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Addition of Intrathecal Dexmedetomidine Prolongs Subarachnoid Block in Orthopaedic Geriatric Population Undergoing Unilateral TKR

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Author`s Contribution

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ABSTRACT

Objective: To evaluate and compare the efficacy of intrathecal dexmedetomidine as an adjuvant to local anesthetic versus local anesthetic alone in prolonging subarachnoid block among geriatric patients undergoing unilateral total knee replacement (TKR).

Methodology: This randomized controlled trial was conducted in the Department of Anesthesiology, Fauji Foundation Hospital, Rawalpindi, from April 1, 2023, to December 30, 2023. A total of 60 geriatric patients (aged ≥60 years) with American Society of Anesthesiologists (ASA) physical status class II or III, scheduled for unilateral TKR, were enrolled and randomized into two equal groups. Primary outcomes included the time to first analgesic requirement and postoperative pain scores at rest and during movement at 24 hours. Secondary outcomes assessed were the duration of sensory and motor blockade.

Results: The mean age of participants was 68.03 ± 4.54 years (range: 60–76 years), with 60% males and 40% females. Group A demonstrated a significantly prolonged time to rescue analgesia compared to Group B (461.37 ± 21.52 vs. 330.91 ± 18.21 minutes; $p = 0.000$). Postoperative pain scores were significantly lower in Group A both at rest (3.29 ± 1.78 vs. 4.86 ± 1.52; $p = 0.000$) and during movement (5.10 ± 1.60 vs. 6.44 ± 1.42; $p = 0.001$). Furthermore, Group A showed a significantly longer duration of sensory block (379.52 ± 63.74 vs. 304.76 ± 17.67 minutes; $p = 0.000$) and motor block (390.03 ± 67.23 vs. 259.80 ± 17.62 minutes; $p = 0.000$) when compared to Group B.

Conclusions: The addition of intrathecal dexmedetomidine to local anesthetic prolongs the subarachnoid block and results in a prolonged duration of need for rescue analgesia and reduces the mean pain score at rest and movement in patients undergoing unilateral TKR.

Keywords: Intrathecal dexmedetomidine, Orthopaedic geriatric population, Subarachnoid block, Total knee replacement.

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Introduction

The analgesic efficacy of dexmedetomidine in patients undergoing different orthopaedic surgeries are well reported in studies. However, the benefits of adding intrathecal dexmedetomidine to local anesthetics for prolonging the subarachnoid block in orthopaedic geriatric population is less documented. Total knee replacement (TKR) is among commonly performed orthopaedic surgical procedures in geriatric patients with a high success rate. Post-operative pain is however most common concern of orthopaedic surgeons as this becomes intolerable for these patients and leads to morbid conditions. Studies conducted on the topic have reported that this post-operative pain after TKR disturbs both the physical and psychological conditions and

disturbs the rehabilitation plan causing delays in hospital discharge, adding up to the total treatment cost.[1] Adequate plans including administration of preemptive analgesics are therefore suggested to reduce morbidity and ensure a rapid recovery.[2]

Orthopaedic surgeries are commonly performed with spinal anesthesia using local anesthetic solutions (Bupivacaine and Ropivacaine are most commonly used in small doses) injected into intrathecal space and causing autonomic as well as sensory and motor nerve blocks. [3,4,5] The use of spinal anesthesia is also recommended due to the lower rate of complications and good perioperative outcomes.[6,7] However, these local anesthetics have a short duration of action and post-operative pain causes a risk of falling and delayed ambulation after TKR. Different drugs are used for prolongation of this duration like epinephrine, opioids, ketamine, magnesium sulfate, and α2 agonists. These agents augment the nerve block and prolong the analgesic effects in the postoperative period. They also allow to use of a lesser amount of local anesthetic agents, therefore, lesser adverse effects for the patients.[8] Neuraxial opioids have been commonly used as an adjuvant to local anesthetic agents to serve the purpose; however, they are linked with adverse effects like nausea/vomiting, pruritus and respiratory depression.[9]

