RCT on the Effect of Dexmedetomidine as an Adjuvant to Ropivacaine in Ultrasound Guided Fascia Iliaca Block for Postoperative Analgesia Following Hemi-Arthroplasty

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# ABSTRACT

Anaesthesia Section

**Introduction:** Fascia Iliaca Compartment Block (FICB) has been employed for post-operative pain relief after hip surgeries. Dexmedetomidine has been found to prolong effect of peripheral nerve blocks but its effect has not been adequately evaluated for FICB.

Aim: To study the effect of addition of dexmedetomidine for FICB.

**Materials and Methods:** The study was conducted at a tertiary level hospital in a randomised double blinded manner. Sixty adult American Society of Anaesthesiologists (ASA) Physical Class I-III patients of either sex scheduled for elective hemiarthroplasty under spinal anaesthesia, were included in the study after ethics committee approval and written informed consent. Patients were administered ultrasound guided FICB in operation theatre at the end of surgery. Group A patients were administered FICB by injecting 3 mg/kg of ropivacaine whereas, Group B patients received FICB using 3 mg/kg of ropivacaine along with 1  $\mu$ g/kg dexmedetomidine as an adjuvant, making injectate volume of 40 mL in each group by the addition of normal saline. Post-operative pain scores using Visual

Analogue Scale (VAS) and total rescue analgesic consumption were recorded in both the groups. Observation data obtained was tabulated and analysed statistically using Student's t-test and Chi-square test. All statistical calculations were done using SPSS (Statistical Package for the Social Science) 21 version statistical program for Microsoft Windows and p-value less than 0.05 was considered to be significant.

**Results:** Both groups were similar in their demographical profile and baseline haemodynamic parameters. Mean time of administration of first rescue analgesic was significantly earlier in group A at  $275.29\pm226.31$  minutes as compared to  $465.8\pm325.56$  minutes in group B. Similarly, group A patients needed rescue analgesic more frequently and mean total tramadol consumption was significantly higher in group A at  $207.24\pm45.17$  mg as compared to  $145.56\pm48.31$  mg in group B. There was no difference in the incidence of adverse effects between the two groups (p=0.072).

**Conclusion:** The addition of dexmedetomidine to ropivacaine significantly prolongs the duration of analgesic effect of FICB without any adverse effects.

Keywords: Hemi-arthroplasty pain, Hip surgery, Nerve block, Pain, Subarachnoid block

# **INTRODUCTION**

Patients with hip fractures generally belong to advanced age and often suffer from significant co-morbidities [1]. Hip fractures are painful and appropriate pain relief is imperative since inadequate pain relief can result in adverse outcomes like increased incidence of adverse cardiovascular events and delirium [2].

However, conventional pain treatment modalities (systemic opioids, non-steroidal anti-inflammatory drugs) have undesirable adverseeffects, many of those being particularly deleterious in elderly patients. [2-4]. This makes the role of multimodal analgesia all the more relevant for patients suffering from hip fractures. Ultrasound guided Fascia Iliaca Compartment Block (FICB) has been found to be effective, safe and reproducible technique for management of post-operative pain following hip surgeries [5]. The effect of single injection of FICB is, however limited by the duration of effect of block. Dexmedetomidine, an  $\alpha$ -2 agonist, has been shown to prolong the duration of peripheral nerve blocks without any significant adverse effects [6,7]. Similarly, intravenous (IV) infusion of dexmedetomidine has successfully been used along with FICB [8].

There is still dearth of literature on the efficacy of dexmedetomidine for FICB, as only a few studies have evaluated this effect [9-11]. The present study was, therefore designed to study the effect of addition of dexmedetomidine to local anaesthetic agent ropivacaine in FICB for patients undergoing hip surgeries under subarachnoid block. The primary aim of the study was to evaluate whether addition of dexmedetomidine to Ropivacaine for Fascia iliaca block results in prolongation of effects of block with secondary aim of looking for any adverse effects.

