

Dexmedetomidine and clonidine as an adjuvant to levobupivacaine in ultrasound guided sciatic nerve block: A randomized, controlled trial

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Abstract: Background and objectives: this study was done to evaluate the effect of adding dexmedetomidine and clonidine 1 μ /kg to levobupivacaine 0.5% with the sciatic nerve block. Patients and methods: Sixty patients scheduled for elective lower limb surgery were randomly allocated into 3 groups to receive ultrasound guided sciatic nerve block with ultrasound guided femoral nerve block to avoid tourniquet pain as follows: Group L received 20 ml levobupivacaine 0.5% for sciatic nerve block and 20 ml levobupivacaine 0.5% for femoral nerve block. Group LD received 20 ml levobupivacaine 0.5% PLUS dexmedetomidine 1 μ /kg for sciatic nerve block and 20 ml levobupivacaine 0.5% PLUS dexmedetomidine 1 μ /kg for femoral nerve block and Group LC received 20 ml levobupivacaine 0.5% PLUS clonidine1 μ /kg for sciatic nerve block and 20 ml levobupivacaine 0.5% PLUS clonidine 1 μ /kg for femoral nerve block. Onset and duration of sensory block, onset and duration of motor block, hemodynamic parameters and quality of operative conditions were assessed. Results: Onset of sensory and motor block in group LD and group LC were significantly faster than that of group L. The duration of sensory and motor block in group LD and group LC were significantly longer than group L. There was a significant decrease in heart rate and mean arterial blood pressure in group LD and group LC in comparison with group L. The quality of operative conditions was better with dexmedetomidine than with clonidine. Conclusion: adding 1 μ /kg dexmedetomidine and clonidine to levobupivacaine for sciatic nerve block leads to more rapid onset and prolongs the duration of sensory and motor block and improves quality of block.

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1. Introduction:

Peripheral nerve blocks have assumed a prominent role in modern anesthesia practice as they provide ideal operative conditions without any sedation or systemic hemodynamic effects (1). Sciatic nerve block is a commonly used regional anesthetic technique for surgeries involving lower limb, especially orthopedic procedures. Always there has been a search for additives to the regional nerve block with drugs that prolong the duration of analgesia but with minimal adverse effects. Alpha-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic and cardiovascular stabilizing effects with reduced anesthetic requirements (2).

Dexmedetomidine, a potent α_2 adrenoceptor agonist, is approximately eight-times more selective towards the α_2 adrenoceptor than clonidine. In previous clinical studies, intravenous dexmedetomidine resulted in significant opioid sparing effects as well as a decrease in inhalational anaesthetic requirements. In various animal studies, dexmedetomidine has been

reported to enhance sensory and motor blockade along with increased duration of analgesia (3, 4, and 5).

Clonidine was initially used for its antihypertensive properties. The central actions are mediated through α_2 adrenoceptors, which are situated at locus coeruleus and dorsal horn of spinal cord. But, specific peripheral effects of clonidine appear to be less obvious because α_2 adrenoceptors are not present on the axon of the normal peripheral nerve (2). This study aimed to evaluate the effect of dexmedetomidine and clonidine as an additive to levobupivacaine in sciatic nerve block.

2. Patients and methods:

After local ethical committee approval and patient informed written consent, this prospective, randomized, double blind, clinical study was conducted on 60 patients above 18 years old ASA I, II and III undergoing elective lower limb surgery. Patients with coagulation disorders or on anticoagulant therapy, patients with local skin infection at the side of injection, patients with psychosis or dementia, patients with known allergy to one of the used drugs, patients

with neurologic or neuromuscular disorder, morbid obesity were excluded from the study.

These patients were randomly allocated by an online randomization program into three equal groups:

Group L: Ultrasound guided sciatic nerve block by 20 ml levobupivacaine 0.5% + Ultrasound guided femoral nerve block by 20 ml levobupivacaine 0.5%.

Group LD: Ultrasound guided sciatic nerve block by 20 ml levobupivacaine 0.5% PLUS dexmedetomidine 1 μ /kg+ Ultrasound guided Femoral nerve block by 20 ml levobupivacaine 0.5% PLUS dexmedetomidine 1 μ /kg.

Group LC: Ultrasound guided sciatic nerve block by 20 ml levobupivacaine 0.5% PLUS clonidine 1 μ /kg+Ultrasound guided Femoral nerve block by 20 ml levobupivacaine 0.5% PLUS clonidine 1 μ /kg.