Selective alpha-2 receptor agonist, Dexmedetomidine (DEX) (a d-enantiomer of medetomidine) which works through hyperpolarization of cation channels has been studied as an adjuvant to local anesthetic bupivacaine in a dosage of 5-10 μg with excellent results for prolonging the analgesic efficacy. Studies have shown prolonged neuraxial blockade and duration of postoperative analgesia with DEX.[10] With a potent and specific agonist effect on α-2 adrenergic receptors, DEX provides analgesic, sedative, and anxiolytic benefits.[11] DEX at a dosage of up to 5μg has also become a preferred choice in ICUs as a sedative agent due to its minimal adverse effects on respiratory and cardiovascular systems and its property of imitating physiological sleep.[11,12]

Neuraxial anesthesia is a useful and preferred choice suggested for orthopedic surgeries; hence it is important to study DEX as add on to local anesthetics in surgeries like TKR as the studies on the outcomes of adding DEX for prolonging the subarachnoid block are limited. This study was therefore planned with the primary outcome of determining the increase in the duration of analgesia with the addition of intrathecal DEX to the local anesthetic compared to local anesthetic alone by prolonging subarachnoid block in orthopaedic geriatric population undergoing unilateral TKR. The results of this study will help orthopaedic surgeons and anesthetists to use evidence-based strategies in their practices to reduce morbidity and ensure earlier recovery and early discharge of their geriatric patients after TKR surgery.

Methodology

This randomized controlled trial was conducted at the Department of Anesthesia, Fauji Foundation Hospital, Rawalpindi, from April, 2023, to September, 2023.

The sample size was calculated using the OpenEpi sample size calculator, with a power of 80% and a two-sided alpha level of 5%. The following parameters were used:

- Mean time to first analgesic requirement in Group 1 (m1) = 459.8 minutes
- Mean time in Group 2 (m2) = 321.85 minutes
- Standard deviation in Group 1 (SD1) = 100.9
- Standard deviation in Group 2 (SD2) = 95.08
- n2/n1= 1, sample size n1=8, n2=8. [14]

The minimum sample size calculated was 16 patients (8 in each group). However, to enhance the statistical validity and reliability of the results, a total of 60 patients were enrolled, with 30 patients allocated to each group.

A total of 60 geriatric patients undergoing unilateral TKR with physical status of class II & III (American Society of Anesthesiologists) were included in this study using consecutive sampling technique and were randomized in to 2 equal groups though computer generated randomization.

Exclusion criteria was set as patients with heart, renal or liver failure, patients with heart block of 2nd or 3rd-degree, patients having low back pain, patients having Body Mass Index> 30 kg/m2 and patients with some psychiatric illnesses which may interfere with pain assessment tools.

All patients were administered with 0.9% normal saline, 2 liters of oxygen/ min and midazolam (0.02 mg/kg) prior to anesthesia. Lumber puncture was carried out at L3-L4 interspace or L4-L5 interspace with the patients in the sitting position.

In Group-A, intrathecal 0.5% hyperbaric bupivacaine 6 mg (1.2 ml) and DEX 5 μg were administrated (0.5 ml of injection DEX diluted with normal saline).

In Group-B, no additional drug was given besides 0.5% hyperbaric bupivacaine 6 mg (1.2 ml).

All the demographic details of patients were noted down. Clinical and laboratory findings including heart rate, blood pressure, ECG, pulse oximetry and ETCO2 (end-tidal carbon dioxide) were also recorded for each patient at the time of admission to operation theatre.

The primary outcome was set as time duration for the first analgesia requirement, post-operative pain score at rest and at movement at 24 hours follow up while the secondary outcomes were duration of sensory and motor blockade.

Severity of postoperative pain were assessed using visual analogue scale (VAS, 0 -10, 0 = no pain while 10 = maximum pain).

Time duration for the first analgesia requirement was calculated as the time calculated from 5 min after subarachnoid block till the patient's complaint of pain (VAS>4). Rescue analgesic given to these patients was Diclofenac (75mg, intramuscular injection).

Assessment of post-operative pain at rest and at movement was done at 4, 6, 12 and 24 hours.