## MATERIALS AND METHODS

The study was conducted in a prospective randomised double blinded manner in a tertiary level hospital after approval from hospital ethics committee (DMCH/R&D/2014/44). Study was conducted from 15<sup>th</sup> January 2013 to 30<sup>th</sup> June 2015. The sample size was calculated by post hoc power analysis conducted using the software package, G power [12]. Based on a previous study by El-Rahmawy GF et al., using reduced analgesic requirement parameter, with an alpha level of p<0.05 and beta of 0.20, assuming 10% error due to chance, a sample size of 26 patients in each of two groups was required for a power of 80% [10]. However, 30 patients were included in each group to account for any possible exclusions or drop outs.

Sixty adult American Society of Anaesthesiologists (ASA) class I-III patients of either sex scheduled for elective hemi-arthroplasty under Subarachnoid Block (SAB) were included in the study after written informed consent. Patients with refusal or failure of SAB, uncooperative patients or patients with communication difficulties, peripheral neuropathies or myopathies on the operative limb, severe liver and kidney dysfunction, history of allergy to any drug being used in study, vascular disease of limbs and history of chronic pain, were excluded from the study. All patients underwent a thorough pre-anaesthetic check up comprising of history, general physical and systemic examination a day prior to surgery. As an institutional protocol, all patients underwent investigations which included complete haemogram, bleeding time, clotting time, prothrombin time index, urine routine examination, Fasting blood sugar, Electrocardiography, X-ray chest and other investigations if indicated.

During the pre anaesthesia interview, patients were introduced to and instructed about Visual Analogue Scale (VAS) as a tool for measuring post-operative pain. VAS scale which consists of a 10 cm line, having markings at 1 cm each, was shown and the patients were explained that they have to bring the slider on the scale on to the point that they feel represents their state of pain with '0' mark corresponding to no pain and '10' mark representing worst imaginable pain. Patients were also educated on the post-operative pain relief plan and informed about their right to request rescue analgesic if needed at any time during the study period.

All the patients were kept nil orally for at least 6-8 hours prior to surgery as per ASA fasting guidelines. Premedication in the form of Tab Alprazolam 0.25 mg orally at night before surgery and 0.25 mg at 6 AM on the day of surgery with a sip of water was given to all the patients. On the day of surgery, after shifting the patient to operation theatre, monitoring of Heart Rate (HR), Non-Invasive Blood Pressure (NIBP), Respiratory Rate (RR), peripheral oxygen saturation (SpO<sub>a</sub>) and Electrocardiogram (ECG) was done. After achieving an intravenous access, patients were preloaded with 0.9% normal saline 10 mL/kg body weight over 20 minutes. Then, under all aseptic precautions, spinal anaesthesia (2.6 mL of plain 0.5% heavy bupivacaine) was given in lateral position. Patients were monitored continuously for HR, RR, SpO<sub>2</sub>, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP). These vital parameters were recorded every 5 minutes by the anaesthetist managing the case. Surgery was allowed to proceed after achieving successful spinal block, defined as absence of pin prick sensation at or above T10 dermatomal level. Patients were randomly allocated to one of the two groups of 30 patients using computer generated random numbers, kept in sealed envelopes which were opened at the end of study. The drug to be administered was prepared by a blinded anaesthetist, not involved in the administration of the FICB or observations. After the completion of procedure, patients were administered FICB under ultrasound guidance by a single trained anaesthetist.

Group A patients were administered FICB by injecting 3 mg/kg of ropivacaine whereas, Group B Patients received FICB using 3 mg/kg of ropivacaine along with 1  $\mu$ g/kg Dexmedetomidine as an adjuvant [11]. The respective drug combinations were made to a fixed volume of 40 mL of normal saline by a person not involved in the study and marked with a coded label to maintain double blind nature of the study.

With patient lying supine and leg extended, area from umbilicus to mid thigh was cleaned with 10% povidone iodine and draped with sterile sheets. A line drawn between the anterior-superior iliac supine and the pubic tubercle was divided into 3 equal parts and labelled with a marking pen. Using linear ultrasound transducer, iliacus muscle, iliacus fascia, femoral nerve, femoral artery and femoral vein were identified. Ultrasound transducer was then moved laterally along the fascia iliaca to its junction at the Sartorius muscle.

