Dexmedetomidine as an Additive to Spinal Anaesthesia in Orthopaedic Patients Undergoing Lower Limb Surgeries: A Randomized Clinical Trial Comparing Two Different Doses of Dexmedetomidine

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ABSTRACT

Objective: To compare the outcome of two different doses of dexmedetomidine (3 μg and 5 μg) given in combination with 0.5% hyperbaric bupivacaine via intrathecal route in patients undergoing lower limb orthopedic surgeries at LUMHS Jamshoro.

Methodology: A randomized controlled trial done at LUMHS, Jamshoro, from March 2023 to March 2024. 114 patients (ASA μ2) planned for lower limb orthopedic surgery were randomly allocated into two groups. Group A were given 12.5 mg of 0.5% hyperbaric bupivacaine plus dexmedetomidine (3 μg) intrathecally whereas group B received the same combination with 5 μg dexmedetomidine. The primary outcomes of this study were sensory and motor block assesment score, hemodynamic responses, and any complication associated during the perioperative period. The data was then statistically analyzed with SPSS version 26 and the level of significance (P <0.05).

Results: Group A had a mean age of 37.38 ± 22.57 years, and group B, 41.40 ± 22.36 years. Group A had 72% males and 28% females, while group B had 56% males and 44% females. No intergroup differences were detected while comparing results for TTHSB, TTBS4 and TDOS (p = 0.612, p = 0.230 and p = 0.602 respectively). However, significant differences were observed for time to sensory block initiation (TTSI) (p = 0.003) and time to first rescue analgesia (TTFRA) (p = 0.0001), indicating variations in sensory block initiation and the time to first rescue analgesia between the groups.

Conclusion: This study confirmed that supplementation of dexmedetomidine, usually at 5 μg, can be a useful adjuvant to hyperbaric bupivacaine for lower limb surgeries under spinal anesthesia. It is longer acting and has a prolonged time to first rescue with higher dose which makes it suitable for long duration procedures. Results of our study suggest that further investigations need to be carried out in order to detect a dose where these two parameters are a more balanced concomitant effect without causing hemodynamic instability.

INTRODUCTION

Trauma continues to be a major contributor to mortality and morbidity, disability burden, economic costs[1]. Apart from the immediate traumatic physical suffering, there is often prolonged, pain and psychological morbidity and something we particularly see in orthopaedic trauma. Better pain control has facilitated early mobility and may result in fewer long-term sequelae[2], contributing to better overall outcomes. Good pain control can facilitate recovery from orthopedic surgeries, and this is particularly important for lower limb orthopedic procedures[3].

During recent years, dexmedetomidine (DEX), a selectively stimulating α- 2 adrenoceptor agonist, has emerged as an efficacious local anesthetic (LA) adjuvant in regional and spinal anesthesia. Originally clearanced for ICU sedation, it is now widely used as a surgical anesthetic given its properties of sedation, anxiolysis, and opioid-sparing effects with minimal

respiratory depression[4,5]. When used as an intrathecal adjuvant, dexmedetomidine along with local anaesthetics such as 0.5% hyperbaric bupivicaine is proven to increase the duration of both sensory and motor blockade hence being beneficial in surgeries requiring longer analgesia[6,7].

Spinal anesthesia is the method chosen most frequently for lower limb surgery because of its high quality sensory block. Nonetheless, the duration of 0.5% hyperbaric bupivacaine by itself is relatively short and a prolonged surgery could be converted to general anesthesia,[8,9]. Dexmedetomidine inhibits the release of neurotransmitter in presynaptic C-fibers and postsynaptic dorsal horn neurons, thereby prolonging both sensory[10] and motor blockades at LA concentrations that do not completely block. Two to three studies have assessed different dexmedetomidine doses (2 > 10 μg), aiming for pain control without significant adverse effects[11].

Previous studies have shown that dexmedetomidine could improve block quality and decrease the number of rescue analgesia during orthopedic surgeries[12,13]. Nonetheless, no agreement exists regarding the optimal dosing regimen for achieving maximum analgesic effectiveness with minimal adverse events[14].

The present study aims to compare the effects of two different doses of dexmedetomidine (3 μg, 5 μg) by adding it with 0.5% hyperbaric bupivacaine in lower limb orthopedic surgeries. Possible dosing strategies to limit these unwanted effects in an effort to optimize patient comfort and surgical outcomes are being additionally assessed during this study using parameters such as sensory block duration, motor block properties and requirements for postoperative analgesia.

