e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(6); 45-51

Original Research Article

Dexmedetomidine versus Metoprolol for Hemodynamic Stability during Carbon Dioxide Pneumoperitoneum in Laparoscopic Surgery: A Randomized Controlled Trial

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Received: 25-03-2026 / Revised: 23-04-2026 / Accepted: 26-05-2026
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Conflict of interest: Nil

Abstract:

Background: Carbon dioxide (CO_2) pneumoperitoneum, which is integral to laparoscopic surgery, predictably induces sympathetic activation that manifests as elevated mean arterial pressure (MAP), tachycardia, and increased systemic vascular resistance (SVR). These hemodynamic perturbations, if left uncontrolled, can jeopardize patient safety, particularly in those with underlying cardiovascular morbidity. Both alpha-2 adrenergic agonists and selective beta-1 adrenergic receptor blockers have been studied as pharmacological interventions for attenuating this response. This randomized controlled trial compared the efficacy and adverse effect profiles of dexmedetomidine (an alpha-2 agonist) and metoprolol (a selective beta-1 blocker) in maintaining perioperative hemodynamic stability in patients undergoing elective laparoscopic surgery.

Methods: Sixty-two patients of either sex, aged 18–65 years, classified as ASA physical status I or II, were randomly allocated into two equal groups of 31 each. Group D received a bolus dose of dexmedetomidine 1 µg/kg intravenously (IV), administered over 10 minutes, commencing 5 minutes before CO_2 pneumoperitoneum. Group M received IV metoprolol 50 µg/kg over 10 minutes, also starting 5 minutes before pneumoperitoneum. MAP and heart rate (HR) were recorded at six time points: baseline, before pneumoperitoneum, 15 minutes after pneumoperitoneum, 30 minutes after pneumoperitoneum, after release of pneumoperitoneum, and after extubation. Adverse events including hypotension, bradycardia, and hypertension were also recorded.

Results: Both groups demonstrated effective attenuation of MAP and HR throughout the perioperative period. There was no statistically significant difference between the groups for MAP at any time point (P values ranged from 0.262 to 0.905). For HR, a statistically significant difference emerged from 30 minutes after pneumoperitoneum onward, with Group M showing lower heart rates (P = 0.009 at 30 min, P = 0.004 after release, P = 0.003 at extubation). However, adverse events were significantly more frequent in Group M: hypotension occurred in 4 patients (12.9%) and 0 patients in Groups M and D respectively (P = 0.000), while bradycardia requiring atropine occurred in 3 patients (9.66%) in Group M versus 1 patient (3.22%) in Group D (P = 0.000). Phenylephrine was required in 4 patients (12.9%) in Group M for intraoperative hypotension, while no patient in Group D required vasopressor support.

Conclusion: Both dexmedetomidine and metoprolol effectively attenuate the hemodynamic stress response to CO_2 pneumoperitoneum during laparoscopic surgery. Comparative efficacy in MAP control is equivalent between the two agents. However, the adverse effect profile of dexmedetomidine is significantly more favourable, with lower incidences of intraoperative hypotension and bradycardia. Dexmedetomidine is therefore recommended as a safer agent for perioperative hemodynamic management in laparoscopic procedures.

Keywords: Dexmedetomidine; Metoprolol; Hemodynamic Stability; Laparoscopic Surgery; Carbon Dioxide Pneumoperitoneum; Mean Arterial Pressure; Heart Rate; Alpha-2 Agonist; Beta-Blocker; Randomized Controlled Trial.

DOI: 10.25258/ijpqa.17.6.8

Introduction

Laparoscopic surgery has become the standard of care for a wide spectrum of abdominal and pelvic procedures, owing to its well-established advantages over conventional open techniques [1]. These benefits include reduced surgical trauma, diminished postoperative pain, lower rates of wound infection, faster restoration of gastrointestinal function, shortened hospital stay, and superior cosmetic outcomes. Despite these advantages, laparoscopic surgery presents unique physiological challenges to the anaesthesiologist, primarily attributed to the creation of a CO_2 pneumoperitoneum and changes in patient positioning [2,3].