The target injection site was determined at the junction of the lateral and middle thirds of the line connecting the anterior-superior iliac spine and the pubic tubercle at the intersection of the iliacus and Sartorius muscles. A 21 gauze, 10 cm needle (stimuplex) was inserted in-plane from lateral to medial at level of the femoral crease to cross the fascia iliaca at the junction of the Sartorius and iliacus muscles. An injection was considered successful when the spread of Local Anaesthesia (LA) reached the femoral nerve medially and at least three cm laterally from the point of injection beneath the fascia iliaca towards the anterior-superior iliac spine. If the medial-lateral spread of LA was not accomplished with a single injection, additional injections were made. Time of administration of FICB was labelled as 0 minutes and patients shifted to Post Anaesthesia Care Unit (PACU). The observations in PACU were made by an independent observer, blinded to the group allocation of the patient. On arrival to PACU, vital parameters and VAS were monitored at 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 12 hours, 16 hours, 20 hours and 24 hours.

Patients were administered rescue analgesia in the form of Inj Tramadol 50 mg IV, whenever they complained of pain or requested analgesia or reported VAS ≥4. Injection tramadol IV could be repeated after 15 minutes if patient still complained of pain, subject to a maximum of 100 mg in 4 hours or 300 mg in 24 hours. If these dose thresholds were breached and patients still complained of pain, such patients were excluded and treated according to discretion of the anaesthetist managing the patient. Time of first administration of rescue analgesic and total analgesic consumption in 24 hours was noted. Patients were also observed for any adverse effects like nausea and vomiting, skin rash, tachycardia (defined as HR > 100/min), bradycardia (defined as HR < 50/min), Hypotension (SBP < 90 mmHg), Hypoxemia (SpO<sub>2</sub> <90%), sedation, or any other side effect, if any, during 24 hours post-operative period. Sedation was assessed using Ramsay sedation scale [13].

## STATISTICAL ANALYSIS

Data was described in terms of mean ±standard deviation (±SD). Comparison of quantitative variables between the study groups was done using Student's t-test. Chi square ( $\chi^2$ ) test was performed and Fisher's-exact test was used when the expected frequency was less than 5. A probability value (p-value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

### RESULTS

All patients entering the study were analysed and none of the patients were excluded [Table/Fig-1]. Both the groups were demographically similar with respect to mean age, weight, height and sex and ASA class distribution [Table/Fig-2].



The mean baseline heart rates were comparable between group A and group B (p-value=0.185). Later on, heart rate was higher in group A as compared to group B at most time intervals, though the difference was statistically insignificant. Mean heart rate however, was significantly higher in group A at 30 minute, 1 hour, 2 hour and 4 hour after administration of FICB [Table/Fig-3].

The mean baseline MAP in group A and group B was statistically similar at 100.60±10.77 and 95.80±16.59 mmHg respectively

	Group A (n=30)	Group B (n=30)	p-value	
Mean age (years)	57.25±14.345	65.15±18.328	0.137	
Sex distribution Male: Female	9:11	9:11	1.000	
Mean weight (kg)	69.30±15.124	64.00±13.338	0.247	
Mean height (cm)	165.00±8.944	162.90±6.719	0.406	
BMI	25.15±3.686	23.85±4.477	0.322	
ASA grade I:II:III	5:13:2	3:13:4	0.558	
Duration of surgery (min)	104.17±24.38	116.38±19.59	0.550	
[Table/Fig-2]: Demographic profile				





(p=0.285). With time, MAP was higher in group A as compared to group B, though the difference was statistically insignificant. However, MAP was statistically significantly greater in group A at 6<sup>th</sup> hour and 16<sup>th</sup> hour post FICB [Table/Fig-4].



Mean baseline VAS was zero in both the groups and mean VAS remained higher in group A at all time intervals though the difference was statistically not significant (p=0.770) [Table/Fig-5].

