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ORIGINAL ARTICLE

Effect of Low-Dose Dexmedetomidine Infusion on Hemodynamic Responses and Anaesthetic Requirements During Laparoscopic Surgery

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Abstract

Introduction: Laparoscopic surgeries conducted under general anaesthesia are associated with peri-operative hemodynamic stress due to tracheal intubation, laryngoscopy, pneumoperitoneum, and extubation. These responses may lead to hypertension, tachycardia, and increased anaesthetic agent requirements. Dexmedetomidine, a selective alpha-2 adrenergic agonist, has been proved to attenuate the sympathetic responses and to reduce the anaesthetic requirements. **Materials and Methods:** This study was done after getting Institutional Ethics Committee approval and the written informed consent from all the study participants. The patients belonging to ASA physical status I and II and those who undergo the elective laparoscopic surgeries were allocated into two groups randomly: Dexmedetomidine group (DX) and Normal Saline group (NS). The DX group received dexmedetomidine infusion at 0.4 µg/kg/hr, and the Normal Saline group received an equivalent volume of saline. Standard general anaesthesia was administered, and the bispectral index monitored the depth of anaesthesia. **Results:** Baseline demographic data and surgical profiles were compared between the two study groups. The dexmedetomidine group demonstrated significant reduction of blood pressure and heart rate responses during the laryngoscopy, intubation, pneumoperitoneum, and extubation compared to the other group (NS). End-tidal isoflurane concentration, isoflurane, total propofol, and fentanyl requirements were significantly lesser in the dexmedetomidine group ($p < 0.001$). Time of awakening was comparable between groups. **Conclusion:** Low-dose dexmedetomidine infusion at 0.4 µg/kg/hr offers effective reduction of peri-operative hemodynamic stress responses during the laparoscopic surgery, which significantly lessens the anaesthetic drug and opioid requirements. It also improves the cardiovascular stability without delaying the recovery time or without increasing the adverse effects.

Keywords: Dexmedetomidine, Hemodynamic response, Laparoscopic surgery, Anaesthetic requirement, Bispectral index

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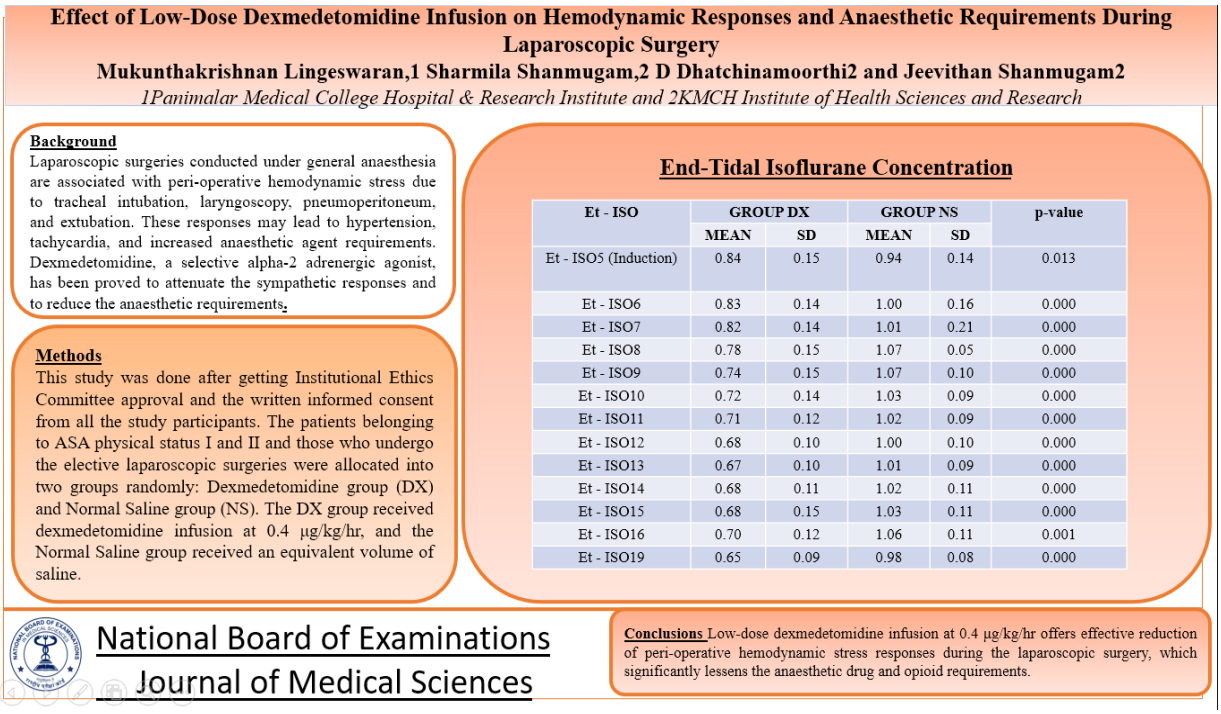
Graphical Abstract