All patients received oral bromazepam 1.5 mg at the night before surgery. In the operating room, wide bore IV line was inserted. Midazolam 0.05 mg/kg was administered and infusion of crystalloid solution was started. Intraoperative monitoring included 5-lead electrocardiogram, noninvasive arterial blood pressure and pulse oximetry.

For sciatic nerve block the patient is placed laterally with the side to be anesthetized uppermost and hip and knee on the operated side flexed at approximately 45degree. The ultrasound transducer positioned perpendicular to skin on the line connecting the ischial tuberosity and greater trochanter, and clear transverse image of the hyperechoic sciatic nerve between them is obtained. After skin sterilization and local infiltration with lidocaine 2% the block is conducted with short bevel 100-mm,21-gauge nerve block needle inserted parallel and in line with ultrasound transducer. Femoral nerve block was done for tourniquet pain. The patient is placed supine the leg in neutral position ultrasound linear probe is placed along inguinal crease search for most visible structures such as femoral artery and fascia iliaca then search in both superior-inferior and medio-lateral directions the nerve appears as a hyperechoic speckled triangular or oval shaped structure just lateral to the artery after skin sterilization and local infiltration with lidocaine 2% the block is conducted with short bevel 100-mm,21-gauge nerve block needle inserted parallel and in line with ultrasound transducer.

The primary outcome was the duration of sensory block defined as time interval between complete loss of sensation (by pin prick method in the dermatomal areas corresponding to sciatic nerve) and complete resolution of sensory block.

Secondary outcomes included: Onset of sensory block was defined as the time elapsed between the end of injection and complete loss of sensation, Onset of motor block was defined as the time elapsed between the end of injection and complete paralysis (absence of dorsiflexion and planter flexion of foot), duration of motor block was defined as time interval between complete paralysis and complete recovery of motor function. Hemodynamic parameters (Mean arterial blood pressure, heart rate) were recorded at 0, 30, 60, 90, 120 minutes after the block. At the end of the procedure quality of operative conditions were assessed according to the following numeric scale (4).

3. Results:

Between February 2013 and December 2015, patients scheduled for lower limb surgery at Benha University hospitals were invited to participate in our trial. Seven patients refused to participate, 10 were excluded (met the exclusion criteria) and 60 patients were randomized after informed written consent. In total, 20 patients were randomized to each group. All patients received the intended treatment, completed the study protocol, and were included in the analysis (Figure 1).

Demographic characteristics and duration of surgery were comparable among groups (Table 2).

In comparison with group L, group LD and group LC showed a significant shorter onset of sensory and motor block and a significant longer duration of sensory and motor block (Table 3). Also in comparison with group LC, group LD showed a non significant shorter onset of sensory and motor block and a non significant longer duration of sensory and motor block (Table 3).

Regarding hemodynamic parameters, there was a significant decrease in heart rate and mean arterial blood pressure in group LD and group LC in comparison with group L. This decrease began 30 minutes after the block and was statistically insignificant, however this decrease continued and became statistically significant ($p < 0.05$) at 60 and 90 minutes after the block. Dexmedetomidine leads to more decrease in heart rate and mean arterial blood pressure than with clonidine and this difference was statistically significant. (Figures 1 and 2)

The quality of operative conditions was better with dexmedetomidine than with clonidine. Grade IV block was achieved in 80% of patients in group LD, 40% in group LC and 25% of patients in group L. (Table 4).

Table 1: Quality of operative conditions

| Grade | | |
|-------|--------------|--|
| IV | Excellent | No complaint from patient |
| III | Good | Minor complaint with no need for the supplemental analgesics |
| II | Moderate | Complaint that required supplemental analgesics |
| I | Unsuccessful | Patient given general anesthesia |

