RESEARCH PAPER

Efficacy of Oral Clonidine On Intraoperative Hemodynamics and Postoperative Analgesia in Patients Undergoing Lumbar Spine Surgeries.

[1]Dr Amruta Vaijanath Chaudhari and [2]Dr. Dr. Subha Teresa Jose Vazhakalayil

[1]Junior Resident Doctor, Department of Anaesthesiology, Clg- Dr.D.Y.Patil Medical College, Hospital and Research Centre, Pimpri, Pune – 411018
[2]Professor, Department of Anaesthesiology, Clg- Dr.D.Y.Patil Medical College, Hospital and Research Centre, Pimpri, Pune – 411018
[1]camruta8@gmail.com and [2]dr.subhajose@gmail.com

Received: 24th April, 2026; Revised: 20th May 2026; Accepted: 30th June, 2026; Available Online: 10th July, 2026

ABSTRACT

Background: Lumbar spine surgery is associated with significant perioperative sympathetic responses and postoperative pain. Clonidine, an α2-adrenergic agonist, may attenuate hemodynamic responses while providing analgesic and anesthetic-sparing effects. This study evaluated the efficacy of oral clonidine as premedication in patients undergoing lumbar spine surgery.

Methods: This prospective, randomized, double-blinded comparative study included 64 ASA I–II patients aged 18–65 years undergoing lumbar spine surgery under general anesthesia. Patients were randomly allocated to receive oral clonidine 100 µg (Group S, n=32) or placebo (Group C, n=32) 45 minutes before surgery. Intraoperative heart rate (HR), systolic, diastolic and mean arterial pressure (MAP), fentanyl and propofol requirements were assessed. Postoperative pain, duration of analgesia, time to first rescue analgesia, rescue analgesic consumption, sedation, and adverse events were evaluated.

Results: Baseline characteristics and hemodynamic parameters were comparable between groups. Intraoperatively, HR and MAP were significantly lower in the clonidine group at all assessed time points after baseline (p<0.001). Fentanyl consumption was significantly lower with clonidine (198.6 ± 9.4 vs 268.3 ± 10.6 µg; p<0.001), while additional propofol was required in 40.6% versus 100% of patients (p<0.001). Postoperative VAS scores were generally lower with clonidine, with significant differences from 60 minutes onward at most assessment points. Duration of analgesia and time to first rescue analgesia were significantly prolonged, while 24-hour rescue analgesic requirements were reduced (p<0.001). Early postoperative sedation was greater with clonidine but resolved by 2 hours. Adverse events were comparable between groups.

Conclusion: Oral clonidine 100 µg administered 45 minutes preoperatively provided effective hemodynamic stabilization, reduced anesthetic and opioid requirements, and improved postoperative analgesia without significant additional adverse effects.

Keywords: Clonidine; Lumbar spine surgery; α2-adrenergic agonist; Hemodynamic stability; Postoperative analgesia; Opioid-sparing; Preemptive analgesia.

How to cite this article: Chaudhari AV, Vazhakalayil STJ, Efficacy of Oral Clonidine On Intraoperative Hemodynamics and Postoperative Analgesia in Patients Undergoing Lumbar Spine Surgeries. Int J Drug Deliv Technol. 2026;16(80s): 1230-1234; DOI: 10.25258/ijddt.16.80s.155
Source of support: Nil.
Conflict of interest: None

INTRODUCTION

Lumbar spine surgery is a complex procedure requiring meticulous anesthetic management to maintain hemodynamic stability, provide adequate analgesia, and facilitate early postoperative neurological assessment. Anesthetic management involves several challenges, including airway control, prevention of hemodynamic fluctuations during positioning and surgical manipulation, appropriate patient positioning to avoid nerve and vascular complications, minimizing intraoperative blood loss, and selecting anesthetic techniques compatible with intraoperative neurophysiological monitoring.[1,2] Rapid emergence from anesthesia with preserved neurological function is particularly important for timely postoperative assessment.[3]

Postoperative pain remains a major concern following lumbar spine surgery. Poorly controlled acute pain can impair respiratory mechanics and secretion clearance, increasing the risk of atelectasis and other pulmonary complications. Severe pain also produces an exaggerated sympathetic response, characterized by increased catecholamine release, tachycardia, and hypertension,

