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Effect of oral clonidine premedication on perioperative hemodynamic response for patients undergoing abdominal surgeries under general anaesthesia

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ABSTRACT

Background: Premedication enhances patient outcomes by minimizing anxiety, stabilizing hemodynamics, and improving perioperative recovery. Clonidine, an alpha-2 adrenergic agonist, has shown promise in anesthesia for its sedative, sympatholytic, and analgesic properties.

Aim:
To evaluate the perioperative effects of a single oral dose of clonidine (150 mcg) on hemodynamic responses, sedation, anesthetic requirements, and postoperative recovery in patients undergoing elective abdominal surgery under general anesthesia.

Methods:
A prospective, randomized, controlled clinical study was conducted on 50 ASA I–II patients aged 20–60 years. Patients were divided into two groups: Group A received oral clonidine (150 mcg) and Group B received a placebo (Vitamin C) 90 minutes prior to surgery. Hemodynamic parameters, sedation scores (Ramsay Sedation Score), and Rate Pressure Product (RPP) were recorded at multiple perioperative time points. Volatile anesthetic requirements and adverse events were also assessed. Statistical analysis was performed using Student's t-test and z-test for proportions.

Results:
Group A demonstrated significantly lower pulse rates, RPP, and better perioperative hemodynamic stability compared to Group B. The hemodynamic response to laryngoscopy, intubation, and surgical stimuli was significantly blunted in the clonidine group. Higher sedation scores were observed preoperatively in Group A. Postoperative nausea, vomiting, and shivering were less frequent in Group A, although incidences of bradycardia and hypotension were higher but manageable.

Conclusion:
Oral clonidine (150 mcg) is an effective premedication agent that provides superior sedation, attenuates hemodynamic responses, reduces anesthetic requirements, and enhances postoperative recovery in patients undergoing elective abdominal surgery.

Keywords: *Clonidine, premedication, hemodynamic stability, sedation, abdominal surgery, anesthesia..*

1. INTRODUCTION

Premedication refers to the drugs given before anesthesia to prepare patients for surgery

Historically, herbal concoctions and alcohol were used to induce stupor for surgery before ether anesthesia was introduced in 1846 by W.T.G. Morton. Ether, while effective, caused excessive secretions and postoperative sickness, leading to the use of atropine and antihistamines to manage these side effects. In the 1940s, the introduction of curare and narcotic analgesics shifted practices toward lighter general anesthesia, with phenobarbitone used to ensure preoperative sleep.

Today, with advances like day surgeries and minimally invasive procedures, short-acting drugs are preferred to manage anxiety, pain, gastric acidity, and postoperative nausea and vomiting (PONV), aiming for quick recovery. Light anesthesia can cause sympathetic stimulation (e.g., during intubation or surgery) leading to dangerous hemodynamic instability, especially in patients with existing health issues. To control this, techniques such as local anesthetics, beta blockers, opioids, and volatile anesthetics are used.

Alpha-2 agonists, especially Clonidine hydrochloride, have become valuable for their ability to reduce sympathetic outflow, maintain hemodynamic stability, provide sedation, control anxiety, reduce pain, prevent nausea, and minimize postoperative shivering. Originally an antihypertensive, Clonidine has been increasingly used in anesthesia, including as an oral premedication. The current study aims to assess whether oral Clonidine can effectively provide sedation, stabilize hemodynamics, and offer postoperative pain relief in patients undergoing abdominal surgery under relaxant anesthesia.

AIM AND OBJECTIVES OF THE STUDY:

1. To evaluate the perioperative hemodynamic effects associated with a single oral dose of clonidine.
2. To assess the efficacy of a single oral dose of clonidine in attenuating hemodynamic responses to laryngoscopy and endotracheal intubation.
3. To determine the requirement of volatile anesthetic agents necessary to maintain pulse rate and blood pressure within ±20% of baseline (preoperative) values.

INCLUSION CRITERIA:

- Patients classified as American Society of Anesthesiologists (ASA) physical status I or II.
- Age between 20 and 60 years.
- Patients scheduled for elective abdominal surgery under general anesthesia.

EXCLUSION CRITERIA:

- Patients who are unwilling to participate or who do not meet the inclusion criteria; patients classified as ASA physical status III or IV.
- Patients with cardiovascular diseases, including hypertension, coronary artery disease (CAD), left ventricular hypertrophy (LVH), left ventricular failure (LVF), cerebrovascular accident (CVA), Asthma, COPD or diabetes mellitus or on monoamine oxidase (MAO) inhibitors.

