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Evaluation of the Effect of Adding Dexmedetomidine to Levobupivacaine in Femoral Sciatic Block for Total Knee Replacement: Randomized Control Study

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Abstract: ***Background:*** In recent years there has been a increasing interest in the practice of regional anaesthesia especially peripheral nerve blocks for surgical anaesthesia and postoperative analgesia. Imaging guidance for nerve localization helps the promise of improving block success with fewer complications. Among the imaging modalities currently available, ultrasonography seems to be the most suitable for regional anaesthesia. One the most significant advantage of ultrasound technology is the availability to provide anatomic examination of the area of interest.

Aim of the Work: To evaluate the additive effect of dexmedetomidine to levobupivacaine in femoral sciatic block in total knee replacement regarding the onset and duration of both sensory and motor blockade, postoperative analgesia requirements.

Patients and Methods: After ethical approval, 60 patients aged 40-60 years old, with an American Society of Anaesthesiologists (ASA) physical class I and II who underwent total knee replacement using combined femoral-sciatic anaesthesia, were included in this prospective, randomized,controlled, double-blinded study. Patients were randomly assigned to receive levobupivacaine alone divided (group B) or dexmedetomidine 100 µg added to levobupivacaine (group BD) [*n* = 30 for each group] for combined femoral–sciatic nerve block.

Results: This study showed that the addition of dexmedetomidine 100 µg to levobupivacaine during ultrasound-guided combined femoral-sciatic nerve block for total knee replacement was associated with +50 % longer duration of analgesia, -20% shorter onset times for sensory and motor block, -25% faster time for surgical readiness, and longer duration of sensory and motor block (+45% and +40%, respectively). Unfortunately, the present study found that the addition of 100 µg dexmedetomidine to levobupivacaine during femoral–sciatic nerve block for total knee replacement was associated with bradycardia and hypotension (30% and 10 %, respectively).

Conclusion: Addition of dexmedetomidine to levobupivacaine during femoral–sciatic nerve block for total knee replacement was associated with faster onset of sensory and motor block, decrease intraoperative and postoperative requirements of analgesia and longer duration of motor block than levobupvicaine alone.

Keywords: *Dexmedetomdine, American Society of Anaesthesiologists, Levobupivacaine*

Introduction

In recent years there has been a growing interest in the practice of regional anaesthesia especially peripheral nerve blocks for surgical anaesthesia and postoperative analgesia.[15]

Regional anaesthesia techniques provide important advantages compared with general anaesthesia and systemic analgesia, including excellent pain control, more stable cardiovascular (CV) hemodynamics, attenuated stress responses, reduced opioid-related complications, reduced side effects, and shortened stay in the hospital. However, these early advantages can be short-lived and limited by the relatively brief duration of action of currently available local anesthetics (LAs), potentially resulting in block resolution before the period of worst postoperative pain.[4]

Imaging guidance for nerve localization holds the promise of improving block success and decreasing complications. Among imaging modalities currently available, ultrasonography seems to be the one most suitable for regional anaesthesia. Perhaps the most significant advantages of ultrasound technology were the availability to provide anatomic examination of the area of interest .[12]

Increasing the volume (dose) of LAs may prolong the duration of analgesia, but may also increase the risk of LA systemic toxicity. Many drugs have been used as adjuvants to LA agents to prolong the duration of peripheral nerve blocks. Clonidine, a partial alpha 2 agonist has been reported to prolong the duration of anaesthesia and analgesia during blocks .[13]

Dexemedetomidine, the pharmacologically active d-isomer of medetomidine is a highly specific and selective α2 adrenoceptor agonist with α2:α1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine, thus decreasing the unwanted side effects of α1 receptors. Presynaptic activation of α2 adrenoceptor in central nervous system (CNS) inhibits the release of norepinephrine, terminating the propagation of pain signals and their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP . [9]

AIM OF THE WORK

To evaluate the additive effect of dexmedetomidine to levobupivacaine in femoral sciatic block in total knee replacement regarding the onset and duration of both sensory and motor blockade, postoperative analgesia requirements.

PATIENTS AND METHODS

After obtaining the approval of the Ethical Committee of Ain Shams University Hospital and an informed consent, 60 patients aged 40 -60 years old, with an American Society of Anaesthesiologists (ASA) physical class from I to II scheduled for total knee replacement under combined femoral-sciatic anesthesia were enrolled in this prospective, randomized, controlled study.

