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Original Research Article

Comparative Analysis of Clonidine and Dexmedetomidine for Hemodynamic Stability and Postoperative Pain Management in Laparoscopic Surgery

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Conflict of interest: Nil

Abstract

Background: Alpha-2 (α2) adrenergic receptor agonists, such as clonidine and dexmedetomidine, are commonly used as adjuvants during anesthesia due to their analgesic, sedative, sympatholytic, and cardiovascular-stabilizing effects. This study aimed to compare the effectiveness of intravenously administered clonidine and dexmedetomidine in achieving hemodynamic stability and postoperative analgesia during laparoscopic surgery.

Methods: This randomized, double-blind, prospective study involved two groups of patients. Group C received 2 µg/kg of clonidine diluted in 10 ml of normal saline, administered as a slow intravenous infusion over 10 minutes before the induction of general anesthesia. Group D received 1 µg/kg of dexmedetomidine, also diluted in 10 ml of normal saline, administered in the same manner.

Results: Data were presented as Mean ± SD. An independent student's t-test was used to compare the groups. A repeated measure analysis of variance (ANOVA) using general linear models (GLM) was also conducted. The mean systolic blood pressure (SBP) scores were higher in Group C throughout the procedure compared to Group D. The mean diastolic blood pressure (DBP) scores were similar in both groups, although slightly higher in Group C, particularly from 30 minutes post-induction until extubation, compared to Group D.

Conclusion: The study concludes that α2 agonists attenuate the hemodynamic response to pneumoperitoneum during laparoscopic surgeries and provide reliable postoperative analgesia and sedation when used as premedication agents.

Keywords: α2 Agonist, General Anesthesia, Pneumoperitoneum, Dexmedetomidine, Hemodynamics, Clonidine.

Introduction

Laparoscopic cholecystectomy is now the gold standard for treating cholelithiasis. This modern surgical technique involves inflating the peritoneal cavity with gas (usually CO2) under pressure. The resulting pneumoperitoneum increases intra-abdominal pressure, which leads to elevated plasma renin activity, higher plasma catecholamine levels, and increased blood volume [1]. Anesthesiologists often encounter challenges managing these hemodynamic changes. Studies have shown a 10–30% reduction in cardiac output during pneumoperitoneum [2]. Increases in arterial pressure can increase the risk of adverse cardiovascular events in patients with pre-existing conditions such as essential hypertension, ischemic heart disease, or elevated intracranial pressure. Hypercapnia and pneumoperitoneum activate the sympathetic nervous system, causing the release of catecholamines and vasopressin [3].

Various strategies have been employed to mitigate these hemodynamic responses, including deepening the level of anesthesia with higher concentrations of inhalational and intravenous anesthetic agents, high doses of opioids, and antihypertensives such as beta-adrenergic blockers and sodium nitroprusside [4]. Additionally, regional or local neural blockades with local anesthetics were used. Clonidine, with an elimination half-life of 6–10

hours, is a centrally acting selective partial α2 agonist (220:1, α-2 to α-1). It is known to induce sedation and improve perioperative hemodynamics by stabilizing blood pressure and heart rate responses to surgical stimulation. Clonidine protects against perioperative myocardial ischemia, providing sympathoadrenal stability and suppressing renin-angiotensin activity. Furthermore, it increases cardiac baroreceptor reflex sensitivity to systolic blood pressure increases, thus stabilizing blood pressure [5].

Dexmedetomidine, with an elimination half-life of 2–3 hours, is a highly selective and potent α2 agonist (1620:1, α-2 to α-1) and is 7–10 times more selective for α2 receptors compared to clonidine [6]. It has a shorter duration of action and is considered a full agonist at α2 receptors, unlike clonidine, which is a partial agonist. Laparoscopic cholecystectomy is a common procedure, and maintaining stable intraoperative hemodynamics is crucial. This study was designed to assess the effects of dexmedetomidine and clonidine, an established antihypertensive, in reducing intraoperative hemodynamic stress responses to pneumoperitoneum when administered intravenously as pre-anesthetic medication [7]. The study aimed to compare the effects of premedication with dexmedetomidine or clonidine on mean arterial pressure (MAP) 10 minutes after pneumoperitoneum in patients undergoing laparoscopic cholecystectomy under general anesthesia (primary outcome). Additionally, changes in heart rate, mean arterial blood pressure, and systolic and diastolic blood pressure at various time points during pneumoperitoneum were evaluated. Any adverse events were also observed.