STUDY DESIGN & STATISTICS:

Study type: Prospective, randomized, controlled, observational clinical investigation.

Statistical methods: The data were analyzed by calculating mean and standard deviation and standard error of mean; comparison was made between two study groups by student's t test and with standard institutional method.

Data on incidence of adverse drug reaction was recorded as the number of patients exhibiting and compared using z-test for difference of proportions.

METHODOLOGY

All patients underwent a thorough preoperative evaluation. A detailed history of the present illness, past medical conditions, and any previous exposure to anesthesia was obtained and recorded in a predesigned proforma. Written informed consent was obtained from each patient prior to inclusion in the clinical study. Patients were randomized based on their case numbers:

- Odd-numbered cases (1, 3, 5, 7, ..., 49) received a placebo tablet of Vitamin C.

- Even-numbered cases (2, 4, 6, 8, ..., 50) received a tablet of clonidine hydrochloride (150 mcg).

On arrival at the reception area of the operation theatres, patients were administered either a clonidine tablet (150 mcg) or a similar-looking Vitamin C tablet 90 minutes prior to the scheduled time of surgery.

Two groups were formed:

- Group A: 25 patients received clonidine 150 mcg orally.
- Group B: 25 patients received a placebo tablet of Vitamin C.

Baseline vital parameters, including heart rate, systolic blood pressure, and diastolic blood pressure, were recorded in Operating Room. After shifting the patient in operating room degree of sedation was assessed using Ramsay sedation score & patient was given general anesthesia.

The arterial pressure was maintained by adjusting the concentration of isoflurane to keep values within ±20% of baseline readings.
In cases of hemodynamic fluctuations, medical interventions were performed in addition to adjustments in the isoflurane dose:

- Bradycardia (heart rate < 60 bpm) was managed with intravenous administration of atropine 0.6 mg.
- Hypotension was initially managed with a 500 ml fluid bolus. If hypotension persisted, intravenous injection of mephentermine 6 mg was administered.

Hemodynamic parameters and electrocardiography (ECG) were monitored continuously and recorded at the following intervals:

- Prior to induction,1 minute, 5 minutes, and 10 minutes after endotracheal intubation, At the time of skin incision & 15 minutes prior to surgical closure.

In the postoperative period, vital signs were recorded at 30 minutes, 60 minutes, and subsequently at 4 and 6 hours after surgery.

The Rate Pressure Product (RPP), an index of myocardial oxygen demand, was calculated at each observation point by multiplying the systolic blood pressure by the heart rate.

The residual effects of neuromuscular blockade were reversed with intravenous neostigmine and glycopyrrolate, following which the patient was shifted to the recovery room.

SEDATION ASSESSMENT:
Sedation was evaluated upon arrival in the operating room and in the recovery room using the six-point Ramsay Sedation Scale:

1. Patient anxious, agitated, or restless.
2. Patient cooperative, oriented, and tranquil.
3. Patient responds to commands only.
4. Patient asleep but with a brisk response to light glabellar tap or loud auditory stimulus.
5. Patient asleep with a sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient exhibits no response to stimulus.

RESULTS

Patients received oral premedication with either clonidine or vitamin C upon arrival in the preoperative room and were observed for 90 minutes. Thereafter, they were shifted to the operating room, where preoperative hemodynamic parameters

(heart rate, ECG, SBP, DBP, MAP) and sedation level, assessed using the six-point Ramsay Sedation Scale, were recorded. Patients were continuously monitored, with observations recorded at key intervals: pre-induction, post-induction, 1 and 5 minutes after intubation, at skin incision, 15- and 30-minutes post-intubation, 15 minutes before closure, during transfer from the operating room, on arrival and discharge from the recovery room, and at 6 hours postoperatively.

PATIENT DEMOGRAPHICS AND INDICATIONS FOR SURGERY

(FIGURE 1) THE MEAN AGE OF PATIENTS WAS 44.0 YEARS, WITH THE MAJORITY IN THEIR LATE THIRTIES TO EARLY FORTIES. A TOTAL OF 66% (33/50) WERE AGED BETWEEN 36 AND 55 YEARS**.**

(Figure 2) Abnormal or dysfunctional uterine bleeding was the most common indication for hysterectomy (17/50), followed by uterine fibroids (12/50). Other indications included menorrhagia, adnexal masses, carcinoma endometrium, adenomyosis, and postmenopausal bleeding.