Patients with significant cardiac, pulmonary, renal, hepatic, neurological, neuromuscular, or psychiatric disorders, coagulopathy, pregnancy, body mass index greater than 35 kg/m^2, those receiving adrenoceptor agonists or antagonists, antiplatelet other than acetylsalicylic acid (aspirin), or anticoagulants were excluded. Patients with history of hypersensitivity to any of the study medications, or those who refused to participate in the study, were also excluded.

Preoperative routine laboratory tests were performed with emphasis on prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR). Preoperative fasting for 8 hours was ensured. Patients were instructed preoperatively about use of the numerical rating scale (NRS) for pain assessment (NRS: 0 = no pain, 10 = worst pain possible).

On arrival to the operating room, after insertion of intravenous catheter, a 5 mL/kg/hour infusion of Lactated Ringer's solution was started before the induction of femoral-sciatic blockade and continued throughout the whole procedure. Standard anesthesia monitors including five-leads ECG, pulse oximeter, and non-invasive blood pressure were applied.

Supplemental oxygen was administered through a nasal cannula at a flow rate of 3-4 L/minute. Patients were given 1–2 mg of midazolam intravenous (IV) as a premedication 10–15 min before beginning each block in

addition to 25-50 µg of fentanyl just prior to block needle insertion. The dose of sedation titrated to keep the patients still responsive for verbal commands.

Patients were randomly assigned into one of two groups (*n = 30* patients in each): using envelope for choosing them. Another doctor not working in the study prepared the drugs and he did not attend the surgery to ensure the blindness of the study.

- **Control group**: patients received a mixture of levobupivacaine and placebo for both femoral and sciatic blockades ***(Group B).***
- **Dexmedetomidine group:** patients received a mixture of levobupivacaine and dexmedetomidine for both femoral and sciatic blockades **(*Group BD*).**

Dexmedetomidine hydrochloride (Precedex®, manufactured by Hospira, Inc. Lake Forest, IL, USA) was supplied in 100 µg/mL. A mixture of 39 ml levobupivacaine 0.5% and 1 ml of dexmedetomidine was prepared (total volume of 40 ml) to use in dexmedetomidine group ***(Group BD)*** taking into consideration not to exceed maximum allowed dose 3 mcg/kg. A mixture of 39 ml levobupivacaine 0.5% and 1 ml of saline (placebo) was prepared (total volume of 40 ml) to use in control group ***(Group B).***

In femoral block:

The patient was placed in the supine position, with the operative lower limb in the neutral position. After skin disinfection with povidone iodine and sterile drapes were applied. A lubricated high-frequency, 8-12 MHz, straight array ultrasound (US) probe covered with a sterile plastic sheath of Sonosite portable US machine (China) was used at depth between 2 to 4 cm.

The transducer probe was placed perpendicular to the skin just beneath the inguinal crease to visualize the femoral artery, using a two-dimensional (2D) ultrasonograph scan through sliding and tilting the probe, and through slightly lateral movements, the femoral nerve was visualized as a hyperechoic structure, 1-2 cm lateral to the femoral artery.

After a negative aspiration of blood, a 15 mL of the previously prepared solution for each group were deposited around the femoral nerve.

In Sciatic block:

Patients were positioned in the lateral decubitus, with the operative side uppermost with flexed hip and knee. The lateral prominence of the greater trochanter and the ischial tuberosity were identified with palpation and a line was drawn between them. After skin disinfection with povidone iodine and sterile drapes were applied, a low-frequency, 5–2 MHz, curved array US probe was covered with a sterile plastic sheath was used to scan the sciatic nerve at depth between 6 and 8 cm.

The 'subgluteal space' appeared as a hypoechoic line between the gluteus maximus and the quadratus femoris muscles. It extended from the greater trochanter laterally to the ischial tuberosity medially. At this level, the sciatic nerve was shown as a hyperechoic triangle with an approximate diameter of 1.5–2 cm within the subgluteal line.

After a negative aspiration of blood, a 25 mL of the previously prepared solution for each group were deposited around the sciatic nerve.

