Original Article

Effect of a low-dose dexmedetomidine infusion on intraoperative hemodynamics, anesthetic requirements and recovery profile in patients undergoing lumbar spine surgery

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Abstract

Background and Aims: Dexmedetomidine has been used as an anesthetic adjuvant; however, hypotension is a concern especially in prone patients. The aim of the study was to evaluate the effect of a low-dose dexmedetomidine infusion on intraoperative hemodynamics, blood loss, anesthetic requirements, and recovery profile in patients undergoing lumbar spine surgery in the prone position.

Material and Methods: The study was conducted in a randomized double-blinded manner in 60 patients scheduled for one- or two-level lumbar laminectomy. After administration of general anesthesia, patients were placed in prone position and allocated to either of two groups of 30 patients each. Patients in Group A received dexmedetomidine infusion at the rate of 0.3 μg kg^{-1} hr^{-1}, whereas, group B patients received a saline infusion. The depth of anesthesia was guided by Bispectral index (BIS) monitoring, maintaining BIS between 40 and 60.

Results: The demographic profile and duration of surgery in both groups were similar. Mean heart rate was statistically similar in both the groups. Mean blood pressure was lower in group A, though the difference was significant only for the initial 30 min. The mean end-tidal sevoflurane requirement in group A was significantly less than that in group B ($P = 0.003$). Patients in group A had better recovery profile with mean emergence, extubation, and recovery times of 8.08 ± 3.48 min, 9.37 ± 3.64 min, and 11.65 ± 4.03 min, respectively, as compared with 11.27 ± 3.05 min, 12.24 ± 2.39 min, and 14.90 ± 2.63 min, respectively, in group B ($P < 0.001$). Mean intraoperative blood loss in group A of 263.47 ± 58.66 mL was significantly lower than 347.67 ± 72.90 ml in group B ($P = 0.0001$).

Conclusion: Group A patients had stable hemodynamic parameters, reduced intraoperative blood loss, less anesthetic requirement, and could be extubated earlier as compared with group B patients.

Keywords: α -2 agonist, dexmedetomidine, prone position, spine surgery

Introduction

Dexmedetomidine, a highly selective alpha-2 agonist, has been widely used in anesthesia practice as an anesthetic adjuvant because of its desirable properties like sedation without respiratory depression and opioid-sparing effects. It decreases sympathetic tone, thereby reducing heart rate and blood pressure; it also attenuates the stress responses to surgery.[1,2] The dose of dexmedetomidine often quoted in

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the literature is a bolus of 1 μg kg^{-1} hr^{-1} over 10 min followed by infusion of 0.2–0.7 μg kg^{-1} hr^{-1}, but this dose frequently results in bradycardia and hypotension.[3,4] As patients undergoing spine surgery already have a propensity to develop hypotension, any additional drug-induced hypotension may further compromise the spinal cord perfusion.[5] Recently, researchers have administered an intraoperative continuous infusion of lower doses of dexmedetomidine without a prior bolus.[6-10] However, the use of low-dose dexmedetomidine infusion without prior bolus administration has not been evaluated in patients undergoing spine surgery. Hence, this study was planned to evaluate the effects of intraoperative IV infusion of a low-dose (0.3 μg kg^{-1} hr^{-1}) dexmedetomidine in patients undergoing lumbar spine surgery. The primary aim of this study was to evaluate the effect of this infusion on the intraoperative hemodynamic profile, blood loss during surgery, and emergence from anesthesia. The secondary aim was to study its effect on intraoperative anesthetic and analgesic requirements.

Material and Methods

The study was conducted in a prospective randomized double-blinded manner in a tertiary level hospital after approval from the hospital ethics committee. The sample size was calculated by *post hoc* power analysis conducted using the software package, G power (Faul and Erdfelder 1992). Based on the previous study by Turgut *et al.*,[11] with an alpha level of $P < 0.05$ and beta of 0.20 with 10% chance of error using reduced anesthetic requirement parameter, a sample size of 30 patients in each of two groups was required for a power of 80%.