PREOPERATIVE SEDATION AND BASELINE HEMODYNAMICS

(Figure 3) Preoperative sedation levels assessed using the Ramsay Sedation Score were significantly better in the clonidine group (Group A), with most patients achieving a score of II or III. In contrast, 21/25 patients in the placebo group (Group B) had a score of I.

(Figure 4) Baseline hemodynamic parameters (pulse rate, SBP, DBP, MAP) were comparable between groups, with no significant differences.

HEMODYNAMIC CHANGES FOLLOWING PREMEDICATION

(FIGURE 5) AFTER 90 MINUTES OF ORAL PREMEDICATION, GROUP A SHOWED SIGNIFICANTLY LOWER PULSE RATES AND RPP COMPARED TO GROUP B. DIFFERENCES IN DBP AND MAP WERE ALSO SIGNIFICANT, THOUGH SBP DIFFERENCES WERE NOT**.**

Response to Anesthetic Induction and Intubation

(Figure 6) Post-induction, Group A had significantly lower pulse rates, SBP, DBP, MAP, and RPP than Group B. One minute after intubation, hemodynamic responses were exaggerated in Group B compared to Group A. RPP exceeded the critical value in the placebo group but remained below it in the clonidine group. Five minutes post-intubation, cardiovascular parameters began to decline but remained significantly higher in Group B.

Hemodynamic Response to Surgical Stimuli

(Figure 7) At skin incision, slight but significant increases in SBP, DBP, and MAP were observed, with Group A maintaining better control.

Intraoperative Hemodynamic Stability: Throughout surgery, parameters remained within ±20% of baseline. Pulse rates and RPP were consistently lower in Group A, with highly significant differences, though SBP, DBP, and MAP differences were not consistently significant.

Postoperative Hemodynamic Trends

(Figure 8) On arrival in the recovery room, Group A had a significantly lower pulse rate and RPP than Group B. SBP, DBP, and MAP were comparable between groups. At discharge from the recovery room, Group A continued to show a significantly lower pulse rate and RPP compared to Group B.
(Figure 9) Six hours postoperatively, cardiovascular parameters in both groups approached preoperative values. Pulse rates, DBP, MAP, and RPP remained significantly lower in Group A.

Adverse Events

(Figure 10) Sinus bradycardia and hypotension were more frequent in the clonidine group but were effectively managed. Postoperative nausea, vomiting, and shivering were significantly more common in the placebo group.

Figures and Tables Legends

Figure 1: Age distribution of patients. (MEAN AGE = 44 years)

Age (in years)	Number of patients
25-35	12
36-45	21

46-55	12
>55	5

Figure 2: Indications for hysterectomy among study subjects.