Material and Methods

This prospective study was conducted on 50 patients in the Department of Anesthesiology, Prathima Institute of Medical Sciences, Naganaoor, Karimnagar. who underwent laparoscopic surgery. It was a prospective, randomized, double-blind study, approved by the Institutional Ethics Committee. Informed written consent was obtained from the patients and their attendants, explaining the study's purpose, methods, risks, and their right to participate.

Inclusion Criteria

1. Aged 20 – 40 years
2. Undergoing laparoscopic surgery
3. ASA grades I and II
4. Males and Females
5. Willing to participate in the study

Exclusion Criteria

1. Cardiovascular diseases
2. Renal and hepatic diseases
3. Pregnant and breastfeeding females
4. Diabetes mellitus
5. On antihypertensives, antipsychotics, and sedative medications

Patients were randomly divided into two groups of 35 each, using a computer-generated random number table. Group C received 2 µg/kg of clonidine, diluted in 10 ml of normal saline, administered slowly via intravenous infusion over 10 minutes before the induction of general anesthesia. Group D received 1 µg/kg of dexmedetomidine, diluted in 10 ml of normal saline, administered in the same manner. Baseline cardio-respiratory parameters, along with electrocardiography, temperature, and end-tidal CO_2, were recorded.

All patients were pre-medicated with intravenous ondansetron 4 mg, glycopyrrolate 0.2 mg, and fentanyl 2 µg/kg. Clonidine for Group C and dexmedetomidine for Group D were administered 10 minutes before induction. General anesthesia was induced with propofol 2 mg/kg, and endotracheal intubation was facilitated with vecuronium bromide 0.1 mg/kg intravenously. Anesthesia was maintained with oxygen and nitrous oxide in a 33:66 ratio, along with halothane at 0.5-1% v/v. Muscle relaxation was sustained with intermittent doses of vecuronium bromide 0.02 mg/kg.

Controlled mechanical ventilation ensured end-tidal CO_2 levels between 30-40 mmHg. Intra-abdominal pressure during pneumoperitoneum was kept between 12-14 mmHg. Patients were placed in a supine position with a 15° left lateral tilt and 30° head elevation. Intraoperative monitoring included non-invasive arterial blood pressure, electrocardiography, capnography, pulse oximetry, and temperature.

At the end of the surgery, residual neuromuscular block was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.2 mg per mg of neostigmine intravenously. Patients were extubated after complete reversal of neuromuscular blockade and restoration of spontaneous respiration, then transferred to the recovery room. Sedation scores were noted according to the Ramsay sedation scores at pre-induction and during the postoperative period.

Ramsay Sedation Scale:

1. Anxious and agitated or restless or both.
2. Cooperative, oriented, and tranquil.
3. Drowsy but responds to commands.
4. Asleep, brisk response to a light glabellar tap, or loud auditory stimulus.
5. Asleep, sluggish response to a light glabellar tap or loud auditory stimulus.
6. Asleep or unarousable.

Pain was assessed using a 10-point Visual Analogue Scale (VAS) at the end of surgery, and at 15, 30, 45, 60, and 90 minutes postoperatively. Patients were observed in the postoperative room until a VAS score of 5 was achieved. Rescue analgesia was provided with an injection of Diclofenac sodium 75 mg IV as the first line and Tramadol 2 mg/kg IV as the second line of analgesia.

Statistical analysis: All the available data was uploaded to an MS Excel spreadsheet and analyzed by SPSS version 21 in Windows format. The continuous variables were represented as mean, standard deviation, and percentage. The categorical variables were calculated by chi-square test for the difference between the two groups and values of p (<0.05) were considered significant.

Results

A total of 50 cases were included in the study and they were equally allotted to two groups. Table 1 presents the demographic characteristics of two groups of patients: Group C (receiving 2 µg/kg of clonidine) and Group D (receiving 1 µg/kg of dexmedetomidine). There are no statistically significant differences in age, sex, weight, or APACHE II score between the two groups (p-value > 0.05 for all comparisons). The results indicate that the two groups are well-matched in terms of demographic characteristics and disease severity (as assessed by APACHE II score).