Introduction

Laparoscopic surgery had shown remarkable evolution since the introduction of diagnostic laparoscopy since 1960s. The pioneering work of Muehe E and Semm K in the early 1980s had established laparoscopy as a definitive surgical procedure, leading to its improved adoption across multiple surgical specialties [1]. Owing to the main advantages like, early mobilization, less postoperative pain, shorter hospital stay, and improved cosmetic outcomes, laparoscopic procedures have become the gold standard for various gastrointestinal and gynaecological surgeries [2-5].

However, laparoscopic surgery under general anaesthesia is commonly associated with significant peri-operative hemodynamic stress. Laryngoscopy, tracheal intubation, pneumoperitoneum, and extubation are the main noxious stimuli which provoke the sympathoadrenal activation, leading to hypertension and tachycardia. The creation of carbon dioxide pneumoperitoneum further leads to hemodynamic instability through increased vasopressin, increased catecholamine release, increased intra-abdominal pressure, and diaphragmatic elevation, causing increased systemic and pulmonary vascular resistance and reduced cardiac output [6-11].

Different pharmacological agents have been tried to reduce these responses, including calcium channel blockers [12,13], beta-blockers [12,14,15], opioids [16], vasodilators [17-18] and lignocaine [16,19]. Among these, alpha-2 adrenergic agonists have gained considerable attention due to their sympatholytic properties. Both clonidine and dexmedetomidine have demonstrated efficacy in blunting peri-operative hemodynamic responses [20-23].

Dexmedetomidine is a highly selective alpha-2 adrenoceptor agonist with an α_2:α_1 selectivity ratio of 1620:1, significantly higher than that of clonidine

[24]. Its pharmacological effects include sedation, anxiolysis, analgesia, and reduction of sympathetic outflow. Several studies have shown that dexmedetomidine reduces anaesthetic requirements and decreases the minimum alveolar concentration of volatile anaesthetics by approximately 30–35% [25]. However, higher doses or rapid bolus administration have been associated with adverse effects such as hypotension and bradycardia [24,26,27-38].

An additional concern with anaesthetic dose reduction is the potential risk of inadequate depth of anaesthesia and intra-operative awareness. Objective monitoring of anaesthetic depth using bispectral index has therefore been advocated to ensure adequate hypnosis during surgery [39-42].

The present study was undertaken to evaluate the efficacy of low-dose dexmedetomidine infusion (0.4 μg/kg/hr) in attenuating hemodynamic responses to laryngoscopy, tracheal intubation, pneumoperitoneum, and extubation in patients undergoing laparoscopic surgery, while assessing its effect on anaesthetic requirements, recovery characteristics, and peri-operative adverse events under bispectral index monitoring.

Materials and Methods

After getting the Institutional Ethics Committee approval, this prospective study was done in patients undergoing elective laparoscopic surgeries under general anaesthesia. The study procedure was explained in detail to all the eligible participants during the pre-anaesthetic evaluation. Written informed consent was obtained from all the willing participants explaining the study objectives, procedures involved, potential benefits, and possible risks. Ethical principles outlined in the Declaration of Helsinki were strictly followed throughout the study. Confidentiality of patient data were maintained, and the participation was purely voluntary, with the option to withdraw at any stage of the study without affecting clinical care.

Sample size was calculated based on expected differences in peri-operative heart rate and mean arterial pressure between the two groups from Ghodki et al. [20]. Assuming an effect size of 0.8, a power of 80%, and an alpha error of 0.05, the minimum required sample size was calculated to be 22 patients per group. To compensate for possible dropouts, 25 patients were recruited in each group, giving a total sample size of 50 patients.

