation.

**Side effects and complications**

Patients were closely observed for bradycardia / tachycardia ( $\pm$  20% of basal value), hypotension / hypertension ( $\pm$  20% of basal value), bradyarrhythmia & desaturation (<85%) during intra and postoperative period. During postoperative period along with above, nausea, vomiting, respiratory depression, sedation and shivering were also recorded if occurred. Any complication if occurred was treated with appropriate medications.

**Statistical analysis**

The observations were recorded and subjected to statistical analysis using students ‘t’ test by statistics

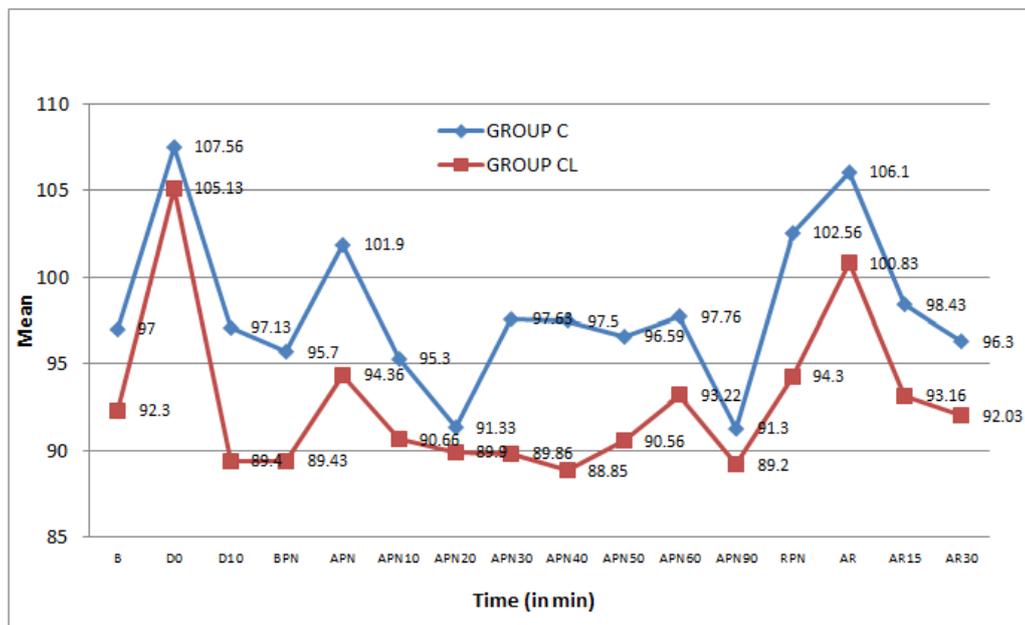
calculator SPSS 17. Student ‘t’-test for inter group comparison was used. p-value>0.05 was taken to be statistically insignificant & p-value <0.05 was taken statistically significant and p-value <0.01 taken to be statistically highly significant.