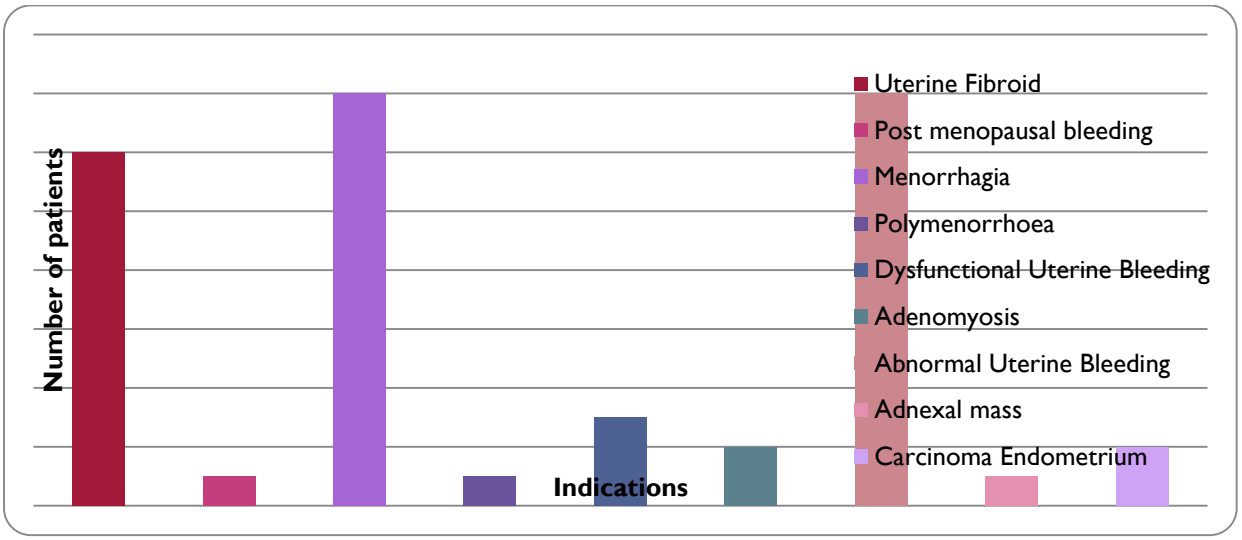


Figure 3: Preoperative sedation levels assessed by Ramsay Sedation Score.

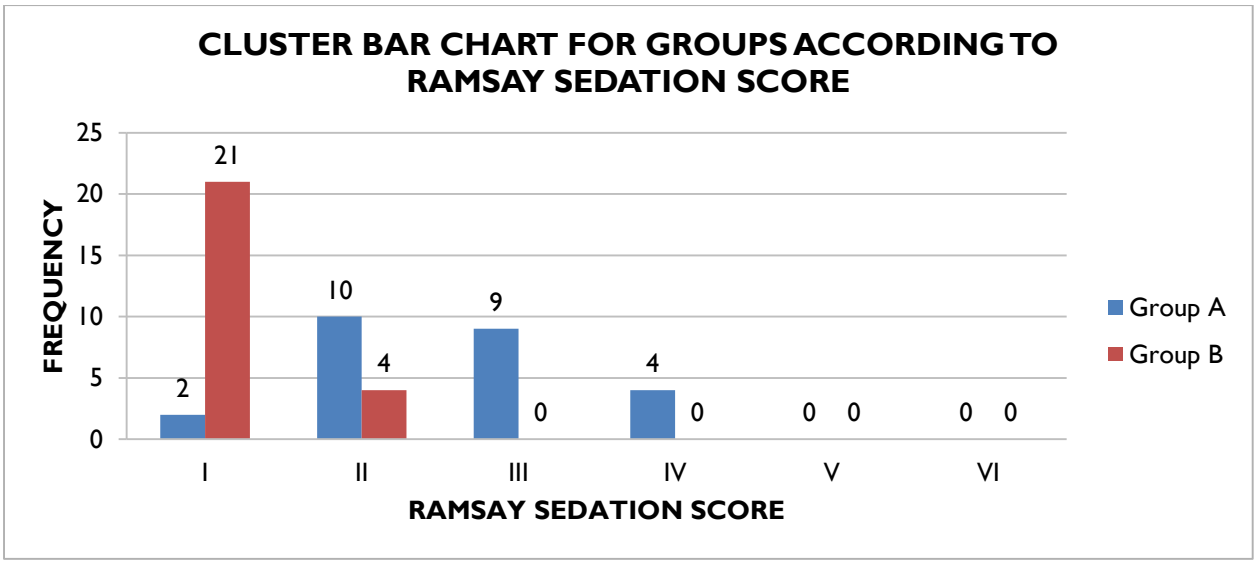
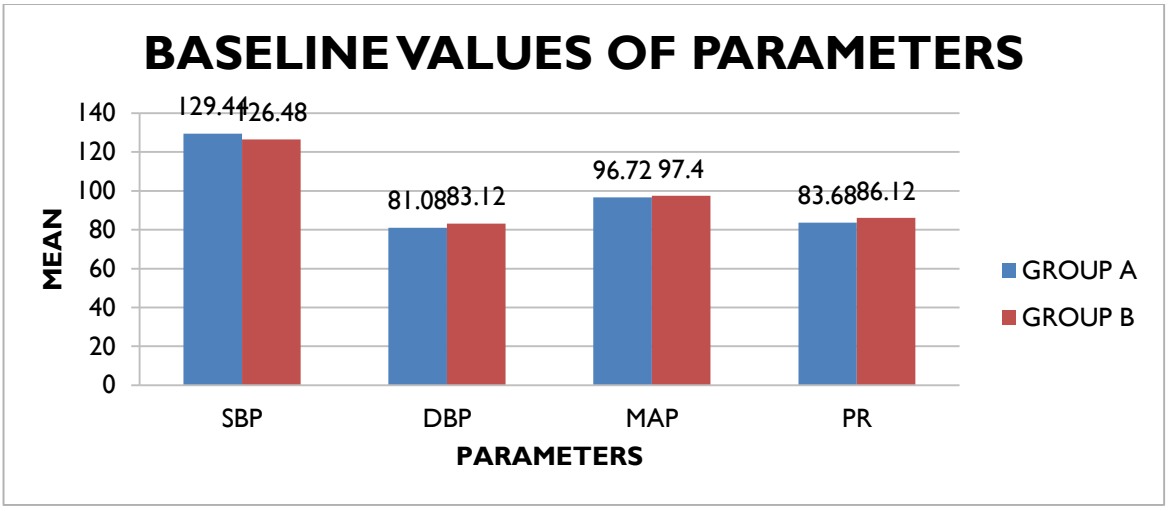
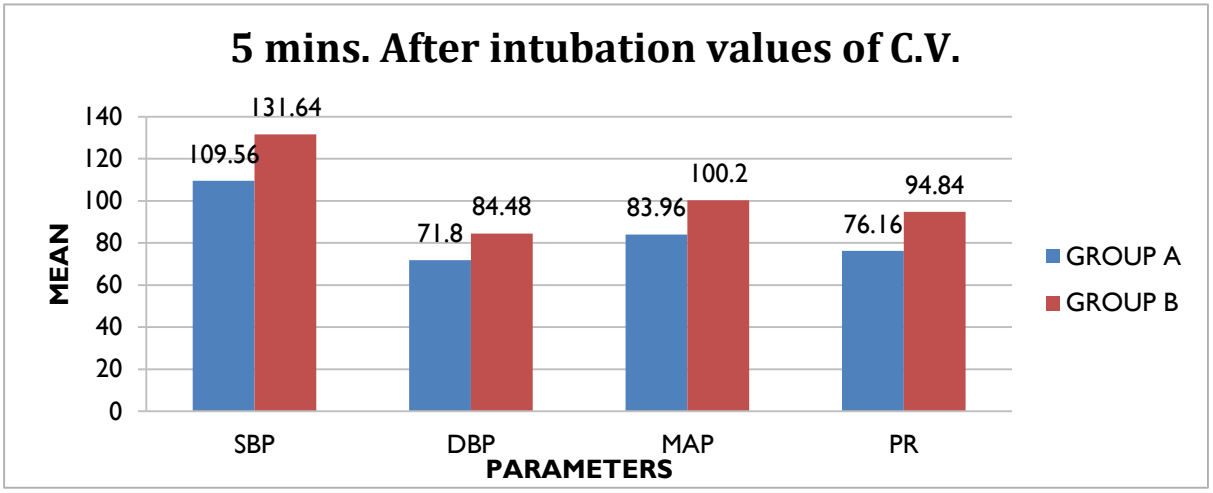