In the present study we used scoring system based on proper assessment of sensory and motor functions along the femoral and sciatic nerves and their branches. This method, although time-consuming, is precise and complete. Dermatomal sensory and motor blockades through the distributions of the femoral and sciatic nerves were assessed every 3 minutes for 30 minutes after completion of both nerve blocks. Patients who did not achieve a complete block, through the two nerves, within 30 minutes were excluded from study.

Assessment of sensory loss, was assessed by pin prick method using a 23 gauge needle across the dermatomal areas innervated with the tibial and common perioneal nerves (namely, lateral aspect of the calf and plantar aspect of the foot) and femoral nerve (namely, anterior aspect of the thigh at the level of the patella and anterior and medial part of the calf for saphenous distribution).

Sensory blockade was assessed using a 3-points numerical rating scale:

Grade 0 = sharp pin felt (normal sensation),
Grade 1 = dull sensation felt i.e., loss of sensation to pinprick only (analgesia),
Grade 2 = no sensation felt i.e., loss of sensation of pain and touch (anaesthesia).

Motor blockade was assessed across the distributions of the common peroneal and tibial nerves through assessing the dorsiflexion and plantar flexion of the foot, respectively, against a manual resistance, and the femoral nerve through assessing the ability to elevate the leg outside the bed or to extend the leg at the knee while the hip is semi-flexed. The degree of motor blockade was assessed using a 3-points numerical scale:

Grade 0 = normal motor function,
Grade 1= reduced motor strength, but with reserved perceptible movement.
Grade 2 = complete motor block.

The **primary outcome** of the study was to measure the onset and duration of both sensory and motor blockade, postoperative analgesia requirements. **Secondary outcomes** were to measure hemodynamics including heart rate, systolic blood pressure, diastolic blood pressure and evidence of adverse drug reaction including hypotension, bradycardia and TUG test as indicator of mobilization ability.

The definition of block onset time showed a great variation between the different studies, in this study we considered two different times to evaluate the blockade.

First, **the *onset time*, sensory onset time** defined as the time interval between the end of local anaesthetic administration (T0) and a loss of sensation to pin prick (grade 1) along the distribution of any of either femoral or sciatic nerves, where **motor onset time** defined as the time interval between the end of local anaesthetic administration (T0) and a reduced motor strength (grade 1) either at knee or ankle levels.

Second, the **surgical anaesthesia time**, defined as the onset time for readiness for surgical procedures that is represented by the time interval between the T0 and the complete sensory blockade at the distribution of both of sciatic and femoral nerves with inability to move the ankle and toes of the operated leg (grade 2).

As a result of the time interval between the onset times of sensory and motor blockade and the occurrence of complete sensory and motor blockade of both femoral and sciatic nerves with their branches, therefore the time needed for readiness to start surgical procedures is clinically important.

The **primary outcome** of the study was to measure the onset and duration of both sensory and motor blockade, postoperative analgesia requirements. **Secondary outcomes** were to measure hemodynamics including heart rate, systolic blood pressure, diastolic blood pressure and evidence of adverse drug reaction including hypotension, bradycardia and TUG test as indicator of mobilization ability.

Hemodynamics parameters including heart rate (HR), systolic arterial blood pressure (SBP), and diastolic arterial blood pressure (DBP) were recorded at 0 (baseline), 5, 10, 15, 30, 45, 60, 90, and 120 minutes after completion of the blockade.

Intraoperative complications including hypotension (defined as a 20% decrease below the baseline value), treated with 6 mg ephedrine, bradycardia (defined as HR lower than 50 beats per minute [bpm]) treated by 0.4 mg Atropine, were recorded.

Durations of sensory and motor blockades, defined as the time interval between the T0 and the fading of both sensory and motor blockades (grade 0) across the distribution of the two blocked nerves, respectively, were measured.

The time between the end of local anaesthetic administration T0 and the first analgesic request was recorded as the duration of the analgesia. Also, number of patients who needed rescue analgesia in form of naluphine were recorded. Total requirements of rescue analgesia over the postoperative 24 h period were also recorded.

A fall was defined as unintentionally coming to rest on the ground, or at some other lower level, not as a result of a major intrinsic event such as a fit, faint or stroke. Time between surgery and falls must be recorded, if patients undergo surgical treatment following their fall, the time from clinical presentation after falling to the surgical intervention is recorded.

