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## Effect of oral clonidine on perioperative haemodynamic response and post-operative requirement of analgesic for patients undergoing laparoscopic surgery

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### Abstract

Laparoscopic surgeries provide direct visualization with small incisions. It reduces postoperative pain and discomfort to patients. It helps in early post-operative recovery and reduces morbidity and mortality. It also reduces the requirement of post-operative analgesics and results in early mobilization. Laparoscopic surgeries generally require creation of pneumoperitoneum which is insufflation of the peritoneal cavity with some gas, usually Carbon Dioxide. Increase in intra-abdominal pressure due to pneumoperitoneum along with position required for better access during surgeries causes several pathophysiological changes in the body. These changes make anesthetic management more challenging as compared to other surgeries.

Since the hemodynamic stress response are inevitable with insufflation of CO<sub>2</sub> [1] In Laparoscopic surgeries, various methods like adequate administration of crystalloids (preloading), different pharmacological agents like opioids, direct vasodilators like nitroglycerine,  $\alpha$ 2-agonists, inhalational anesthetics are used.

In our study, we determined to observe and compare the effects of oral preparation of clonidine on patients undergoing elective laparoscopic surgeries. We observed the effect of clonidine as premedication for attenuation of hemodynamic changes perioperatively, and postoperative sedation, analgesia.

**Keywords:** Laparoscopic surgery, Hemodynamic changes, Oral Clonidine, Pneumoperitoneum

### Introduction

Laparoscopic surgeries are the modern methods for better visualization of internal anatomy of abdomen with advantages of minimal invasiveness as compared to conventional methods of surgeries.

Among the  $\alpha$ 2-agonist class, Clonidine is one of the drugs to be found effective in controlling the hemodynamic stress response associated with laparoscopic surgeries especially after pneumoperitoneum. Oral tablets can be safely given before surgery as it has good absorption and long half-life and better compliance for patients.

We observed the effect of clonidine as premedication for attenuation of hemodynamic changes perioperatively, and postoperative sedation, analgesia.

### Objectives

1. To observe the efficacy of Oral Clonidine in prevention of hemodynamic stress response to laryngoscopy, intubation and surgical stimulus and during extubation.
2. To study the hemodynamic changes that occur during laparoscopy and pneumoperitoneum.
3. To see side effects of Oral Clonidine in perioperative period.
4. Effect of Oral Clonidine for postoperative vital stability as well as sedation and analgesia.

**Materials and Methodology**

After approval from Institutional Review Board of NHL Medical College, the study was carried out at VS Hospital on 50 patients who were admitted for elective laparoscopic surgeries.

**Inclusion criteria**

1. Normotensive patients between the age group 18-60 years of both gender.
2. Patients of American Society of Anaesthesiologists (ASA) Grade I undergoing laparoscopic surgeries for various indications.

**Exclusion criteria**

1. Patients not coming under defined inclusion age criteria.
2. Patients with systemic diseases like diabetes, hypertension, IHD and others.
3. ASA grade II, III, IV, V.

Detailed general and systemic examination and necessary investigations were done preoperatively. Written informed consent was obtained from patients and their relatives after giving complete explanation regarding procedure and the study. Patients were explained regarding VAS score for grading of postoperative pain.

**Anaesthetic management**

- Patients were kept nil-by-mouth for 6 hours prior to surgery and shifted to the preoperative room 2 hour prior to surgery.
- Preoperative PR, BP and SpO2 were recorded.
- Wide bore I.V. cannula inserted.
- Preloading over 20-30 minutes done with crystalloid solution 10 ml/kg before induction.

Patients were divided into two groups

- Group A (Clonidine): Patients who received Oral Clonidine tablet 150 µg 90 minutes before induction.
- Group B (Control): Patients who received Vitamin C tablets 90 minutes before induction.

Vital parameters like Pulse, NIBP (SBP, DBP, MAP) and SpO2 were recorded with the help of multipara monitors in the pre-operative room 30 min and 60 min after giving oral drug.

On arrival in the operating room, digital multipara monitors were attached to the patients and Pulse, NIBP (SBP, DBP, MAP) and SpO2 were recorded in all the patients intraoperatively. After intubation EtCO<sub>2</sub> was monitored continuously.