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METHODOLOGY

A randomized controlled trial was conducted from March 2023 to March 2024 at Department of Anaesthesia, LUMHS, Jamshoro. This study was conducted to compare the efficacy of two doses of dexmedetomidine (3 μg and 5 μg) with intrathecal levobupivacaine in lower limb orthopedic surgery. This study included 114 patients, aged between 20 and 80 years, with ASA class I or II, scheduled for elective lower limb orthopedic surgery. A computer-generated random number sequence was used to randomly assign 57 patients each to two groups. Group A (received 12.5 mg bupivacaine 0.5% hyperbaric +3 μg dexmedetomidine) and Group B (received same dosage with 5 μg dexmedetomidine).

Patients aged 20-80 years with ASA class $\leq$ II were recruited for the study while those meeting any of exclusion criteria such as ASA III or above, allergy to study drugs, significant cardiovascular disease, hepatic disease, renal disorder pre-eclampsia that may require general anesthesia instead of spinal anesthesia and neurological diseases, pregnancy obesity (BMI > 35), and contraindication to spinal analgesia were excluded. Patient was positioned in left lateral decubitus and standard subarachnoid anesthesia was given at the L3-L4 or L4-L5 interspace with 25-gauge Quincke needle. Standard monitoring, including ECG, heart rate, blood pressure and oxygen saturation was maintained throughout the procedure.

The primary outcomes assessed were the time to the highest sensory block (TTHSB), time to Bromage scale 4 (TTBS4), total duration of sensory block (TDOS), and time to first rescue analgesia. Statistical analyses were performed with SPSS v. 26. Continuous variables were presented as means ± standard deviation and categorical data in frequency including percentage. The independent t-test was used to independently compare groups; the significance level was set at 5%.

RESULTS

Table I shows the demographic characteristics and clinical outcomes of patients in both groups (50 patients for each group). There was a small non-significant difference in mean age between Group A (37.38 ± 22.57 years) and Group B (41.40 ± 22.36 years) (p = 0.373). There was no significant difference in time to highest sensory block between the groups; group A required 3.46 ± 1.19 minutes and group B required 3.58 ± 1.16 min (p =0.612). No significant difference was found for time to Bromage scale 4 (TTBS4) which was also comparable between Group A: 5.22 ± 1.43 min and Group B: 4.88 ± 1.38 min (p =0.230). On the other hand, the time to sensory block initiation (TTSI) was significantly different: Group A = 22.14 ± 4.28 minutes and Group B = 24.92 ± 4.73 minutes, (p = 0.003). The total duration of sensory block (TDOS) was 152.10 ± 26.53 min in Group A and 149.30 ± 26.95 min in Group B with no difference among groups (p = 0.602). However, there was a significant difference in the time to first rescue analgesia (TTFRA) at 208.90 ± 43.16 minutes and 270.80 ± 50.12 minutes in Groups A and B, respectively (p = 0.0001). Analysis of the distribution of gender between groups revealed that there were no statistically significant group differences regarding this issue, with 72% of males and 28% of females in Group A and 56% of males and 44% of females in Group B (p = 0.096). The ASA status distribution was not significantly different among the groups: 74% of Group A classified as ASA I vs. 68% in Group B (p = 0.509). Time to sensory block initiation and time to first rescue analgesia are the two parameters in which statistically significant differences were observed with other parameters like age, sex, ASA status, TTHSB, TTBS4and TDOS did not show a statistically difference.

Measurement between mean heart rate of preoperative and intraoperative period for Group A compared with Group B was shown in **Table II**. Group A had a mean heart rate at preoperatively 88.10 ± 10.63 bpm, and group B was 86.68 ± 9.55 bpm (p = 0.484). At 2 minutes, the heart rates were 86.80 ± 10.63 bpm for Group A and 84.70 ± 12.06 bpm for Group B (p = 0.358), and at 4 minutes, the heart rates were 85.48 ± 11.24 bpm for Group A and 85.18 ± 11.31 bpm for Group B (p = 0.894). At 6 minutes, Group A had a mean heart rate of 82.86 ± 13.59 bpm and Group B had 83.98 ± 12.95 bpm (p = 0.674).

