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Research Article

Effects Of Oral Clonidine as a Premedication On perioperative hemodynamic changes and post-operative analgesia requirement in patient undergoing laproscopic Surgeries: A Prospective Observational Study

Dr. Dharaviben Mahendrabhai Patel[1], Dr. Urvisha V. Tarpara[2], Dr. Tejal D. Gohel[2], Dr. Dipti N. Anandani[4]

[1]Senior Resident, Department of Anaesthesiology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India
Assistant Professor, Smt. NHLMMC & SVPIMSR, Paldi, Ahmedabad Gujarat, Bharat
[3]Senior Resident, Department of Anesthesiology, Baba Saheb Ambedkar Hospital, Rohini, New Delhi, India
[4]Associate Professor, Department of Anaesthesiology, Narendra Modi Medical College & Sheth L.G. General Hospital, Ahmedabad, Gujarat, India

Corresponding Author:

Dr. Dharaviben Mahendrabhai Patel
Senior Resident, Department of Anaesthesiology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India
Email: pateldharavi@gmail.com

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ABSTRACT

Background: Laparoscopic surgery offers multiple advantages but is associated with significant hemodynamic changes due to pneumoperitoneum and intubation. This study evaluates the effectiveness of oral clonidine premedication in attenuating these responses compared to placebo in elective laparoscopic surgeries.
Materials and Methods: After ethics committee approval and informed consent, this prospective observational study was conducted from 2022 to 2024 on 60 patients (ASA Grade I–II), aged 20–60 years, undergoing elective laparoscopic surgery under general anaesthesia. Patients were randomly divided into two groups (n=30 each): Group C received oral clonidine 100 µg, and Group P received oral vitamin C 100 mg, both administered 90 minutes prior to induction.
Result: Oral clonidine (100 µg) as premedication provides better perioperative hemodynamic stability, increased sedation, and prolonged postoperative analgesia with minimal side effects compared to control in laparoscopic surgeries.
Conclusion: Oral clonidine 100 µg given 90 minutes preoperatively is a simple, effective, and cost- efficient premedication that provides hemodynamic stability, attenuates perioperative stress responses, and reduces postoperative analgesic requirements with minimal side effects, making it a useful anesthetic adjuvant.

Keywords: *Hemodynamic response, Oral clonidine, Analgesia, Laproscopic surgery.*

INTRODUCTION

Laparoscopic surgery has become a widely adopted modern technique in abdominal procedures due to its advantages over open surgery, including smaller incisions, reduced blood loss, less postoperative pain, shorter recovery time, and lower morbidity and mortality.1

A key component of laparoscopic surgery is the creation of CO_2 pneumoperitoneum, which can significantly impact cardiopulmonary physiology. It may lead to systemic CO_2 absorption, decreased cardiac output, increased systemic and pulmonary vascular resistance, and potential complications such as gas embolism and organ injury. These effects arise from both increased intra-abdominal pressure and the chemical properties of CO_2, making anesthetic management more challenging.2

Various strategies have been employed to attenuate pneumoperitoneum-induced hemodynamic changes, including fluid preloading and pharmacological agents such as nitroglycerin, α_2-agonists (e.g., clonidine), esmolol, and magnesium sulfate, each with variable efficacy and limitations.3

Additionally, laryngoscopy and endotracheal intubation provoke sympathetic stimulation, leading to tachycardia, hypertension, arrhythmias, and possible myocardial ischemia due to increased catecholamine release.4

Clonidine, an α_2-adrenergic agonist with good oral bioavailability and a half-life of 9–12 hours, exerts central sympatholytic, sedative, and analgesic effects. It attenuates perioperative stress responses by reducing catecholamine, cortisol, and vasopressin release, thereby stabilizing heart rate and blood pressure.5

This study aims to evaluate the efficacy of oral clonidine as a premedication in attenuating hemodynamic responses to laryngoscopy, intubation, and pneumoperitoneum in patients undergoing elective laparoscopic surgery.

Material and method:
After obtaining ethics committee approval and written informed consent, this prospective observational study was conducted from 2022 to 2024 in 60 patients aged 20–60 years of either gender, classified as ASA Grade I and II, undergoing elective laparoscopic surgery under general anesthesia.

Patients were randomly divided into two groups of 30 each:
- Group C: Received oral clonidine 100 µg, 90 minutes prior to induction.
- Group P: Received oral vitamin C 100 mg, 90 minutes prior to induction.

Exclusion criteria
- Patient not fulfilling eligibility criteria
- Lack of patient consent
- History of bronchial asthma
- Concomitant use of monoamine oxidase inhibitors, tricyclic antidepressants or opioids.
- Patient allergic to clonidine
- Hypertensive and diabetic patients

Preoperative Evaluation
All patients underwent a detailed preanesthetic assessment, including history, general and systemic examination, and airway evaluation using the Mallampati score. Baseline vital parameters (temperature, pulse, blood pressure, respiratory rate, and SpO_2) were recorded.

Relevant investigations including CBC, RFT, LFT, serum electrolytes, blood sugar, coagulation profile, and ECG were reviewed.

Patients received either oral clonidine or vitamin C 90 minutes prior to surgery. An intravenous wide-bore cannula was secured. Patients were kept nil per os for 6–8 hours and were explained the Visual Analogue Scale (VAS). Written informed consent was obtained.

Preoperative Preparation (Operating Room)
Standard anesthesia equipment and emergency drugs were checked. Upon arrival in the operating room, monitors including ECG, non-invasive blood pressure, and pulse oximetry were attached, and baseline parameters were recorded.