**Premedication**

Inj. Glycopyrrolate 0.004 mg/kg I.V. Inj. Ondansetron 0.08 mg/kg I.V. Inj. Fentanyl 1 µg/kg I.V.

**Induction**

Inj. Thiopentone Sodium 5-7mg/kg in titrated doses I.V. Inj. Succinylcholine 2 mg/kg I.V.  
Inj. Lignocaine 1mg/kg I.V.  
Intubation: with disposable portex cuffed oral endotracheal tube

**Maintenance of anaesthesia**

O<sub>2</sub> + N<sub>2</sub>O + Sevoflurane with controlled ventilation on closed circuit + Inj. Vecuronium Bromide 0.12 mg/kg I.V. + intermittent doses of Vecuronium Bromide 0.02 mg/kg. PR, NIBP (SBP, DBP, MAP), SpO<sub>2</sub> and EtCO<sub>2</sub> were recorded:

1. At the time of intubation
  2. 5 mins post intubation
  3. Before pneumoperitoneum
  4. 5 min after pneumoperitoneum
  5. Every 10mins later on till completion of surgery
  6. During extubation
- Rise or fall in PR & BP of up to 20% from the baseline was considered acceptable. Any rise or fall was managed by inhaled anesthetics and deepening the plane of anesthesia or vasoconstrictors respectively.
  - Mean intra-abdominal pressure was kept around 12 mmHg and EtCO<sub>2</sub> was kept between 25-35 mmHg throughout the surgery.
  - I.V. fluids in the form of crystalloids 2ml/kg/hr.
  - At the end of surgery, patients were reversed with Inj. Glycopyrrolate mg/kg I.V. and Inj. Neostigmine 0.05 mg/kg I.V. and patients were extubated..

In the postoperative ward, patients were monitored for PR, BP and sedation using Ramsay Sedation Scale at 0, ½, 1, 2, 4 and 6 hours. Post-operative analgesia was assessed by Visual Analogue Scale (VAS) score and Rescue Analgesia in form of I.V. diclofenac (1.5 mg/kg) was given when score was ≥ 4.

**Table 1:** Ramsay sedation scale

Score	Response
1	Anxious or restless or both
2	Cooperative, orientated and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus



**Fig 1:** Visual analogue scale

The common side-effects of clonidine were hypotension and bradycardia. These side effects were observed.

Presence of other side effects were dizziness, headache, pruritus, dry mouth, urinary retention, dry eyes were observed during postoperative period.

Hypotension was prevented by adequately preloading with I.V. fluid (10 ml/kg). If the BP fell below 20% of the baseline value, Inj. Ephedrine 6 mg I.V. in incremental doses was kept ready.

For bradycardia, Inj. Glycopyrrolate 0.2 mg was given and

Inj. Atropine 0.6 mg was kept ready. Close monitoring for other side effects was done and if reported, were treated accordingly.

Statistical analysis of observations was done using Excel software. Inter-group data analysis was done with independent t-Test. Data were presented as Mean  $\pm$  Standard Deviation (S.D.). *P* value  $< 0.05$  was considered statistically significant.

## Results

The following table is comparison of both groups

**Table 2: Results**

Changes in mean pulse rate	No statistical significant difference in baseline mean pulse rate ( <i>P</i> value $>0.05$ ). There is a significant difference in mean pulse rate 60 min after giving the drug, before induction, at the time of intubation and after intubation. Significant changes in mean pulse rate were seen from 5 min after pneumoperitoneum till postoperative period up to 6 hours ( <i>P</i> value $<0.05$ ).
Changes in mean systolic BP (SBP)	No statistical significant difference in baseline mean SBP ( <i>P</i> value $>0.05$ ). Significant statistical differences were found in mean SBP starting from 60 min after oral drug up to postoperative period of 6 hours at all recorded time intervals ( <i>P</i> value $<0.05$ ).
Changes in mean diastolic BP (DBP)	No statistical significant difference in baseline mean DBP ( <i>P</i> value $>0.05$ ). Significant statistical differences were found in mean DBP starting from 60 min after oral drug up to postoperative period of 6 hours at all recorded time intervals ( <i>P</i> value $<0.05$ ).