Adult patients of either sex belonging to American Society of Anaesthesiologists (ASA) physical status I and II scheduled for elective laparoscopic procedures were enrolled in the study. Patients with known hypersensitivity to the study drugs, significant cardiovascular, hepatic, renal, or neurological disease, anticipated difficult airway, or those receiving medications affecting autonomic function were excluded. Eligible patients were randomly allocated into two groups using a computer-generated random number table. Allocation concealment was ensured using sealed opaque envelopes, which were opened only at the time of initiation of the study drug. The anesthesiologist administering anaesthesia was aware of group allocation, while the investigator recording hemodynamic parameters and postoperative outcomes was blinded to group assignment.

All the participants had undergone standard pre-anaesthetic evaluation and they were kept nil per oral as per the

institutional protocol. During the surgery, standard monitoring including non-invasive blood pressure, electrocardiography, pulse oximetry, end-tidal carbon dioxide, and bispectral index monitoring were utilised. Baseline heart rate, blood pressure, and bispectral index values were recorded. An intravenous line (IV) was secured, and participants in the DX group received dexmedetomidine infusion at a rate of 0.4 μg/kg/hr, while the participants in the NS group received an equivalent volume of normal saline. The infusion was started, just prior to the induction and it continued throughout the intra-operative period.

Anaesthesia was induced with intravenous (IV) propofol, titrated to loss of consciousness, and guided by bispectral index monitoring to maintain the necessary depth of anaesthesia. Neuromuscular blockade was done using a suitable muscle relaxant to perform tracheal intubation and Fentanyl was administered for analgesia. Laryngoscopy and endotracheal intubation were conducted using standard techniques. Anaesthesia was maintained with air, oxygen and isoflurane, with end-tidal isoflurane concentration adjusted to maintain an appropriate bispectral index range. Pneumoperitoneum was created using carbon dioxide, and intra-abdominal pressure was maintained within acceptable standards as per the surgical requirements.

Hemodynamic parameters including systolic blood pressure, diastolic blood pressure, heart rate, and mean arterial pressure were noted at predefined intervals: At the Baseline, after administering the drug, following the induction, after laryngoscopy and intubation, during the period of pneumoperitoneum (CO_2) at regular intervals, after release of the pneumoperitoneum, and following the extubation. Total consumption of isoflurane, propofol, and fentanyl were recorded. Recovery parameters including the time to awakening were recorded. Episodes of tachycardia, hypertension, hypotension, and bradycardia were noted and managed according to the institutional standard protocols.

The primary outcome was the peri-operative hemodynamic response like heart rate and blood pressure changes. Secondary outcomes included anaesthetic and opioid requirements, recovery characteristics, and incidence of adverse events.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 27. Continuous variables were expressed as mean and standard deviation (SD), while categorical variables were expressed as frequencies and percentages. The independent sample t-test was used for Intergroup comparisons for continuous variables and categorical variables were assessed using the Fisher's exact test or Chi-square test. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1 shows that both the Dexmedetomidine (DX) group and the Normal Saline (NS) group were comparable with respect to baseline demographic and operative parameters. The average age of patients in the DX group was 40.92 ± 13.07 years when compared to 42.36 ± 11.22 years in the NS group ($p = 0.678$). Mean body weight (72.28 ± 7.94 kg vs. 71.36 ± 9.83 kg; $p = 0.717$) and body mass index (27.33 ± 3.31 vs. 27.08 ± 2.68; $p = 0.973$) were also statistically comparable between the two groups. The duration of surgery was nearly same (74.6 ± 13.30 minutes in DX group vs. 74.4 ±

19.33 minutes in NS group; p = 0.966). The intergroup differences in anaesthetic requirements and hemodynamic responses can be attributed to the study drug rather than the baseline confounding variables.

Table 1. Baseline Demographic and Operative Characteristics

Parameter	Dexmedetomidine gp		Normal saline gp		P value
	Mean	SD	Mean	SD	
AGE	40.92	13.07	42.36	11.22	0.678
Body weight	72.28	7.94	71.36	9.83	0.717
BMI	27.33	3.31	27.08	2.68	0.973
Duration of surgery	74.6	13.30	74.4	19.33	0.966

Table 2 gives an even distribution of categorical variables between the study groups. Both groups had similar sex distribution, with males constituting females 13 patients (52%) and 12 patients (48%in each group). **ASA physical status I** is accounted for 18 patients (72%) in the NS group 19 patients (76%) in the DX group, while **ASA status II** comprised of 7 patients (28%) in the NS group, and 6 patients (24%) in the DX group. (p = 0.753). The types of laparoscopic procedures were also well matched, with laparoscopic appendicectomy, cholecystectomy, inguinal hernia repair, and umbilical hernia repair being similarly distributed between groups (p = 0.90).