Sixty ASA grade I and II patients of either sex, aged 18–65 years, undergoing elective laminectomy at one- or two-lumbar levels in the prone position under general anesthesia were included in the study after written informed consent. The exclusion criteria were pregnant patients, patients suffering from hypertension (blood pressure >140/90 mm Hg), uncontrolled diabetes mellitus, morbid obesity (BMI >35 kg m^{-2}), severe respiratory disease, such as asthma, chronic obstructive pulmonary disease, severe hepatic, renal, endocrine disease, cardiac dysfunction, such as ischemic heart disease, arrhythmias, and valvular heart disease. Patients having a history of drug abuse or undergoing spine fixation or corrective spine surgery or those who have undergone previous spine surgery were also excluded.

A thorough preanesthetic evaluation including detailed history, general physical examination, and systemic examination was done a day prior to the surgery. Routine investigations like complete hemogram, prothrombin time (PT), international normalized ratio (INR), renal function tests, random blood sugar, chest X-ray, and electrocardiogram (ECG) were done prior to the surgery. All patients were kept nil per oral for at least 6 h prior to surgery and premedicated with 150 mg of ranitidine and 0.5 mg of alprazolam orally the night before and on the morning of surgery.

On arrival to operation theatre, intravenous (IV) fluids were started after securing an 18 G cannula, preferably on the left dorsum of the hand. Routine monitoring which included five lead ECG, pulse oximetry, noninvasive blood pressure (NIBP) were applied and baseline vital parameters were recorded. Anesthesia was induced with glycopyrrolate 0.2 mg fentanyl 2 μg kg^{-1} sodium thiopentone 3–5 mg kg^{-1} and atracurium 0.5 mg kg^{-1}. Before intubation, an additional dose of sodium thiopentone (2 mg kg^{-1}) was administered. Trachea was intubated with an appropriate sized cuffed orotracheal flexometallic tube in all the patients.

Anesthesia was maintained using oxygen (O_2) and nitrous oxide (N_2O) (40:60), and sevoflurane (1%–3%) with closed circuit using a total fresh gas flow of 2 L min^{-1}. Atracurium, in increments of 5 mg, was administered as guided by neuromuscular monitoring maintaining a train of four (TOF) count of 0. Lungs were ventilated with a tidal volume of 6–8 mL/kg and respiratory rate of 10–12 per minute to maintain an end-tidal carbon dioxide ($EtCO_2$) of 30–40 mm Hg. Depth of anesthesia was monitored using the Bispectral index (BIS) targeting BIS values between 40 and 60, by adjusting the dial settings of sevoflurane. The end-tidal concentration of sevoflurane (Et_{sevo}) was recorded.

The patients were placed in prone position, and once properly positioned, this time was labeled as 0. From here onwards, vital parameters including HR, NIBP-systolic, diastolic, and mean blood pressure, SpO_2, BIS score, $EtCO_2$, and Et_{sevo} were recorded at an interval of 5 min throughout the procedure.

The patients were randomly assigned to one of the two groups of 30 patients each using computer-generated random numbers, which were enclosed in a sealed envelope. The study drug was prepared in identical 50 mL syringes by an anesthesiologist not involved in the study.

At '0' time, an IV infusion of dexmedetomidine was started at a rate of 0.3 μg kg^{-1} hr^{-1} in patients in Group A. For this, 200 μg (2 mL) of dexmedetomidine was added to 0.9% saline (48 ml) (resulting concentration was 4 μg L^{-1}). Patients in Group B were administered an infusion of 0.9% saline, at the same rate and at the same time.

An episode of tachycardia (defined as heart rate >20% of baseline value) and hypertension (defined as blood pressure >20% of baseline value), lasting for more than a minute, was controlled by a bolus of fentanyl (1 μg kg^{-1}) given intravenously. Another bolus of fentanyl 0.5 μg kg^{-1} was repeated after 15 min if the episode of heart rate and blood pressure did not revert to normal. Tachycardia and hypertension if not controlled with fentanyl boluses then were controlled with labetalol 5 mg IV boluses, at the discretion of anesthesiologist conducting the case and the same was recorded.

