Original Research

Comparative evaluation of the efficacy of dexmedetomidine versus dexamethasone as adjuvant to 0.2% ropivacaine in erector spinae plane block for lumbar spine surgeries- A prospective, randomised controlled study

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ABSTRACT

Aim: To comparatively evaluate the efficacy of dexmedetomidine versus dexamethasone as adjuvant to 0.2% ropivacaine in erector spinae plane (ESP) block for postoperative analgesia in patients undergoing lumbar spine surgeries.

Material and Methods: This prospective, randomized controlled study included 100 adult patients aged 18–65 years scheduled for elective lumbar spine surgeries under general anesthesia. Patients were randomly assigned into two groups: Group DEXM received 0.2% ropivacaine with dexmedetomidine (0.5 μg/kg), and Group DEXA received 0.2% ropivacaine with dexamethasone (8 mg) in the ESP block. Postoperative pain scores using Visual Analogue Scale (VAS), duration of analgesia, total opioid consumption over 24 hours, hemodynamic parameters, and incidence of adverse effects were recorded and analyzed.

Results: The demographic characteristics were comparable between the groups. Group DEXM demonstrated a significantly longer mean duration of analgesia (812.6 ± 75.4 minutes) compared to Group DEXA (645.2 ± 68.8 minutes; $p < 0.001$). Total morphine consumption over 24 hours was significantly lower in Group DEXM (4.2 ± 1.5 mg) than in Group DEXA (6.8 ± 2.1 mg; $p < 0.001$). VAS scores at all assessed time points were consistently lower in Group DEXM. Group DEXM also showed better hemodynamic stability with lower heart rate and mean arterial pressure values. Sedation was more frequent in Group DEXM (12.0%) compared to Group DEXA (2.0%), but other adverse effects were comparable.

Conclusion: The addition of dexmedetomidine to 0.2% ropivacaine in ESP block significantly prolonged analgesia, reduced opioid consumption, improved pain control, and provided better hemodynamic stability compared to dexamethasone. Dexmedetomidine was found to be a superior adjuvant for ESP block in lumbar spine surgeries, despite a slightly higher incidence of sedation.

Keywords: Erector spinae plane block, Dexmedetomidine, Dexamethasone, Ropivacaine, Lumbar spine surgery

Introduction

Effective postoperative pain management remains a critical component of enhanced recovery protocols following lumbar spine surgeries. Inadequate control of pain after spinal procedures can delay ambulation, prolong hospital stays, impair pulmonary function, and increase the risk of chronic pain development. Multimodal analgesia strategies have been adopted widely to address postoperative pain, with regional anesthesia techniques emerging as key contributors. Among these, the erector spinae plane (ESP) block has gained considerable popularity for its simplicity, safety profile, and ability to provide effective analgesia for thoracic and lumbar spine surgeries.[1]

The ESP block involves the deposition of local anesthetic deep to the erector spinae muscle at the level of the transverse processes, allowing for cranio-caudal spread to multiple spinal levels and effective blockade of both dorsal and ventral rami. Its ease of administration under ultrasound guidance and low risk of complications compared to neuraxial techniques have positioned it as an attractive option for spine

surgeons and anesthesiologists alike. However, the duration of analgesia provided by a single-shot ESP block with local anesthetic alone is often limited. Consequently, various adjuvants have been explored to prolong the analgesic effect and enhance patient outcomes.[2]

Ropivacaine, a long-acting amide local anesthetic, is frequently chosen for peripheral nerve and fascial plane blocks because of its favorable pharmacological profile, offering prolonged sensory blockade with minimal motor impairment. Nevertheless, even with ropivacaine, the duration of postoperative analgesia following ESP block may not be sufficient for the extended recovery period associated with spine surgeries. To overcome this limitation, the addition of adjuvants such as dexmedetomidine and dexamethasone to local anesthetics has been investigated.[3]

