Original Article

Efficacy of dexmedetomidine as an adjuvant in femoral nerve block for post-op pain relief in hip surgery: A prospective randomized double-blind controlled study

Chetna P. Goel, Sameer Desai

Department of Anesthesia, SDM College of Medical Sciences and Hospital, Sattur, Dharwad, Karnataka, India

Abstract

Background and Aims: To determine whether the addition of dexmedetomidine either in peripheral block or via systemic route leads to prolongation of the duration of analgesia is inconclusive. The present study aimed to assess the duration of postoperative analgesia with dexmedetomidine used as an additive with bupivacaine for ultrasound-guided femoral nerve block (FNB) and to compare it with intramuscular dexmedetomidine along with FNB.

Material and Methods: A prospective, double-blind randomized clinical trial involving adult patients undergoing elective hip surgery, performed under subarachnoid block. When sensory block receded to T12 after the surgery, FNB was given for postoperative analgesia. Patients were randomized into three groups; Group A received FNB with 40 mL 0.25% bupivacaine and 0.5 mL saline as IM injection, Group B received FNB with 39.5 mL of 0.25% bupivacaine + 0.5 mL (50 mcg) of dexmedetomidine in the affected limb and 0.5 mL saline IM injection, and Group C received FNB with 40 mL of 0.25% bupivacaine and 0.5 mL (50 mcg) of dexmedetomidine as IM injection. Postoperative pain was assessed and for pain with VAS score >3, intravenous tramadol was given as rescue analgesia. Chi-square test for categorical variables and one-way ANOVA for continuous variables.

Results: The mean duration of analgesia in groups A, B, and C was 671, 676, and 490 min, respectively which was not significant. A 24 h analgesic requirement was also not different between the groups.

Conclusion: The use of dexmedetomidine perineurally or systemically did not prolong the duration of analgesia as compared to bupivacaine alone for femoral nerve block.

Keywords: Bupivacaine, dexmedetomidine, hip surgery, postoperative pain, USG-guided femoral nerve block

Introduction

Hip fracture is one of the most common fractures seen in the elderly, leading to significant morbidity.[1] Hip fractures are painful and therefore, providing good analgesia throughout the perioperative period is very important for patients to gain comfort as well as for early mobilization. Peripheral block not only helps in reducing pain but also limit the postoperative physiologic complications.[2-4] Studies have shown ultrasound-guided femoral nerve block (USG-FNB) does provide effective analgesia for fractured neck of femur, but the main limitation of the USG-FNB is the limited duration of postoperative analgesia when local anesthetics are used alone.[5-12] To prolong the duration of analgesia many additives such as fentanyl, ephedrine, dexamethasone, clonidine, and dexmedetomidine have been studied as an adjuvant along with the local anesthetic blocks.[13] Dexmedetomidine is a new alpha-2-agonist, studies have shown that it's beneficial when used as an additive for peripheral nerve block. Studies

Address for correspondence: Prof. Sameer Desai,
Department of Anesthesia, SDM College of Medical Sciences and Hospital, Sattur, Dharwad, Karnataka, India.
E-mail address sameeranaes@gmail.com

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indicate that perineural dexmedetomidine improves the quality of block, fastens the onset of action, and prolongs the duration of the block.[14-20] However, earlier meta-analysis indicated that prolongation of the duration of block by addition of dexmedetomidine may not be statistically significant.[21] Studies also indicate that the duration of perineural dexmedetomidine is comparable to systemically administered dexmedetomidine along with the block.[22-24] Dexmedetomidine given by the systemic route also leads to prolongation of regional anesthesia.[25] Therefore, whether dexmedetomidine is useful as an adjuvant for the block is still not clear.

Our study aimed to evaluate whether the addition of dexmedetomidine prolongs the duration of analgesia when used along with local anesthetic for USG-FNB and if it prolongs the duration of analgesia, to assess whether dexmedetomidine acts locally at the peripheral nerve or act after systemic absorption. Duration of analgesia was the primary endpoint of this study and analgesic consumption in 24-h duration, number of patients requiring rescue analgesia in the 24-h postoperative period and its side effects were the secondary endpoints of the study.