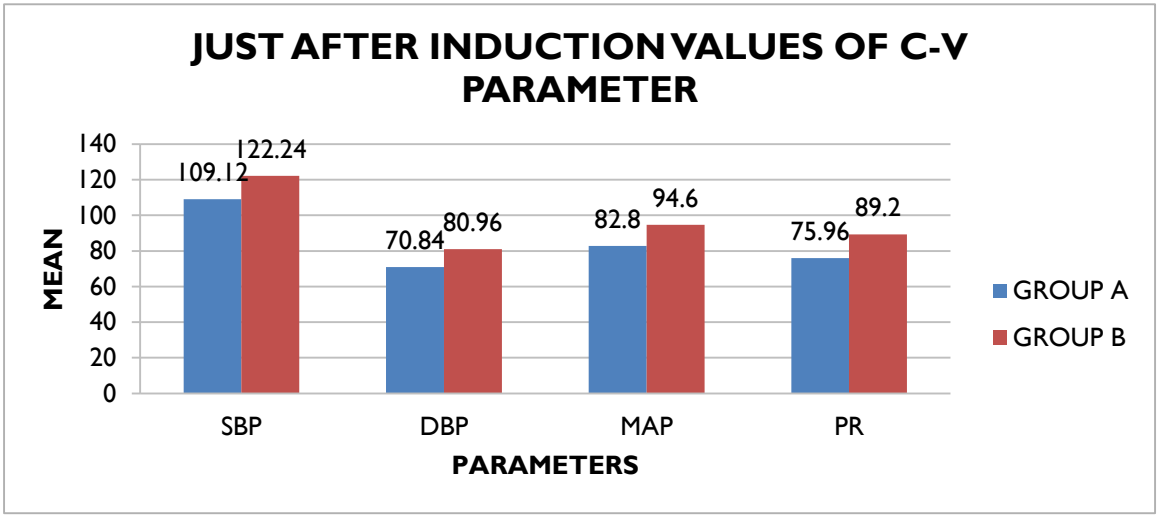
Figure 4: Baseline preoperative hemodynamic parameters.