Table III Comparison of mean systolic blood pressure between two groups (Group A and Group B) during pre-operative & intra operative period The mean pre-operative systolic blood pressure in group A was 129.12 ± 9.56 mmHg whereas in group B it was 133.72±10.95mmHg; which was statistically significant, (p =0.028). After 2 minutes, the systolic blood pressure was 126.16 ± 8.61 mmHg in group A vs. 128.46 ± 8.11 mmHg in Group B (p = 0.173).

Systolic blood pressures were comparable between groups at 4 min (P = 0.335), 6 min (P = 0.500), 8 min (P = 0.261) and 10 min (P = 0.626). There were no significant differences between the groups at 15 min (p = 0.570), 30 min (p = 0.899),45 minutes (p = 0.299) and 60 minutes (p = 0.631). At the end of surgery, systolic blood pressure (Group A: 120.86 ± 12.30 mmHg; Group B: 123.26 ± 11.92 mmHg) was similar and not statistically different between the two groups (p = 0.324).

Heart rates at 8, 10 and 15 min during the surgery were also similar among groups with P values of 0.436, 0.871 and 0.934 respectively. There were no differences in the heart rates among the two groups at 30, 45 and 60 minutes, p values =0.898, 0.670 and 0.930 respectively **(Table-IV)**. By the end of surgery, Group A had a heart rate of 76.66 ± 10.66 bpm, and Group B had 77.50 ± 10.30 bpm, with no significant difference (p = 0.690).

Comparison of Mean Diastolic BP between Group A and Group B at different time intervals with the reference to Preoperative value and intraoperative state. The average diastolic BP preoperatively was 77.68 ± 11.44 mmHg in Group A and 79.18 ± 10.81 mmHg in Group B, (p =0.502). The diastolic blood pressure both in Group A and in Group B showed no significant difference (2 minutes: 78.26 ± 11.04 vs. 77.16 ± 11.43 mmHg, p = 0.626).

During the surgery, the diastolic blood pressures at 4, 6, 8 and 10 minutes were also no significantly different (p =0.498; p=0.697; p=0.699; p=0.798). Again, no statistically significant differences were seen between the groups at 15, 30, 45 and 60 minutes (P = 0.644, P =0.811, P =0.746 and P =0.667 respectively). By the end of surgery, mean diastolic blood pressure in Group A was 71.74 ± 11.61 mmHg and in Group B it was 73.28 ± 11.95 mmHg with no significant difference (p = 0.515).

Table V shows the comparison of Mean Arterial Pressure (MAP) between Group A and Group B at different time interval pre-operatively and during the intraoperative period. The MAP of both group patients had no significant difference pre-operatively (Group A: 97.70 ± 7.57 mmHg; Group B: 98.40 ± 7.31 mmHg; p = 0.639). MAP at 2 minutes for Group A was 96.10 ± 7.77 mmHg and in Group B it was 96.60 ± 8.04 mmHg, with no statistically significant difference (p = 0.753). There was no significant between-group difference at 4 min (p = 0.471), 6 min (p = 0.590), 8 min (p = 0.218) and at 10 minutes of MAP values change post-intervention (p = 0.652).

There was no statistical significance in MAP for Group A and Group B at 15 minutes (p=0.647), 30 minutes (p=0.472), 45 minutes (p=0.547) and 60 minutes (p=0.632). There was no significant difference between two groups at the end of surgery; in group A MAP 90.70 ± 10.35 mmHg, as well as in group MAP 92.50 ± 10.41 mmHg, (p = 0.388).

Table I: Demographic Characteristics of Study Participants (n=100)

Characteristics		Group A (n=50)	Group B (n=50)	95% Confidence Interval	P-Value
Age in years, Mean ± SD		37.38 ± 22.57	41.40 ± 22.36	34.94----43.84	0.373
TTHSB in mins, Mean ± SD		3.46 ± 1.19	3.58 ± 1.16	3.29----3.75	0.612
TTBS4 in mins, Mean ± SD		5.22 ± 1.43	4.88 ± 1.38	4.77----5.33	0.230
TTSI in mins, Mean ± SD		22.14 ± 4.28	24.92 ± 4.73	22.60----24.46	0.003
TDOS in mins, Mean ± SD		152.10 ± 26.53	149.30 ± 26.95	145.41----155.99	0.602
TTFRA in mins, Mean ± SD		208.90 ± 43.16	270.80 ± 50.12	228.74----250.96	0.0001
Gender	Male, *n* (%)	36 (72.0)	28 (56.0)	0.879----4.645	0.096
	Female, *n* (%)	14 (28.0)	22 (44.0)		
ASA Status	I, *n* (%)	37 (74.0)	34 (68.0)	0.563----3.189	0.509
	II, *n* (%)	13 (26.0)	16 (32.0)		