Material and Methods

This study was a prospective, double-blind, randomized clinical trial conducted after obtaining approval from the institutional ethical committee (Reference Number: SDMIEC: 8062:2016) from November 2016 to October 2018. Patients in the age group of 18–80 years, undergoing elective surgery for fracture femur neck and belonging to ASA I, II, and III were included in this study. Those patients with poly-trauma and head injury, those consuming long-term beta-blocker and steroids were excluded from the study. The patients were explained about the study and informed consent was obtained.

Patients were preoperatively adequately optimized and necessary intraoperative monitoring was performed. Surgery was conducted under spinal anesthesia using 0.5% hyperbaric bupivacaine. The patients did not receive any additional analgesia during the surgery while anxious patients were given intravenous midazolam 1 mg.

At the end of the surgery, when the sensory level of spinal anesthesia receded to T12 then the USG-FNB was performed using the medication as below.

With the patient in the supine position, the skin over the femoral crease disinfected. The procedure was performed using SAMSUNG SONOACER7 Ultrasound machine's linear transducer, with a frequency range of 5–12 MHz. The transducer was positioned to identify the femoral artery and/or nerve. Once the femoral nerve was identified, a 22 G 10 cm needle was inserted in-plane, lateral-to-medial orientation, and advanced towards the femoral nerve. Besides, a needle passage through the fascia iliac was often felt like a "pop" sensation. Once the needle tip was witnessed adjacent to the nerve, after careful aspiration, 40 mL of the study solution was injected around the nerve. The pressure was applied below the injection site for 5 min. The high volume of drug and the distal pressure directs the local anesthetic solution proximally and blocks the lateral cutaneous nerve of the thigh and obturator nerve (three in one block) and provide analgesia for hip surgery.

Patients were then randomized to one of the three groups using a randomization table.

Group A: Patients received USG-FNB with 39.5 mL of 0.25% bupivacaine +0.5 mL of normal saline in the operated side and 0.5 mL of normal saline was given as an intramuscular injection in the opposite gluteal region.

Group B: Patients received USG-FNB with 39.5 mL of 0.25% bupivacaine +0.5 mL (50 mcg) of dexmedetomidine in the affected limb and 0.5 mL of normal saline as an intramuscular injection in the opposite gluteal region.

Group C: Patients received USG-FNB with 39.5 mL of 0.25% bupivacaine +0.5 mL of normal saline in the affected limb and 0.5 mL (50 mcg) of dexmedetomidine was given an intramuscular injection in the opposite gluteal region.

An anesthesiologist loaded the local anesthetic and added in 20 mL syringes and label it as "For block" and prepared a second 2 mL syringe loaded with a drug to be given intramuscularly and label it as "IM." He/she prepared the solutions as per the randomization table and did not participate in the performance of the block or assessment of the patient subsequently. The patients were unaware of the group he/she belongs to; thus, ensuring the double-blinding nature of the study.

Postoperatively, all the patients were monitored in the post-anesthetic care unit for 2 h after the block and in the ward subsequently for 24 h. Patients were assessed in the ward for postoperative pain using a visual analog scale (VAS). If patient complaints of pain VAS >3, it was considered breakthrough pain and was treated with intravenous tramadol 50 mg diluted in normal saline. Time for rescue analgesia was noted. If pain did not subside (VAS >3), then intravenous paracetamol 1 g was given. The total analgesic needed in 24 h was noted. Significant hypotension defined as (mean arterial pressure decreased by 30% compared to baseline was treated with

intravenous injection ephedrine 6 mg and bradycardia (heart rate <45/min) was treated with 0.6 mg of intravenous atropine. Incidence of any adverse effects such as hypotension, bradycardia, and respiratory depression were noted.

The primary endpoint of the study was the duration of analgesia, which was defined as the time from the performance of FNB to the onset of breakthrough pain. The patient's heart rate, blood pressure were monitored every 2nd hourly after the USG-FNB up to 24 h of the postoperative period. Several patients needing rescue analgesia and total doses of analgesics required in a 24-h study period were assessed.

Statistical analysis

An initial pilot study indicated that the mean duration of analgesia was 420 ± 74 min in the control group. So for prolongation of analgesia by an additional 60 min with the 80% power and with an α error of 0.05, 24 patients were required in each group. Considering the possible drop out, we included 25 patients in each group. Data were analyzed using SPSS software version 20 (SPSS Inc., Chicago, IL). Categorical variables such as groups, gender, ASA status, indication for surgery, diagnosis, and analgesics needed or not within 24 h of the block, and several analgesics used in the postoperative period were compared using Chi-square test. Continuous variables such as age, duration of analgesia, duration of surgery, heart rate, and blood pressure were compared using one-way ANOVA. Data were presented by mean ± SD, ratios, and percentages. $P < 0.05$ was considered to be statistically significant.