Author for Correspondence: camruta8@gmail.com

which may contribute to thromboembolic complications and increased perioperative morbidity.[4] Furthermore, inadequate analgesia can delay mobilization and physiotherapy, prolong hospital stay, and increase healthcare costs.[5] Consequently, contemporary perioperative analgesia emphasizes preemptive and multimodal approaches that combine agents with different mechanisms of action to improve pain control while reducing opioid requirements.[4,5] Preemptive analgesia may also reduce central sensitization and postoperative pain perception.[5]

Alpha-2 adrenergic agonists have an important role in perioperative medicine because of their sedative, anxiolytic, analgesic, muscle-relaxant, and sympatholytic properties.[6] Clonidine, a selective alpha-2 adrenergic agonist, has been used as a premedication to attenuate perioperative hemodynamic responses and reduce postoperative analgesic requirements.[6] It can be administered through several routes, including oral, intravenous, epidural, and intrathecal routes, with oral administration offering a simple and practical approach for preoperative use. Through central alpha-2 receptor activation, clonidine provides sedation, anxiolysis, analgesia, and sympatholysis while reducing the requirement for anesthetic and opioid agents. This opioid-sparing effect is particularly relevant in the context of efforts to minimize perioperative opioid exposure.

Therefore, the present prospective, randomized, double-blinded comparative study was undertaken to evaluate the efficacy of **oral clonidine as premedication in patients undergoing lumbar spine surgery**, with particular emphasis on its effects on perioperative hemodynamic responses and postoperative analgesic requirements.

MATERIALS AND METHODS

This prospective, randomized, double-blinded comparative study was conducted at Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune, after obtaining Institutional Ethics Committee approval. The study included 64 patients (32 in each group), aged 18–65 years, of either sex, with American Society of Anesthesiologists (ASA) physical status I or II, scheduled for lumbar spine surgery under general anesthesia. The study was conducted over two years, including 18 months for data collection and six months for analysis and reporting. Sample size was calculated using WINPEPI version 11.3, based on previously reported mean arterial pressure values, with 95% power and a 5% significance level.[7] Written informed consent was obtained from all participants following pre-anesthetic evaluation and relevant investigations.

Patients meeting the inclusion criteria of ASA I–II status, age 18–65 years, hemodynamic stability, normal routine investigations, absence of significant comorbidities, and willingness to participate were enrolled. Patients with ASA III–IV status, liver dysfunction, allergy to study medications, pregnancy, scoliosis or major spinal deformity, procedures involving more than five levels of fusion, uncontrolled systemic disorders, bleeding or coagulation abnormalities, or unwillingness to participate were excluded. Participants were randomly allocated using computer-generated randomization into two groups: Group S received oral clonidine 100 µg, while Group C received oral calcium 100 mg as placebo, both administered 45 minutes before surgery.

Preoperative Evaluation and Anesthetic Technique

A comprehensive preoperative assessment was performed on the day before surgery, including history, general and systemic examination, and relevant laboratory investigations. Standard preoperative fasting instructions were followed, and patients were educated regarding postoperative pain assessment using the visual analogue scale (VAS). Baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded in the supine position before induction. Standard monitoring with electrocardiography, pulse oximetry, and non-invasive blood pressure measurement was used, and intravenous access was secured with an 18–20 G cannula.

General anesthesia was induced using intravenous fentanyl 2 µg/kg followed by propofol 2 mg/kg and vecuronium 0.1 mg/kg. After three minutes of mask ventilation with 100% oxygen, orotracheal intubation was performed. HR, SBP, DBP, and MAP were recorded at baseline, immediately before induction, during intubation, and after intubation. Anesthesia was maintained with 40% oxygen and 60% air at a fresh gas flow of 1 L/min, with end-tidal isoflurane titrated to a MAC of approximately 1.0. Intravenous paracetamol 1 g was administered for additional analgesia. Hemodynamic parameters were recorded at 15-minute intervals. Hypertension was managed initially with incremental propofol and, if persistent, fentanyl, while hypotension was treated with ephedrine or phenylephrine as required.