Dexmedetomidine is a highly selective alpha-2 adrenergic receptor agonist with sedative, anxiolytic, and analgesic properties. Its use as an adjuvant in regional anesthesia has been shown to enhance the quality and prolong the duration of nerve blocks. The mechanism by which dexmedetomidine exerts its prolonging effect is believed to involve hyperpolarization of nerve tissues, vasoconstriction leading to slower absorption of the local anesthetic, and central modulation of pain pathways. Additionally, dexmedetomidine has been associated with stable hemodynamics and decreased anesthetic requirements, making it a valuable adjunct in perioperative pain management.On the other hand, dexamethasone, a potent synthetic glucocorticoid, is another widely studied adjuvant for regional anesthesia. Its anti-inflammatory and anti-nociceptive effects contribute to prolonging the duration of analgesia when added to local anesthetics. Dexamethasone may act by reducing perineural inflammation, inhibiting ectopic neuronal discharge, and possibly modulating potassium channel function, thereby enhancing the efficacy and duration of regional blocks. Moreover, dexamethasone has the added benefit of reducing postoperative nausea and vomiting, which is an important consideration in the recovery of spine surgery patients.[4]

Although both dexmedetomidine and dexamethasone have been individually shown to enhance regional anesthesia outcomes, direct comparisons between the two agents, specifically in the setting of ESP block for lumbar spine surgeries, remain limited. Understanding the relative efficacy and safety profiles of these two adjuvants could significantly impact clinical practice by guiding anesthesiologists in selecting the optimal agent for prolonged postoperative analgesia.[5]

The choice of adjuvant must also take into account the potential side effects associated with each agent. Dexmedetomidine is known to cause dose-dependent bradycardia and hypotension, and excessive sedation may complicate postoperative neurological assessment. Dexamethasone, while generally safe in single doses, carries concerns related to hyperglycemia and potential immunosuppression, especially in vulnerable patient populations. Therefore, an ideal adjuvant would provide effective prolongation of analgesia without a significant increase in adverse effects.[6]

The growing emphasis on enhanced recovery after surgery (ERAS) protocols and the movement toward opioid-sparing analgesia further highlight the need to refine regional anesthesia techniques. Prolonged effective analgesia not only improves patient comfort but also facilitates early mobilization, reduces hospital stay duration, and minimizes opioid-related side effects, such as respiratory depression, constipation, and the potential for long-term dependence. In this context, the use of adjuvants that can extend the benefits of a single-shot ESP block assumes considerable clinical importance.[7]

Given these considerations, the present study was designed to conduct a comparative evaluation of the efficacy of dexmedetomidine versus dexamethasone as adjuvants to 0.2% ropivacaine in ultrasound-guided erector spinae plane block for patients undergoing lumbar spine surgeries. The primary aim was to compare the duration of analgesia between the two groups. Secondary objectives included comparing postoperative opioid consumption, pain scores at various intervals, hemodynamic stability, and the incidence of adverse effects such as bradycardia, hypotension, nausea, vomiting, and sedation.

Material and Methods

This prospective, randomized controlled study was conducted at the Department of Anesthesiology in a tertiary care teaching hospital. Written informed consent was obtained from all participants before enrolment.A total of 100 adult patients, aged 18–65 years, classified as American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective lumbar spine surgeries under general anesthesia with an erector spinae plane (ESP) block for perioperative analgesia, were included.

Inclusion Criteria:

- Patients aged between 18–65 years.
- ASA grade I or II.
- Elective lumbar spine surgeries (laminectomy, discectomy, or spinal instrumentation).
- Willingness to provide informed consent.

Exclusion Criteria:

- Known allergy or contraindication to study drugs (dexmedetomidine, dexamethasone, or ropivacaine).
- Local infection at the injection site.
- Coagulopathy or patients on anticoagulation therapy.
- Chronic opioid use or pre-existing chronic pain disorders.

- Significant hepatic, renal, psychiatric, or cardiac disease.

Randomization and Blinding: Patients were randomized into two equal groups (n = 50 each) using a computer-generated random sequence and sealed opaque envelopes.