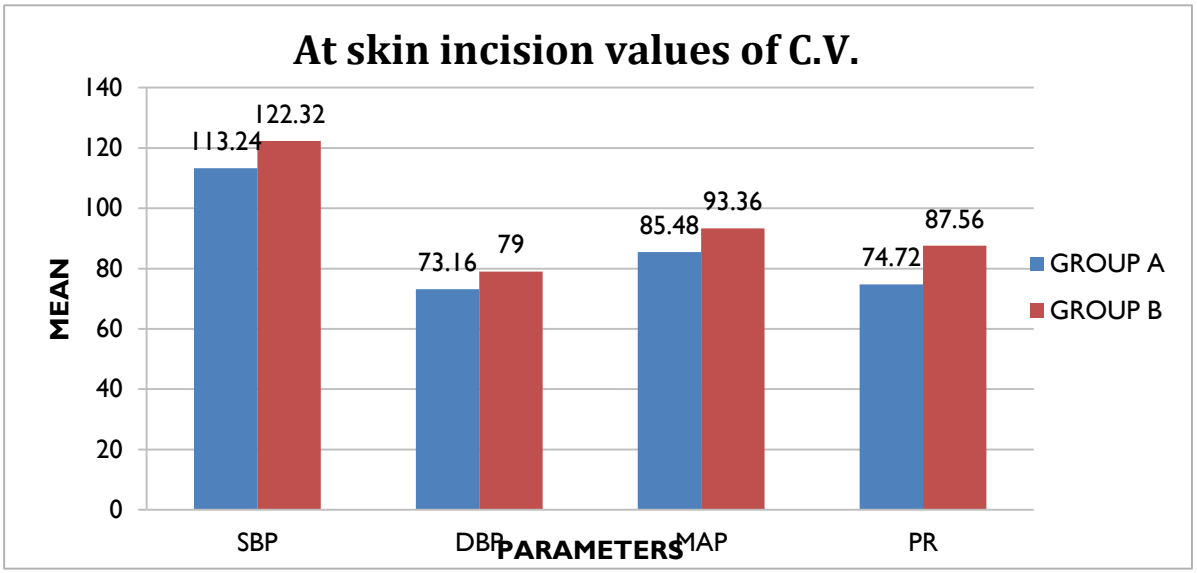
- **Figure 5**: Hemodynamic parameters after 90 minutes of premedication.



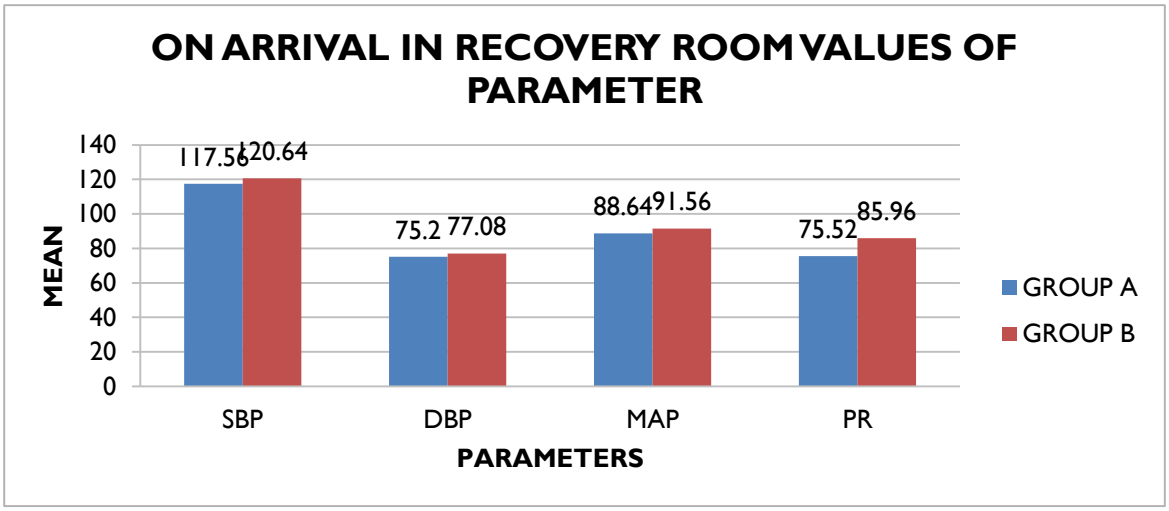
- **Figure 6**: Hemodynamic changes following induction of anesthesia.