Premedication included:
- Ondansetron 0.1 mg/kg IV
- Glycopyrrolate 0.004 mg/kg IV
- Midazolam 0.02 mg/kg IV
- Fentanyl 1 µg/kg IV

ANESTHETIC TECHNIQUE
After preoxygenation, general anesthesia was induced with:
- Lignocaine 1 mg/kg IV
- Propofol 1.5 mg/kg IV
- Atracurium 0.5 mg/kg IV

Endotracheal intubation was performed using an appropriate-sized tube. Anesthesia was maintained with 40% oxygen, 60% nitrous oxide, and 1–1.5% sevoflurane. Controlled ventilation was adjusted to maintain end-tidal CO_2 between 30–40 mmHg.

Intraoperative Management
Hemodynamic fluctuations were managed as follows:
- Bradycardia (HR <60 bpm): Atropine 0.6 mg IV

- Hypotension (MAP <60 mmHg): Fluids and/or mephentermine 6 mg IV bolus
- Hypertension (MAP >110 mmHg): Nitroglycerin infusion (0.5–5 µg/kg/min)

Monitoring Parameters

Heart rate, SBP, DBP, MAP, SpO_2, and $EtCO_2$ were recorded at:

- Baseline (pre-induction)
- 1 and 5 minutes post-intubation
- Before pneumoperitoneum
- 15, 30, 60, and 120 minutes after pneumoperitoneum
- 10 minutes after release of pneumoperitoneum
- After extubation

Postoperative Management

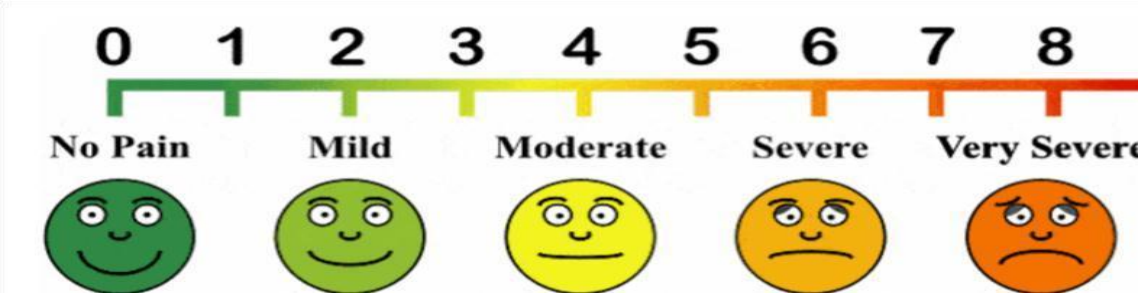
Neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Patients were extubated and shifted to the recovery room.

In the PACU, patients were monitored for complications. Sedation was assessed using the Ramsay Sedation Score, and pain was evaluated using the VAS. Rescue analgesia was administered when VAS >4.

Duration of Analgesia

Postoperative pain was assessed using the Visual Analogue Scale (VAS) to determine the duration of analgesia.

VISUAL ANALOGUE SCALE6



Pain Assessment and Analgesia

Postoperative pain was assessed using a 10-cm Visual Analogue Scale (VAS), where 0 indicated no pain and 10 indicated worst imaginable pain. The time to first analgesic request (TAR) was recorded as the duration from the end of surgery to the first request for analgesia (VAS >4). Rescue analgesia was administered as intravenous diclofenac sodium 75 mg.VAS scores were recorded at 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours postoperatively.

RAMSAY SEDATION SCORE7

Sedation and Adverse Events

Postoperative sedation was assessed using the Ramsay Sedation Score (1–6). Patients were monitored for adverse events, including nausea, vomiting, hypotension, hypertension, bradypnea, and urinary retention.

Sedation scores were recorded at 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours postoperatively.

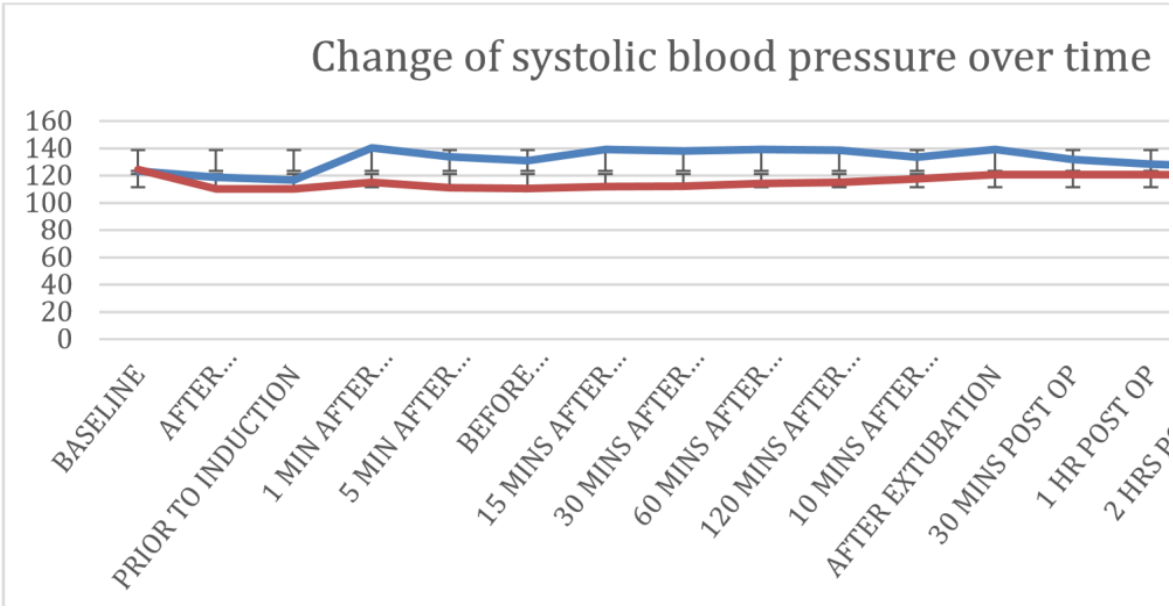
SCORE	RESPONSE
1	Anxious, restless or both
2	Cooperative, oriented and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Brisk response to stimulus
6	No response to stimulus

Statistical Analysis

Data were collected using a predesigned proforma and entered into Microsoft Excel for tabulation. Statistical analysis was performed using SPSS version 20.