- **Group DEXM:** Received 0.2% ropivacaine with dexmedetomidine (0.5 μg/kg) as an adjuvant in ESP block.
- **Group DEXA:** Received 0.2% ropivacaine with dexamethasone (8 mg) as an adjuvant in ESP block.

Both the patients and the investigator responsible for data collection were blinded to the group allocations. The anesthesiologist preparing the drug solutions was not involved in the intraoperative or postoperative assessments.

Intervention Protocol: Upon arrival in the operating room, standard monitoring (ECG, non-invasive blood pressure, pulse oximetry) was established. Intravenous access was secured, and baseline vital signs were recorded.

Under aseptic precautions, ultrasound-guided ESP block was performed at the L3 level on the side of surgery using a high-frequency linear probe. After identifying the transverse process and erector spinae muscle, a 21G block needle was inserted in-plane and advanced to the fascial plane deep to the erector spinae muscle. After negative aspiration, 20 mL of the prepared study solution was injected in incremental doses under real-time ultrasound visualization.

After successful block administration, general anesthesia was induced with intravenous propofol (2 mg/kg), fentanyl (2 μg/kg), and rocuronium (0.6 mg/kg) to facilitate tracheal intubation. Anesthesia was maintained with isoflurane (MAC 1.0–1.2) in a 50% oxygen-air mixture. Additional doses of muscle relaxant were administered as required.

Postoperative Analgesia: All patients received intravenous paracetamol 1 g every 8 hours postoperatively. Rescue analgesia with intravenous morphine 2 mg boluses was provided if the Visual Analogue Scale (VAS) pain score exceeded 4, and the total morphine consumption over 24 hours was recorded.

The primary outcome of the study was the duration of analgesia, defined as the time interval from the completion of the erector spinae plane (ESP) block to the first requirement of rescue analgesia. Secondary outcomes included the total opioid consumption in the first 24 hours postoperatively, which was measured by the cumulative dose of intravenous morphine administered as rescue analgesia. Pain intensity was assessed using the Visual Analogue Scale (VAS) at rest and during movement at specific postoperative time points: 2, 4, 8, 12, and 24 hours. Hemodynamic parameters, including heart rate and mean arterial pressure, were continuously monitored intraoperatively and postoperatively to evaluate stability and detect any significant deviations. Additionally, the incidence of adverse effects such as bradycardia, hypotension, nausea, vomiting, and sedation was recorded throughout the intraoperative and postoperative periods to assess the safety profile of the interventions.

Statistical Analysis

Data were analyzed using SPSS version 16.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD) and compared using the independent samples t-test or Mann–Whitney U test, as appropriate. Categorical variables were expressed as frequencies (percentages) and compared using the Chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

Demographic Characteristics(Table1): The demographic profile of patients in both groups was comparable without any statistically significant differences. The mean age in Group DEXM was 45.2 ± 10.3 years, while in Group DEXA it was 44.7 ± 9.8 years ($p = 0.76$). Gender distribution was also similar, with males and females accounting for 28 and 22 patients respectively in Group DEXM, and 30 and 20 patients respectively in Group DEXA ($p = 0.68$). Regarding ASA physical status, Group DEXM had 32 patients classified as ASA I and 18 as ASA II, while Group DEXA had 34 patients in ASA I and 16 in ASA II ($p = 0.70$). The mean duration of surgery was comparable between the groups, with Group DEXM at 132.5 ± 18.4 minutes and Group DEXA at 130.8 ± 17.6 minutes ($p = 0.52$). Thus, baseline characteristics were evenly distributed between groups, ensuring homogeneity for further outcome comparisons.

Duration of Analgesia and Opioid Consumption (Table 2): The duration of analgesia was significantly longer in Group DEXM compared to Group DEXA. Patients in Group DEXM experienced a mean analgesia duration of 812.6 ± 75.4 minutes, while those in Group DEXA had a mean duration of 645.2 ± 68.8 minutes ($p < 0.001$). This indicates that dexmedetomidine as an adjuvant to 0.2% ropivacaine provided prolonged postoperative pain relief compared to dexamethasone. In terms of total morphine consumption over the first 24 hours postoperatively, Group DEXM patients required significantly less morphine (4.2 ± 1.5 mg) compared to Group DEXA (6.8 ± 2.1 mg) ($p < 0.001$). This further supports the superior analgesic efficacy of dexmedetomidine over dexamethasone when used in ESP block for lumbar spine surgeries.