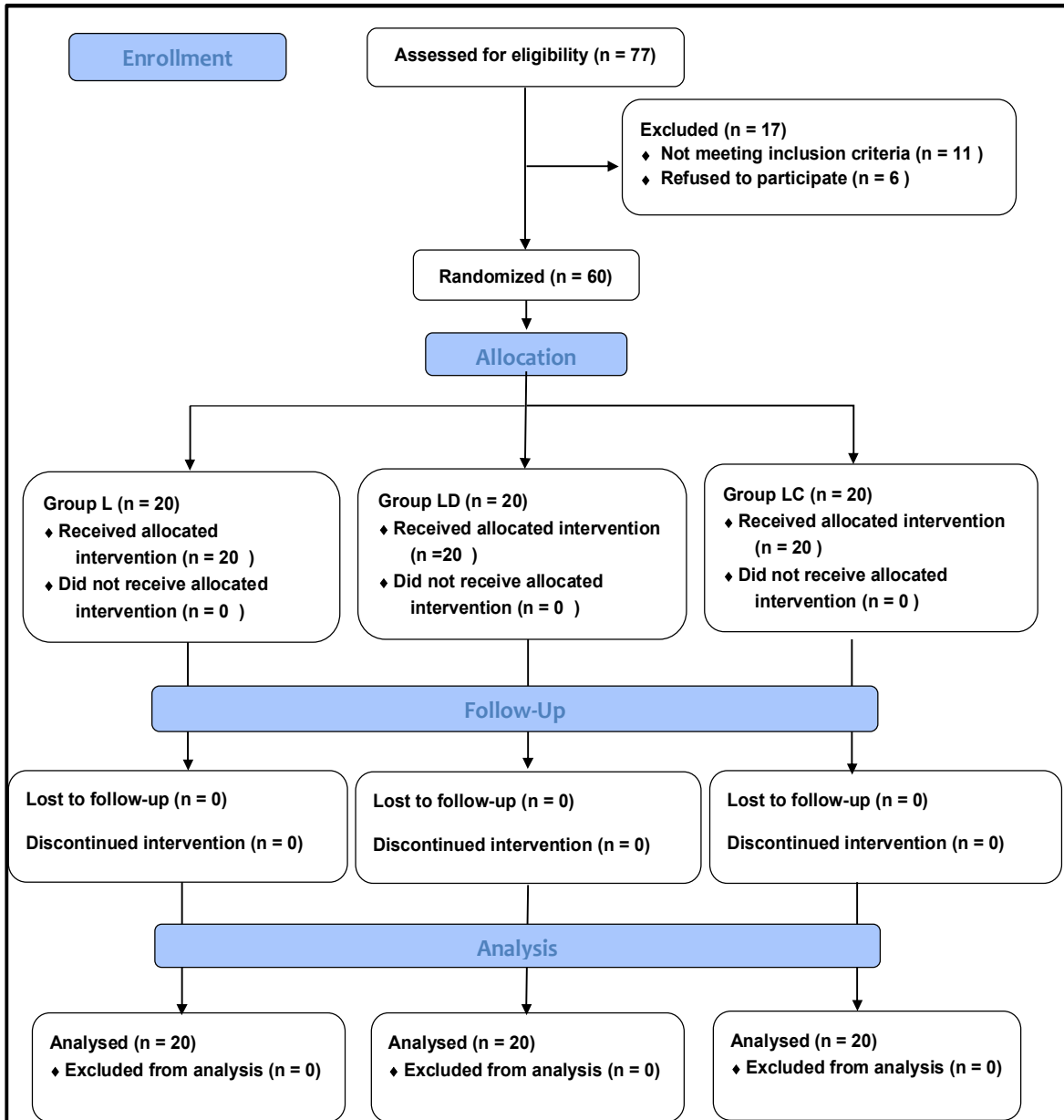


Figure 1: Consort flow diagram

Table 2: Demographic characteristics and duration of surgery

| | | Group L | Group LD | Group LC | p-value |
|-----------------------------------|------------|------------|------------|-------------|---------|
| Age(Years) | | 41.65±15.2 | 47.7±12.7 | 42.9±13.49 | 0.34 |
| BMI (Kg/m²) | | 29.6±3 | 27.7±2.7 | 27.5±3.6 | 0.06 |
| Sex | M | 13 | 12 | 10 | 0.6 |
| | F | 7 | 8 | 10 | |
| | I | 15 | 14 | 16 | 0.7 |
| ASA | II | 3 | 4 | 1 | |
| | III | 2 | 2 | 3 | |
| Duration of surgery (min.) | | 89.4±21.36 | 104.7±33.2 | 103.15±26.7 | 0.16 |

Data are presented as mean±SD except for sex and ASA as numbers and percentage.