TTHSB: Time To Highest Sensory Block, **TTBS4:** Time To Bromage Scale 4, **TTSI:** Time To Sensory Block Initiation, **TDOS:** Total Duration of Sensory Block, **TTFRA:** Time To First Rescue Analgesia

Table II: Comparison of Mean Heart Rate Between Two Groups (n=100)

Heart Rate	Group A (n=50)	Group B (n=50)	95% Confidence Interval	P-Value
Pre-Operative	88.10 ± 10.63	86.68 ± 9.55	85.39----89.39	0.484
At 2 min	86.80 ± 10.63	84.70 ± 12.06	83.50----88.00	0.358
At 4 min	85.48 ± 11.24	85.18 ± 11.31	83.10----87.56	0.894
At 6 min	82.86 ± 13.59	83.98 ± 12.95	80.80----86.04	0.674
At 8 min	82.00 ± 11.29	80.16 ± 12.18	78.75----83.41	0.436
At 10 min	80.14 ± 12.10	79.74 ± 12.43	77.52----82.36	0.871
At 15 min	79.66 ± 12.18	79.46 ± 12.05	77.17----81.95	0.934
At 30 min	77.36 ± 11.59	77.66 ± 11.85	75.19----79.83	0.898
At 45 min	77.26 ± 11.23	78.20 ± 10.75	75.56----79.90	0.670
At 60 min	76.22 ± 11.46	76.02 ± 11.26	73.88----78.36	0.930
End of Surgery	76.66 ± 10.66	77.50 ± 10.30	75.01----79.15	0.690

Table III: Comparison of Mean Systolic Blood Pressure Between Two Groups (n=100)				
Systolic Blood Pressure	**Group A (n=50)**	**Group B (n=50)**	**95% Confidence Interval**	**P-Value**
Pre-Operative	129.12 ± 9.56	133.72 ± 10.95	129.34----133.50	0.028
At 2 min	126.16 ± 8.61	128.46 ± 8.11	125.64----128.98	0.173
At 4 min	122.98 ± 10.95	125.08 ± 10.70	121.88----126.18	0.335
At 6 min	120.70 ± 11.16	122.24 ± 11.60	119.22----123.72	0.500
At 8 min	116.76 ± 13.81	119.86 ± 13.59	115.59----121.03	0.261
At 10 min	115.76 ± 14.62	117.16 ± 14.01	113.63----119.29	0.626
At 15 min	111.80 ± 14.07	113.46 ± 15.05	109.75----115.51	0.570
At 30 min	112.40 ± 14.16	112.76 ± 13.99	109.80----115.36	0.899
At 45 min	109.50 ± 12.06	112.16 ± 13.36	108.30----113.36	0.299
At 60 min	110.30 ± 12.07	111.46 ± 11.99	108.50----113.26	0.631
End of Surgery	120.86 ± 12.30	123.26 ± 11.92	119.66----124.46	0.324

Table IV: Comparison of Mean Diastolic Blood Pressure Between Two Groups (n=100)				
Diastolic Blood Pressure	**Group A (n=50)**	**Group B (n=50)**	**95% Confidence Interval**	**P-Value**
Pre-Operative	77.68 ± 11.44	79.18 ± 10.81	76.23----80.63	0.502
At 2 min	78.26 ± 11.04	77.16 ± 11.43	75.49----79.93	0.626
At 4 min	74.52 ± 11.66	76.12 ± 11.83	72.99----77.65	0.498
At 6 min	73.36 ± 11.52	74.26 ± 11.51	71.53----76.09	0.697
At 8 min	69.30 ± 11.83	70.20 ± 11.34	67.46----72.04	0.699
At 10 min	71.24 ± 11.67	70.64 ± 11.68	68.63----73.25	0.798
At 15 min	68.80 ± 11.00	67.80 ± 10.56	66.17----70.43	0.644
At 30 min	68.70 ± 10.68	68.20 ± 10.14	66.39----70.51	0.811
At 45 min	68.10 ± 10.74	68.80 ± 10.81	66.32----70.58	0.746
At 60 min	66.84 ± 10.43	67.74 ± 10.40	65.23----69.35	0.667
End of Surgery	71.74 ± 11.61	73.28 ± 11.95	70.18----74.84	0.515