## Discussion

### Changes in the vital parameters (PR, SBP, DBP) pulse rate

In group A (clonidine) before induction mean PR dropped for 4.3% from baseline not significant. During intubation rise in mean PR was about 5.84% from baseline and in pneumoperitoneum mean pulse rate increased by 5.6% and during extubation raised by 10.61%. Mean pulse rate returned at baseline value around 2 hours postoperatively and remained near the baseline value up to 6 hours postoperatively.

In group B (control) During intubation rise in mean PR was about 15.54% from baseline and in pneumoperitoneum mean pulse rate increased by 14.45% and during extubation raised by 19.77% and remained raised or 14.28 from baseline postoperative period for 6 hours.

Our results matches with the results of the following studies: Jean L. Joris *et al.* (1998) 26 concluded that clonidine causes significant reduction in rise in Heart Rate(HR), Mean Arterial Pressure(MAP), Systolic Blood Pressure and catecholamine levels caused by CO<sub>2</sub> pneumoperitoneum.

### Systolic BP

The mean SBP in Group A (Clonidine) decreased for about 5.68 % 60 min after administration of oral clonidine from the baseline value which was clinically not significant. No significant rise above baseline value was found during and after intubation (2.44 % from baseline value) till initiation of pneumoperitoneum. After pneumoperitoneum maximum rise in mean SBP was only about 4.12% from baseline and during extubation rise of about 4.5%. During the postoperative period, SBP declined to baseline level by the time of 2 hours and remained at that level upto 6 hours. Maximum rise in mean SBP in Group A (Clonidine) is 4.5% from baseline value.

In the Group B (Control), mean SBP showed a rise of 9.8% from baseline value during intubation and it kept on rising by 11.06% after pneumoperitoneum and remained elevated

11.13% from baseline value during extubation. This was controlled by hyperventilation, analgesics and by increasing depth of anesthesia, still it remained above the baseline value. Mean SBP of Group B (Control) remained raised above the baseline value by 5.51% in the postoperative period up to 6 hours. Maximum rise in mean SBP in Group B (Control) is 11.13% from baseline value.

### Diastolic BP

The mean DBP in Group A (Clonidine) declined by 6.12% only from baseline value before induction and remained near baseline value after intubation. Mean DBP increased up to 4.96% from baseline value during pneumoperitoneum. This was probably due to the ability of clonidine to prevent stress response to pneumoperitoneum. The rise in mean DBP during extubation was only 7.08% from baseline value. And mean DBP declined to baseline level at 2 hours postoperatively and remained at the baseline values up to 6 hours postoperatively. Maximum rise in mean DBP in Group A (Clonidine) was 7.08% from baseline value.

The Group B (Control) showed rise in mean DBP level by 11.74% from baseline value during intubation and mean DBP kept on rising after pneumoperitoneum by 13.09% and remained elevated by 13.14% from baseline during extubation. Mean DBP of Group B (Control) remained raised above the baseline value by 8.54% even in the postoperative period up to 6 hours. Maximum rise in mean DBP value in Group B (Control) was 13.14% from baseline value. In Group A (Clonidine), the changes were less marked as compared to Group B (Control).

### SPO<sub>2</sub>

No statistically significant difference was found in mean SpO<sub>2</sub> between two groups intraoperatively and postoperatively up to 6 hours.

### ETCO<sub>2</sub>

No statistically significant difference was found in mean

EtCO<sub>2</sub> between two groups intraoperatively.

### **Extubation**

During extubation, changes in mean values of vital parameters of both groups showed significant differences. According to vital parameters group A (Clonidine) patients were more stable than group B (Control) (*P* value <0.05). Thus, patients given oral clonidine preoperatively showed a stable hemodynamic profile than the Group B (Control).

### **Post-operative sedation**

All the patients were monitored for sedation and common side effects of oral clonidine e.g. hypotension, bradycardia etc. in the postoperative period up to 6 hours. No statistically significant difference was found between sedation score in the postoperative period between two groups. Patients of both groups were tranquil and cooperative, less anxious and less agitated.

### **Conclusion**

Thus it can be concluded from this study that premedication with oral clonidine given 90 minutes before induction in dose of 150 µg is significantly effective in attenuating hemodynamic stress response during induction, laryngoscopy and pneumoperitoneum in laparoscopic surgery. It provides postoperative hemodynamic stability and analgesia.

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### **Conflict of interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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