Table 2. Distribution of Sex, ASA Status, and Type of Surgical Procedure

Parameter	Sub classification	Dexmedetomidine gp		Normal saline gp		P Value
		F	%	F	%	
Sex	Male	12	48	12	48	1
	Female	13	52	13	52	
ASA	1	19	76.00%	18	72.00%	0.753
	2	6	24.00%	7	28.00%	
Type of Surgical Procedure	Laparoscopic appendicectomy	5	20	4	16	0.90
	Laparoscopic cholecystectomy	8	32	7	28	
	Laparoscopic inguinal hernia repair	8	32	8	32	
	Laparoscopic umbilical hernia repair	4	16	6	24	

This balanced distribution ensures homogeneity of surgical stress and anaesthetic exposure, strengthening the internal validity of the comparative outcomes.

Analysis of systolic blood pressure, diastolic blood pressure, heart rate, and mean arterial pressure across the critical peri-operative time periods revealed a significant reduction of hemodynamic stress responses in the Dexmedetomidine group compared to the Normal Saline group. Following the laryngoscopy, tracheal intubation, pneumoperitoneum, and extubation, the NS group showed marked hypertensive and tachycardia responses, whereas these changes were blunted significantly in the DX group. The intergroup differences were observed immediately after intubation, during the early pneumoperitoneum, and following extubation, with various comparisons reaching the statistical significance ($p < 0.001$). Over time, hemodynamic parameters in both the groups had gradually returned towards the baseline values (Figure 1).