Table 1: Shows the distribution of demographic details among two groups

Parameters	Group C (N=25) 2 µg/kg of clonidine	Group D (N=25) 1 µg/kg of dexmedetomidine	P value
Age (years)	32.55.28 ± 8.54	31.55 ± 8.75	0.229
Sex (M: F)	13:12	14:11	0.432
Weight (kgs)	53.35.00 ± 7.62	55.19 ± 6.21	0.198
APACHE II-score	12.21 ± 1.95	12.52 ± 1.89	0.992

Table 2 presents the distribution of Ramsay Sedation Scores among two groups of patients: Group C (receiving 2 µg/kg of clonidine) and Group D (receiving 1 µg/kg of dexmedetomidine). Both groups primarily exhibited sedation scores of 3 and 4, indicating a moderate level of sedation. The mean Ramsay Sedation Score was significantly lower in Group D (dexmedetomidine group) compared to Group C (clonidine group). There were differences in the distribution of scores between the two groups, with Group D showing a higher proportion of patients with lower sedation scores (2 and 3). The results indicate that dexmedetomidine (Group D) provided a lower level of sedation compared to clonidine (Group C).

Table 2: Shows the distribution of Ramsay Sedation Score among 2 groups

Ramsay score	Group C (N=25) 2 µg/kg of clonidine	Group D (N=25) 1 µg/kg of dexmedetomidine
1	4	3
2	1	2
3	8	14
4	5	6
5	2	0
6	5	1
Mean ± SD	3.85 ± 2.94	3.02 ± 0.14
P value	0.0491*	

*Significant

Figure 1 shows that at baseline, Group C has a slightly higher average SBP than Group D, but Group C also shows more variability (higher SD). At 5 minutes: Group-C: Mean SBP increases to 126.6 mmHg (SD = 5.26). Group-D: Mean SBP is 120.89 mmHg (SD = 3.77). Group C shows a slight increase in mean SBP with reduced variability, while Group D remains stable with minimal change. At 10 minutes: Both groups show an increase in SBP, but Group C shows less variability compared to Group D. Group D experiences a noticeable decrease in SBP, suggesting a response to induction, while Group C shows a minor decrease. Intubation: at 15 minutes Both groups show an increase in SBP during intubation, with Group C showing a larger increase. Skin Incision: Both groups show a decrease in SBP after the initial rise, with Group C having more variability. CO_2 Insufflation: Both groups experience an increase in SBP during CO_2 insufflation, with Group-C slightly higher. Extubation: 90 to 120 minutes SBP rises for both groups, with Group-C consistently having higher mean SBP than Group-D. Throughout the periods, Group D tends to have higher variability in SBP compared to Group D,

especially at baseline and during certain procedural stages.

