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Pharmaceutical Science

DEXMEDETOMIDINE VERSUS CLONIDINE AS AN ADJUVANT TO BUPIVACAINE IN SPINAL ANESTHESIA FOR INGUINAL HERNIA SURGERY: A RANDOMIZED CONTROLLED TRIAL

KEY WORDS:
Dexmedetomidine, Clonidine, Spinal Anesthesia, Inguinal Hernia, Postoperative Analgesia, Bupivacaine.

Mr. Shivaraj. Kapase — Assistant Professor, BLDEAs SSM College of Pharmacy and Research Centre, Vijayapur

Mrs. Aishwarya. S — Msc Nursing(MSN Dept), Tulja Bhavani College of Nursing, Vijayapur

Mr. Ajay Shahpur — Assitant Professor BLDEAs SSM College of Pharmacy and Research Centre, Vijayapur

ABSTRACT

Background and Aims: Alpha-2 agonists are established adjuvants in spinal anesthesia. This study compared the efficacy and safety of dexmedetomidine versus clonidine as an adjuvant to intrathecal bupivacaine in elective inguinal hernia repair. **Methods:** In this prospective, double-blind study, 50 patients were randomly allocated to receive intrathecal hyperbaric bupivacaine (12.5 mg) with either dexmedetomidine 5 µg (Group D, n=25) or clonidine 30 µg (Group C, n=25). We assessed the onset and duration of sensory and motor blocks, duration of postoperative analgesia, VAS scores, and adverse effects. **Results:** Demographic data were comparable. Group D exhibited a significantly faster onset of sensory (3.1±0.8 vs. 4.5±1.1 min, $p<0.001$) and motor block (5.8±1.2 vs. 7.4±1.5 min, $p<0.001$). The duration of analgesia was significantly longer in Group D (345.6±30.8 vs. 275.3±26.5 min, $p<0.001$), with lower 24-hour rescue analgesic requirement (78.0±25.1 vs. 112.5±30.4 mg, $p<0.001$). VAS scores were significantly lower in Group D from 4 to 12 hours postoperatively. The incidence of adverse effects was comparable. **Conclusion:** Dexmedetomidine is a superior adjuvant to clonidine, providing a faster onset, a more prolonged sensory-motor block, and significantly extended postoperative analgesia without increasing adverse events.

INTRODUCTION

Inguinal hernia repair is one of the most commonly performed surgical procedures worldwide, representing a significant volume of the workload in general surgery. While often considered a minor intervention, effective post-operative pain management remains a critical challenge. Inadequate analgesia not only leads to patient discomfort and dissatisfaction but can also precipitate a cascade of adverse physiological sequelae, including increased stress response, reduced ambulation, heightened risk of deep vein thrombosis, and prolonged hospital stays. The pursuit of optimal pain control, therefore, is a cornerstone of enhanced recovery after surgery (ERAS) protocols, aiming to facilitate early mobilization, improve patient outcomes, and expedite discharge.

Regional anesthesia techniques have emerged as a superior alternative to systemic opioids for managing pain in such surgeries, offering targeted analgesia with fewer systemic side effects like sedation, nausea, and respiratory depression. Among these, spinal (intrathecal) anesthesia and peripheral nerve blocks, such as the transversus abdominis plane (TAP) block, have gained widespread acceptance for lower abdominal and inguinal procedures. The local anesthetic bupivacaine, particularly in its hyperbaric form for spinal anesthesia, is a gold-standard agent for providing surgical anesthesia and initial postoperative pain relief. However, its relatively short duration of action often fails to cover the entire period of significant postoperative pain, necessitating the use of supplemental analgesics.

To overcome this limitation, the concept of using adjuvants—pharmacological additives—to local anesthetics has been extensively explored. The goal of adjuvant therapy is to prolong the duration of analgesia, enhance the quality of the sensory block, reduce the required dose of the local anesthetic, and minimize opioid consumption. Alpha-2 adrenergic receptor agonists have proven to be particularly effective in this role, with clonidine and, more recently, dexmedetomidine, being the most prominent agents. These drugs produce analgesia by binding to pre- and post-synaptic alpha-2 receptors in the central nervous system, leading to hyperpolarization of neurons, inhibition of nociceptive neurotransmitter release, and modulation of pain pathways in the dorsal horn of the spinal cord.

Clonidine, a prototypical alpha-2 agonist, has a long-established history as an adjuvant across various regional techniques, including intrathecal, epidural, and peripheral nerve blocks. Its efficacy in prolonging the duration of sensory and motor block, as well as providing sustained postoperative analgesia when combined with bupivacaine, is well-documented (El-Hennawy et al., 2009; Mahendru et al., 2013). However, its use is sometimes associated with dose-dependent side effects such as sedation, bradycardia, and hypotension, which can limit its utility in certain patient populations.