We adopted TUG test (timed up and First go), as indicators of mobilization ability to assess nerve blockade following TKA. Interpretation of the outcomes must be made with caution due to the relatively small sample size and different dose of the analgesia.

Power analysis was based on a pilot study of five patients in the control group that showed a main duration of analgesia of 420 min (± 80). Twenty-seven patients were required in each group to detect one hour difference in the duration of analgesia, with an alpha error of 0.05 and a power of 80%. To compensate for dropout cases and shifting from normality in data distribution, 30 patients were studied in each group.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric. Also qualitative variables were presented as number and percentages. The comparison between groups with qualitative data was done by using ***Chi-square test***. The comparison between two groups with quantitative data and parametric distribution were done by using ***Independent t-test***. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P > 0.05: Non significant, P < 0.05: Significant, P < 0.01: Highly significant.

RESULTS

The study was conducted at Ain Shams University Hospital. Sixty adult patients underwent below knee surgery and received ultrasound-guided femoral–sciatic nerve block.

Patients were randomly allocated into two groups: Group BD (*n=30*), who received ultrasound guided femoral–sciatic nerve block with bupivacaine 0.5% and 100 µg dexmedetomidine, and Group B (*n=30*) who received ultrasound guided femoral–sciatic nerve block with bupivacaine 0.5% alone.

I. Patients Demographic Data

Table (1): Comparison between B group and BD group regarding demographic data

		B group	**BD group**	**Test value**	**P-value**	**Sig.**
		No. = 30	**No. = 30**			
Age	Mean ± SD	54.77 ± 5.33	56.33 ± 5.09	-1.165•	0.249	NS
Sex	Female Male	14 (46.7%) 16 (53.3%)	13 (43.3%) 17 (56.7%)	0.067*	0.795	NS
Weight	Mean ± SD	89.13 ± 7.66	87.47 ± 5.85	0.947•	0.347	NS
Height	Mean ± SD	165.17 ± 8.42	167.67 ± 9.28	-1.093•	0.279	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS),
*:Chi-square test; •: Independent t-test

II. Onset Time of Sensory and Block Motor and surgical anaesthesia time:

Table 2 showed the time taken to the onset of sensory block in group (BD) was faster (15.53 ± 1.80 min) Than group (B) (19.87 ± 1.87) , also the onset of motor block was (19.93 ± 1.66) min in group (BD), earlier than group (B) (25.20 ± 2.01) min . This led to earlier start of surgery in group (BD) (23.03 ± 1.67)min , than group (B) (27.77 ± 2.43)min.

Table (2): Comparison between two groups regarding onset time of sensory and motor blockade and surgical anesthesia time:

		B group	**BD group**	**Test value**	**P-value**	**Sig.**
		No. = 30	**No. = 30**			
Sensory onset	Mean ± SD	19.87 ± 1.87	15.53 ± 1.80	9.155	0.000	HS
Motor onset	Mean ± SD	25.20 ± 2.01	19.93 ± 1.66	11.077	0.000	HS
Surgical anaesthesia time	Mean ± SD	27.77 ± 2.43	23.03 ± 1.67	8.789	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test

III. Duration of Sensory and Motor Block and duration of analgesia.

Table (3): Comparison between two groups regarding sensory duration, motor duration and duration of analgesia.

		B group	BD group	Test value	P-value	Sig.
		No. = 30	No. = 30			
Sensory duration	Mean ± SD	422.83 ± 48.84	646.50 ± 38.06	-19.784	0.000	HS
Motor duration	Mean ± SD	243.83 ± 34.91	327.33 ± 24.59	-10.711	0.000	HS
Duration of analgesia	Mean ± SD	451.83 ± 45.48	710.50 ± 38.20	-23.855	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

•: Independent t-test

The table showed that there was highly statistically significant difference found between two groups as regard sensory, motor onset and start surgical procedure.

IV. Hypotension and Bradycardia.

Table (4): Comparison between two groups regarding hypotension and bradycardia.