At the end of surgery, neuromuscular blockade was reversed with neostigmine 0.5 mg/kg and glycopyrrolate 0.008 mg/kg, followed by extubation after adequate spontaneous ventilation and recovery of airway reflexes. Postoperatively, patients were assessed at recovery-room arrival and at 30 minutes, 1, 2, 4, 6, 8, 12, and 24 hours. Pain intensity was assessed using the 0–10 VAS. Duration of analgesia, time to first rescue analgesic requirement, and cumulative analgesic consumption during the first 24 hours were recorded. Intravenous paracetamol 1 g was administered as rescue analgesia when required.

Postoperative sedation was evaluated at the same intervals using the modified Ramsay Sedation Scale (RSS), ranging from 1 (anxious/agitated) to 6 (no response to stimuli). Adverse events, including nausea, vomiting, bradycardia, hypotension, and other clinically relevant side effects, were documented throughout the postoperative observation period.

Primary outcomes included intraoperative HR, SBP, DBP, and MAP, total intraoperative fentanyl consumption, and postoperative VAS pain scores. Secondary outcomes

included duration of postoperative analgesia, number of rescue analgesic doses required within 24 hours, postoperative RSS, and the incidence of intraoperative and postoperative adverse events, including hypotension, hypertension, bradycardia, nausea, vomiting, urinary retention, and requirement for vasopressor support.

Statistical Analysis

Data were collected using standardized forms, entered into Microsoft Excel, and analyzed using SPSS version 24.0. Quantitative variables were analyzed using Student's *t*-test and qualitative variables using the Chi-square test, with appropriate parametric or non-parametric methods applied where required. Comparisons between groups included demographic, hemodynamic, analgesic, sedation, and adverse-event parameters. Statistical significance was assessed using two-tailed tests at the 5% level, with a 95% confidence level.

RESULTS

A total of 64 patients were included, with 32 patients each in the clonidine (Group S) and control (Group C) groups. All participants completed the study and were included in the final analysis.

Table 1. Demographic and baseline characteristics

Variable	Group S (n=32)	Group C (n=32)	*p*-value
Age, years	45.3 ± 4.9	45.9 ± 5.1	0.62
Male/Female	16/16	17/15	0.80
Weight, kg	69.6 ± 2.7	69.8 ± 2.9	0.74
ASA I/II	17/15	16/16	0.80
Baseline HR, bpm	80.2 ± 2.1	79.8 ± 2.4	0.41
Baseline MAP, mmHg	92.1 ± 1.3	91.8 ± 1.4	0.36

The two groups were comparable with respect to age, sex, weight, ASA grade, baseline heart rate, and MAP, with no statistically significant differences ($p>0.05$), indicating balanced baseline characteristics.

Table 2. Intraoperative hemodynamic parameters

Time	HR (bpm) Group S	HR (bpm) Group C	*p*	MAP (mmHg) Group S	MAP (mmHg) Group C	*p*
Baseline	79.8 ± 2.4	80.2 ± 2.1	0.41	91.8 ± 1.4	92.1 ± 1.3	0.36
15 min	75.1 ± 2.3	86.8 ± 2.5	<0.001	95.3 ± 1.8	109.4 ± 2.1	<0.001
30 min	74.2 ± 2.2	84.9 ± 2.3	<0.001	94.6 ± 1.7	107.8 ± 2.0	<0.001
45 min	73.3 ± 2.2	83.7 ± 2.4	<0.001	93.8 ± 1.7	106.9 ± 1.9	<0.001
60 min	72.4 ± 2.1	82.6 ± 2.4	<0.001	93.1 ± 1.6	105.9 ± 1.9	<0.001
90 min	71.4 ± 2.0	81.7 ± 2.3	<0.001	92.5 ± 1.5	105.1 ± 1.8	<0.001
120 min	70.3 ± 2.0	80.8 ± 2.2	<0.001	91.9 ± 1.5	104.2 ± 1.8	<0.001
180 min	69.2 ± 2.1	79.4 ± 2.3	<0.001	90.8 ± 1.4	102.6 ± 1.7	<0.001

Baseline HR and MAP were comparable between groups. Following induction and throughout surgery, Group S demonstrated significantly lower HR and MAP than Group C at all measured time points ($p<0.001$). Heart rate remained approximately 10 bpm lower in the clonidine group, while MAP remained close to baseline in Group S but was substantially higher in controls, indicating attenuation of the perioperative sympathetic response.