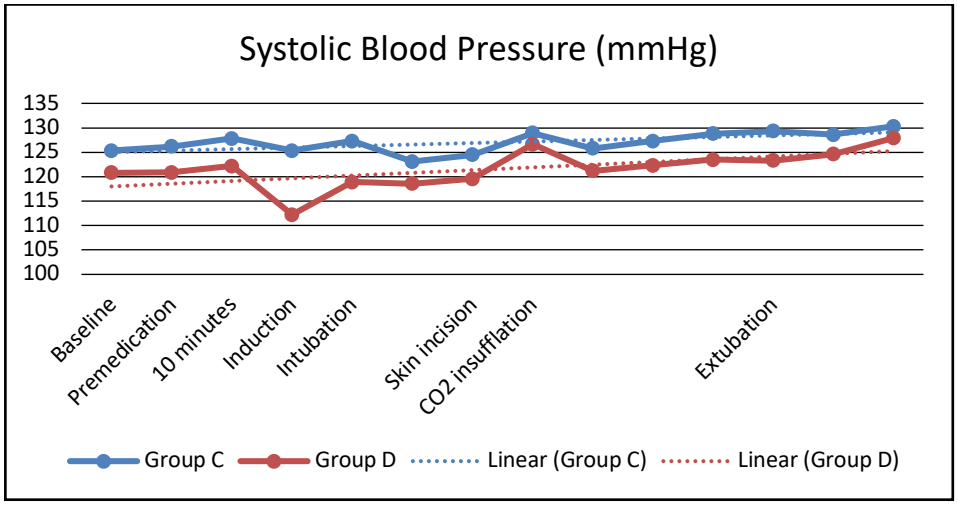

Figure 1: Shows Mean Systolic blood pressure (mm/Hg) in two groups

Figure 2 presents the diastolic blood pressure (DBP) values for two groups (C and D) at various time points during a procedure. Both groups exhibited similar DBP values at baseline. Both groups experienced a slight decrease in DBP during the early phases of the procedure (up to induction), followed by a gradual increase towards baseline levels. There were minimal differences in DBP between the two groups throughout the monitoring period. This suggests that both groups experienced similar hemodynamic responses to the procedure, with a transient decrease in DBP followed by a return toward baseline levels. The small differences observed between the groups were not clinically significant.

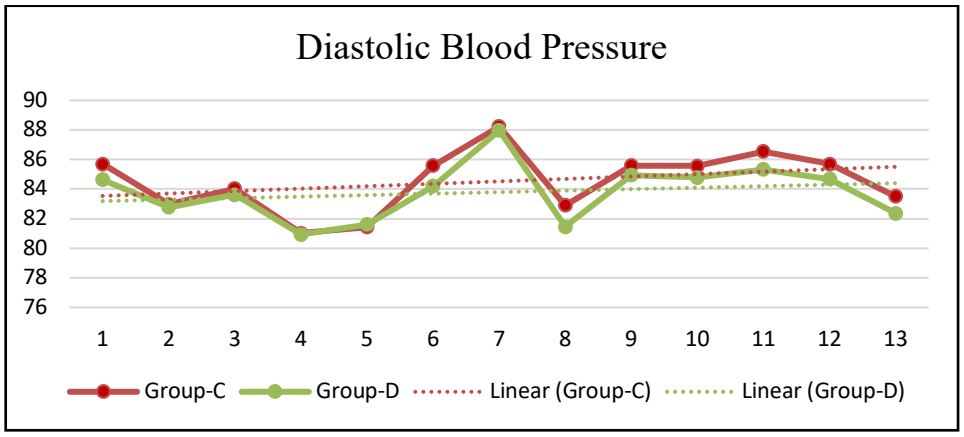

Figure 2: Shows Mean Diastolic blood pressure (mm/Hg) in two groups

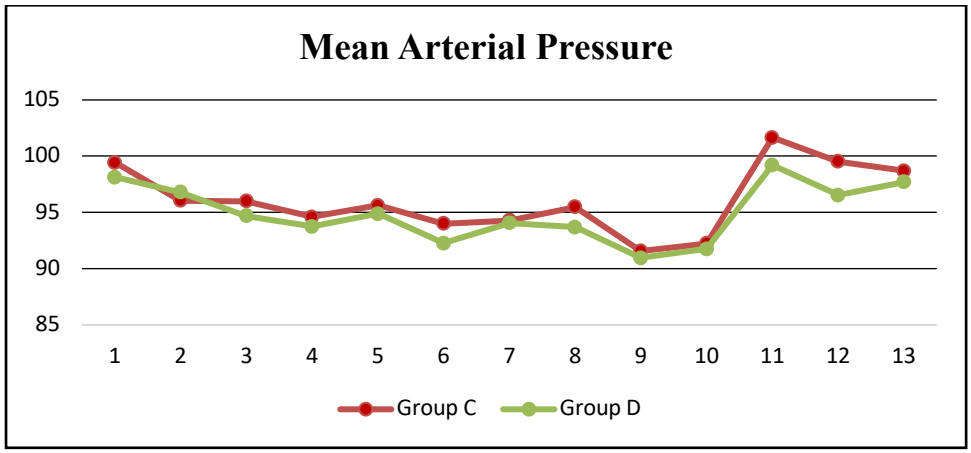

Figure 3: Shows Mean Arterial blood pressure (mm/Hg) in two groups

Figure 3 presents the mean arterial pressure (MAP) values for two groups (C and D) at various time points during a procedure. Both groups exhibited similar MAP values at baseline. Both groups experienced a slight decrease in MAP during the early phases of the procedure (up to induction), followed by a gradual increase toward baseline levels. There were minimal differences in MAP between the two groups throughout the monitoring period. The data suggests that both groups had similar hemodynamic responses to the procedure, with a transient decrease in MAP followed by a return toward baseline levels. The small differences observed between the groups were not clinically significant.