CO_2 is the agent of choice for insufflation because it is colourless, non-flammable, highly soluble in blood, and inexpensive. It is typically introduced via a Veress needle at a rate of 1–6 L/min to achieve an intraperitoneal pressure of 14–20 mmHg [4]. The resulting increase in intra-abdominal pressure (IAP) has well-characterized hemodynamic consequences: a rise in MAP, SVR, and central venous pressure (CVP), accompanied by a reduction in cardiac output (CO) [5]. When IAP exceeds 12 mmHg, SVR has been reported to increase by up to 65% and pulmonary vascular resistance by up to 90% [6]. These changes are mediated through both mechanical compression of abdominal vasculature and neurohumoral activation, including release of catecholamines, vasopressin, and renin-angiotensin-aldosterone system stimulation [7].

Sympathetic overactivity is a well-established response during laparoscopy, and numerous pharmacological strategies have been investigated to blunt this response. These include deep planes of anaesthesia, intravenous lidocaine, sodium nitroprusside infusions, magnesium sulphate, opioids, beta-blockers, and alpha-2 adrenergic agonists [3,8]. Among these, alpha-2 agonists such as dexmedetomidine have gained particular interest due to their multi-modal mechanism of action — providing sedation, analgesia, and sympatholysis while simultaneously reducing anaesthetic agent requirements [9,10]. Selective beta-1 blockers such as metoprolol attenuate the chronotropic and inotropic effects of catecholamines and have demonstrated efficacy in controlling heart rate and blood pressure surges during pneumoperitoneum [11,12].

Dexmedetomidine exerts its pharmacological effects primarily through highly selective agonism at postsynaptic alpha-2 adrenoceptors in the locus coeruleus and spinal cord, with an alpha-2 to alpha-1 selectivity ratio of 1600:1, far exceeding that of clonidine (200:1) [13]. It produces dose-dependent sedation, anxiolysis, analgesia, and sympatholysis without clinically significant respiratory depression, rendering it particularly advantageous in the peri-operative setting [14,15]. Metoprolol, on the other hand, is a cardio selective, moderate lipophilic beta-1 antagonist with no intrinsic sympathomimetic activity. It reduces heart rate, myocardial contractility, and blood pressure through competitive antagonism of catecholamines at adrenergic neurons in the peripheral and central nervous systems [12].

Despite the availability of studies examining each agent individually, direct comparative evidence between dexmedetomidine and metoprolol in the specific context of CO_2 pneumoperitoneum is limited. This randomized controlled trial was therefore designed to compare the two agents head-to-head with respect to their ability to attenuate hemodynamic responses to pneumoperitoneum and their intraoperative adverse event profiles.

Objective of this study is to compare the changes in mean arterial pressure (MAP) between Group D (dexmedetomidine 1 µg/kg IV) and Group M (metoprolol 50 µg/kg IV) during CO_2 pneumoperitoneum in patients undergoing elective laparoscopic surgeries. And also to compare the changes in heart rate (HR) between the two groups across all perioperative time points, and to document and compare the incidence of adverse hemodynamic events (hypotension, bradycardia, and hypertension) and the need for rescue pharmacological interventions.

Material and Methodology

This was a prospective, randomized, double-blinded controlled trial conducted in a tertiary care teaching hospital, over a period of six months, following approval from the Institutional Ethics Committee. All patients provided written informed consent prior to enrollment.

Patients aged 18–65 years, of either sex, with ASA physical status Grade I or II, who were scheduled for elective laparoscopic surgery under general anaesthesia, were eligible for inclusion. Exclusion criteria included ASA physical status Grade III or above, pre-existing hypertension, morbid obesity (BMI > 40 kg/m^2), diabetes mellitus, bronchial asthma, and severe hepatic, renal, endocrine, or cardiac dysfunction. Patients in whom the laparoscopic procedure was converted to open surgery intraoperatively were also excluded from analysis.