		B group		BD group		Test value	P-value	Sig.
		No.	%	No.	%			
Hypotension	Negative Positive	30 0	100.0% 0.0%	26 4	86.7% 13.3%	4.286	0.038	S
Bradycardia	Negative Positive	27 3	90.0% 10.0%	20 10	66.7% 33.3%	4.812	0.028	S

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

: Independent t-test

V. Total postoperative analgesia consumption

Table (5): Comparison between two groups regarding total postoperative analgesia consumption

		B group		BD group		Test value	P-value	Sig.
		No.	%	No.	%			
Post-op analgesia requirement	Negative Positive	0 30	0% 100%	4 26	13.3% 86.7%	4.286	.038	S
IV naluphine (mg) consumption over 24 h		25 ± 6.62		12 ± 3.54		4.582	<0.01	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

: Independent t-test

VI. TUG TEST:

Table (6): Comparison between two groups regarding TUG test.

		B group		BD group		Test value	P-value	Sig.
		No.	%	No.	%			
TUG test after 12 hours	Negative Positive	29 1	96.7% 3.3%	28 2	93.3% 6.7%	.351	0.554	NS
TUG test after 24 hours	Negative Positive	30 0	100% 0%	30 0	100% 0%	0.946	0.364	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

: Independent t-test

VII. Hemodynamic Changes

Table (7): Heart rate (HR)

		B group	BD group	Test value	P-value	Sig.
		No. = 30	No. = 30			
HR preoperative	Mean ± SD	67.67 ± 7.51	67.00 ± 6.51	0.367	0.715	NS
HR 0	Mean ± SD	64.50 ± 4.80	68.83 ± 8.48	-2.437	0.018	S
HR 5	Mean ± SD	62.83 ± 6.52	68.00 ± 10.05	-2.362	0.022	S
HR 10	Mean ± SD	69.50 ± 11.77	75.83 ± 11.90	-2.073	0.043	S
HR 15	Mean ± SD	68.00 ± 8.87	68.00 ± 7.38	0.000	1.000	NS
HR 30	Mean ± SD	67.17 ± 7.84	66.83 ± 6.36	0.181	0.857	NS
HR 45	Mean ± SD	66.67 ± 7.58	65.67 ± 5.98	0.567	0.573	NS
HR 60	Mean ± SD	66.67 ± 7.58	66.00 ± 6.21	0.372	0.711	NS
HR 90	Mean ± SD	66.50 ± 7.56	65.83 ± 6.17	0.374	0.710	NS
HR 120	Mean ± SD	66.33 ± 7.18	65.67 ± 5.68	0.399	0.692	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

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HR 0	Mean ± SD	64.50 ± 4.80	68.83 ± 8.48	-2.437	0.018	S
HR 5	Mean ± SD	62.83 ± 6.52	68.00 ± 10.05	-2.362	0.022	S
HR 10	Mean ± SD	69.50 ± 11.77	75.83 ± 11.90	-2.073	0.043	S
HR 15	Mean ± SD	68.00 ± 8.87	68.00 ± 7.38	0.000	1.000	NS
HR 30	Mean ± SD	67.17 ± 7.84	66.83 ± 6.36	0.181	0.857	NS
HR 45	Mean ± SD	66.67 ± 7.58	65.67 ± 5.98	0.567	0.573	NS
HR 60	Mean ± SD	66.67 ± 7.58	66.00 ± 6.21	0.372	0.711	NS

HR 90	Mean ± SD	66.50 ± 7.56	65.83 ± 6.17	0.374	0.710	NS
HR 120	Mean ± SD	66.33 ± 7.18	65.67 ± 5.68	0.399	0.692	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

•: Independent t-test

Table (8): Systolic arterial blood pressure (SAP)

		B group	**BD group**	**Test value**	**P-value**	**Sig.**
		No. = 30	**No. = 30**			
SAP 0	Mean ± SD	135.27 ±15.18	137.5 ± 17.18	.532	.596	NS
SAP 5	Mean ± SD	133.63 ± 13.93	126.32 ± 14.81	1.969	.0537	NS
SAP 10	Mean ± SD	134.05 ± 11.47	122.07 ± 5.65	3.245	.0019	HS
SAP 15	Mean ± SD	131.83 ± 14.24	117.17 ± 16.24	3.717	.0005	Hs
SAP 30	Mean ± SD	127.25 ± 18.59	115.83 ± 18.58	2.3798	.0206	S
SAP 45	Mean ± SD	129.83 ± 16.24	113.83 ± 18.23	3.589	.0007	HS
SAP 60	Mean ± SD	125.93 ± 10.94	111.33 ± 14.17	4.5235	.01	HS
SAP 90	Mean ± SD	121.23 ± 15.67	111.33 ±14.17	2.5666	.0129	S
SAP 120	Mean ± SD	123.33 ± 13.95	124.16 ± 14.94	.2221	.8248	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table (9): Diastolic arterial blood pressure (DAP)