Table 3. Intraoperative blood pressure and anesthetic drug consumption

Parameter	Group S (n=32)	Group C (n=32)	*p*-value
Total fentanyl consumption, µg	198.6 ± 9.4	268.3 ± 10.6	<0.001
Additional propofol required, n (%)	13 (40.6)	32 (100)	<0.001
Baseline SBP, mmHg	119.8 ± 2.9	120.1 ± 3.1	0.62
Baseline DBP, mmHg	77.9 ± 2.3	78.4 ± 2.2	0.48
SBP at 15 min, mmHg	124.6 ± 4.2	138.9 ± 4.8	<0.001
DBP at 15 min, mmHg	81.9 ± 2.9	94.6 ± 3.4	<0.001
SBP at 180 min, mmHg	119.4 ± 3.5	131.8 ± 4.0	<0.001
DBP at 180 min, mmHg	77.9 ± 2.3	88.4 ± 2.8	<0.001

Clonidine significantly attenuated intraoperative blood pressure responses, with SBP and DBP remaining close to baseline compared with substantially higher values in controls ($p<0.001$). Total fentanyl consumption was significantly lower with clonidine (198.6 vs. 268.3 µg), representing approximately a 26% reduction. Additional propofol was required in 40.6% of Group S compared with 100% of Group C ($p<0.001$), demonstrating an anesthetic-sparing effect.

Table 4. Postoperative pain and analgesic requirements

Parameter	Group S	Group C	*p*-value
VAS at 60 min, median (range)	1 (0–1)	1 (1–2)	<0.001
VAS at 90 min	2 (1–3)	3 (2–4)	<0.001
VAS at 2 h	3 (2–4)	4 (3–5)	<0.001
VAS at 6 h	4 (3–5)	3 (2–4)	0.02

VAS at 12 h	2 (1–2)	2 (2–4)	0.03
VAS at 24 h	1 (0–2)	2 (1–3)	0.02
Duration of analgesia, min	354 ± 17	121 ± 14	<0.001
Time to first rescue analgesia, min	389 ± 15	148 ± 18	<0.001
Rescue analgesic doses/24 h, median (range)	1 (1–2)	3 (3–4)	<0.001

Postoperative pain scores were significantly lower in the clonidine group at 60 minutes, 90 minutes, 2 hours, 12 hours, and 24 hours, although pain was transiently higher at 6 hours (p=0.02). Clonidine significantly prolonged the duration of analgesia and delayed the first rescue analgesic requirement. Patients receiving clonidine required fewer rescue analgesic doses during the first 24 hours (p<0.001).

Table 5. Postoperative sedation and adverse events

Parameter	Group S	Group C	*p*-value
RSS at 30 min, median (range)	3 (2–4)	2 (1–2)	<0.001
RSS at 60 min	3 (2–4)	2 (1–2)	<0.001
RSS at 2 h	2 (1–2)	2 (1–2)	0.41
RSS at 24 h	1 (1–1)	1 (1–1)	0.88
Nausea/vomiting, n (%)	5 (15.6)	10 (31.3)	0.23
Bradycardia, n (%)	6 (18.8)	7 (21.9)	0.77
Urinary retention, n (%)	1 (3.1)	2 (6.3)	1.00

Clonidine produced significantly greater sedation during the first postoperative hour, with higher RSS scores at 30 and 60 minutes (p<0.001). Sedation scores were comparable by 2 hours and identical at 24 hours, indicating resolution of the early sedative effect. Nausea/vomiting was numerically less frequent with clonidine, but the difference was not statistically significant. Bradycardia and urinary retention were comparable between groups.

DISCUSSION

Effective perioperative analgesia and hemodynamic stability are important goals during lumbar spine surgery because surgical stimulation, airway manipulation, and prolonged tissue trauma can produce significant sympathetic responses and postoperative pain. In the present prospective, randomized, double-blinded study of 64 patients, oral clonidine 100 µg administered 45 minutes before surgery significantly attenuated intraoperative hemodynamic responses, reduced anesthetic and opioid requirements, and improved postoperative analgesia compared with placebo, without a significant increase in adverse events.