**RESULTS**

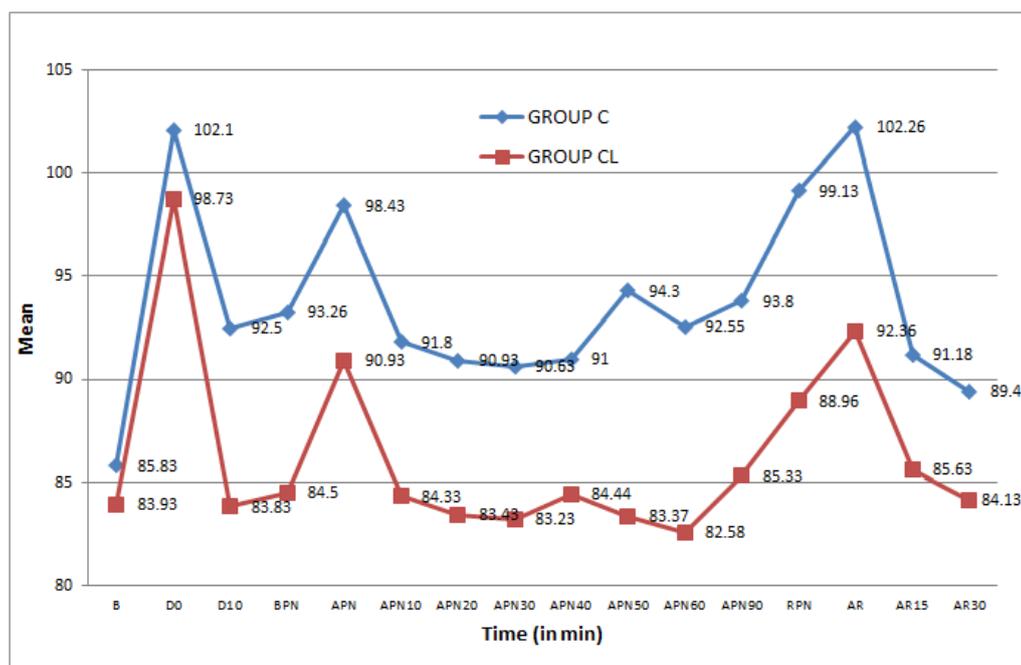
Data obtained from the patients involved in the study were analyzed. The mean age, weight, sex, type of surgery, duration of pneumoperitoneum, duration of anaesthesia, type of surgery and Ramsay sedation score after extubation were comparable in all the three study groups as shown in table. Preoperative heart rate, systolic, diastolic and mean blood pressure and blood sugar level were comparable in all the two groups.

**Table- 1: Showing demographic variables of two groups**

DEMOGRAPHIC DATA	Group A	Group B
Age	34.43 $\pm$ 8.75	35.16 $\pm$ 8.49
Weight (Kg)	53.23 $\pm$ 7.20	53 $\pm$ 6.45
Sex (Female)	73.33%	86.67%
Duration Of Pneumoperitoneum (Min)	62.96 $\pm$ 18.14	58.4 $\pm$ 17.78
Duration Of Anaesthesia (Min)	89.16 $\pm$ 19.47	85 $\pm$ 9.73
Type Of Surgery Laparoscopic Cholecystectomy	93.33	93.33
2. Laparoscopic Hernia	6.67	6.67
Ramsay Sedation Score After Extubation(Mean $\pm$ SD)	1.43 $\pm$ 0.56	1.73 $\pm$ 0.69



**Graph-1: Statistical analysis of mean ( $\pm$  SD) mean arterial pressure (mmHg)**



Graph-2: Statistical analysis of mean pulse rate (bpm)

## DISCUSSION

Pneumoperitoneum used for laparoscopic procedure is a complex patho-physiologic phase with significant haemodynamic variation. Pneumoperitoneum (PNP) is produced by administration of carbon dioxide (CO<sub>2</sub>) during laparoscopic surgical procedure [9, 10]. Both pneumoperitoneum and CO<sub>2</sub> cause adverse cardiovascular effects due to increase of plasma levels of epinephrine, nor-epinephrine, vasopressin, neurophysin and plasma renin activity increase [26]. All these changes contribute to increase in heart rate, arterial pressure, systemic and pulmonary vascular resistance and reduced cardiac output. In addition trendelenburg position causes diminished venous return and reduction in cardiac output [7].

Various studies have been done over the years for attenuating these unwanted detrimental effects which occur during pneumoperitoneum and intraoperative period. Drugs like beta blockers, magnesium sulphate, opioids, nitroglycerine, lidocaine, pregabalin, calcium channel blockers and gasless approach [27] to negate the haemodynamic variations. In modern anesthesia practice  $\alpha$ -2-agonist due to their beneficial effects like sedation, analgesia, attenuation of stress response and reduction of anesthesia requirement has been studied to attenuation of these responses. Clonidine is one such drug of alpha-2 agonist category that significantly reduces the release of catecholamines, predominantly having an effect on systemic vascular resistance and improves intra and postoperative haemodynamic stability by stabilizing the changes in heart rate, arterial pressure and cardiac output.