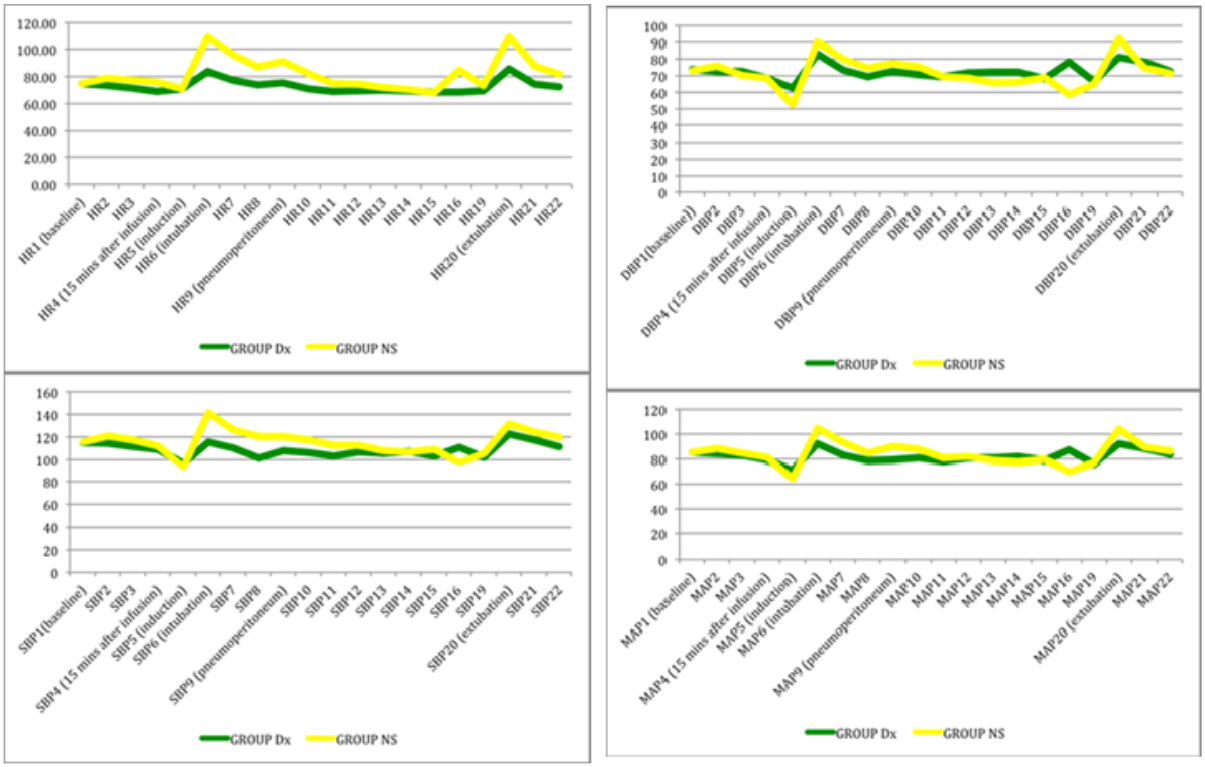


Figure 1. Peri-operative Hemodynamic Responses

Table 3 shows consistently lower end-tidal isoflurane requirement in the Dexmedetomidine group throughout the anaesthesia maintenance. From induction onwards, the mean end-tidal isoflurane concentrations were significantly decreased in the DX group, when compared to the NS group at all the measured intervals, with p-values reaching the significant statistical significance ($p \leq 0.001$) at most of the time periods. These results clearly indicate a dose-sparing effect of dexmedetomidine on the inhalational anaesthetic requirements, showing its anaesthetic-adjunct properties while maintaining the expected depth of anaesthesia.

Table 3. End-Tidal Isoflurane Concentration

Et - ISO	GROUP DX		GROUP NS		p-value
	MEAN	SD	MEAN	SD	
Et - ISO5 (Induction)	0.84	0.15	0.94	0.14	0.013
Et - ISO6	0.83	0.14	1.00	0.16	0.000
Et - ISO7	0.82	0.14	1.01	0.21	0.000
Et - ISO8	0.78	0.15	1.07	0.05	0.000
Et - ISO9	0.74	0.15	1.07	0.10	0.000
Et - ISO10	0.72	0.14	1.03	0.09	0.000
Et - ISO11	0.71	0.12	1.02	0.09	0.000
Et - ISO12	0.68	0.10	1.00	0.10	0.000
Et - ISO13	0.67	0.10	1.01	0.09	0.000
Et - ISO14	0.68	0.11	1.02	0.11	0.000
Et - ISO15	0.68	0.15	1.03	0.11	0.000
Et - ISO16	0.70	0.12	1.06	0.11	0.001
Et - ISO19	0.65	0.09	0.98	0.08	0.000

Table 4 demonstrates a significant reduction in opioid and anaesthetic consumption in patients receiving dexmedetomidine. The average propofol requirement in the DX group (75.60 ± 13.56 mg) was significantly lesser than in the NS group (135.60 ± 15.30 mg; $p < 0.001$). Similarly, total isoflurane consumption (11.88 ± 2.33 vs. 15.92 ± 1.61; $p < 0.001$) and total fentanyl requirement (2.29 ± 0.26 vs. 3.47 ± 0.44; $p < 0.001$) were significantly reduced in the DX group. Despite reduced anaesthetic dosing, time to awakening was comparable between the two study groups ($p = 0.751$), indicating that dexmedetomidine did not delay recovery while providing effective anaesthetic sparing.

Table 4: Anesthetic Drug Requirements and Recovery Profile

Parameter	Dexmedetomidine gp		Normal saline gp		P value
	Mean	SD	Mean	SD	
Time to Awakening	5.92	1.32	6.04	1.34	0.751
Propofol requirement	75.60	13.56	135.60	15.30	<0.001
TOTAL ISOFLURANE REQUIRED	11.88	2.33	15.92	1.61	<0.001
TOTAL FENTANYL REQUIRED	2.29	0.26	3.47	0.44	<0.001

Table 5 demonstrates a marked reduction in episodes of hypertension and tachycardia in the Dexmedetomidine group. 18 patients (72%) in the DX group, experienced no episodes of hypertension, compared to only 2 patients (8%) in the NS group (p = 0.002). Multiple episodes of hypertension were frequently seen in the NS group, with 12 patients (48%) experiencing two episodes in the DX group.

Table 5. Incidence of Hemodynamic Adverse Events

Parameter	Sub classification	Dexmedetomidine gp		Normal saline gp		P Value
		F	%	F	%	
Episodes of hypertension	0	18	72.00	2	8.00	0.002
	1	3	12.00	8	32.00	
	2	4	16.00	12	48.00	
	3	0	0.00	2	8.00	
	4	0	0	1	4	
Episodes of Tachycardia	0	15	60.00	1	4.00	<0.001
	1	9	36.00	2	8.00	
	2	1	4.00	4	16.00	
	3	0	0.00	12	48.00	
	4	0	0.00	5	20.00	
	6	0	0.00	1	4.00	
Episodes of hypotension	0	20	80.00	14	56.00	0.21
	1	4	16.00	11	44.00	
	2	1	4.00	0	0.00	
Episodes of bradycardia	Nil	25	100.00	25	100.00	1

Similarly, No tachycardia was observed in 15 patients (60%) in the DX group compared to only 1 patient (4%) in the NS group (p < 0.001), while recurrent tachycardia episodes were seen notably in the NS group. Episodes of hypotension were comparable between groups (p = 0.21), and no episodes of bradycardia were observed in both the groups (100% in both).