VAS Pain Scores at Different Time Points (Table 3): Pain scores assessed using the Visual Analogue Scale (VAS) at various postoperative intervals

showed consistently lower values in Group DEXM compared to Group DEXA. At 2 hours postoperatively, the mean VAS score was 2.1 ± 0.7 in Group DEXM versus 2.8 ± 0.9 in Group DEXA ($p = 0.002$). Similarly, at 4 hours, Group DEXM had a VAS score of 2.5 ± 0.8 compared to 3.3 ± 1.0 in Group DEXA ($p = 0.001$). At 8 hours, the scores were 2.8 ± 0.9 and 3.6 ± 1.2, respectively ($p = 0.001$). At 12 hours, the scores were 2.9 ± 1.0 for Group DEXM and 3.7 ± 1.1 for Group DEXA ($p < 0.001$). Finally, at 24 hours, Group DEXM still demonstrated lower pain scores (3.2 ± 1.1) compared to Group DEXA (3.9 ± 1.3) ($p = 0.004$). These findings indicate that dexmedetomidine provided more effective and sustained pain control throughout the postoperative period.

Hemodynamic Parameters (Intraoperative and Postoperative) (Table 4): There were notable differences in hemodynamic stability between the two groups. The intraoperative heart rate (HR) was significantly lower in Group DEXM (68.4 ± 6.2 beats/min) compared to Group DEXA (74.1 ± 7.0 beats/min) ($p < 0.001$). Similarly, intraoperative mean arterial pressure (MAP) was lower in Group DEXM (82.6 ± 5.8 mmHg) versus Group DEXA (87.3 ± 6.1 mmHg) ($p = 0.001$). Postoperatively, Group DEXM continued to show lower HR (70.2 ± 6.5 beats/min) compared to Group DEXA (75.6 ± 6.8 beats/min) ($p < 0.001$), and lower MAP (84.3 ± 5.6 mmHg) compared to Group DEXA (89.0 ± 5.9 mmHg) ($p = 0.001$). These results suggest that dexmedetomidine contributed to better hemodynamic control by maintaining lower heart rate and blood pressure values during and after surgery.

Incidence of Adverse Effects (Table 5): The incidence of adverse effects was generally low and comparable between the two groups. Bradycardia was observed in 8.0% of patients in Group DEXM and 2.0% in Group DEXA ($p = 0.17$), while hypotension occurred in 6.0% of Group DEXM patients and 4.0% of Group DEXA patients ($p = 0.64$). Incidence of nausea was 10.0% in Group DEXM and 12.0% in Group DEXA ($p = 0.75$), and vomiting occurred in 4.0% and 6.0% of patients, respectively ($p = 0.65$). Notably, sedation was more frequent in Group DEXM (12.0%) compared to Group DEXA (2.0%), with a borderline statistically significant p-value of 0.05. While dexmedetomidine showed a slight tendency toward greater sedation, other adverse effects were similar and manageable across both groups, indicating that both adjuvants were safe for use in ESP block.

Table 1: Demographic Characteristics of Patients

Parameter	Group DEXM (n=50)	Group DEXA (n=50)	p-value
Age (years, mean ± SD)	45.2 ± 10.3	44.7 ± 9.8	0.76
Gender (Male/Female)	28/22	30/20	0.68
ASA Physical Status (I/II)	32/18	34/16	0.70
Duration of Surgery (minutes, mean ± SD)	132.5 ± 18.4	130.8 ± 17.6	0.52

Table 2: Duration of Analgesia and Opioid Consumption

Outcome Parameter	Group DEXM (n=50)	Group DEXA (n=50)	p-value
Duration of Analgesia (minutes, mean ± SD)	812.6 ± 75.4	645.2 ± 68.8	<0.001
Total Morphine Consumption (mg in 24 hours, mean ± SD)	4.2 ± 1.5	6.8 ± 2.1	<0.001