The present study was conducted to evaluate and compare the effects and efficacies of clonidine on HR, SBP, DBP and MAP during pneumoperitoneum. This study was also aimed to observe any untoward effects of study drugs and effect on sedation after extubation.

Selected groups were comparable for the demographic variables like age and weight parameters, type of surgery, sex, duration of pneumoperitoneum and duration of anaesthesia with  $P > 0.05$ . Effect of intubation and laryngoscopy induced stress response, creation of pneumoperitoneum, reversal of pneumoperitoneum and extubation was seen over heart rate, SBP, DBP and MAP in both the groups but was significantly less in the clonidine (CL) group compared to the control (C) group showing better stability of the hemodynamic vitals in the patients given clonidine intraoperatively.

Joris JL *et al.* conducted a study in which clonidine (8  $\mu$ g/kg) was given before pneumoperitoneum reduced the release of catecholamines and thus significantly attenuated the increase in MAP and heart rate in comparison to placebo.

Singh S *et al.* [28] observed significant rise in MAP in placebo group compared to oral clonidine group (150  $\mu$ g) after pneumoperitoneum.

Passi Y *et al.* [29] observed that with oral clonidine (150  $\mu$ g) premedication 60-90 minutes before laparoscopy, change in MAP was significantly lower and MAP varied between 88  $\pm$  9 to 95  $\pm$  9 mmHg as

compared to control group (vit B complex tablets) in which MAP varied between  $97 \pm 14$  to  $106 \pm 5$  mmHg.

Sung CS *et al.* [30] also found that isoflurane requirements were less by 30% in patients who received clonidine premedication. Aho *et al.* [31] used  $4.5 \mu\text{g}/\text{kg}$  and  $3 \mu\text{g}/\text{kg}$  iv clonidine 15 minute prior to induction. They observed significant reduction in MAP in the  $4.5 \mu\text{g}/\text{kg}$  group before induction of anaesthesia. They recommended  $3 \mu\text{g}/\text{kg}$  of clonidine for perioperative haemodynamic stability.

Similar findings were observed by Altan *et al.* [32], where they used  $3 \mu\text{g}/\text{kg}$  of clonidine IV over a period of 15 minutes before induction and followed by  $2 \mu\text{g}/\text{kg}/\text{hr}$  as continuous infusion. Ray *et al.* [33] also used  $3 \mu\text{g}/\text{kg}$  clonidine as IV bolus followed by  $1 \mu\text{g}/\text{kg}/\text{hr}$  infusion intraoperatively and found significant reduction in blood pressure compared to the control group.

Roy S *et al.* [34] used clonidine as  $2.25 \mu\text{g}/\text{kg}$  iv 15 minutes before induction followed by  $0.9 \mu\text{g}/\text{kg}/\text{hr}$  infusion intraoperatively while comparing iv clonidine with iv lignocaine. Arterial pressure was better controlled in clonidine group, with no episode of hypotension and bradycardia.

Our findings were also supported by Kumkum G *et al.* [35], Kalra *et al.* [36] and Malek *et al.* [37]. Tripathi DC *et al.* [38] who studied two different doses of clonidine ( $1 \mu\text{g}/\text{kg}$  and  $2 \mu\text{g}/\text{kg}$ ).

According to previously done studies, clonidine has better and positive effect over the haemodynamic stability of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

## CONCLUSION

Study conducted can be concluded as the creation of pneumoperitoneum in laparoscopic abdominal surgeries produces significant increase of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) and clonidine decreases and thus stabilizes all haemodynamic parameters (HR, SBP, DBP and MAP) during pneumoperitoneum in laparoscopic abdominal surgeries.

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