Postoperative Analgesic Effect of Morphine added to Ropivacaine for Fascia Iliaca Compartment Block following Femoral Fracture Surgeries: A Randomized Controlled Trial

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Citation

Background: Fascia iliaca compartment block (FICB) following femoral fracture surgery provides effective analgesia. Reports of morphine added to ropivacaine for peripheral nerve blocks are limited. We designed this study to investigate the effects of morphine as an adjuvant to ropivacaine in FICB for femoral fracture surgery.

Methods: Seventy patients undergoing spinal anaesthesia for femoral fracture surgery were randomized to undergo ultrasound aided FICB with ropivacaine alone (n = 35) or in combination with morphine (n = 35). FICB was performed postoperatively with 20 ml of 0.375% ropivacaine plus 2 ml normal saline or 20 ml of 0.375% ropivacaine plus 2 ml (1 mg/ ml) morphine. Primary outcome parameter was the duration of analgesia. Secondary outcome parameters were total doses of rescue analgesics, sedation scores, Numeric Rating Scale (NRS) scores for pain and patient satisfaction.

Results: Demographic data were similar between the two groups. Patients receiving morphine adjuvant had longer duration of postoperative analgesia (541 ± 167 vs 634 ± 164 mins, p = 0.01; Mean difference -92.71; 95% CI: -171.95 − -13.47). Requirement of postoperative rescue analgesics for the first 24h was significantly lesser (tramadol 77 ± 25 vs 62 ± 22 mg, p = 0.01; Mean difference 14.28 ;95% CI: 2.95 − 25.63) in patients receiving morphine adjuvant. Postoperative NRS scores and sedation scores were comparable between the two groups.

Conclusion: Morphine as an adjuvant to ropivacaine for FICB significantly prolongs the duration of postoperative analgesia.

Keywords: FICB; Morphine; Postoperative analgesia; Ropivacaine; Ultrasonography

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Declarations

Femoral fractures are common and associated with a higher risk of perioperative morbidity including pain [1]. Pain has many undesirable effects on several physiological processes [2]. Increased catecholamine release leading to tachycardia and hypertension is detrimental [3]. Pain negatively affects the immune system and delays the normal process of healing [4]. These facts highlight the need for fast and effective treatment of pain in patients with femur fractures in perioperative period. Oral analgesics, parenteral analgesics or regional analgesia techniques can be used for pain management. Clinicians are frequently reluctant to administer adequate parenteral analgesia to these patients for fear of worsening intercurrent disease or of precipitating adverse effects [5].

The fascia iliaca compartment block (FICB) has been proven to be a simple, inexpensive, and effective method of prehospital analgesia for femoral shaft fracture [6, 7]. Compared to bupivacaine, ropivacaine, an enantiomer of bupivacaine produces more intense analgesia with lesser motor blockade, cardiac or neurotoxic effects [8]. The role of peripheral opioids for analgesia is still controversial. Although some studies have reported no peripheral effects of opioids, other studies have suggested the presence of opioid receptors on the sensory neurons, which are transported into neuronal process and are detectable on peripheral sensory nerve terminals [9 - 12]. Some reports even suggest that systemically injected opioids may act through peripheral receptors [13, 14]. Morphine injected perineurally in patients with chronic pain has significantly longer duration of action than that of systemically administered morphine [15 - 17]. It is not illogical to speculate that morphine administered as adjuvant to local anaesthetic may enhance analgesia. Since the reports of its use in FICB are limited, we designed this prospective, randomized double blinded study to investigate the analgesic effects of morphine as an adjuvant to ropivacaine on FICB. The primary objective of this study was to assess the duration of postoperative analgesic effect of morphine as an adjunct to ropivacaine in a single shot ultrasound (USG) guided FICB in patients undergoing open reduction and internal fixation for fracture femur under spinal anaesthesia. Secondary objectives were to compare the requirement of rescue analgesics, NRS score and MRSS score between those who received ropivacaine alone and those who received ropivacaine with morphine adjuvant.

METHODS

The study was carried out from April 2017 to December 2017 in B. P. Koirala Institute of Health Sciences, a tertiary care hospital of eastern Nepal. Ethical clearance was obtained from the Institutional Review Committee. Informed written consent was obtained from all the patients. All consecutive patients of 18 - 65 years of age with ASA physical status I and II, undergoing elective femur surgery under spinal anesthesia were included. Patients not willing to participate, patients with other painful co-morbidities (neuropathies), allergy, any contraindication to study medication, psychiatric disorder, coagulopathy, infection at the site of the block, or use of other modes of anesthesia or analgesia besides spinal anesthesia were excluded.