Duration of sensory blockade was assessed as the time calculated from 5 min after subarachnoid block till the sensory levels reached back to less than S1 dermatome level. Duration of motor blockade was assessed as the time calculated from 5 min after subarachnoid block till modified Bromage score of 6. (Bromage scale: where 0= no paralysis, 1= no rise of extended legs, 2=no knee flexion, 3=no ankle dorsiflexion).

Assessment of the level of sensory and motor block was done at every 15 min in the post-surgical period till the restoration of normal sensations.

Ethical approval for the study was obtained from the Institutional Ethics Committee of Fauji Foundation Hospital, Rawalpindi Ref no.798/RC/FFH/RWP, dated 12 Feb 2023. The study objectives and procedures were explained in detail to all participants, and written informed consent was obtained prior to enrollment.

Data analysis was performed using SPSS version 26. Mean±SD of quantitative variables were calculated for the analysis while frequency and percentages were calculated for qualitative variables. Independent t-test and Chi-squar tests were applied to compare the results between the two groups while $p \leq 0.05$ was taken as significant.

Results

The Mean±SD of age in this study was 68.03±4.54 years with an age range of 60 to 76 years. The ratio of male gender was 60% while female gender was 40% in overall study population. The group-wise details of demographic and clinical findings are given in table I.

Table I: Demographic and clinical details in both the groups. (n=60)

Demographics and clinical findings		Group A (n=30)	Group B (n=30)
Age (Mean±SD) years		69.16±4	66.9±4.82
Gender	Male n (%)	17 (56.66)	19 (63.33)
	Female n (%)	13 (43.33)	11 (36.66)
BMI (Mean±SD)		26.6 ±2.42	27.13±1.90
ASA*	I	4 (13.33)	3 (10)
	II	26 (86.66)	27 (90)
Duration of surgery	(Mean±SD) minutes	140.73±7.15	144.13±8.09

The primary outcomes of the study demonstrated a significantly longer duration before the first rescue analgesia was required in Group A compared to Group B. Additionally, mean pain scores at rest and during movement were significantly lower in Group A than in Group B. Regarding the secondary outcomes, both sensory and motor blockade durations were significantly prolonged in Group A compared to Group B. A detailed comparison of primary and secondary outcomes between the two groups is presented in table II**.**

The difference in the incidence of adverse events among the two groups was found to be non-significant fas shown in table III.

Table II: Primary and secondary outcomes of the study. (n= 60)

Study Outcomes	Group-A (n=30)	Group-B (n=30)	p-value
Primary outcomes			
Mean±SD			
Time duration for rescue analgesic min	461.37±21.52	330.91±18.21	0.000
Pain Score at Rest	3.29±1.78	4.86±1.52	0.000
Pain Score at Movement	5.1±1.60	6.44±1.42	0.001
Secondary outcomes			
Duration of sensory Blockade (min)	379.52±63.74	304.76±17.67	0.000
Duration of Motor Blockade (Min)	390.03±67.23	259.8±17.62	0.000

Discussion

The use of DEX as an adjuvant to local anesthesia has been discussed in various studies for its effects of

prolonging the motor and sensory blockade in the sub umbilical, perianal, orthopaedic, and other lower limb surgeries; however, few have discussed its utility when administrated intrathecally for geriatric orthopaedic patients undergoing the procedure of TKR.

Table III: Primary and secondary outcomes of the study. (n= 60)

Adverse events	Group-A (n=30)	Group-B (n=30)	p-value
Hypotension	5	4	0.717
Bradycardia	6	4	0.488
Hypertension	5	3	0.447
Nausea/Vomiting	3	2	0.218

Gupta K studied the prolongation of the subarachnoid block when DEX was administered intravenously in sub-umbilical surgical procedures. The results of the study showed a prolonged sensory block in the DEX group compared to the group where the subarachnoid block was only done with 0.5% hyperbaric bupivacaine (259.7 ± 46.8 min Vs 216.4 ± 31.4 min, P < 0.001).[15]