Results

In our study, we assessed 110 patients, out of which 80 patients who met study criteria were included. Out of 80 patients, 75 were randomized into three groups' containing 25 patients each [Figure 1]. There was no significant difference in the age, sex, ASA status, indication for surgery procedure, and duration of surgery between the study groups [Table 1]. The mean duration of analgesia in the control group was 671.4 ± 529.9 min as compared to 676.7 ± 495.6 min perineural dexmedetomidine, and 490.8 ± 346.1 min with intramuscular dexmedetomidine and FNB, which was statistically not significant [Figure 2]. There was no difference between the groups for several patients needing analgesia and the total doses of analgesic used up to 24 h of the postoperative period [Table 2]. There was no significant difference in postoperative heart rate and blood pressure between the groups. None of the patients in the study group had bradycardia and hypotension requiring treatment or any other significant complication.

Discussion

In the present study, we noted that the mean duration of analgesia in the control group was comparable to patients receiving perineural dexmedetomidine and intramuscular dexmedetomidine along with FNB. Thus, we conclude that the addition of dexmedetomidine did not prolong the duration of analgesia, either when used perineurally or when given by the intramuscular route.

Contrary to our study, most of the studies indicate that perineural dexmedetomidine prolongs the duration of analgesia after the surgeries. Abdulatif *et al*. studied the effects of different doses of perineural dexmedetomidine on the pharmacodynamics profile of FNB in patients undergoing arthroscopic knee surgery.[26] In their study, USG-FNB was performed before general anesthesia using 25 mL of bupivacaine 0.5% combined with normal saline in the control group, and 25 mcg, 50 mcg, or 75 mcg of dexmedetomidine in three treatment groups. The use of the 50 mcg and 75 mcg dose levels of dexmedetomidine were associated with a reduction of the onset time, prolongation of the duration of the block, and prolonged time to the first postoperative request for rescue analgesia. In another study, dexmedetomidine 100 mcg was added to bupivacaine during USG combined femoral and sciatic block for below-knee surgery.[27] They studied the time to the first postoperative analgesic request which was found to be 462.5 ± 54.3 in plain bupivacaine group and 807.7 ± 112.9 in group bupivacaine with dexmedetomidine ($P < 0.01$). A meta-analysis by Vorobeichik regarding the use of dexmedetomidine in the brachial block concluded that perineural dexmedetomidine not only hastened the onset of the block but also led to a prolonged duration of analgesia by at least 63%.[28]

Dexmedetomidine also reduced postoperative oral morphine consumption by 10.2 mg ($P < 0.0001$), improved pain control and enhanced satisfaction. In another meta-analysis by Schnabel, the use of dexmedetomidine perineurally and systemically in the peripheral nerve block increases postoperative analgesia for around 5 h but there were no significant differences in the duration of analgesia between perineural or intravenous dexmedetomidine combined with local anesthetics.[29] Therefore, these studies indicate that the use of dexmedetomidine as an adjuvant for the peripheral nerve block prolongs the duration of analgesia.

Besides, few other studies have shown the addition of dexmedetomidine to local anesthetic did not prolong the duration of postoperative analgesia compared to local anesthetic alone. In 2013, Abdallah conducted a meta-analysis to study the facilitatory effect of dexmedetomidine in peripheral nerve block and compared studies on perineural dexmedetomidine