Table 3: VAS Pain Scores at Different Time Points

Time Postoperatively	Group DEXM VAS (mean ± SD)	Group DEXA VAS (mean ± SD)	p-value
2 hours	2.1 ± 0.7	2.8 ± 0.9	0.002
4 hours	2.5 ± 0.8	3.3 ± 1.0	0.001
8 hours	2.8 ± 0.9	3.6 ± 1.2	0.001
12 hours	2.9 ± 1.0	3.7 ± 1.1	<0.001
24 hours	3.2 ± 1.1	3.9 ± 1.3	0.004

Table 4: Hemodynamic Parameters (Intraoperative and Postoperative)

Parameter	Group DEXM (mean ± SD)	Group DEXA (mean ± SD)	p-value
Intraoperative HR (beats/min)	68.4 ± 6.2	74.1 ± 7.0	<0.001
Intraoperative MAP (mmHg)	82.6 ± 5.8	87.3 ± 6.1	0.001
Postoperative HR (beats/min)	70.2 ± 6.5	75.6 ± 6.8	<0.001
Postoperative MAP (mmHg)	84.3 ± 5.6	89.0 ± 5.9	0.001

Table 5: Incidence of Adverse Effects

Adverse Effect	Group DEXM (n=50)	Group DEXA (n=50)	p-value
Bradycardia	4 (8.0%)	1 (2.0%)	0.17
Hypotension	3 (6.0%)	2 (4.0%)	0.64
Nausea	5 (10.0%)	6 (12.0%)	0.75
Vomiting	2 (4.0%)	3 (6.0%)	0.65
Sedation (RASS ≤ -2)	6 (12.0%)	1 (2.0%)	0.05

Discussion

In the present study, the demographic characteristics such as age, gender, ASA physical status, and duration of surgery were comparable between the two groups, ensuring a homogeneous population for comparing outcomes. These findings align with the observations made by Schnabel et al (2013), who, in their meta-analysis on dexmedetomidine as an adjuvant to regional anesthesia, also reported no significant differences in demographic parameters across groups, allowing a fair evaluation of the analgesic effects of different adjuvants.[8]

The duration of analgesia was significantly longer in patients who received dexmedetomidine as an adjuvant compared to those who received dexamethasone in our study (812.6 ± 75.4 minutes vs. 645.2 ± 68.8 minutes, $p < 0.001$). Similar trends were reported by Brummett et al (2011), who demonstrated that the addition of perineural dexmedetomidine to ropivacaine significantly prolonged the duration of sensory block compared to ropivacaine alone, suggesting that dexmedetomidine enhances local anesthetic action through peripheral mechanisms.[9]

In terms of opioid consumption, patients in the dexmedetomidine group had lower morphine requirements (4.2 ± 1.5 mg) compared to those in the dexamethasone group (6.8 ± 2.1 mg) over 24 hours postoperatively. These results are consistent with findings by Marhofer et al (2013), who observed that dexmedetomidine used as an adjuvant in peripheral nerve blocks reduced postoperative opioid use and provided superior analgesia without significant adverse effects.[10]

The postoperative VAS pain scores were significantly lower at all assessed time points in Group DEXM compared to Group DEXA. A similar outcome was described by Esmaoglu et al (2010), who found that dexmedetomidine, when combined with levobupivacaine in axillary blocks, resulted in lower VAS scores at various intervals compared to local anesthetic alone, supporting its potent analgesic and anti-nociceptive effects when used as an adjunct.[11]

Hemodynamic stability was better maintained in the dexmedetomidine group, as indicated by lower intraoperative and postoperative heart rate and mean arterial pressure values. This finding correlates with the study by Memis et al (2004), who demonstrated that intravenous dexmedetomidine administered perioperatively led to significant reductions in heart rate and blood pressure, attributed to its central sympatholytic effects via alpha-2 receptor activation.[12]