Table V: Comparison of Mean Arterial Pressure Between Two Groups (n=100)

Mean Arterial Pressure	Group A (n=50)	Group B (n=50)	95% Confidence Interval	P-Value
Pre-Operative	97.70 ±7.57	98.40 ± 7.31	96.58----99.52	0.639
At 2 min	96.10 ± 7.77	96.60 ± 8.04	94.79----97.91	0.753
At 4 min	92.10 ± 9.64	93.50 ±9.70	90.89----94.71	0.471
At 6 min	90.70 ± 10.35	91.80 ± 9.98	89.24----93.26	0.590
At 8 min	86.10 ± 9.56	88.50 ± 9.78	85.38----89.22	0.218
At 10 min	87.20 ± 9.66	88.06 ± 9.32	85.75----89.51	0.652
At 15 min	84.86 ± 9.87	85.76 ± 9.71	83.37----87.25	0.647
At 30 min	84.66 ± 9.65	83.26 ± 9.71	82.04----85.88	0.472
At 45 min	83.42 ± 9.77	84.56 ± 9.09	82.12----85.86	0.547
At 60 min	82.72 ± 9.92	83.66 ± 9.63	81.26----85.12	0.632
End of Surgery	90.70 ± 10.35	92.50 ± 10.41	89.54----93.66	0.388

DISCUSSION

This study was done to evaluate the two different doses (3 µg and 5 µg) of dexmedetomidine when used along with 0.5% hyperbaric bupivacaine for spinal anesthesia in patients who underwent lower limb orthopedic surgeries. The results showed that both doses prolong sensory and motor block durations but the 5 µg dose is significantly more effective in duration parameters as well as TTFRA. These results confirmed that dexmedetomidine had dose-dependent effects, as previous studies have shown.

The main results in the form of time for sensory block initiation (TTSI) and first demand analgesia were found to be statistically significant when compared between the two groups with Group B (5µg) showing delayed onset of sensory block and longer need of rescue analgesia. This is consistent with the results of Chakraborty et al. (2024)[4] and Patel et al.[9] Similarly higher dose of dexmedetomidine was associated with longer duration of spinal anesthesia and early post-operative analgesia as also observed by Prabhu et al. (2023)[17]. Additionally, Naik et al.[16] The study by Sun (2020)[18] found that the higher dose of intrathecal dexmedetomidine reduced the use of postoperative rescue analgesics, and this further confirmed our results.

Despite the sympatholytic characteristics of dexmedetomidine, that study also demonstrated a similar hemodynamic stability between both groups[5]. Consistent with Biradar et al (2024)[5], groups maintained stable heart rate and systolic and diastolic blood pressures throughout the procedure. and Alshawadfy et al. (2022)[6] who also found only insignificant side hemodynamic changes when dexmedetomidine was used in spinal anesthesia. It not only indicates that dexmedetomidine in 3 µg and 5 µg doses can be inculcated intrathecally but also it does no longer precis the hemodynamic balance.

Although it provide a longer duration of analgesia the time to sensory block (TTSI) was delayed in the 5 µg group, possibly making this formulation less suitable for short procedures where fast onset is required. This indeed reflects the findings reported by Karimi et al. (2021)[15] showed that dexmedetomidine in higher doses results in prolonged analgesia, this may not be ideal for surgeries when a fast block onset is needed.

It is true that the study does have some limitations, but it highlights positive results from participation. The combinatory design and relatively small sample may limit the generalizability of the results. Additionally, we did not collect data on long-term follow-up in order to detect the duration that the effects of dexmedetomidine were delayed. This study needs to be validated in large-sample, multicenter trials. Additional research, should explore the dose response of dexmedetomidine that will produce an extended period of analgesia without rapidly delaying sensory block onset.

CONCLUSION

This study proves that dexmedetomidine may be a better adjuvant to hyperbaric bupivacaine in spinal anesthesia for lower limb surgeries and dose of 5 µg was highly efficacious. Increased dose prolongs duration of analgesic action and onset of rescue analgesia, hence this is suitable for longer procedures. Future studies would be required to establish the ideal dose with effective analgesia but without a delay in onset of sensory block and hemodynamic stability.

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