- **Figure 7**: Hemodynamic changes at skin incision.



- **Figure 8**: Hemodynamic parameters on arrival in recovery room.



- **Figure 9**: Hemodynamic parameters six hours postoperatively.

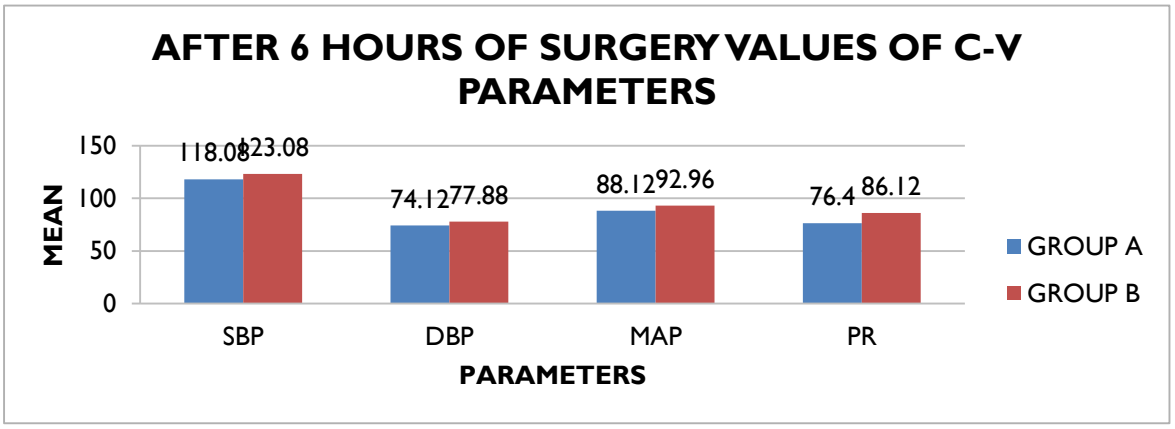


Figure 10: Incidence of adverse events in study and control groups.

Complication	Group A	Group B	Z value	P value
Bradycardia	14	3	3.28	0.001
Hypotension	6	2	1.54	0.123
Vomiting	1	8	2.57	0.009
Shivering	2	10	2.64	0.008

DISCUSSION

In the current era of day-care surgeries, medications with short to intermediate durations of action are preferred to help patients meet discharge criteria as early as possible. During surgery, events such as laryngoscopy, endotracheal intubation, skin incisions, and manipulation of internal organs often trigger acute surgical stress, leading to temporary increases in heart rate and blood pressure. While such fluctuations are typically well tolerated by normotensive patients without cardiovascular disease, they can pose significant risks for individuals with uncontrolled hypertension, coronary artery disease, valvular heart conditions, or a history of cerebrovascular accidents, potentially precipitating serious cardiac events. Clonidine and other alpha-2 adrenergic agonists (such as dexmedetomidine) are being extensively studied as adjuncts to anesthesia. Their desirable effects during the perioperative period include sedation, analgesia, and anti-shivering action. The use of clonidine, in particular, enhances cardiovascular stability by mitigating the body's stress response to surgical and anesthetic stimuli**.**

This study was conducted on 50 adult female patients undergoing total abdominal hysterectomy and other gynecological surgeries under general anesthesia, all procedures associated with moderate to severe surgical stress. The objective was to assess the cardiovascular protective effects of a single oral dose of clonidine, along with its other pharmacological benefits.