Categorical variables were expressed as number and percentage [n (%)], while continuous variables were presented as mean ± standard deviation or median (minimum–maximum), as appropriate. The Chi-square test was used for analysis of qualitative data.

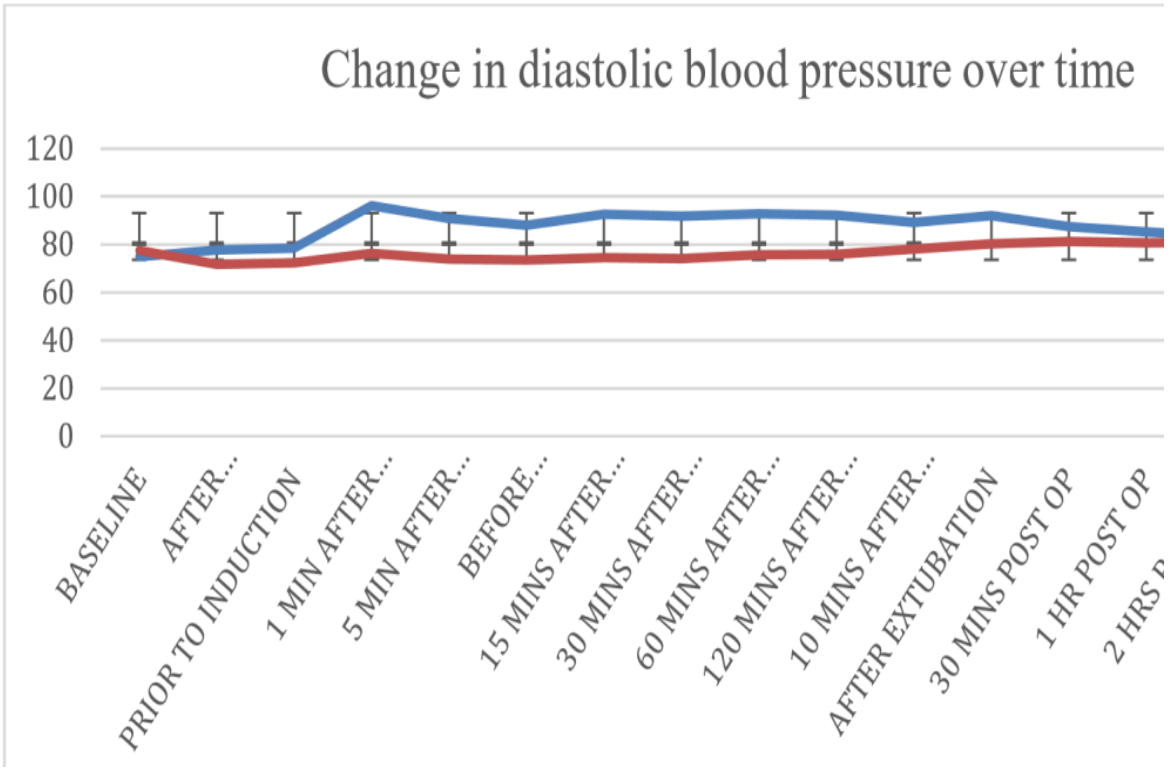
OBSERVATION AND RESULTS



GRAPH: 1 – Changes of systolic blood pressure over time

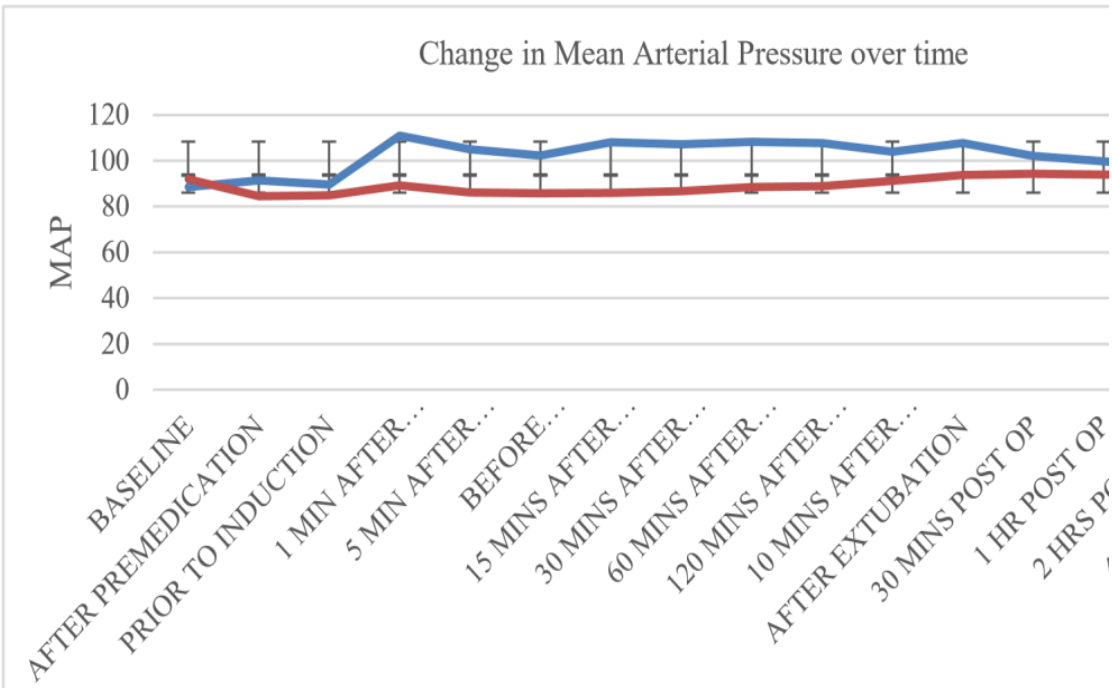
Systolic Blood Pressure (SBP)