Any episode of bradycardia, that is, heart rate <50/min was treated by reducing the dial setting of sevoflurane and atropine 0.6 mg intravenously. Any episode of hypotension, that is, mean arterial blood pressure <60 mm Hg was managed by administering a bolus of IV fluids and ephedrine 3 mg intravenously. Infusion of study drug was discontinued if hypotension/bradycardia was resistant to treatment with two doses of atropine and ephedrine. Such patients were excluded from the study. Total IV fluids, fentanyl, labetalol, and blood products if administered were recorded as an indirect measure for intraoperative hemodynamic lability. Intraoperative blood loss was estimated by both subjective and objective methods.

Blood loss was measured by weighing gauze pieces and surgical sponges before the start of surgery and again at the end of surgery and noting down the difference between their weights. Also, the contents from the suction bottle were noted and intraoperative saline used for irrigation was subtracted from this. Blood loss was obtained by summation of these two. In addition, subjective assessment of blood loss was made by the neurosurgeon operating on the patient by the level of impairment of the surgical field as follows:[12]

0 – No impairment
1 – Slightly impaired
2 – Impaired
3 – Heavily impaired.

To minimize the interobserver variability of such an evaluation, cases operated upon by only one neurosurgeon were enrolled for the study.

At the end of surgery, all patients were administered paracetamol 1 g IV and ondansetron 8 mg IV at the beginning of skin closure. The infusion of study medication was stopped on starting of skin closure and sevoflurane was stopped once dressing of the incision site was complete. After wound dressing, the patient was made supine and fresh gas flow was changed to 4 L min^{-1} of oxygen, the residual neuromuscular block was reversed with neostigmine 2.5 mg IV and glycopyrrolate 0.4 mg IV, and tracheal extubation was performed.

Timing of the following events was recorded:[12]

1. Emergence time: It was measured as the time between anesthetic discontinuation and the time at which patients opened their eyes (spontaneously or on verbal prompting repeated every 2 min after turning the patient supine)
2. Tracheal extubation time: This was measured as the time elapsed from anesthetic discontinuation to extubation (performed when the patient obeyed verbal commands and maintained adequate spontaneous ventilation, i.e., regular respiratory pattern with tidal volume 4 mL kg^{-1})
3. Recovery time: This was measured as the time elapsed from discontinuation of anesthetic agent to the time when patients were able to recall their names and dates of birth (on verbal prompting every 2 min after extubation).

Statistical analysis

Statistical analysis was performed using the SPSS (Statistical Package for Social Sciences) for Windows. Data were reported as mean value, with variability expressed as standard deviation (SD). The two-tailed Student's unpaired *t*-test and analysis of variance (ANOVA) were used for parametric data. All non-parametric data were analyzed using the χ^2 test. A P value < 0.05 was considered statistically significant.

Results

The demographic profile like mean age, weight, body mass index (BMI), and sex distribution is given in Table 1. The mean platelet counts, PTI, and INR in is also shown.

The duration of surgery was similar in both the groups; it was 164.0 ± 56.0 min in group A and 172.0 ± 46.7 min in group B ($P = 0.550$). The difference in the total amount of fentanyl administered in either group was also statistically insignificant ($P = 0.200$).

The mean HR was statistically similar in both the groups throughout surgery [Figure 1]. The MAP was significantly lower in group A as compared with group B for the initial 30 min, after which the difference in MAP among the two groups was statistically not significant [Figure 2].

The mean ET_{sevo} was significantly less in group A as compared with group B ($P = 0.003$) [Figure 3].

The mean total intraoperative blood loss of 263.5 ± 58.7 mL in group A was significantly less as compared with 347.7 ± 72.9 mL in group B ($P<0.001$). Similarly,

mean fall in hemoglobin in group A (0.5 ± 0.1 g/dL) was significantly lesser as compared with group B. (0.7 ± 0.2 g/dL) ($P = 0.017$). The objective assessment of the impairment of the surgical field by the surgeon was also statistically higher in group B ($P = 0.039$) [Figure 4].