Table 3: Onset and duration of sensory and motor block

| | Group L | Group LD | Group LC |
|---|-------------|---------------|----------------|
| Onset of sensory block (min.) | 25.85±2.5 | 20.7±3* | 22.6±2.16* |
| Onset of motor block (min.) | 30.65±2.9 | 25.85±2.45* | 27.75±1.5* |
| Duration of sensory block (min.) | 805.5±40.93 | 1280.8±51.6* | 1263.95±57.88* |
| Duration of motor block (min.) | 724.7±53.69 | 1213.9±46.02* | 1202.35±54.11* |

Data are presented as mean±SD

* P- value significant in comparison with group L

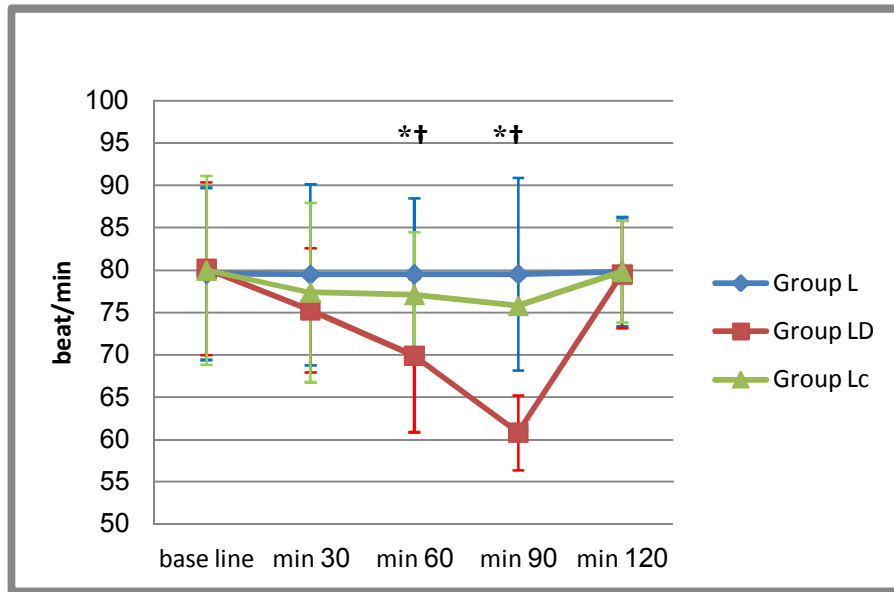


Figure 1: Heart rate

* P- value significant in comparison with group L

† P- value significant between group LD and group LC

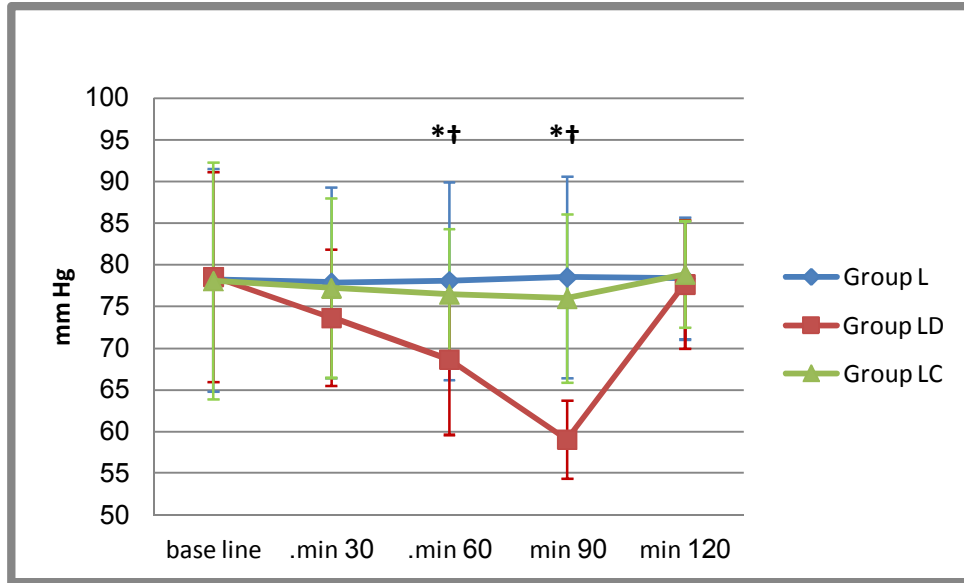


Figure 2:MAP

* P- value significant in comparison with group L

† P- value significant between group LD and group LC

Table 4: Quality of operative conditions between groups

| Grade | Group L | Group LD | Group LC | P- value |
|-------|---------|----------|----------|----------|
| VI | 5(25%) | 16(80%) | 8(40%) | 0.001* |
| III | 14(70%) | 4(20%) | 12(60%) | 0.003* |
| II | 1(5%) | 0 | 0 | 0.3 |
| I | 0 | 0 | 0 | |

4. Discussion:

The results of the present study demonstrated that Adding 1 µ/kg dexmedetomidine or clonidine to 20 ml of 0.5% levobupivacaine reduced the onset and increased the duration of sensory and motor block and improves the quality of operative conditions.