		B group	**BD group**	**Test value**	**P-value**	**Sig.**
		No. = 30	**No. = 30**			
DAP 0	Mean ± SD	77.83 ± 8.79	75.83± 7.49	.9486	.3468	NS
DAP 5	Mean ± SD	74.83 ± 3.72	71.97 ± 9.61	1.52	.133	NS
DAP 10	Mean ± SD	72.14 ± 7.28	70.07 ± 6.31	1.176	.244	NS
DAP 15	Mean ± SD	71.104 ± 7.43	69.66 ± 7.43	.75	.455	NS
DAP 30	Mean ± SD	71.17 ± 10.23	67.16 ± 9.22	1.79	.0786	NS

DAP 45	Mean ± SD	69.63 ± 9.47	63.83 ± 8.74	2.465	.0167	S
DAP 60	Mean ± SD	68.17 ± 11.12	62.76 ± 8.13	2.151	.0356	S
DAP 90	Mean ± SD	66.33 ± 8.93	60.33 ± 10.73	2.354	.022	S
DAP 120	Mean ± SD	65.94 ± 13.89	66 ± 9.29	.019	.984	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test

DISCUSSION

This prospective, randomized,controlled, double-blinded study was designed to evaluate the efficacy of adding 100 μg dexmedetomidine to levobupivacaine 0.5% during ultrasound-guided combined femoral–sciatic nerve blockade as the sole anaesthesia for patients undergoing total knee replacement.

The main findings of the present study was increase in the duration of postoperative analgesia, accelerated sensory and motor block onset , and lengthened the duration of sensory and motor blockade.

Some recent investigations have studied the effects of mixing dexmedetomidine with local anaesthetics during peripheral nerve block in humans. All these studies have shown that the perineural dexmedetomidine as a local anaesthetic adjuvant for peripheral nerve blocks can prolong the duration of blockade and post-operative analgesia compared with local anaesthetics alone in numerous regional blocks **.** [6]

In agreement with this study, Agarwal and colleagues found that the addition of 100 μg dexmedetomidine to bupivacaine during supraclavicular brachial plexus blockade for upper limb operations prolongs the duration of analgesia by (+220%). Although, the investigators used the same dose of dexmedetomidine and the same type of local anaesthetic solution, this difference may relate to differences in the complexity nature of the surgical operations in the present study that associated with tense postoperative pain.

Additionally, the present study demonstrated accelerated **onset for sensory blockade** (-20%) after the addition of dexmedetomidine 100 μg to levobupivacaine during ultrasound-guided femoral–sciatic nerve block for total knee surgery. Similarly, others reported reduced onset time for sensory blockade with the administration of dexmedetomidine for supraclavicular brachial plexus block (-40%), infraclavicular brachial plexus block (-40%),and axillary block (-40%) **.** [2]

This work approved that the addition of dexmedetomidine 100 μg to levobupivacaine accelerated the **onset for motor blockade** (100%) after femoral–sciatic nerve blockade for below knee surgery. This is similar to previous studies. In contrast, other investigators found comparable times in motor blockade **.** [11]

Although Kaygusuz and colleagues found significant shortening in the onset time for sensory blockade (40%), their results did not find a significant shortening in the onset time for motor blockade after the addition of dexmedetomidine 100 μg to levobupivacaine during axillary brachial plexus blockade.

The present study reported prolonged **durations of sensory and motor blockades** (45% and 40%, respectively) after addition of dexmedetomidine 100 μg to levobupivacaine during femoral–sciatic nerve blockade in patients who underwent below knee surgery. However, the prolongation of motor block has been associated with minimal patient discomfort on movement in the postoperative period.