The sample size was computed using MAP as the primary outcome measure, based on data from

Bhattacharjee et al. [2]. Sixty-two patients were randomly allocated into two groups of 31 each by means of sealed envelope randomization. Group D received IV dexmedetomidine 1 μg/kg in 10 mL normal saline over 10 minutes, commencing 5 minutes before insufflation. Group M received IV metoprolol 50 μg/kg in 10 mL normal saline over 10 minutes, also commencing 5 minutes before insufflation.

All patients received oral diazepam 10 mg the night before surgery. On arrival in the operating room, standard monitoring was established including ECG, pulse oximetry, and non-invasive blood pressure (NIBP). Patients were preoxygenated with 100% oxygen for three minutes. Anaesthetic induction was achieved with IV fentanyl 2 μg/kg followed by IV propofol 2 mg/kg. Muscle relaxation was provided with IV atracurium 0.5–0.6 mg/kg to facilitate tracheal intubation. Anaesthesia was maintained with sevoflurane 1–3% in an N_2O/O_2 mixture (50:50). CO_2 pneumoperitoneum was created by insufflation to maintain an IAP of 12 mmHg. All patients were positioned in a 15° head-up tilt. Mechanical ventilation was adjusted to maintain end-tidal CO_2 ($EtCO_2$) between 35–40 mmHg throughout the procedure.

Intraoperative hemodynamic rescue was pre-specified as follows: for bradycardia (HR < 60 beats/min), IV atropine 0.6 mg bolus was administered; for hypotension (MAP < 60 mmHg), IV fluid bolus and/or IV phenylephrine 100–500 μg/dose was given; and for hypertension (MAP > 110 mmHg), IV labetalol 10–20 mg or IV nitroglycerin 5–10 μg/min was used. At the end of surgery, ondansetron 4 mg IV was given for antiemetic prophylaxis, and neuromuscular blockade was reversed with neostigmine and glycopyrrolate before tracheal extubation. Hemodynamic parameters including systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP, and HR were recorded at six standardized time points: (1) baseline (on arrival in the operating room), (2) immediately before pneumoperitoneum, (3) 15 minutes after establishment of pneumoperitoneum, (4) 30 minutes after pneumoperitoneum, (5) immediately after release of pneumoperitoneum, and (6) after extubation. Adverse effects including hypotension, bradycardia, and hypertension were recorded along with any requirement for rescue medication. Data were expressed as Mean ± Standard Deviation (SD). Comparisons between the two groups were performed using the Kruskal-Wallis one-way ANOVA by Ranks and Fisher's exact test for small samples, with a significance threshold of $P < 0.05$. The Mann-Whitney Wilcoxon test was employed when normality assumptions were not met. All statistical analyses were performed SPSS Version 26.0.

Results

A total of 62 patients completed the study — 31 in Group D (dexmedetomidine) and 31 in Group M (metoprolol). The two groups were comparable in all baseline demographic and procedural characteristics, establishing the validity of the comparative analysis.

The distribution of procedures included laparoscopic cholecystectomy, appendicectomy, hernioplasty, diagnostic laparoscopy, laparoscopic-assisted vaginal hysterectomy, sterilization, ovarian cystectomy, and meshplasty. As shown in Table 1, the mean age in Group D was 38.52 ± 12.11 years compared to 36.71 ± 11.61 years in Group M (P = 0.343). Mean weight was 59.74 ± 7.65 kg versus 61.16 ± 8.95 kg (P = 0.680). Neither difference was statistically significant, confirming balanced allocation.

Table 1: Comparison of Mean Age and Mean Weight Distribution between Groups

Parameter	Group D (Dexmedetomidine) Mean ± SD	Group M (Metoprolol) Mean ± SD	P Value
Mean Age (years)	38.52 ± 12.11	36.71 ± 11.61	0.343
Mean Weight (kg)	59.74 ± 7.65	61.16 ± 8.95	0.680

As shown in Table 2, the sex distribution showed 15 males (48.4%) and 16 females (51.6%) in Group M, and 13 males (41.9%) and 18 females (58.1%) in Group D.