The recovery characteristics, which included mean emergence time, mean tracheal extubation time, and mean recovery times, were significantly earlier in group A ($P < 0.001$) as compared with group B [Figure 5].

The incidence of adverse events between both groups was statistically similar [Table 2]. None of the patients in either of the groups had hypotension or bradycardia, severe enough to warrant stoppage of infusion of study drug. The need for ephedrine to manage hypotension and labetalol to control hypertension in the two groups was also statistically similar [Table 2].

Discussion

Low-dose dexmedetomidine infusion of 0.25–0.5 μg kg^{-1} hr^{-1} without a prior bolus has been reported to result in a more predictable decrease of heart rate and blood pressure.[13,14] We also noted a similar mean HR among the two groups. Similarly, the MAP was lower in group A only for the initial 30 min, after which it was similar in both the groups. This initial fall in blood pressure in group A might be because of the fall in the cardiac index because of dexmedetomidine, which probably, later on, normalized by compensatory hemodynamic changes. Feld *et al.*[15] also observed a similar decrease in blood pressure while comparing dexmedetomidine with fentanyl in bariatric surgery. Similarly, Tanskanen *et al.* and Batra *et al.* also reported stable hemodynamics in patients undergoing intracranial surgery when dexmedetomidine infusion without a preceding bolus was administered.[9,13]

MAP has been considered to be the chief determinant of intraoperative blood loss with higher MAP expected to result in greater blood loss.[16] We, however, observed significantly lesser blood loss in group A as compared with group B, which reflected in lesser drop in hemoglobin also. The surgeon also reported less subjective impairment of the surgical field. This was an unexpected finding, suggesting that probably factors other than MAP are also important determinants of intraoperative blood loss during spine surgery. In this context, Lee *et al.* had reported differing paraspinal muscle blood flow at the same levels of hypotension.[17]

Similarly, Taghipour *et al.* reported that oral clonidine premedication resulted in significantly less blood loss during posterior spine fusion, despite similar MAP in both the

Table 1: Demographic profile

	Group A		Group B	
	Mean	SD	Mean	SD
Age (years)	47.03	14.34	49.53	14.42
Weight (kg)	74.18	12.38	78.07	16.00
BMI	26.12	3.37	27.54	4.55
Male:Female ratio	19:11		17:13	
Platelet count ($10^3/\mu L$)	207.57	58.85	226.93	58.59
PT (s)	11.23	0.91	11.00	2.11
INR	1.02	0.07	1.05	0.11

BMI=Body mass index, INR=International normalized ratio, PT=Prothrombin time, SD=Standard deviation