There was no statistically significant difference in baseline SBP between the two groups. However, SBP was significantly lower in the clonidine group at 90 minutes after premedication, prior to induction, at 1 and 5 minutes post-intubation, during pneumoperitoneum (15, 30, 60, and 120 minutes), 10 minutes after release of pneumoperitoneum, after extubation, and in the postoperative period up to 6 hours.



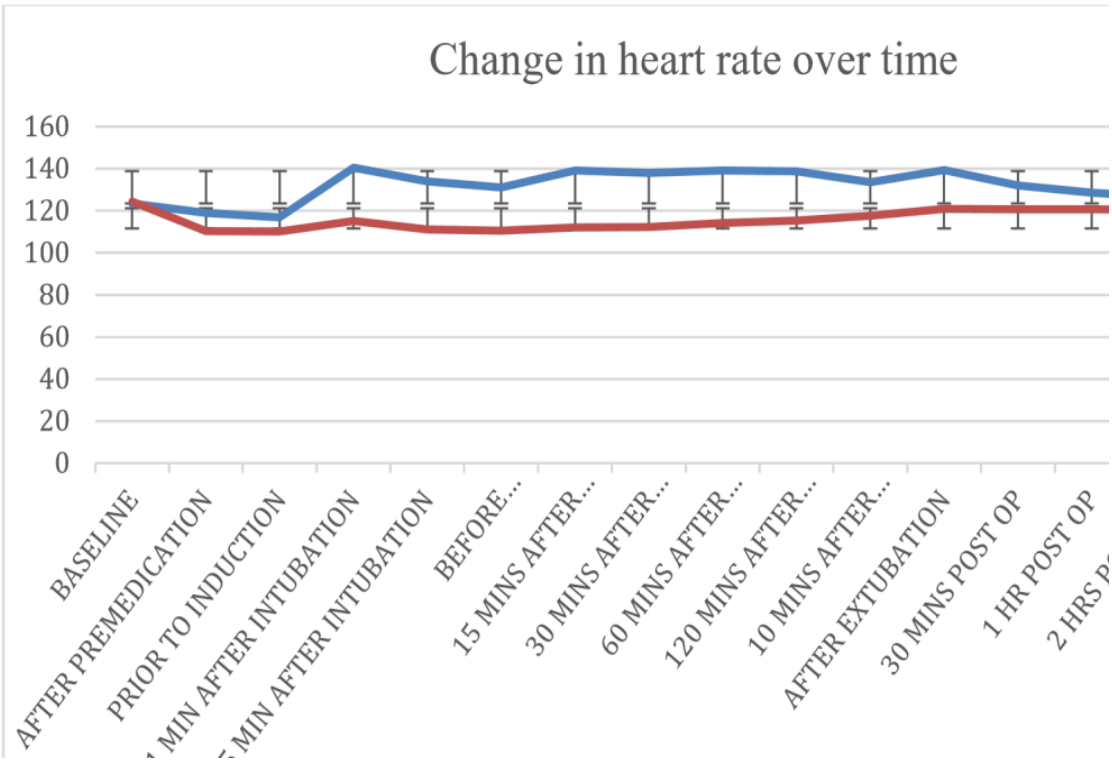
GRAPH:2- Change in diastolic blood pressure over time

Graph 2 shows no statistically significant difference in baseline diastolic blood pressure (DBP) between the two groups. However, DBP was significantly lower in the clonidine group at 90 minutes after premedication, prior to induction, at 1 and 5 minutes post-intubation, during pneumoperitoneum (15, 30, 60, and 120 minutes), 10 minutes after release of pneumoperitoneum, after extubation, and in the postoperative period up to 6 hours.



GRAPH:3- Change in Mean Arterial Pressure over time

Graph 3 shows no statistically significant difference in baseline mean arterial pressure (MAP) between the two groups. However, MAP was significantly lower in the clonidine group at 90 minutes after premedication, prior to induction, at 1 and 5 minutes post-intubation, during pneumoperitoneum (15, 30, 60, and 120 minutes), 10 minutes after release of pneumoperitoneum, after extubation, and in the postoperative period up to 4 hours.