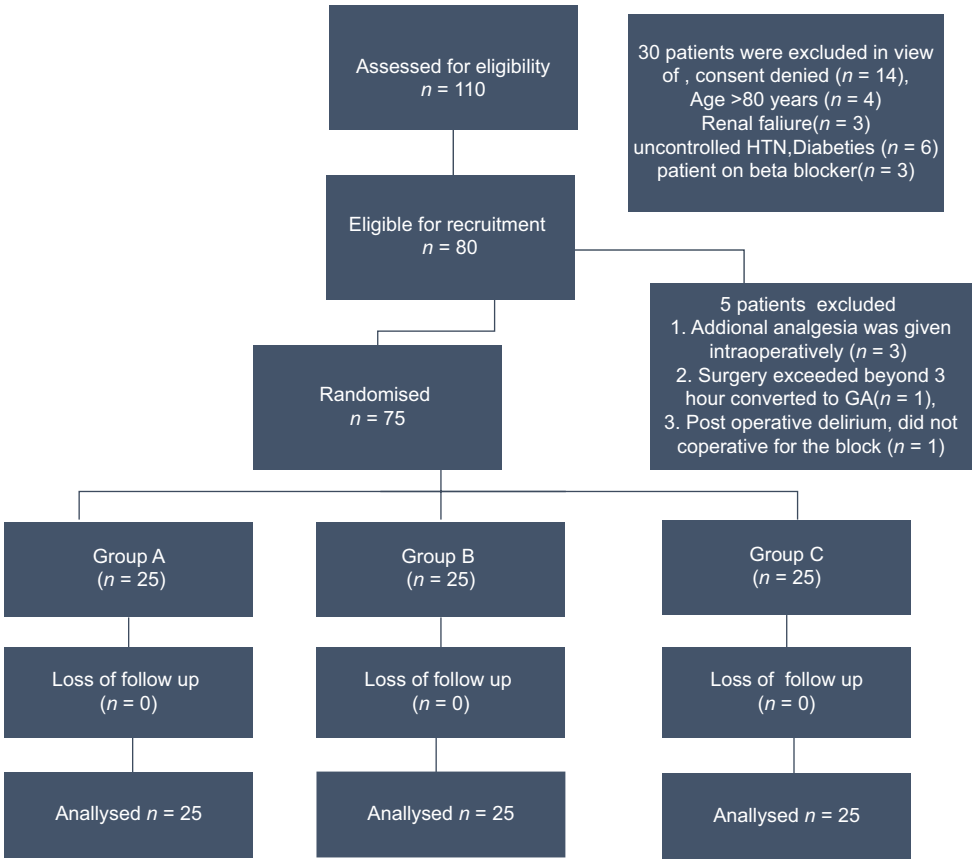

Figure 1: Consort Flow chart

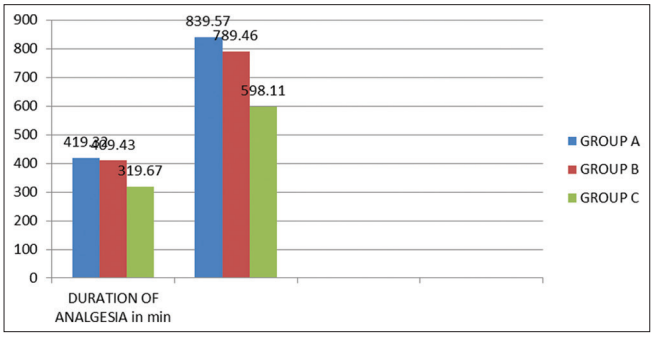

Figure 2: Analgesic duration for three groups

with local anesthetic to local anesthetic alone.[21] They found that sensory block duration with perineural dexmedetomidine was prolonged, with the mean sensory duration by 284 min, but this did not reach statistical significance. Packiasbapathy *et al*., in their study compared two doses of dexmedetomidine, in FNB, for postoperative analgesia after total knee arthroplasty (TKA). They performed FNB using 20 mL of 0.25% bupivacaine with 1 and 2 mcg/kg of dexmedetomidine.[30] They noted significant lower pain scores only with 2 mcg/kg dexmedetomidine group and there was no difference in pain scores or duration of analgesia between 1 mcg/kg dexmedetomidine group and control group. The mean duration of analgesia was significantly longer with 2 mcg/kg dexmedetomidine (6.66 h) compared to 1 mcg/kg dexmedetomidine (5.7 h) and control (4.55 h). They concluded that the use of dexmedetomidine at 2 mcg/kg doses in FNB is superior to 1 mcg/kg for providing analgesia after TKA and 1 mcg/kg dose dexmedetomidine is inadequate for FNBs.

We did not observe any prolonged duration of analgesia by using dexmedetomidine adjuvant. One of the possible reasons for the failure of dexmedetomidine in prolonging the duration of analgesia may be related to the dose of dexmedetomidine used. We used 50 mcg of dexmedetomidine perineurally as recommended by Abdulatif *et al*. in their dose-finding study.[26] However, this is less than 1 mcg/kg. Another study by Packiasbapathy *et al*. indicated that 1 mcg/kg may not be effective in prolonging the duration of analgesia compared to control.[30] Hence, an inadequate dose of dexmedetomidine may be one of the reasons for the lack of prolongation of analgesia compared to the control group in our study.