After FICB administration, mean duration of time when patient complained of pain in group A was  $275.29\pm226.31$  minutes while in group B, it was  $465.8\pm325.56$  minutes and the difference was statistically significant (p=0.036). Mean VAS at that time was  $5.59\pm1.06$  in group A while in group B, it was  $5.71\pm0.77$ . The difference in mean VAS when patient complained of pain which was statistically not significant (p=0.716) [Table/Fig-6].



	Group A (n=30)	Group B (n=30)	p-value	
Median number of rescue analgesics given along with Interquarantile Range (IQR)	3 (2-3.5)	2 (1-3)	0.015	
Mean total analgesic consumption in 24 hours	207.24±45.17	145.56±48.31	0.015	
Mean time of administration of first analgesic (min)	275.29±226.31	465.8±325.56	0.036	
VAS at time of first rescue analgesic	5.59±1.064	5.71±0.772	0.716	
[Table/Fig-6]: Mean rescue analgesic consumtion.				

Similarly, patients in group A required rescue analgesia more frequently in the initial 24 hours as compared to group B and this difference was statistically significant [Table/Fig-6]. The median number of times along with Interquartile range when rescue analgesia was required in group A was 3 (IQR 2-3.5) whereas in group B, it was 2 (IQR 1-3). (p=0.015) [Table/Fig-6]. Mean total analgesic consumption in 24 hours was also significantly less in group B at 145.56 ±48.31 mg as compared to 207.24±45.17 mg in group A (p=0.015) [Table/Fig-6].

None of the patients in either of the groups had adverse effects such as hypotension, skin rash, tachycardia, bradycardia or hypoxemia. Three patients in group B had sedation score of 4, while all patients in Group A had sedation scores of 3 or less. However, the difference in sedation scores was statistically not significant. (p=0.072).

### DISCUSSION

Fascia iliaca block is a safe, reproducible and effective technique for pain management [14]. The benefits of adequate analgesia employing FICB as one of the modalities includes improved cognition, better patient satisfaction and reduction of complications [11]. FICB blocks have been found to be more effective than femoral nerve blocks in alleviating post operative pain after hip surgeries [15,16]. Ropivacaine was chosen as local anaesthetic agent as it has significantly less neurotoxic and cardiotoxic potential compared to bupivacaine and is also longer acting compared to lignocaine. Its vasoconstrictive property makes it less toxic by preventing sharp increase in plasma concentration of the local anaesthetic [17]. Dexmedetomidine, used as an adjunct to ropivacaine for FICB in our study is a highly selective central alpha-2 agonist and has sedative, anxiolytic and analgesic properties [18,19]. IV infusion of dexmedetomidine has been found to reduce pain scores when used in conjunction with FICB [8]. Various studies conducted in the past have reported that addition of dexmedetomidine as an adjuvant to ropivacaine for peripheral nerve block prolonged the duration of analgesia and time to first rescue analgesia with improved quality of block [6,20]. In our study, none of the patients were excluded and both the groups were statistically comparable with respect to age, weight and ASA grade. It was observed that patients in group B, received rescue analgesic after a mean of 465.8 minutes as compared to 275.29 minutes in group A. This implies that group B patients required analgesia for a mean 190.51 minutes later as compared to group A and this difference was statistically significant. Our results were similar to the findings of Lin YN et al., who also reported prolongation of the duration of sensory block by mean of 1 hour after addition of dexmedetomidine to ropivacaine for cervical plexus block [6]. In another study, by Fritsch G et al., the median duration of sensory block was prolonged by 4 hours in dexmedetomidine group when used in interscalene block [20].

Rescue analgesia was required less often in group B, thus indicating that dexmedetomidine reduces analgesic requirement. Similarly, mean total analgesic consumption in 24 hours was significantly less in group B (145.56±48.31 mg) than in group A patients (207.24±45.17 mg), thus implying that addition of dexmedetomidine to ropivacaine in FICB has opioid sparing effect. El-Rahmawy GF et al., also observed that time to administration of rescue was significantly later in the patients who received dexmedetomidine in local anaesthetic for FICB. In addition, dexmedetomidine group had significantly lower VAS scores and decreased rescue analgesic consumption [10].