Discussion

The current study assessed the effectiveness of low-dose dexmedetomidine infusion (0.4 µg/kg/hr) in suppressing the peri-operative hemodynamic responses and reducing anaesthetic requirements in patients undergoing laparoscopic surgery under general anaesthesia. The findings of the current study prove that dexmedetomidine offered the excellent hemodynamic stability during the critical peri-operative events such as laryngoscopy, tracheal intubation, pneumoperitoneum (CO_2), and extubation, without increasing the recovery period or increasing the adverse events.

Laparoscopic surgery provokes significant sympathoadrenal responses due to airway manipulation and carbon dioxide pneumoperitoneum, leading to hypertension and tachycardia [6-11]. In the current research, the patients in the normal

saline (NS) group showed, significant raise in blood pressure and heart rate following intubation, during the pneumoperitoneum, and after extubation. In contrast, the dexmedetomidine group show cased, significant decrease in these responses, particularly during intubation, early pneumoperitoneum, and extubation. These results prove the sympatholytic effect of dexmedetomidine, which is mediated through central alpha-2 adrenoceptor activation, leading to reduced sympathetic outflow [20-23].

The observed hemodynamic stability with dexmedetomidine in this research is consistent with earlier findings showing reduction of pressor responses to laryngoscopy and intubation [24,26-29,35]. Previous studies evaluating the dexmedetomidine during the laparoscopic surgery have reported similarly with tachycardia and arterial pressure responses during pneumoperitoneum [21,37,42]. The present study reinforces these findings using a low-dose continuous infusion, thereby minimizing the risk of adverse cardiovascular effects reported with higher doses or rapid bolus administration [24,26,27].

An important finding of this study was the significant reduction in anaesthetic and opioid requirements in the dexmedetomidine group. End-tidal isoflurane concentrations were consistently lower throughout the intra-operative period, and total consumption of propofol, isoflurane, and fentanyl was significantly reduced. This anaesthetic-sparing effect of dexmedetomidine has been well documented in previous studies, which have demonstrated reductions in minimum alveolar concentration and total anaesthetic consumption [24,25,35,36]. The current study proves that even low-dose dexmedetomidine infusion can bring meaningful reduction in anaesthetic dosage.

Despite the decrease in anaesthetic requirements, the recovery characteristics were not affected so much. Time to awakening was similar between the two groups, indicating that dexmedetomidine did not delay the early emergence from anaesthesia. Similar observations were reported in the earlier studies, where dexmedetomidine provided anaesthetic and hemodynamic benefits without prolonging the recovery period [29,36,37]. The present study used the bispectral index monitoring and ensured the adequate depth of anaesthesia despite reduction in the anaesthetic dosing, addressing concerns regarding intra-operative awareness [39-42].

The incidence of less adverse hemodynamic events supports the safety profile of the drug low-dose dexmedetomidine. Episodes of tachycardia and hypertension were significantly lesser in the dexmedetomidine group compared to the normal saline group, while the incidence of hypotension was comparable between the two groups. Notably, no episodes of bradycardia were observed in either of the groups. These findings contrast with the studies using more bolus doses of dexmedetomidine initially, where hypotension and bradycardia were more frequently noted [24,26,27,35] and showcased the advantage of low-dose infusion in maintaining the cardiovascular stability.

This study has certain limitations. It was conducted in ASA I–II patients only, limiting generalizability to higher-risk populations. Blinding of the anaesthesiologist was not feasible. Neuroendocrine markers were not

measured, and hemodynamic parameters were used as indirect indicators of stress response. Larger multicentre studies are required to confirm these findings.

Conclusion

The findings of this research have significant clinical implications. Low-dose dexmedetomidine infusion offers effective reduction in peri-operative stress responses, decreases opioid and anaesthetic requirements. It also improves hemodynamic stability without compromising the recovery time. This makes dexmedetomidine infusion, an essential anaesthetic adjuvant, particularly in laparoscopic surgeries where the sympathetic stimulation is pronounced.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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