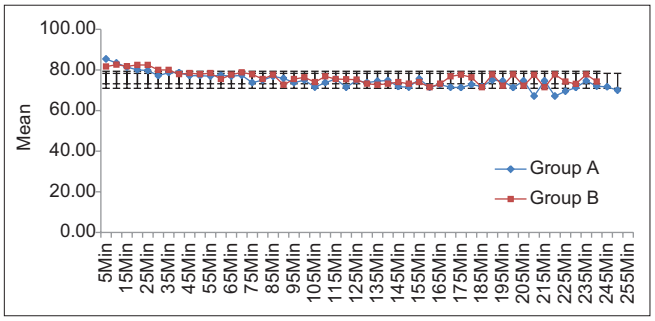

Figure 1: Comparison of mean heart rate

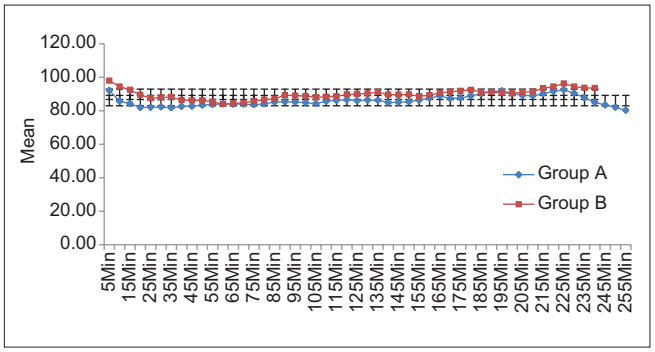

Figure 2: Comparison of mean blood pressure

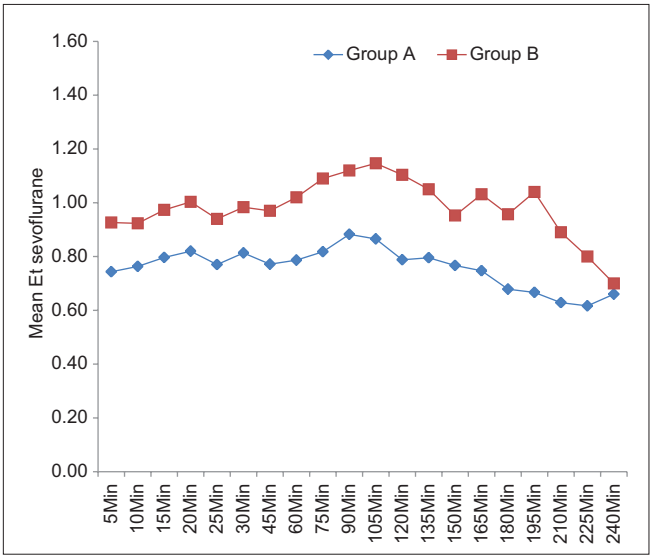

Figure 3: Mean end-tidal sevoflurane concentration

Table 2: Adverse effects

Adverse effect	Group A	Group B	Total	Treatment given	*P*
Tachycardia and hypertension	0 (0%)	4 (13.3%)	4	Inj. labetalol 5 mg	0.056
Bradycardia	3 (10%)	0 (0%)	3	Inj. atropine 0.6 mg	0.119
Hypotension	8 (26.7%)	5 (16.7%)	13	Inj. ephedrine 3 mg	0.266
Nausea/Vomiting	0 (0%)	0 (0%)		None	-
None	19	21	40	None	-