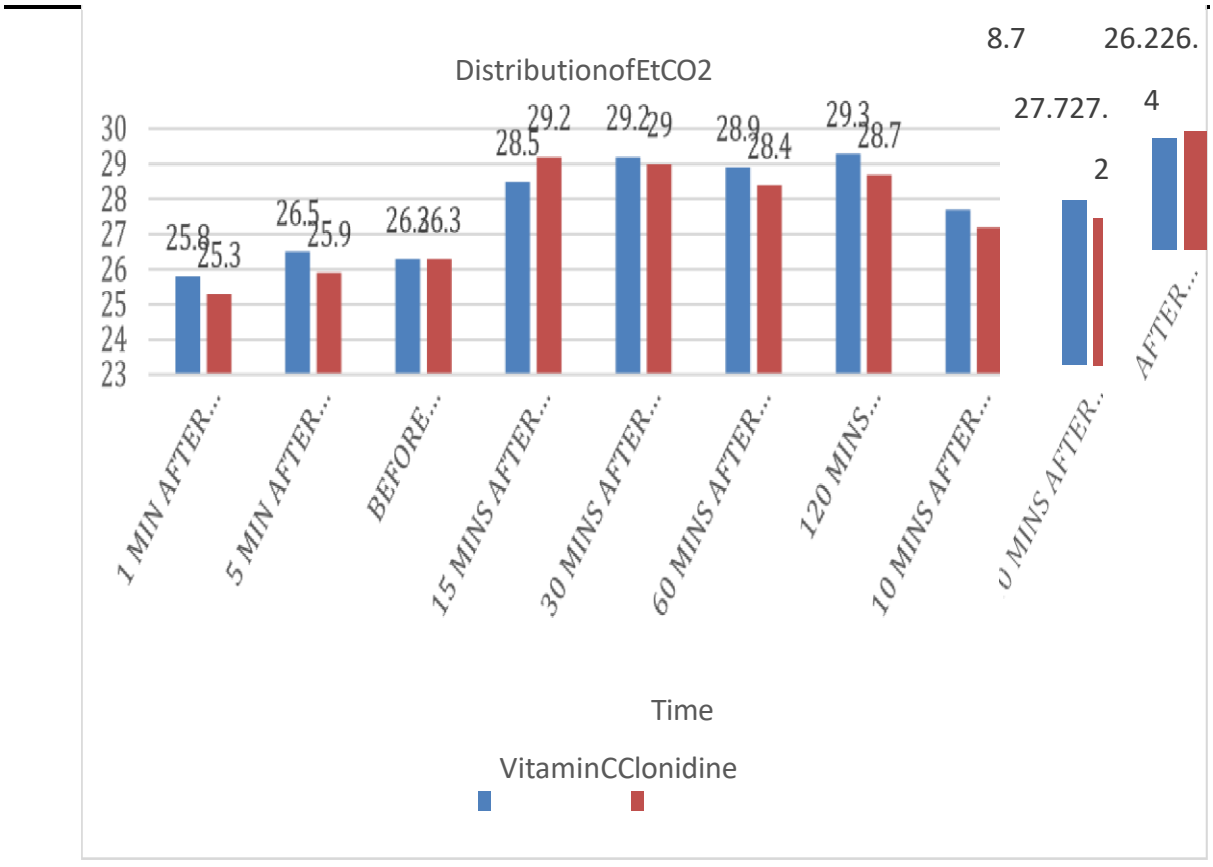
GRAPH:4- Change in heart rate over time

Graph 4 shows a statistically significant reduction in heart rate (HR) in the clonidine group at 90 minutes after premedication, prior to induction, at 1 and 5 minutes post-intubation, during pneumoperitoneum (15, 30, 60, and 120 minutes), 10 minutes after release of pneumoperitoneum, after extubation, and in the postoperative period up to 6 hours.

GRAPH: 5- Change in SPO2 over time

A p-value < 0.05 was considered statistically significant.

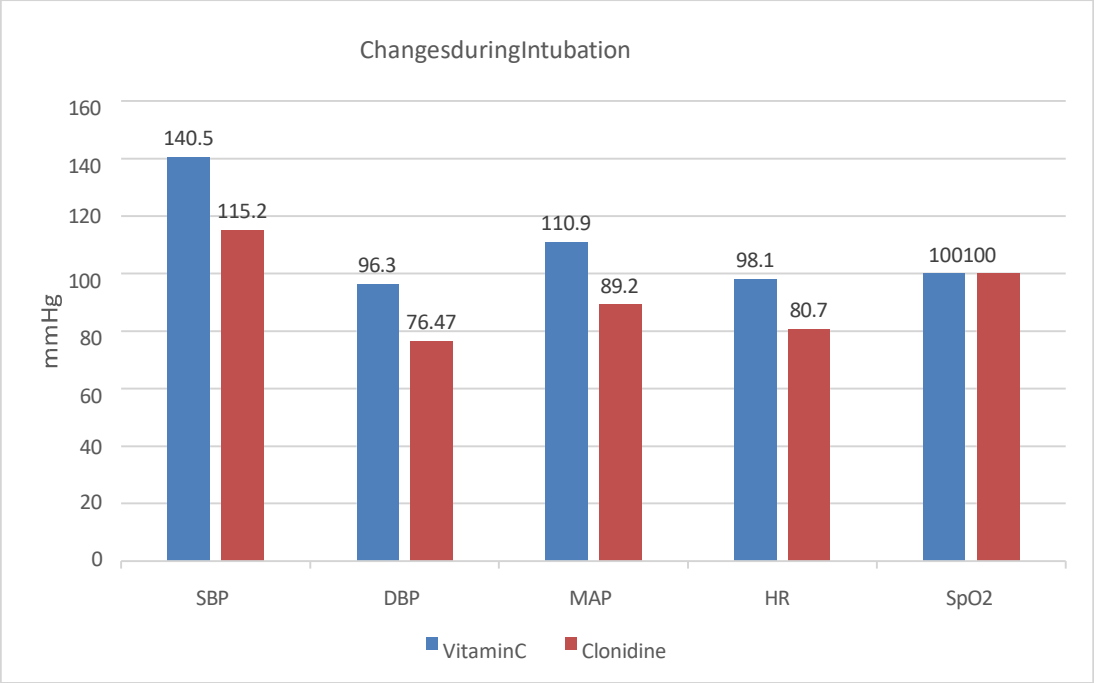
Graph 5 shows no statistically significant difference in oxygen saturation (SpO_2) between the two groups at any time interval.