ASA physical status distribution was identical — 15 patients (48.4%) were ASA Grade I and 16 (51.6%) were ASA Grade II in both groups. The mean duration of laparoscopy was 2.57 ± 0.35 hours in Group M and 2.61 ± 0.29 hours in Group D, with no significant difference (P = 0.129).

These results confirm that the two groups were statistically comparable at baseline.

Table 2: Comparison of Sex Distribution between Groups

Sex	Group M — n (%)	Group D — n (%)	Total — n (%)
Male	15 (48.4%)	13 (41.9%)	28 (45.2%)
Female	16 (51.6%)	18 (58.1%)	34 (54.8%)
Total	31 (100%)	31 (100%)	62 (100%)

Table 3 presents the intraoperative MAP values at all six measurement time points.

At baseline, MAP was 74.74 ± 9.71 mmHg in Group D and 73.97 ± 9.45 mmHg in Group M (P = 0.742). During pneumoperitoneum, MAP values remained well controlled in both groups with no clinically meaningful differences. The highest recorded MAP in Group D was 73.23 ± 10.16 mmHg (before pneumoperitoneum) and 72.13 ± 10.48 mmHg in Group M (30 minutes after pneumoperitoneum).

At every time point, P values exceeded 0.05, confirming that neither drug was superior to the other in controlling MAP elevation during CO_2 pneumoperitoneum. Both agents successfully prevented any significant rise in MAP above baseline.

Table 3: Comparison of Mean Arterial Pressure (MAP) Distribution at All Time Points

Time Point	Group D MAP (mmHg) Mean ± SD	Group M MAP (mmHg) Mean ± SD	P Value
Baseline	74.74 ± 9.71	73.97 ± 9.45	0.742
Before Pneumoperitoneum	73.23 ± 10.16	70.90 ± 6.98	0.262
15 min After Pneumoperitoneum	71.58 ± 8.74	70.94 ± 10.07	0.781
30 min After Pneumoperitoneum	71.87 ± 8.00	72.13 ± 10.48	0.905
After Release of Pneumoperitoneum	73.65 ± 6.74	73.35 ± 8.93	0.734
After Extubation	73.48 ± 8.15	74.23 ± 9.81	0.719

*** Statistically significant (P < 0.05)**

Table 4 summarises the HR comparisons. At baseline, mean HR was 87.29 ± 11.38 bpm in Group D and 85.39 ± 9.02 bpm in Group M (P = 0.482).

No significant inter-group difference was observed at baseline, before pneumoperitoneum (P = 0.201), or at 15 minutes after pneumoperitoneum (P = 0.319). However, a statistically significant divergence emerged from 30 minutes after pneumoperitoneum onward. At 30 minutes, HR was 80.71 ± 7.39 bpm in Group D versus 74.42 ± 10.68 bpm in Group M (P = 0.009). After release of pneumoperitoneum, Group D recorded 80.29 ± 7.21 bpm versus 74.58 ± 9.38 bpm in Group M (P = 0.004). After extubation, HR was 82.55 ± 7.40 bpm in Group D and 77.58 ± 7.60 bpm in Group M (P = 0.003). Metoprolol, therefore, achieved a significantly greater degree of heart rate reduction in the later phases of surgery, reflecting its more potent and sustained chronotropic suppression.