Heart rate was higher in group A than in group B and the difference was statistically significant at 30 minute, 1<sup>st</sup> hour, 2<sup>nd</sup> hour, 4<sup>th</sup> hour post FICB. Similarly, MAP was lower in group B than group A and the difference was statistically significant at 6<sup>th</sup> hour and 16<sup>th</sup> hour post FICB. Our findings of greater haemodynamic stability in group B are similar to the finding by Lin YN et al., where MAP level and HR level were significantly lower in patients receiving ropivacaine and dexmedetomidine as compared to patients who received ropivacaine alone [6]. EL-Rahmawy GF et al., also reported lower HR and MAP in the dexmedetomidine group [10]. The reason for greater haemodynamic stability may be attributed to be due to better pain relief in Group B. The mean VAS was similar in both the groups and this could be explained by the fact that whenever, patients reported VAS  $\geq$ 4, a dose of rescue analgesic was administered. The possible mechanism by which dexmedetomidine exerts its effect include its peripheral and central actions. Peripherally,  $\alpha$ -2 agonists produce analgesia by reducing release of norepinephrine and causing  $\alpha$ -2 receptor-independent inhibitory effects on nerve fibre action potentials. Centrally,  $\alpha$ -2 agonists produce analgesia and sedation by inhibiting substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activating  $\alpha 2$  adrenoceptors in the locus coeruleus [21,22]. Therefore, addition of dexmedetomidine as an adjuvant to ropivacaine for post-operative pain relief in FICB block prolonged the duration of block and improved its quality. In group B, sedation was observed in three patients, which might have occurred from absorption of dexmedetomidine from the local site while there were no side effects seen in group where only ropivacaine was used for FICB. The efficacy of dexmedetomidine as an adjuvant for peripheral neuraxial blocks like brachial plexus block has been reported by various studies [6,7,20]. The results of present study suggest that the addition of dexmedetomidine in a dose of 1 mcg/kg to ropivacaine is effective in prolonging the effect of FICB in patients undergoing hemiarthroplasty, without any significant adverse effects.

## LIMITATION

The limitation of our study which is worth mentioning is that only a single dose of dexmedetomidine as an adjuvant for FICB was evaluated and the patients operated upon by different surgeons were included, thus introducing possibilities of differences in tissue handling and resulting pain. Further dose-response studies may be planned to find out an optimal dose for its use as an adjuvant in FICB.

# CONCLUSION

The addition of dexmedetomidine to ropivacaine for FICB block significantly prolongs the effect of block and decreases total dose of rescue analgesic consumption in patients undergoing hemiarthroplasty.

#### REFERENCES

 Foss NB, Kehlet H. Mortality analysis in hip fracture patients: Implications for design of future outcome trials. Br J Anaesth. 2005;94:24-29.