GRAPH :6- Distribution of ETCO2

P value < 0.05 considered as statistical significance.

Graph 6 shows no significant difference observed in both groups in EtCO2. Graph 7: Changes during intubation

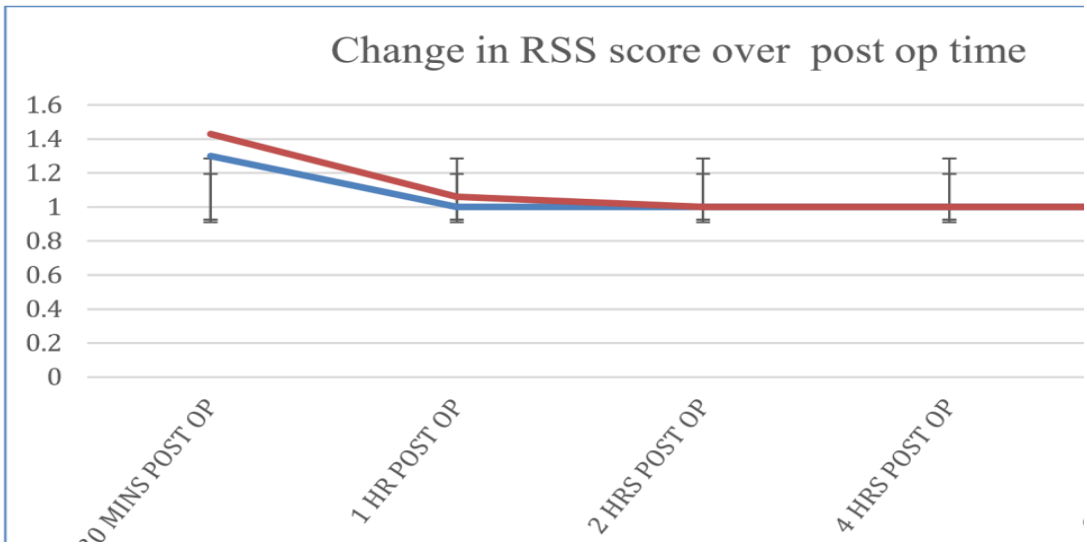


Graph 7 shows difference between SBP, DBP, MAP and HR in both groups during intubation which was clinically significant. SpO2 shows no clinically significant difference.

GRAPH 8: Changes after extubation

Graph 8 shows difference between SBP, DBP, MAP and HR in both groups after extubation which was clinically significant. SpO2 shows no clinically significant difference.

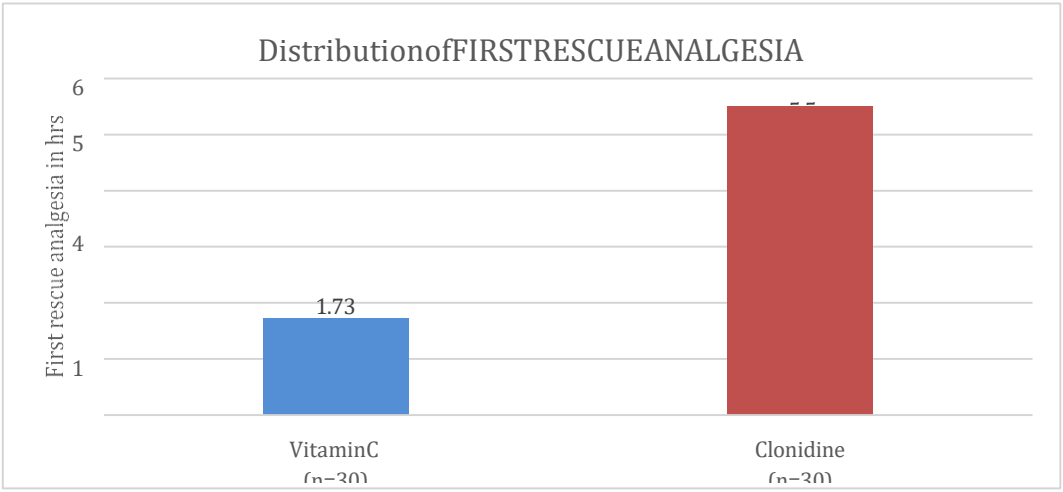
NE=Not Evaluated



GRAPH 9: Change in RSS score over post op time

P value < 0.05 considered as statistical significance.

Graph 9 shows that no significant statistical difference in mean post-operative sedation score.



GRAPH 10: Distribution of First Rescue Analgesia

A p-value < 0.05 was considered statistically significant.

The mean (± SD) time to first rescue analgesia was 1.73 ± 0.45 hours in the Vitamin C group and 5.5 ± 0.50 hours in the clonidine group. This difference was statistically significant on independent sample t-test (p = 0.0001).

Ethical Considerations

The study included only ASA Grade I and II patients. Written informed consent was obtained from all participants. All drugs used in the study are widely accepted, approved, and have a well-established safety profile with no major adverse effects.

DISCUSSION

Our research supports previous findings that a low dose of oral Clonidine (100µg) taken before surgery reduces the body's stress response during laparoscopy and surgery. Laparoscopic abdominal surgery can cause unstable blood pressure and heart rate due to surgical stress, patient positioning, and pneumoperitoneum (inflating the abdomen with gas).