In similar to our results, a meta-analysis done by Abdallah and his colleagues in 2013 showed prolonged mean durations of analgesia, sensory blockade and motor block (70%, 76%, and 87%; respectively) after administration of perineural dexmedetomidine. This meta-analysis identified all randomized controlled trials (January 1985–August 2012) that examined the effects of adding perineural dexmedetomidine to LA

(dexmedetomidine group) compared with LA alone (control group) on neuraxial or peripheral nerve block characteristics, postoperative analgesia, and dexmedetomidine related side-effects in surgical patients undergoing regional anaesthesia **.** [1]

In the present study, heart rate levels in the group which received 100 μg dexmedetomidine with levobupivacaine were significantly lower than those in the group that received levobupivacaine alone. Bradycardia was observed in10 patients in the group that received 100 μg dexmedetomidine, but without any hemodynamic instability, and all of these patients were treated with 0.4 mg atropine. There were no episodes of bradycardia in the control group.

The decrease in pulse rate and blood pressure might be related to the post-synaptic activation of central α2-adrenoceptors, leading to decreased sympathetic activity that decrease the blood pressure and slower HR. Baroreceptor reflex is well preserved with the use of dexmedetomidine. Thus bradycardia are easily treatable conferring hemodynamic stability **.** [14]

This work showed a significant fall in systolic blood pressure that started after 10 min in the dexmedetomidine group in comparison to the control group.. Both systolic and diastolic blood pressures start to return to their basal values after 90 min. Hypotension was observed in 4 patients in the group that received 100 μg dexmedetomidine, and all of these patients were treated with 9 mg ephedrine.

There is a diverse dose range of perineural dexmedetomidine in previous studies. The used dose of perineural dexmedetomidine in the present study is comparable to the dose range used in previous studies when based upon patient body weight (1.25 μg/kg vs. 0.5 μg/kg to 1.5 μg/kg, respectively) . In an experimental study, the use of large doses of perineural dexmedetomidine up to 40 μg/kg had no effect on either nerve axons or myelin sheaths **.** [5]

As for complications, there has been more risk of falls linked to peripheral nerve blocks. In our study, FNB increased the risk of falls post TKA. Several studies have reported that FNB results in weakness of all four components of the quadriceps muscle increasing fall risks **.** [10]

Falling recorded firstly in four cases in three different orthopedic centres in london in 2004-2005 and 3 of them had fractures and need another operation **.** [8]

Although the cause of these falls may be multifactorial, and 3 of our patients were over 65 years of age, these cases highlight a complication related to the use of FNB and early mobilization. Multidisciplinary research by anaesthetists, orthopaedic surgeons, and physiotherapists is warranted.

Quadriceps strength for FNB was reduced compared with baseline. A study on volunteers by **Kwofie *et al***. demonstrated that FNB reduced quadriceps strength balance scores compared with baseline.

We adopted TUG test as indicator of mobilization ability to assess nerve blockade following TKA. In the current study, After 12 hours only 2 Patients cannot perform this test , after 24 hours all patients can do this test. The result is non significant due to the relatively small sample size and different dose of the analgesia.

We recommend that, after having a FNB, patients should undergo enhanced postoperative evaluation of blockade and proprioceptive function (in particular 2-point discrimination, light touch, and vibration sense) to ensure safe neurological function before mobilization.

In the Canadian study, In 135 patients who underwent TKA, researchers from the Universite Laval in Quebec City, Canada, found that those who received either continuous or single-shot femoral nerve blocks had less quadriceps strength at six weeks, six months, and 12 months than those who did not receive a nerve block, Two TKA patients in the single-shot femoral nerve group suffered falls in the first postoperative week that necessitated further surgery **.** [3]

Current evidence support that ACB provide same analgesic efficacy and facilitate earlier mobilization by sparing quadriceps strength compared with FNB **.** [7]

CONCLUSION

The results of the current study demonstrated that the addition of perineural dexmedetomidine 100 μg to levobupivacaine for combined femoral- sciatic nerve block prolonged the duration of analgesia, shortened

onset times for sensory and motor block, hastened the time for surgical readiness, and extended the motor and sensory block durations. However, dexmedetomidine may be associated with bradycardia and hypotension. Qudriceps femoris weakness shows weakness after femoral nerve block in about 40 % of patients which lead to falling in about 2% of patients.

Recommendation:

To avoid quadriceps weakness and its consequencs it is better to prefer adductor canal block with sciatic nerve block in total knee replacement**.**

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