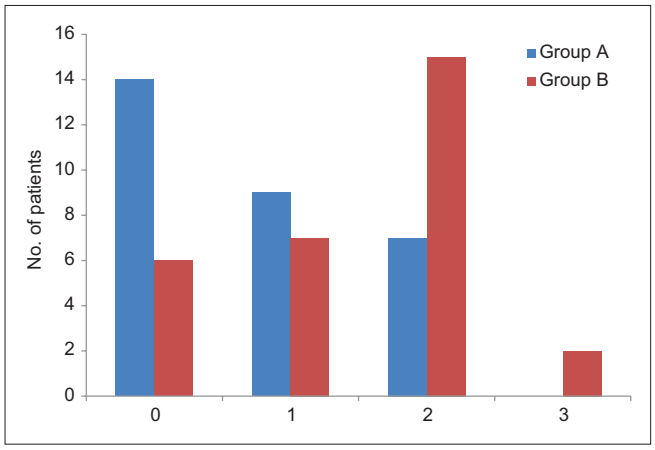

Figure 4: Surgeon's assessment of impairment of visual field by blood

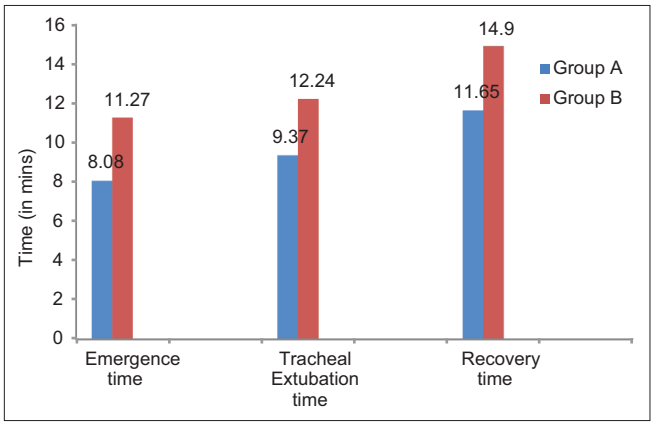

Figure 5: Emergence characteristics

groups.[18] The explanation offered was that clonidine acts on the α–2β subtype of adrenoreceptors in peripheral vascular smooth muscle to cause vasoconstriction.[19] As clonidine and dexmedetomidine are chemically related and act on same receptors, differing only in terms of relative selectivity for α-2 receptors,[1,4] it is plausible that mechanisms similar to those described above resulted in significantly less blood loss despite similar MAP in our study as well. Okuyama *et al.* also observed that clonidine and prostaglandin E_1 reduce blood loss during paranasal sinus surgery without inducing hypotension.[20]

In our study, the mean perioperative fentanyl requirements were lesser in group A as compared with group B. However, the difference between the two groups was statistically not significant ($P = 0.131$). Thus, we could not demonstrate the opioid-sparing effect of dexmedetomidine as has been reported in some of the studies. Mohamed *et al.*[21] and Nazir *et al.*[22] reported a significant reduction in fentanyl requirement with dexmedetomidine during spine surgery. However, the dose of dexmedetomidine used in their studies (bolus of 1 μg kg^{-1} followed by infusion of 0.4–0.8 μg kg^{-1} hr^{-1}) is much higher than the used in this study. In addition, there is no accurate parameter to evaluate the dose and timing when a patient needs additional analgesic. Often, tachycardia and hypertension are used to guide the opioid administration. However, this method has its own limitations and opioids are usually administered as per the subjective judgment and experience of the anesthesiologist. We did, however, observe anesthesia sparing effects of dexmedetomidine infusion as $Et_{(sevo)}$ required to maintain a BIS of 40–60 in our study was observed to be significantly lesser in the group A as compared to the control group. Turgut *et al.* and Ozkose *et al.* also reported decreased anesthetic requirements in patients receiving dexmedetomidine.[11,23]

The time of emergence from anesthesia, tracheal extubation time and recovery time were observed to be significantly earlier in group A as compared to group B. Early emergence is desirable in neuroanesthesia as it allows early neurological assessment. Published studies have highlighted that balanced anesthesia with dexmedetomidine hastens postoperative recovery in patients undergoing prolonged spinal surgery procedures.[24] Tanskanen *et al.*[9] and Batra *et al.*[13] have also reported earlier emergence and extubation times when dexmedetomidine was used as an anesthetic adjuvant in patients undergoing intracranial tumor surgery.

Dexmedetomidine has been reported to reduce the incidence of postoperative nausea and vomiting.[25] However, none of the patients in our study reported any episode of nausea and vomiting. This was probably because all the patients had received an adequate dose of antiemetics before extubation.

The incidence of bradycardia and hypotension was statistically similar in both the groups. Our findings are similar to those of Batra *et al.*,[13] who reported 8% incidence of bradycardia and 20% incidence of hypotension in patients administered

a constant infusion of dexmedetomidine during intracranial surgery.

Limitation of study

The study did not measure intra-abdominal pressure, which can have a bearing on the intraoperative blood loss. Measurement of plasma levels of dexmedetomidine and cardiac output could have added more value to our findings, but the facility for measuring these was not available at our hospital. We could not demonstrate opioid-sparing properties, whereas some other studies have reported opioid-sparing effect when using dexmedetomidine. More studies are needed to find the reason for this and whether the analgesia-sparing properties of dexmedetomidine are dose-dependent.

We conclude that dexmedetomidine in a dose of 0.3 $\mu g\ kg^{-1}\ hr^{-1}$ reduces intraoperative blood loss and results in earlier emergence from anesthesia without any significant adverse effects.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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