Clonidine, a medication that acts on specific nerve receptors is effective when taken orally, with peak levels reached within 60-90 minutes. Previous studies used a 150µg dose, which maintained stable blood pressure during surgery but had some adverse effects. Shivinder Singh and Kapil Arora (5) study. In our study, we used a lower dose of 100µg, 90 minutes before surgery, and found it maintained stable heart rate and blood pressure during the procedure. Clonidine works by reducing

the release of norepinephrine and slowing heart rate. While bradycardia (slow heart rate) can occur with clonidine overdose, it rarely happens at prescribed doses.

Clonidine, a medication similar in structure to norepinephrine, works by stimulating specific nerve receptors which opens potassium and calcium channels. This reduces nerve transmission leading to pain relief and sedation. In our study, we found that there was no significant difference between ramsay sedation score the end of the surgery compared placebo group.

The analgesic effects of clonidine are by both central and peripheral action. Centrally, it acts on α2 receptors in the substantia gelatinosa of dorsal horn of the spinal cord, where it increases release of acetylcholine (ACh) and suppress the release of substance P and glutamate. Peripherally, it blocks C- fibers and interact with inhibitory G-proteins.

Oral clonidine (100 µg), administered 90 minutes prior to surgery, is an effective and safe premedicant for patients undergoing laparoscopic surgery under general anesthesia. It significantly attenuates the hemodynamic responses to laryngoscopy, endotracheal intubation, pneumoperitoneum, and extubation.

Clonidine provides better perioperative stability of heart rate and blood pressure compared to placebo, without causing significant respiratory depression or excessive sedation.

Additionally, it prolongs the duration of postoperative analgesia and reduces analgesic requirements.

The use of low-dose oral clonidine is associated with minimal and manageable side effects, making it a simple, cost-effective, and valuable anesthetic adjuvant in laparoscopic procedures.

SYSTOLIC BLOOD PRESSURE DISTRIBUTION:
The SBP in both groups at baseline was comparable and clinically insignificant. The SBP prior to induction in clonidine group and vitamin C group was 110.2±8.59 and 116.8±13.61 respectively. SBP at 1 min after intubation was 115.2±9.26 in clonidine group and 140.5±9.94 in vitamin C group, 15 mins after pneumoperitoneum was 112.2±7.91 in clonidine group and 139.2±5.51 in vitamin C group, after extubation was 120.9±7.75 in clonidine group and 139.4±6.45 in vitamin C group which was clinically significant.

The systolic blood pressure remained better controlled in clonidine group as compared to placebo group throughout the study period. The clonidine group also showed significant difference in systolic blood pressure at extubation as compared to placebo group throughout the study period.

Jehangir AB, Roshan Ara and Mushtaq SM (8) shows that marked variation in SBP throughout the procedure while in clonidine group showed controlled SBP. Shivinder Singh and Kapil Arora (5) showed greater reduction systolic blood pressure in clonidine group as compared to placebo group. There was greater rise in systolic blood pressure in post intubation period in placebo group. Malti J Pandya, Dhruvi J Patel and, Divyang V Shah (9) showed that there is a significant difference in SBP before induction, at intubation, 10 min, 30 min and 60 min after CO2 insufflation. At extubation there is no significant difference in SBP in both groups.

DIASTOLIC BLOOD PRESSURE DISTRIBUTION:
The DBP in both groups at baseline was comparable which was clinically insignificant. The DBP prior to induction in clonidine and vitamin C group was 72.4±7.08 and 76.2±8.52 respectively. DBP at 1min after intubation was 76.4±9.26 in clonidine group and 96.3±8.11 in vitamin C group, 15 mins after pneumoperitoneum was 74.5±6.97 in clonidine group and 92.6±6.24 in vitamin C group, after extubation DBP was 80.3±5.44 in clonidine group and 92.0±5.07 in vitamin C group which was clinically significant.

The diastolic blood pressure of clonidine group was lower significantly at induction and remained until 15 mins after intubation. It was also controlled at extubation which was statistically significant

Jehangir AB, Roshan Ara and Mushtaq SM (8) showed marked variation in DBP throughout the operative procedure while clonidine group showed controlled DBP. Malti J Pandya, Dhruvi J Patel and, Divyang V Shah (9) showed that there is a significant difference in DBP before induction, at intubation, 10 min, 30 min and 60 min after CO2 insufflation. At extubation there is no significant difference in DBP in both groups.

MEAN ARTERIAL PRESSURE DISTRIBUTION:
MAP in both groups at baseline was comparable which was clinically insignificant. The MAP prior to induction in clonidine group was 84.8±7.15 and in vitamin C group was 89.6±9.9, 1 min after intubation 89.2±7.60 in clonidine group and 110.9±8.40 in vitamin C group, 15 mins after pneumoperitoneum 86.0±7.40 in clonidine group and 108.0±6.24 in vitamin C group, after extubation 93.7±5.75 in clonidine group and 107.6±5.28 in vitamin C group which was clinically significant.

Jehangir AB, Roshan Ara and Mushtaq SM (8) showed marked variation in MAP throughout the operative procedure while clonidine group showed controlled MAP. Shivinder Singh and Kapil Arora (5) showed that greater reduction in MAP in clonidine group compared to placebo group. Malti J Pandya, Dhruvi J Patel and, Divyang V Shah (9) showed that there is a significant difference in MAP before induction, at intubation, 10 min, 30 min and 60 min after CO2 insufflation. At extubation there is no significant difference in MAP in both groups. Ramki J (18) showed that the baseline MAP

between the two groups before ingestion of premedication (Clonidine or vitamin C) was comparable. There were no statistical differences ($p > 0.05$) between the groups. In both groups, the highest spike in MAP occurred at one minute after intubation and at the start of pneumoperitoneum. In comparison to group II, the MAP was lower and stable in clonidine group perioperatively.