The demographic and baseline characteristics were comparable between the groups, including age, sex, weight, ASA grade, baseline heart rate, and mean arterial pressure. This similarity confirms successful randomization and provides a balanced basis for comparison of subsequent outcomes. [8,9]

Clonidine produced a marked attenuation of the intraoperative cardiovascular response. Although baseline heart rates were comparable, heart rate was significantly lower in the clonidine group from 15 minutes after intubation and remained lower throughout surgery (p<0.001). Similarly, SBP, DBP, and MAP remained closer to baseline in patients receiving clonidine, whereas controls demonstrated significantly higher values throughout the operative period. At 15 minutes, SBP was 124.6 ± 4.2 mmHg versus 138.9 ± 4.8 mmHg and MAP was 95.3 ± 1.8 mmHg versus 109.4 ± 2.1 mmHg in the clonidine and control groups, respectively (both p<0.001). These findings are consistent with the sympatholytic action of clonidine through central α2-adrenergic receptor stimulation and are in agreement with previous studies reporting attenuation of cardiovascular responses to laryngoscopy, intubation, and surgical stimulation. [7,8,9]

The hemodynamic benefit was accompanied by an anesthetic-sparing effect. Total intraoperative fentanyl consumption was significantly lower with clonidine (198.6 ± 9.4 µg vs 268.3 ± 10.6 µg; p<0.001), representing an approximately 26% reduction. Additional propofol was required in only 40.6% of clonidine-treated patients compared with all patients in the control group (p<0.001). These findings are consistent with the analgesic and sedative properties of α2-adrenergic agonists and support the opioid- and anesthetic-sparing effects reported in previous studies. [10,11]

Postoperative pain outcomes further supported the benefit of clonidine. Pain scores were similar immediately after recovery and at 30 minutes but were significantly lower in the clonidine group from 60 minutes through 2 hours. Although a transiently higher VAS score was observed at 6 hours, pain scores were again significantly lower at 12 and 24 hours. The duration of analgesia was significantly longer in the clonidine group (354 ± 17 vs 121 ± 14 minutes; p<0.001), while the time to first rescue analgesia was substantially prolonged (389 ± 15 vs 148 ± 18 minutes; p<0.001). Patients receiving clonidine also required fewer rescue analgesic doses during the first 24 hours. These findings support the role of preoperative clonidine in improving postoperative analgesia and reducing supplemental analgesic requirements.[11,12]

Clonidine was associated with greater sedation during the early postoperative period. RSS was significantly higher at 30 and 60 minutes, indicating greater early sedation; however, the difference disappeared by 2 hours and scores were identical between groups at 24 hours. Thus, although clonidine produced transient early sedation, there was no evidence of prolonged sedation or delayed neurological

recovery. This is particularly relevant in spine surgery, where early postoperative neurological assessment is important.

The overall safety profile was favorable. Hypertensive episodes were less frequent in the clonidine group, while the incidence of bradycardia was comparable between groups. Postoperative nausea and vomiting were numerically lower with clonidine, although the difference was not statistically significant. Urinary retention was also uncommon and comparable between groups. These findings suggest that the hemodynamic and analgesic benefits of clonidine were not accompanied by a significant increase in clinically relevant adverse events. [13,14]

CONCLUSION

Oral clonidine premedication (100 micrograms administered 45 minutes preoperatively) represents an effective, safe, and clinically beneficial adjunct to standard anesthetic protocols in patients undergoing lumbar spine surgery. The drug consistently produces superior hemodynamic stability, reduces perioperative opioid requirements, and substantially enhances postoperative analgesia. These benefits align with contemporary emphasis on opioid-sparing anesthesia techniques and enhanced recovery after surgery pathways.

The demonstrated reduction in perioperative opioid exposure carries particular significance given emerging public health concerns regarding opioid-related complications and addiction. Incorporation of clonidine into routine perioperative protocols offers an evidence-based strategy to minimize opioid exposure while achieving superior pain control.

Furthermore, the hemodynamic stabilization afforded by clonidine premedication reduces cardiovascular stress responses to anesthesia and surgical manipulation, potentially benefiting patients at heightened cardiac risk. The favorable safety profile supports widespread implementation in appropriately selected patient populations.

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