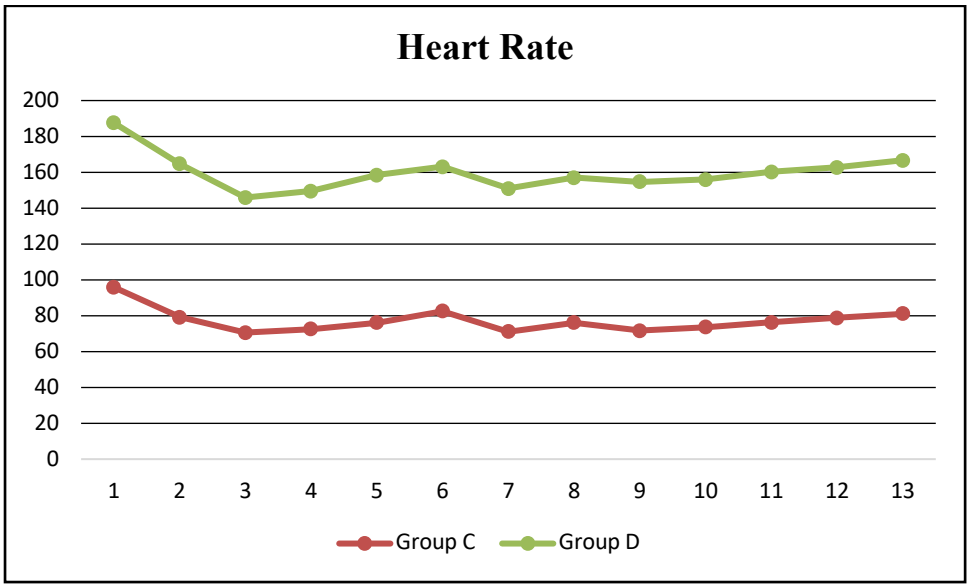

Figure 4: Shows Mean Heart Rate in beats per minute in two groups

Figure 4 presents the mean arterial pressure (Heart Rate) values for two groups (C and D) at various time points during a procedure. Group C consistently exhibited lower Heart Rate values compared to Group D at all measured time points. The p-value of 0.01 for all time points indicates a statistically significant difference in Heart Rate between the two groups. Both groups showed a general trend of decreasing Heart Rate during the initial phases of the procedure, followed by a gradual increase. The results demonstrate a clear and consistent difference in Heart Rate between Group C and Group D throughout the procedure. Group C maintained significantly lower Heart Rate values compared to Group D. At the end of the surgery, the mean Visual Analog Scale (VAS) score was significantly lower in Group D compared to Group C (3.69 ± 1.12 vs. 1.39 ± 1.56, $p<0.0001$). In this study, bradycardia was observed in 3 patients (12%) in Group C and D patients (8%) in Group D, with no significant difference between the two groups ($p=0.64$).

Discussion

Several agents are employed for premedication and induction, with a tendency to counteract hemodynamic changes during laparoscopic interventions. Several interventions have been developed by researchers, including beta-blockers, α2 agonists, magnesium sulfate, opioids, vasodilators, and gasless methods. Thus, the choice of this study was based on the fact that it involved a comparison of the two most widely used α-2 agonists in anesthetic practice to determine their ability to suppress stress responses and hemodynamic alterations related to laparoscopy as well as the efficacy of postoperative analgesia [8, 9]. In our study, both groups showed an improvement in at least one clinically significant parameter, namely a decrease in SBP. SBP was lower with dexmedetomidine at intubation, during pneumoperitoneum, at extubation, and during the postoperative period, and the difference was statistically significant as compared to clonidine. Both drugs helped narrow the fluctuations of SBP and even reduced augmentation during different phases of anesthesia as well as during laparoscopy, which conforms to the studies conducted by Kumar et al. [10]. A Comparison was made between clonidine and dexmedetomidine at the time of extubation, and clonidine increased the SBP level. This also means that, unlike dexmedetomidine, the effect of clonidine in raising SBP was not sustained beyond the intubation phase, which directly affected the postsurgical outcomes because clonidine was not as effective in preventing hemodynamic changes when the patients were extubated. These two drugs also dampened the