Heart rate

Heart rate in both groups at baseline was comparable which was clinically insignificant. Prior to induction mean heart rate in clonidine group and vitamin C group was 76.2±7.87 and 80.5±6.36 respectively. Mean heart rate at 1 min after intubation was 80.7±7.90 in clonidine group and 98.1±4.86 in vitamin C group, 15 mins after pneumoperitoneum 79.4±7.48 in clonidine group and 97.2±5.21 in vitamin C group, after extubation was 88.5±7.15 in clonidine group and 96.7±5.05 in vitamin C group which was clinically significant.

The preinduction heart rate changes were comparable between the two groups. The fall in heart rate in clonidine group is significant at induction, upto 5 mins after intubation and during pneumoperitoneum as compared to vitamin C group. ($p<0.05$).

Jehangir AB, Roshan Ara and Mushtaq SM (8) shows that administration of placebo showed lots of fluctuations in heart rate but heart rate in clonidine is under control. Shivinder Singh and Kapil Arora (5) showed That basal heart rate was not comparable. There was a rise in pulse rate post-intubation the difference being statistically significant only at 5 min after intubation. Perioperatively the mean heart rate was lower in clonidine group compared to placebo group. Ramki J (10) showed that the baseline HR between the two groups before ingestion of premedication drugs (Clonidine or vitamin C) was comparable. There were no statistical differences ($p > 0.05$) between the groups. There was an increase in HR at 1 minute following intubation with the difference becoming statistically significant ($p < 0.05$) after 5 minutes only. In comparison to placebo group, the mean HR was lower and stable in clonidine group at all times perioperatively.
HR, SBP, DBP, MAP in clonidine group are constantly stable comparison to vitamin C group (p value <0.05).

There was not a significant difference found in mean spo2 between two groups intraoperatively and post operatively up to 6 hours. Megha tyagi, Arvin preetkour and Ram Nandan Prasad (11) showed no significance difference was observed in spo2 between two groups.

No significant changes were observed in etCO2 in any patients in both groups. Malti J Pandya, Dhruvi J Patel and Divyang V Shah (9) showed that no significant changes in etCO2 observed in any patients in both groups at any stage of surgery.

Changes 1 min after intubation and after extubation.

Changes in mean values of vital parameters of both groups showed significant differences. Clonidine group patients were more stable than vitamin C patients at 1 min after intubation and after extubation as shown in table 8 & 9. Thus patients given oral clonidine preoperatively showed more stable hemodynamic profile than vitamin C group.

The results of this study correlates with below mentioned study.

Ramki J(10) showed that the statistically significant difference found between the two groups 1 min after intubation. There were statistically significant difference seen with vital parameters such as SBP, DBP, MAP, HR. C.B. Sridhar and Sulfiqdeen K(12) were observed that patient premedicated with low dose oral clonidine had more stable Hemodynamic than those premedicated with placebo drug. The arterial blood pressures (SBP, DBP, MAP) were significantly lower in clonidine group at 15 min and 30 mins of pneumoperitoneum and after extubation.

Sedation

Mean RSS in clonidine group 1.43±0.49 and 1.30±0.45 in vitamin C group. P value is 0.423. There was a no significant difference found between ramsay sedation score in post- operative period.

Ramki J (10) showed that clonidine Group patients were slightly sedated at 30 minutes following surgery when compared to placebo Group, but there were no statistically significant differences measured at 30 min intervals until 2 hours after surgery ($p > 0.05$).

C.B. Sridhar and Sulfiqdeen K (12) were observed that patient premedicated with low dose oral clonidine compared with the placebo group. Degree of sedation was comparable between both the groups and there was no significant difference.

Duration of post-operative analgesia

In our study there was a significant difference found in duration of post- operative analgesia between two groups as shown in table 11which means that clonidine group patients had better pain relief when compared to placebo group. Similar findings were seen in a study by Shivender Singh and kapil arora.(5) Patients in clonidine group they found requirement of analgesia 6-8 hours postopratively than control group. Ramki J (10) shows that VAS score was lower in clonidine group when compared with placebo group, being statistically significant at 30 min intervals till 2 hours postoperatively ($p < 0.05$). C. B. Sridhar et al (12) demonstrated a decreased need for postoperative analgesia with Clonidine use. Similarly, in our study, TAR was shown to be longer in the Clonidine group in comparison with the vitamin C group. This is because of its synergistic analgesic action with opioids and antinociceptive properties.

Side effects

In our study, only two patients in the Clonidine group had hypotension who required i.v. mephentermine 6mg single dose because we used low dose clonidine. One patient developed bradycardia in clonidine group which was treated by inj. atropine 0.6 mg i.v. Y. Passi et al (13) and Altan et al (14) also had similar findings of bradycardia and hypotension at higher doses of Clonidine. No other post-operative side effects such as headache, dizziness, dry mouth, dry eyes and urinary retention were found in either group.

CONCLUSION

Preoperative administration of oral clonidine (100 µg), given 90 minutes before induction, is an effective, simple, and cost-effective strategy in patients undergoing laparoscopic surgery. It provides better intraoperative hemodynamic stability and attenuates the stress response to laryngoscopy, intubation, pneumoperitoneum, and surgical stimulation under general anesthesia. Additionally, clonidine offers dose-dependent sedation, reduces postoperative analgesic requirements, and is associated with minimal side effects, making it a valuable anesthetic adjuvant.

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