Clonidine is a selective α2adrenergic agonist with some α1agonist property. In clinical studies (1, 2, and 7), the addition of clonidine to local anesthetic improved peripheral nerve blocks by reducing the onset time, improving the efficacy of the block during surgery and extending postoperative analgesia. In various experimental studies, dexmedetomidine had been reported to enhance sensory and motor blockade along with increased duration of analgesia when it added to local anesthetics solution (8). The beneficial effects of adding dexmedetomidine to local anesthetics for peripheral nerve block procedures have proved to be efficacious in humans(9, 10).

The peripheral effects of α2-adrenoceptor agonist appear to be less obvious because α2-adrenoceptors are not present on the axon of the normal peripheral nerve (11). There have been four proposed mechanisms for the action of α2-adrenoceptoragonist in peripheral nerve blockades. These mechanisms are centrally mediated analgesia, α2B-adrenoceptor

mediated vasoconstrictive effects, attenuation of the inflammatory response, and direct action on a peripheral nerve(12).

In our study we found that onset of sensory and motor block was faster with the addition of clonidine and dexmedetomidine and it was more rapid onset with dexmedetomidine than with clonidine but this was statistically not significant. Duration of sensory and motor block was prolonged with the addition of clonidine and dexmedetomidine and it was longer with dexmedetomidine than with clonidine but again this was statistically insignificant. Quality of operative conditions was better with dexmedetomidine than with clonidine. These results are similar to Swami *et al.*(2) who added clonidine and dexmedetomidine to bupivacaine in supraclavicular brachial plexus block, however In the present study, theduration of block was longer than Swami *et al*, a possible explanation for that, Swami has used bupivacaine 0.25% instead of bupivacaine 0.5% in our study. However when Helal *et al.*(8), used a total dose of 39 cc bupivacaine 0.5% plus 100 µg dexmedetomidine and was used for both femoral and sciatic nerve block the duration of block was shorter than our study, a possible explanation for that in our study we used a total dose of 2µg/kg dexmedetomidine for both sciatic and femoral nerve

block one of the proposed mechanisms for the action of α_2 -adrenoceptor agonist in peripheral nerve blockades is centrally mediated analgesia (12), Abdallah *et al.*, demonstrates that dexmedetomidine, whether applied perineurally or intravenously, is an effective local anesthetic adjunct capable of selectively prolonging the duration of interscalene brachial plexus analgesia (10). However, this hypothesis needs to be appropriately investigated in the clinical setting.

Alpha 2 agonists are not devoid of side effects, dexmedetomidine when used for IV sedation, it leads to biphasic (low, then high) dose related effect on MAP. It may also lead to bradycardia and has sedative effects (13). In our study we found that MAP and heart rate decreased at 30,60 and 90 minutes after the block the decrease in HR and MAP was more with dexmedetomidine than with clonidine and was statistically significant this may be due to dexmedetomidine has alpha 2/alpha 1 selectivity ratio that is eight times higher than that of clonidine(14).

The long duration of sensory block is desirable as it leads to decrease the need for postoperative analgesia, however prolonged motor block leads to delayed ambulation and risk of falls is reported in patients undergoing lower limb surgeries (15). All patients in the present study received ultrasound-guided standard sciatic nerve block at the sub gluteal region using levobupivacaine 0.5%. It is possible that the use of dexmedetomidine or clonidine in smaller doses with a lower concentration of local anesthetic will be associated with extended duration of sensory block and preserved motor function and less hemodynamic effects. However, this hypothesis needs to be appropriately investigated in the clinical setting. When Beebe *et al.*(16) used bupivacaine 0.125% for continuous femoral nerve block provided adequate postoperative analgesia and did not prevent early ambulation in patients undergoing total knee arthroplasty. And Yao *et al.*(17) reported that the use of ropivacaine 0.2% for single-shot femoral-sciatic nerve block in knee arthroscopy provided satisfactory post-operative analgesia, while preserving the ability of motion. However Maria Bauer *et al.*(18) demonstrated that lowering the concentration of local anesthetic is not an effective component of a strategy to minimize undesired motor weakness during continuous femoral nerve block. In contrast, decreasing local anesthetic concentration at a given infusion rate resulting in a lower total dose will decrease muscle weakness during continuous femoral nerve block, but at the expense of reduced analgesia.

Conclusion:

This study demonstrate that adding dexmedetomidine and clonidine to levobupivacaine

prolongs the duration of sensory and motor block and improves quality for sciatic nerve block.

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