SS Nethra studied the effects of intrathecal administration of DEX 5 μg when added to hyperbaric bupivacaine on increasing the duration of analgesia and sensory/motor blockade. The results showed a significantly increased duration of time required for rescue analgesic compared to the group where no DEX was added (459.8 ± 100.9 Vs 321.85 ± 95.08min). Similarly, time for the regression of motor and sensory blockage was also significantly increased in the DEX group compared to the other group (430.05 ± 89.13 Vs 301.10 ± 94.86 min and 323.05 ± 54.58 Vs 220.10 ± 63.61 min).[14]

Bansal I, conducted a randomized control trial to compare the efficacy of DEX and an opioid (Buprenorphine) when added to 0.5% hyperbaric bupivacaine intrathecally in patients undergoing bilateral TKR. The results of the study showed that motor and sensory blockade was significantly prolonged in patients in the DEX group compared to the Buprenorphine group. Similarly, the time to need the rescue analgesic was significantly longer in the DEX group compared to the opioid group (581.933 ± 122.0251 Vs 295.547 ± 45.1462, p<0.0001). The study therefore concluded that intrathecal DEX provides prolonged anaesthesia and delays the need for rescue analgesic. These advantages are accompanied by fewer adverse events compared to opioids.[16]

A meta-analysis of patients undergoing TKR published in 2020 focused on the efficacy of DEX when added with local anesthetic agents for nerve block. The primary outcomes were duration of analgesia, mean pain score, and patient satisfaction while the secondary outcomes were degree of sedation, motor strength, and the incidence of adverse events. The results concluded that DEX was effective in nerve block when added to a local anesthetic agent, in patients undergoing TKR in shape of relieving post-operative pain, prolonging the duration of analgesia, and increasing patient satisfaction.[17]

A meta-analysis on DEX 5 μg to study its effects on the quality of motor and sensory block, when used intrathecally as an adjuvant to a local anesthetic agent in orthopaedic surgeries, was published recently in 2023. This meta-analysis included 8 RCTs and the results showed a significantly increased time duration for regression of one sensory block (mean difference 13 9.72 min, P = 0.009) and two sensory blocks (mean difference 54.8 min, P < 0.001) in the DEX groups. The Bromage score of zero was also prolonged in the DEX group with a statistically significant difference (mean difference 93.66 min, p=0.004).[18]

The Mean±SD of age in this study was 68.03±4.54 years with an age range of 60 to 76 years. The ratio of male gender was 60% while female gender was 40% in overall study population. Primary outcomes of the study showed that the mean time to need rescue analgesia was significantly longer in Group A compared to Group B (461.37±21.52 Vs 330.91±18.21 Min, p=0.000). Similarly, the mean pain scores at rest (3.29±1.78 Vs 4.86±1.52, p=0.000) and at movement (5.1±1.60 Vs 6.44±1.42, p=0.001) were significantly less in Group-A compared to Group-B. The results of secondary outcomes also showed a prolonged duration of nerve block in Group-A compared to Group-B (379.52±63.74 Vs 304.76±17.67, p=0.000 and 390.03±67.23 Vs 259.8±17.62, p=0.000, respectively). The comparison of adverse effects between the two groups showed no statistically significant difference regarding the incidences of bradycardia, hypotension, hypertension, nausea, and vomiting.

The results of our study are in line with studies discussed above over the subject as the results of this study and studies previously conducted with the same type of orthopedic patients show that the addition of intrathecal DEX to local anesthetic prolongs the subarachnoid block benefiting in the shape of increased duration of need for rescue analgesia and reduction in mean pain score at rest and at movement in geriatric patients undergoing unilateral TKR.[14-18]

These benefits ultimately improve patient satisfaction, reduce the length of hospital stay, and help to cut the cost of treatment.

Conclusion

The results of this study demonstrate that the addition of intrathecal DEX to local anesthetic prolongs the subarachnoid block which is apparent by prolonged sensory and motor block. This results in significant advantages in the shape of increased duration for rescue analgesia and reduction in mean pain score in orthopaedic geriatric patients undergoing unilateral TKR. All these benefits lead to increased patient satisfaction, reduce the length of hospital stay, and help reduce the overall treatment cost.

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The major limitation of this study is the small sample size. Future studies at a larger scale will help prove stronger evidence for recommending intrathecal DEX in addition to local anesthetic agents in geriatric patients undergoing TKR.

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