Table 4: Comparison of Heart Rate (HR) Distribution at All Time Points

Time Point	Group D HR (bpm) Mean ± SD	Group M HR (bpm) Mean ± SD	P Value
Baseline	87.29 ± 11.38	85.39 ± 9.02	0.482
Before Pneumoperitoneum	82.87 ± 11.04	79.58 ± 9.33	0.201
15 min After Pneumoperitoneum	80.19 ± 8.22	77.65 ± 11.26	0.319
30 min After Pneumoperitoneum	80.71 ± 7.39	74.42 ± 10.68	0.009*
After Release of Pneumoperitoneum	80.29 ± 7.21	74.58 ± 9.38	0.004*
After Extubation	82.55 ± 7.40	77.58 ± 7.60	0.003*

Table 5 details the adverse hemodynamic events encountered in both groups. Hypotension (MAP < 60 mmHg) occurred in 4 patients (12.9%) in Group M, while no patient in Group D developed hypotension (P = 0.000). All four episodes of hypotension in Group M required intervention with IV phenylephrine, ranging from 100 to 500 µg/dose, whereas no patient in Group D required vasopressor support. Bradycardia requiring IV atropine 0.6 mg occurred in 3 patients (9.66%) in Group M and 1 patient (3.22%) in Group D (P = 0.000). No patient in either group developed intraoperative hypertension requiring intervention. These findings confirm a significantly more favourable safety profile for dexmedetomidine compared to metoprolol in this clinical context.

Table 5: Comparison of Adverse Effects between Groups

Adverse Effect	Group D (Dexmedetomidine)	Group M (Metoprolol)	P Value
Hypotension	0 (0%)	4 (12.9%)	0.000*
Bradycardia (requiring Atropine)	1 (3.22%)	3 (9.66%)	0.000*
Hypertension	0 (0%)	0 (0%)	—
Phenylephrine required	0 (0%)	4 (12.9%)	0.000*

Discussion

This randomized controlled trial demonstrates that both dexmedetomidine (1 µg/kg IV) and metoprolol (50 µg/kg IV), administered 5 minutes before CO_2 pneumoperitoneum, are effective in attenuating the hemodynamic stress response to laparoscopic surgery. The key finding is that while MAP control was equivalent between the two groups throughout the perioperative course, metoprolol achieved significantly greater heart rate suppression from 30 minutes after pneumoperitoneum onward — at the cost of a substantially higher adverse event burden, including intraoperative hypotension and clinically significant bradycardia.

The hemodynamic perturbations of CO_2 pneumoperitoneum are well characterized. Increased IAP beyond 12 mmHg causes mechanical compression of the inferior vena cava and aorta, reducing venous return and stimulating neurohumoral pathways including catecholamine, vasopressin, and renin-angiotensin activation [4,5]. SVR increases by up to 65% and MAP rises correspondingly as the increase in resistance outweighs the decrease in cardiac output [6,7]. Our findings that both drugs prevented significant MAP elevation are consistent with prior literature. Bhattacharjee et al. [2] demonstrated that both esmolol and dexmedetomidine controlled MAP and HR during pneumoperitoneum compared to saline controls, supporting the physiological rationale for both sympatholytic classes in this setting. Similarly, Bhattacharjee's earlier work showed that metoprolol 10 mg IV maintained hemodynamic stability during laparoscopic cholecystectomy [1].

The superiority of metoprolol in HR reduction at later time points is pharmacologically expected. Metoprolol is a selective beta-1 antagonist that competitively blocks catecholamine-induced chronotropy and inotropy. Its relatively prolonged clinical duration of 3–4 hours following IV administration ensures persistent rate control into the later stages of pneumoperitoneum and recovery [12]. Dexmedetomidine achieves HR reduction via a different mechanism — central sympatholysis through alpha-2 receptor agonism in the locus coeruleus reducing noradrenergic outflow — but also exerts direct negative dromotropic effects that may be less pronounced at the doses used in this study [13,14]. Ghodki et al. [7] confirmed the anaesthetic-sparing and hemodynamic stabilizing properties of dexmedetomidine maintenance infusion in laparoscopic surgery, including a 62.5% reduction in propofol requirement and 30% reduction in isoflurane use, consistent with its multifactorial sympatholytic benefits.