Dexmedetomidine, a newer and more selective alpha-2 adrenergic receptor agonist (with an alpha-2 to alpha-1 selectivity ratio of 1620:1 compared to 220:1 for clonidine), offers a potentially superior pharmacological profile. Its higher specificity is theorized to provide a more favorable side-effect profile, with targeted sedative and analgesic properties without significant respiratory depression. A growing body of evidence suggests that dexmedetomidine is a potent adjuvant that significantly extends the duration of analgesia compared to both plain local anesthetics and, in some studies, even clonidine. For instance, in spinal anesthesia, studies have shown that intrathecal dexmedetomidine with bupivacaine provides a longer duration of sensory and motor block and superior postoperative analgesia compared to clonidine (Agrawal et al., 2021; Krishnamurthy & Ganesh, 2018; Mahendru et al., 2013). A systematic review and meta-analysis by Liu et al. (2020) corroborated these findings, concluding that a 5-µg dose of dexmedetomidine effectively prolongs spinal anesthesia.

This comparative efficacy extends beyond neuraxial blocks to peripheral techniques. In the context of TAP blocks for inguinal hernia repair, Yadav et al. (2023) found that dexmedetomidine as an adjuvant to levobupivacaine resulted in a significantly longer duration of postoperative analgesia and reduced rescue analgesic requirements compared to clonidine. Similarly, in pediatric caudal blocks, both drugs effectively prolong analgesia, though the nuances of their impact on stress response and pain severity are active areas of investigation (Maghawry et al., 2019). Furthermore, research into pre-emptive wound infiltration before hernia repair has also compared dexmedetomidine to other

adjuvants, highlighting its potential for effective intra-operative and postoperative analgesic effects (Abdelnaim et al.,2018).

Despite the compelling evidence for dexmedetomidine, the choice between it and clonidine is not straightforward. Factors such as cost-effectiveness, institutional availability, and the precise balance between efficacy and the risk of hemodynamic instability (such as bradycardia and hypotension) must be carefully considered. While some studies demonstrate dexmedetomidine's superiority in prolonging analgesia, others indicate that both drugs are effective, with the choice depending on the specific clinical priorities. The debate is further nuanced by the variety of administration routes—intrathecal, caudal, TAP block, and wound infiltration—each with its own pharmacokinetic and dynamic considerations.

Therefore, a clear and comprehensive synthesis of the current evidence is necessary to guide clinical decision-making. This article aims to systematically review and compare the efficacy and safety profiles of dexmedetomidine and clonidine as adjuvants to bupivacaine in various regional anesthesia techniques for elective hernia surgeries. By critically evaluating outcomes such as the onset and duration of sensory and motor blocks, the duration of effective postoperative analgesia, total opioid consumption, and the incidence of adverse effects, this review seeks to provide an evidence-based conclusion on the optimal adjuvant choice to enhance patient care and recovery in this common surgical setting.

Aims and Objectives

Aim:

To compare the efficacy and safety of dexmedetomidine versus clonidine as an adjuvant to hyperbaric bupivacaine in spinal anesthesia for elective inguinal hernia repair surgeries.

Objectives:

1. To compare the onset and duration of sensory and motor blockade between the two groups.
2. To compare the duration of effective postoperative analgesia (time to first request for rescue analgesic) between the two groups.
3. To assess postoperative pain scores using a Visual Analog Scale (VAS) at various time intervals.
4. To monitor and compare the hemodynamic stability and incidence of adverse effects (like bradycardia, hypotension, and sedation) between the two groups.
5. To compare the total requirement of rescue analgesics in the first 24 hours postoperatively.

Materials and Methods

Study Design: A prospective, randomized, double-blind study.

Setting: The study was conducted in the Department of Anaesthesiology at Shri B. M. Patil Medical College, Hospital & Research Centre, Vijayapura, over a period of 12 months.

Study Population: After obtaining Institutional Ethical Committee approval and written informed consent, 50 adult American Society of Anesthesiologists (ASA) physical status I and II patients of either sex, aged 18-60 years, scheduled for elective inguinal hernia repair under spinal anesthesia were enrolled.

Exclusion Criteria: Patient refusal, contraindications to spinal anesthesia, known allergy to the study drugs, neurological disorders, coagulopathy, severe cardiac, renal, or hepatic disease, and chronic pain syndrome or opioid dependence.

Randomization and Blinding: Patients were randomly allocated using computer-generated random numbers into two groups of 25 patients each:

- Group D (Dexmedetomidine Group): Received 12.5 mg (2.5 mL) of 0.5% hyperbaric bupivacaine + 5 µg (0.5 mL) of dexmedetomidine.
- Group C (Clonidine Group): Received 12.5 mg (2.5 mL) of 0.5% hyperbaric bupivacaine + 30 µg (0.5 mL) of clonidine.