This variation in the duration of analgesia provided by dexmedetomidine in various surgeries could be attributed to the difference in the location of the block performed, a different type of local anesthetic used, and the difference in the nature of surgeries performed or due to difference in the method of pain evaluation. The femoral nerve is the major

Table 1: Demographic parameters

Data	Group A *n*=25	Group B *n*=25	Group C *n*=25	*P*
Age (years)	64.4±13.6	65.9±9.7	64.36±10.6	0.865
Sex Male/Female	11/14	14/11	8/17	0.232
ASA status I/II/III	10/11/04	11/11/03	07/15/03	0.737
Indication for surgery Intertrochantric fracture/Fracture neck of femur	14/11	13/12	13/12	0.948
Procedure PFN/HRA	14/11	13/12	13/12	0.948
Duration of surgery (min)	105±23.1	104±22.17	92±22.17	0.070

Values presented as mean±SD or absolute numbers. P<0.05 considered as significant

Table 2: Analgesic parameters

Data	Group A	Group B	Group C	*P*
Duration of analgesia (min)	629.4±531.18	599.4±499.5	458.8±351.1	0.363
Number of patients needing rescue analgesics in 24 h needed/not needed	18/07	20/05	23/02	0.189
Number of doses of postoperative analgesics consumed	0.72±0.45	0.84±0.47	1.08±0.5	0.042

Values presented as mean±SD or absolute numbers. P<0.05 considered as significant

sensory supply of the hip joint but the contribution from the lateral cutaneous nerve of thigh, obturator, and sciatic nerve remains significant.[31,32] Even though chances of blocking lateral cutaneous nerve of the thigh and obturator nerve is high by using 40 mL of local anesthetics solution (three in one block), but there are chances that this nerve may be spared despite using a high volume of local anesthetic solution. Since only three in one block were used in our study; the sciatic nerve innervation area will be spared in all cases, which might have contributed to the higher pain scores in all the patients. We also had used high volume i.e., 40 mL of local anesthetics which would have diluted the dexmedetomidine concentration at the block site and reduced its efficacy.

Most of the above studies which indicated the beneficial effect of dexmedetomidine have used ropivacaine rather than bupivacaine 0.25% used in our study.[33,34] It is possible that dexmedetomidine prolonged duration of ropivacaine, which has a slightly shorter duration of action than bupivacaine. Previous studies have shown that clonidine another alpha-2 adrenergic agonist was shown capable of prolonging the duration of shorter-acting local anesthetics (lignocaine and mepivacaine) but, it did not significantly prolong the duration of longer-acting local anesthetics (bupivacaine). In our study, we have used longer-acting anesthetic bupivacaine for FNB. Consequently, prolonged duration of analgesia provided by bupivacaine might have masked the facilitatory action of dexmedetomidine.

We have used intramuscular dexmedetomidine in the systemic group in our study, expecting that the intramuscular preparation will have a longer duration of action whereas all the other studies have used dexmedetomidine infusion intravenously along with the block, which would have a different pharmacokinetic effect.

Publication bias against the studies with negative results may be one of the reasons for the lack of sufficient literature against perineural dexmedetomidine. Hence, further detailed studies are warranted to investigate whether dexmedetomidine is helpful as an adjuvant for peripheral nerve block if so, the mechanisms of its action on peripheral nerve block. Further studies are necessary on the perineural effect-site concentration of dexmedetomidine, which otherwise has a very short duration of action in prolonging the block. The lack of FDA approval for perineural application of dexmedetomidine also raises doubts regarding the need for using a drug which has doubtful benefit in prolonging the analgesia.

Conclusion

We conclude that the addition of dexmedetomidine either perineurally or systemically (intramuscular) did not prolong the duration of analgesia when used along with bupivacaine for FNB after a hip surgery. The requirement of analgesics did not vary among any of the three groups during the 24-h follow-up period. Therefore, adding dexmedetomidine may not be very beneficial for prolonging the duration after FNB for hip surgeries.

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Conflicts of interest
There are no conflicts of interest.

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