This study aimed to evaluate the effectiveness of oral clonidine premedication in perioperative sedation, cardiovascular stability, and hemodynamic responses. The findings suggest that clonidine administration has a significant impact on sedation levels, pulse rate, blood pressure, and the rate pressure product (RPP) in patients undergoing surgery. These results align with various other studies that support the use of clonidine as a reliable premedicant.

Dose and Timing of Administration

A fixed dose of 150 mcg of clonidine, roughly 2.5-3 mcg/kg for patients weighing between 50-60 kg, was administered 90 minutes before anesthesia induction. Pharmacokinetic studies indicate that clonidine reaches peak plasma concentration within 60-90 minutes post-oral administration. This is consistent with findings from studies by Dr. Dipak L. Rawal and Dr. Malini K. Mehta[1], who used similar doses in their clinical trials. Additionally, studies by Shuichi Yokota[2] and others have demonstrated a dose-dependent relationship between clonidine administration and its sedative as well as cardiovascular effects.

Level of Sedation

The preoperative sedation level was measured using the Ramsay Sedation Score (RSS), with 19 out of 25 patients in the clonidine group achieving a sedation score of 2 or 3. This compares favorably to the 21 out of 25 patients in the control group who had a score of 1. Patients in the clonidine group were mostly cooperative, oriented, and responsive to commands. Studies by Braz L.G. et al.[3] (2002) and Shuichi Yokota[2] (1998) have similarly reported clonidine's sedative and analgesic properties. Furthermore, Dr. Rita Singh[4] and colleagues (2015) found clonidine premedication significantly reduced preoperative anxiety compared to placebo, a finding also supported by others researchers in this field. These observations suggest that clonidine is an effective agent for sedation and anxiety reduction, particularly in preoperative settings.

Changes in Pulse Rate (Heart Rate)

Regarding heart rate, the clonidine group showed a slight reduction in pulse rate (4.0 bpm) 90 minutes after premedication, with values stabilizing before induction. Both groups exhibited an increase in heart rate immediately after induction, laryngoscopy, and intubation, but the clonidine group demonstrated a significantly lower heart rate during this stressful period. Studies, including those by Savitha K.S. et al. (2014)[5] and Idit Matot et al.[6] (2000), have similarly noted that clonidine reduces heart rate changes during stressful events like intubation and laryngoscopy. This suggests that clonidine premedication may help attenuate the sympathetic response during the perioperative period, providing cardiovascular protection, especially in high-risk patients.

Changes in Systemic Blood Pressure

Systemic blood pressure was closely monitored throughout the perioperative period, including at anesthesia induction,

laryngoscopy, skin incision, and during operative manipulation. The clonidine group showed significantly lower systolic, diastolic, and mean arterial pressures (MAP) compared to the control group at key points such as induction and skin incision.

Changes in Rate Pressure Product (RPP)

The rate pressure product (RPP), an indicator of myocardial workload and energy demand, was also assessed. The results indicated that the RPP in the clonidine group remained lower than in the control group throughout the perioperative period. During periods of maximum stress (e.g., airway instrumentation), the clonidine group showed an RPP that stayed well below the critical threshold for cardiovascular events, while the control group reached near-critical levels. These findings are in line with previous studies, such as those by Rashmi Rani and S.S. Nesargi (2015)[7], which reported that clonidine helps maintain RPP within safe limits, reducing the risk of cardiac events during surgery.

Adverse Effects

While clonidine showed significant benefits in terms of sedation and cardiovascular stability, it was also associated with some adverse effects, particularly bradycardia and hypotension. These effects were managed effectively with atropine, fluid administration, or vasopressors, a finding consistent with other research in this area. Additionally, clonidine's anti-shivering properties led to fewer incidences of shivering and vomiting in the study group compared to the control group. These results align with the observations made by Joan W. Flacke et al.[8] (1987) and Dr. Rita Singh et al. (2015)[4], who also noted a reduced incidence of shivering with clonidine premedication.

CONCLUSION

In conclusion, oral clonidine premedication effectively reduces preoperative anxiety, provides sedative and analgesic effects, and stabilizes cardiovascular parameters during the perioperative period. It helps attenuate the hemodynamic stress response, including increases in heart rate and blood pressure, thereby improving perioperative outcomes. While clonidine can cause bradycardia and hypotension, these side effects are generally manageable, and the benefits of clonidine in high-risk patients may outweigh these risks. Given its ability to enhance sedation and cardiovascular stability, clonidine remains a valuable agent for premedication in patients undergoing surgical procedures.

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