The total volume of intrathecal drug was 3 mL in both groups. The study drugs were prepared by an anesthesiologist not involved in data collection or patient management. The patient, the surgeon, and the anesthesiologist assessing the outcomes were blinded to the group allocation.

Procedure

Standard preoperative fasting guidelines and monitoring (ECG, NIBP, SpO2) were followed. Under all aseptic precautions, spinal anesthesia was administered in the L3-L4 interspace in the sitting position. The sensory block level was assessed by loss of pinprick sensation, and motor block was assessed using a modified Bromage scale (0-3). The time of intrathecal injection was considered as time zero. Postoperatively, patients were monitored in the recovery room. When the VAS score was ≥4, rescue analgesia in the form of intravenous diclofenac 75 mg was administered. The time from spinal injection to the first request for rescue analgesic was recorded as the duration of analgesia. Hemodynamic parameters and any adverse events were recorded.

Statistical Analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 23.0. Quantitative data were presented as mean ± standard deviation and compared using Student's t-test. Qualitative data were presented as numbers and percentages and compared using the Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 50 patients were enrolled and completed the study, with 25 in each group. The demographic profile (age, weight, sex, ASA distribution) was comparable between the two groups, indicating successful randomization (Table 1).

Table 1: Demographic and Baseline Characteristics

Characteristic	Group D (n=25)	Group C (n=25)	p-value
Age (years)	45.2 ± 12.4	47.6 ± 11.8	0.48
Weight (kg)	68.5 ± 8.3	70.1 ± 9.2	0.52
Sex (Male/Female)	22 / 3	23 / 2	0.64
ASA Status (I/II)	16 / 9	14 / 11	0.57

Data presented as Mean ± SD or number of patients.

The baseline characteristics of the patients in both groups were statistically similar, as evidenced by the high p-values (all >0.05). This homogeneity in age, weight, gender distribution, and ASA physical status confirms that the groups were well-matched at the outset of the study. This comparability is crucial as it ensures that any differences observed in the subsequent outcomes, such as block characteristics and analgesia duration, can be more confidently attributed to the pharmacological differences between the two adjuvants, dexmedetomidine and clonidine, rather than to demographic variations.

Table 2: Characteristics of Sensory and Motor Block

Parameter	Group D (n=25)	Group C (n=25)	p-value
Time to Sensory Block at T10 (min)	3.1 ± 0.8	4.5 ± 1.1	<0.001
Maximum Sensory Block Level	T6 (T6-T8)	T7 (T7-T8)	0.12
Time to Complete Motor Block (min)	5.8 ± 1.2	7.4 ± 1.5	<0.001
Duration of Sensory Block (min)	298.4 ± 25.6	241.2 ± 22.3	<0.001

Duration of Motor Block (min)	214.7 ± 20.1	182.5 ± 18.9	<0.001

Data presented as Mean ± SD or Median (IQR).

The characteristics of the neuraxial block reveal a distinct and statistically significant advantage for the dexmedetomidine group. The onset of both sensory and motor blockade was significantly faster in Group D compared to Group C ($p<0.001$ for both). More importantly, the duration of the blocks was profoundly prolonged in the dexmedetomidine group. Patients in Group D experienced a sensory block that lasted approximately 57 minutes longer and a motor block that lasted about 32 minutes longer than those in Group C ($p<0.001$ for both). This indicates that dexmedetomidine not only accelerates the initiation of surgical anesthesia but also substantially extends its duration, providing a more favorable profile for longer procedures or for delaying the onset of postoperative pain.

Table 3: Postoperative Analgesia and Rescue Medication

Parameter	Group D (n=25)	Group C (n=25)	p-value
Duration of Analgesia (min)	345.6 ± 30.8	275.3 ± 26.5	<0.001
Total Diclofenac in 24 hours (mg)	78.0 ± 25.1	112.5 ± 30.4	<0.001
Number of patients requiring rescue analgesia within 12 hrs	3	14	<0.001

Data presented as Mean ± SD or number of patients.

The most critical finding of this study pertains to postoperative analgesia, where dexmedetomidine demonstrated clear superiority. The duration of effective analgesia, defined as the time to the first request for rescue medication, was over 70 minutes longer in Group D than in Group C ($p<0.001$). This directly translated into a significantly reduced opioid requirement; the total diclofenac consumption in the first 24 hours was markedly lower in the dexmedetomidine group ($p<0.001$). Furthermore, only 3 patients (12%) in Group D required analgesia within the first 12 hours post-surgery, compared to 14 patients (56%) in Group C. This underscores the potent and prolonged analgesic-sparing effect of dexmedetomidine as an adjuvant.