- [2] Lin YT, Lan KM, Wang LK, Chu CC, Wu SZ, Chang CY, et al. Incidence, risk factors, and phenomenological characteristics of post-operative delirium in patients receiving intravenous patient-controlled analgesia: A prospective cohort study. Neuropsychiatr Dis Treat. 2016;12:3205-12.
- [3] Buvanendran A, Kroin JS. Multimodal analgesia for controlling acute postoperative pain. Curr Opin Anaesthesiol. 2009;22:588-93.
- [4] Vadivelu N, Mitra S, Narayan D. Recent advances in post-operative pain management. Yale J Biol Med. 2010;83:11-25.
- [5] Castillón P, Veloso M, Gómez O, Salvador J, Bartra A, Anglés F. Fascia iliaca block for pain control in hip fracture patients. Rev Esp Cir Ortop Traumatol. 2017;61(6):383-89.
- [6] Lin YN, Li Q, Yang RM, Mao ZX, Liu JC. Addition of dexmedetomidine to ropivacaine improves cervical plexus block. Acta Anaesthesiol Taiwan. 2013;51:63-66.
- [7] Rancourt MP, Albert NT, Cote M, Létourneau DR, Bernard PM. Posterior tibial nerve sensory blockade duration prolonged by adding dexmedetomidine to ropivacaine. Anesth Analg. 2012;115:958-62.
- [8] Kunisawa T, Ota M, Suzuki A, Takahata O, Iwasaki H. Combination of high dose dexmedetomidine sedation and fascia iliaca compartment block for hip fracture surgery. J Clin Anesth. 2010;22(3):196-200.
- [9] Bang S, Chung J, Jeong J, Bak H, Kim D. Efficacy of ultrasound-guided fascia iliaca compartment block after hip hemiarthroplasty: A prospective, randomized trial. Medicine (Baltimore). 2016;95(39):e5018. doi:10.1097/MD.00000000005018.
- [10] EI-Rahmawy GF, Hayes SMS. Efficacy of dexmedetomidine addition to bupivacaine on the quality of blind fascia iliaca compartment block in children undergoing femur fracture surgery. Egypt J Anaesth. 2013;29:137-42.
- [11] Hua X, Hu Y, Chen D, Xiao Y, Luo L. Efficacy and safety of ultrasound-guided fascia iliaca compartment block using dexmedetomidine combined with ropivacaine in aged patients undergoing hip replacement. Int J Clin Exp Med. 2017;10(12):16484-91.
- [12] Faul F, Erdfelder E. G power. A priori, post hoc, and compromise power analyses (or MS-DOS [Computer program]. Germany, Bonn: Bonn University; 1992.
- [13] Rasheed AM, Amirah MF, Abdallah M, Parameaswari PJ, Issa M, Alharthy A. Ramsay sedation scale and richmond agitation sedation scale: A cross-sectional study. Dimens Crit Care Nurs. 2019;38(2):90-95.
- [14] Odo PM, Chris Sterl, Wilkinson I, Sage F. Effect of admission fascia iliaca compartment blocks on post-operative abbreviated mental scores in elderly fractured neck of femur patients : A retrospective cohort study. BMC Anesthesiol. 2017;17(1):2-8.
- [15] Lako SJ, Steegers MA, Van E, Gardeniers J, Staals LM, Van G. Incisional continuous fascia iliaca block provides more effective pain relief and fewer side effects than opioids after pelvic osteotomy in children. Anesth Analg. 2009;109:1799-1803.
- [16] McMeniman TJ, McMeniman PJ, Myers PT, Hayes DA, Cavdarski A, Wong MS, et al. Brisbane Orthopaedic and Sports Medicine Centre Writing Committee. Femoral nerve block vs fascia iliaca block for total knee arthroplasty post-operative pain control: A prospective, randomized controlled trial. J Arthroplasty. 2010;25(8):1246-49.
- [17] Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth. 2006;53:646-52.
- [18] Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. BUMC Proceedings. 2001;14:13-21.
- [19] Murthy TVSP, Singh R. Alpha 2 adrenoceptor agonist- Dexmedetomidine role in anaesthesia and intensive care: A clinical review. J Anaesth Clin Pharmacol. 2009;25:267-72.
- [20] Fritsch G, Danninger T, Allerberger K, Tsodikov A, Felder TK, Kapeller M, et al. Dexmedetomidine added to ropivacaine extends the duration of interscalene brachial plexus blocks for elective shoulder surgery when compared with ropivacaine alone: A single-center, prospective, triple-blind, randomized controlled trial. Reg Anesth Pain Med. 2014;39:37-47.
- [21] Eisnach JC, De Kock M, Klimscha W. Alpha-2-adrenergic agonists for regional anesthesia. A clinical review of clonidine. Anesthesiology. 1996;85:655-74.
- [22] Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into locus coeruleus produces antinociception. Anesthesiology. 1996;84:873-81.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: Feb 10, 2019 Date of Peer Review: Mar 07, 2019 Date of Acceptance: Apr 18, 2019 Date of Publishing: Jun 01, 2019