early stages of DBP but failed to blunt the extubation-stimulated DBP rise, comparable to the study by Prasad et al. [11]. Regarding MAP, the two groups were not statistically different during the first phase of the procedure. Ultimately, both drugs were able to reduce the increase in MAP, yet to a lesser extent than clonidine, mainly because this drug did not act as a potent inhibitor of the increase in MAP in response to surgical stress.

It emerged that the mean heart rate was significantly lower in the clonidine group throughout the whole procedure compared to the dexmedetomidine group. Both groups revealed a reduced heart rate compared to the baseline, and the change differed significantly from the baseline. However, some of the patients taking clonidine also experienced a considerable degree of bradycardia that necessitated intervention or dose modification. In patients with coronary artery disease the ability of both drugs to decrease the heart rate therefore decreasing myocardial oxygen demand was advantageous. This was particularly true of dexmedetomidine – in agreement with the findings of the study carried out by Naz Anjum et al. [12] The drugs maintained intraoperative hemodynamic stability and the efficacy of dexmedetomidine was similar to that of clonidine during laparoscopic surgeries. In a similar study by Pravin Ubale et al [13] it was also observed that oral clonidine premedication can produce a similar effect as observed in this study. Compared with clonidine as preoperative medication and intraoperative infusion, dexmedetomidine has been evidenced to lessen the sympathoadrenal response to tracheal intubation from previous studies as well. As compared to pneumoperitoneum and intubating stresses, clonidine at the dose of 1 μg/kg IV was less effective for preventing hemodynamic alterations during extubation. Hemodynamic responses to pneumoperitoneum, intubation, and extubation were prevented using clonidine at a dose of 2 μg/kg. In this study, 2 μg/kg of clonidine was able to inhibit the response to laryngoscopy and intubation but not extubation although the p-value was not very much different compared to 1 μg/kg of dexmedetomidine. Therefore, we found that 1 μg/kg of dexmedetomidine was more effective than 1 μg/kg of clonidine and as effective as 2 μg/kg of clonidine.

Regarding the postoperative pain assessed using the VAS, clonidine infusion was associated with VAS of 3/10 and all subjects required analgesics at 60 minutes after the surgery 8 of 25 patients requested additional analgesia at the time of extubation. On the other hand, the mean VAS score at the end of the procedure in the dexmedetomidine group was 1.39, the majority of the patients demonstrated adequate analgesia for up to 90 minutes. Thus, in the comparison of analgesic efficacy, dexmedetomidine proved to be more effective than clonidine in the duration of analgesia. Sedation scores in the two groups were 3.85 for clonidine and 3.02 for dexmedetomidine respectively with p=0.30, hence the difference is not statistically significant. Therefore, the patient's sedation level was equally compromised in both brackets. The sedation status, postoperative observation, and cooperation degree of the patients in the two groups were superior, which indicated that dexmedetomidine had a sedation effect and analgesia effect in proportion to each other so no airway or ventilator assistance was required. As for the adverse effects described in the study, no serious complications were observed except for bradycardia in 3 patients treated with clonidine and 2 patients treated with dexmedetomidine; however, this difference was not statistically significant and did not require any actions. The incidence of hypotension was found to be statistically significant and required intervention; this was manifested in 12 patients under clonidine and 4 patients under dexmedetomidine. No patients had any rebound hypertension thus it can be deduced that both drugs are safe.

Conclusion

The analysis of hemodynamic parameters in groups C (clonidine) and D (dexmedetomidine) revealed significant differences in SBP and heart rate, and the differences between the groups regarding DBP and MAP were not found to be clinically significant. Both α2 agonists effectively attenuated hemodynamic responses during laparoscopic surgery and provided reliable postoperative analgesia and sedation when used as premedication agents.

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