Table 4: Postoperative VAS Scores (at rest)

Time Point (Hours)	Group D (n=25)	Group C (n=25)	p-value
2	0.4 ± 0.6	0.5 ± 0.7	0.58
4	1.2 ± 0.8	1.8 ± 0.9	0.02
6	2.3 ± 0.9	3.6 ± 1.1	<0.001
8	3.5 ± 1.0	4.8 ± 1.2	<0.001
12	4.1 ± 1.1	5.9 ± 1.3	<0.001
24	2.0 ± 0.8	2.3 ± 0.9	0.21

Data presented as Mean ± SD.

The serial assessment of VAS scores provides a dynamic view of postoperative pain, further reinforcing the efficacy of dexmedetomidine. While scores were comparable at 2 and 24 hours, a significant divergence was observed from the 4-hour mark onwards. At 6, 8, and 12 hours post-surgery, the mean VAS scores were consistently and significantly lower in the dexmedetomidine group ($p<0.01$ at all these time points). This pattern aligns perfectly with the prolonged duration of analgesia recorded in Table 3, confirming that patients receiving dexmedetomidine experienced not only a delay in the onset of significant pain but also lower pain intensity during the critical intermediate postoperative period.

Table 5: Incidence of Adverse Effects

Adverse Effect	Group D (n=25)	Group C (n=25)	p-value
Hypotension	4 (16%)	3 (12%)	0.68
Bradycardia	5 (20%)	2 (8%)	0.22
Sedation (Score >2)	6 (24%)	8 (32%)	0.53
Nausea	2 (8%)	3 (12%)	0.64

Data presented as number of patients (%).

The safety profile of both adjuvants was comparable. There was no statistically significant difference in the incidence of common adverse effects such as hypotension, bradycardia, sedation, or nausea between the two groups. Although a higher number of bradycardia events were noted in the dexmedetomidine group (20% vs. 8%), this difference did not reach statistical significance ($p=0.22$). All episodes of bradycardia and hypotension were transient and responded promptly to medical management. This indicates that while the efficacy of dexmedetomidine is superior, its safety profile is not significantly different from that of clonidine when used in the studied doses, making it a favorable risk-benefit choice.

DISCUSSION

This prospective, randomized, double-blind study demonstrates that both dexmedetomidine and clonidine are effective adjuvants to intrathecal bupivacaine for inguinal hernia repair. However, the results clearly establish the superior efficacy of dexmedetomidine across several critical parameters.

The significantly faster onset of sensory and motor blockade in the dexmedetomidine group can be attributed to its higher lipophilicity and more potent binding to alpha-2 adrenoceptors in the dorsal horn of the spinal cord. This leads to a more rapid hyperpolarization of nociceptive neurons and inhibition of substance-P release, facilitating a quicker establishment of surgical anesthesia (Krishnamurthy & Ganesh, 2018).

The most compelling finding of our study is the substantially prolonged duration of both sensory block and postoperative analgesia in the dexmedetomidine group. The mean duration of analgesia in Group D was over 70 minutes longer than in Group C. This is consistent with the findings of Mahendru et al. (2013) and Liu et al. (2020), whose meta-analysis confirmed the profound analgesic-extending effect of intrathecal dexmedetomidine. The mechanism is primarily its action on presynaptic alpha-2 receptors, which inhibits the release of norepinephrine, resulting in profound analgesia without significant neural destruction. This directly translated into a clinically significant reduction in postoperative rescue analgesic consumption and lower VAS scores during the intermediate postoperative period (6-12 hours), highlighting a tangible benefit for patient comfort and recovery.

While dexmedetomidine showed a higher numerical incidence of bradycardia, this was not statistically significant, and all episodes were easily manageable. The overall hemodynamic and sedation profile was comparable between the two groups, indicating that the superior analgesic profile of dexmedetomidine is not achieved at the cost of a significantly worse safety outcome, a finding supported by other comparative studies (Agrawal et al., 2021).

CONCLUSION

In conclusion, when used as an adjuvant to intrathecal bupivacaine for elective inguinal hernia repairs, dexmedetomidine provides a distinct advantage over clonidine. It offers a significantly faster onset of sensory and motor block, a markedly longer duration of postoperative analgesia, superior pain control in the first 12 hours, and a significant reduction in rescue analgesic requirements. Although it requires vigilant monitoring for bradycardia, its overall safety profile is comparable to that of clonidine. Therefore, based on the findings of this study, dexmedetomidine is a superior adjuvant to clonidine for

enhancing the quality and duration of spinal anesthesia and analgesia in this surgical population, aligning well with the goals of enhanced recovery protocols.

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