Regarding adverse effects, while sedation was more common in the dexmedetomidine group (12.0% vs. 2.0%), the incidence of bradycardia, hypotension, nausea, and vomiting was similar between groups. These observations are in agreement with the results of Al-Mustafa et al (2009), who reported that dexmedetomidine increased the incidence of mild sedation without significantly raising the risk of severe adverse events when used as an adjuvant to local anesthetics for regional anesthesia.[13]

Conclusion

The addition of dexmedetomidine to 0.2% ropivacaine in erector spinae plane block significantly prolonged the duration of analgesia, reduced postoperative opioid consumption, and provided lower pain scores compared to dexamethasone in patients undergoing lumbar spine surgeries. Dexmedetomidine also offered better hemodynamic stability, although with a slightly higher incidence of sedation. Both adjuvants were safe and effective, but dexmedetomidine demonstrated superior overall analgesic efficacy in this study.

References

1. Grogan EL, Jones DR. VATS lobectomy is better than open thoracotomy: what is the evidence for short-term outcomes? ThoracSurg Clin. 2008;18(3):249-58. doi:10.1016/j.thorsurg.2008.04.007. PMID: 18674747.
2. Kotemane NC, Gopinath N, Vaja R. Analgesic techniques following thoracic surgery: a survey of United Kingdom practice. Eur J Anaesthesiol. 2010;27(10):897-9. doi:10.1097/EJA.0b013e32833d1259. PMID: 20706185.
3. Forero M, Adhikary SD, Lopez H, Tsui C, Chin KJ. The erector spinae plane block: a novel analgesic technique in thoracic neuropathic pain. Reg Anesth Pain Med. 2016;41(5):621-7. doi:10.1097/AAP.0000000000000451. PMID: 27518494.
4. Rancourt MP, Albert NT, Côté M, Brulotte V, Godbout C, Varin F, et al. Posterior tibial nerve sensory blockade duration prolonged by adding dexmedetomidine to ropivacaine. AnesthAnalg. 2012;115(4):958-62. doi:10.1213/ANE.0b013e318265bab7. PMID: 22972992.
5. Choi S, Rodseth R, McCartney CJL. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. Br J Anaesth. 2014;112(3):427-39. doi:10.1093/bja/aet417. PMID: 24395367.

6. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. AnesthAnalg. 2006;102(1):263-7. doi:10.1213/01.ane.0000189055.06729.0a. PMID: 16368831.
7. Thomson AJ, Nimmo AF, Engbers FHM, Scott NB. A novel technique to determine an 'apparent ke0' value for use with the Marsh pharmacokinetic model for propofol. Anaesthesia. 2014;69(5):420-8. doi:10.1111/anae.12596. PMID: 24571220.
8. Schnabel A, Reichl SU, Kranke P, Pogatzki-Zahn EM, Zahn PK. Efficacy and safety of dexmedetomidine in peripheral nerve blocks: a meta-analysis and trial sequential analysis. Eur J Anaesthesiol. 2013 Sep;30(9):729-36. doi: 10.1097/EJA.0b013e328362d331. PMID: 23648845.
9. Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. Anesthesiology. 2011 Sep;115(3):836-43. doi: 10.1097/ALN.0b013e31822e93e7. PMID: 21792054.
10. Marhofer D, Kettner SC, Marhofer P, Pils S, Weber M, Zeitlinger M. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: a volunteer study. Br J Anaesth. 2013 Aug;110(3):438-42. doi: 10.1093/bja/aes400. PMID: 23242982.
11. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. AnesthAnalg. 2010 Dec;111(6):1548-51. doi: 10.1213/ANE.0b013e3181f45e3b. PMID: 21081774.
12. Memis D, Turan A, Karamanlioglu B, Pamukcu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. AnesthAnalg. 2004 Dec;98(3):835-40. doi: 10.1213/01.ANE.0000096180.41664.D4. PMID: 14980947.
13. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J. 2009 Mar;30(3):365-70. PMID: 19271060.