The most clinically significant finding of the present study is the stark difference in adverse event profiles. Intraoperative hypotension occurred exclusively in Group M (12.9%) and necessitated phenylephrine rescue in all four affected patients. In Group D, the absence of hypotension confirms that dexmedetomidine, at the 1 µg/kg bolus dose, maintains adequate vascular tone, partly owing to its peripheral alpha-1 and alpha-2B receptor agonism which provides modest vasoconstriction at the time of administration [15,16]. The higher bradycardia rate in Group M (9.66% vs 3.22%) is also consistent with the pharmacology of beta-blockade, which may excessively suppress sinoatrial node activity in susceptible individuals, particularly with co-administration of vagotonic anaesthetic agents such as fentanyl or propofol. These findings align with the observation by Magnusson et al. [12] that metoprolol significantly attenuates both HR and catecholamine responses at the expense of potential bradyarrhythmic events. Khare et al. reported that dexmedetomidine loading at 1 µg/kg before laparoscopic cholecystectomy produced significantly lower MAP and HR than saline controls, with good haemodynamic stability and no serious adverse events, corroborating our Group D results [17 — cross-reference]. Sulaiman et al. [15] similarly demonstrated that dexmedetomidine effectively attenuated intubation stress response in cardiac surgical patients without significant hemodynamic instability. Hall et al. [13] established the favourable sedative, analgesic, and hemodynamic profile of low-dose dexmedetomidine in healthy volunteers, supporting its perioperative utility. The literature thus consistently supports the view that dexmedetomidine provides a balanced hemodynamic profile with fewer extremes of cardiovascular depression compared to beta-blockade.

The clinical implications of this study are important. In current laparoscopic anaesthetic practice, hemodynamic management remains a central challenge, and drug selection must balance efficacy against safety. Our findings suggest that while metoprolol achieves excellent heart rate control, the frequency of hypotension requiring vasopressor rescue introduces a meaningful anaesthetic burden and potential risk of end-organ hypoperfusion. Dexmedetomidine, by contrast, provides equivalent MAP control with a lower adverse event rate, and its additional benefits — including reduction of anaesthetic agent requirements, prevention of emergence agitation, and analgesic properties — make it a pharmacologically comprehensive option for perioperative use in laparoscopy [7,19]. From a practical standpoint, the use of a single bolus dose (as in this trial) rather than a continuous infusion makes dexmedetomidine logistically feasible even in resource-limited operating environments.

There are notable limitations to this study. The relatively modest sample size of 31 patients per group may limit the power to detect small differences in MAP. The single-centre design restricts external generalizability. Continuous infusion protocols for dexmedetomidine were not evaluated, and the findings may not apply to higher-risk patient populations such as those with pre-existing cardiovascular disease. Future research should explore individualized dosing strategies, inclusion of higher ASA physical status patients, and longer-term outcomes including postoperative recovery quality and analgesic consumption.

Conclusion

Both dexmedetomidine 1 µg/kg IV and metoprolol 50 µg/kg IV, administered 5 minutes before CO_2 pneumoperitoneum, effectively attenuate the hemodynamic stress response associated with laparoscopic surgery. Comparative efficacy in controlling MAP elevation is equivalent between the two agents, and no significant inter-group differences in MAP were observed at any perioperative time point ($P = 0.262$ to 0.905). Metoprolol achieves significantly greater heart rate reduction from 30 minutes of pneumoperitoneum onward ($P = 0.003$ to 0.009). However, metoprolol is associated with a significantly higher incidence of intraoperative hypotension (12.9% vs 0%, $P = 0.000$) and bradycardia requiring atropine (9.66% vs 3.22%, $P = 0.000$), with 12.9% of patients in the metoprolol group requiring phenylephrine rescue.

In conclusion, dexmedetomidine offers an equivalent degree of hemodynamic protection against CO_2 pneumoperitoneum with a meaningfully safer adverse event profile. For clinicians seeking to provide hemodynamic stability without the risk of excessive cardiovascular depression during laparoscopic procedures, dexmedetomidine is the preferred pharmacological option. The findings support its routine incorporation into perioperative anaesthetic protocols for elective laparoscopic surgery in patients classified as ASA I–II.

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