A total of 70 patients were enrolled. Based on the computer-generated random number sequence, patients were assigned to either ropivacaine alone group or ropivacaine with morphine adjuvant group. Ropivacaine alone group patients received ropivacaine 0.375% 20 ml with normal saline 2 ml and ropivacaine with morphine adjuvant group patients received ropivacaine 0.375% 20 ml with morphine (1 mg/ml) 2 ml for FICB. Ultrasound guidance was used for location of the site and injection of the drug. Sequentially numbered opaque white envelopes were used with study medication mentioned inside. The investigator (PB) observing and recording the outcome parameter was unaware regarding the medication group. At the same time, participants were unaware of the nature of the study drug used. The group allocation was revealed only after analysis of the data.

All the patients were pre-medicated with tab lorazepam 2 mg given orally the night before and in the morning of surgery. During the preoperative assessment, patients were familiarized and explained about Numeric Rating Scale (NRS) for pain in simple understandable language. On arrival to operation theatre, venous access was established (if not in situ) on the dorsum of non-dominant hand with 18 G intravenous (IV) cannula and lactated Ringer's solution was infused.

In the operating table, electrocardiogram, heart rate, oxygen saturation and non-invasive blood pressure were monitored. Spinal anesthesia was administered in sitting position using 3 ml 0.5% hyperbaric bupivacaine. The level of sensory block was checked using sterile needle. Motor block was assessed by grading the motor power of the muscles (0 to 5). After the completion of surgery and application of dressing on the surgi-

cal wound the patients were positioned supine. The skin was disinfected and the transducer of Sonosite M-Turbo ultrasound machine with linear transducer (6-14 MHz) was positioned over the inguinal crease to identify the femoral artery, iliopsoas muscle and fascia iliaca. The transducer was moved laterally until the sartorius muscle was identified. After a skin wheal was made, the needle was inserted in-plane. As the needle eventually pierced through the fascia, a pop was felt and the fascia was seen to "snap" back on the ultrasound image. The block was performed by injecting the drug in aliquots
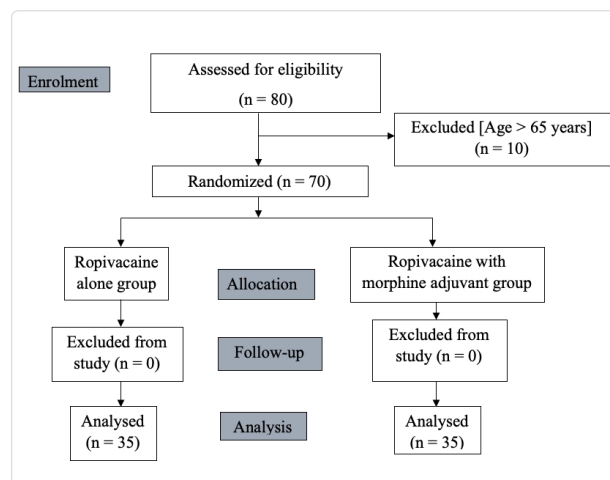

Figure 1: Consort flow diagram of the study

of 5ml alternating with aspiration. This time point was considered as zero hour for our study. The block was performed by an experienced anesthesiologist not involved in the study and anaesthetic care of the patient. Sedation score and NRS for pain were recorded at 0 h, 4 h, 8 h, 12 h and 24 h postoperatively. Sedation was assessed using Modified Ramsay's sedation scale (MRSS) [18].

Patients were given injection paracetamol 15 mg/kg, (not exceeding 1 gm) after the surgery and then every six hours postoperatively. Inj. tramadol 50 mg IV was administered slowly when NRS was more than 3 (rescue analgesia). Inj. ondansetron 4 mg IV was administered at the same time to offset nausea and vomiting caused by tramadol. The time between the block and the first analgesic request was recorded as the duration of analgesia. Total dose of rescue analgesic (tramadol) consumed in the postoperative period was recorded. In the post-operative period in the ward, acceptance of the procedure and satisfaction level was assessed using a 5- point Likert scale (a psychometric response scale

in which responders specify their level of agreement to a statement typically in five points: strongly disagree; disagree; neither agree nor disagree; agree; strongly agree) [19].

For calculation of sample size, we conducted a pilot study. It showed a mean duration of analgesia ± standard deviation of 396 ± 135 min in ropivacaine alone group and 516 ± 137 min in ropivacaine with morphine adjuvant group. Using these values, with clinically significant mean difference of 120 min and keeping confidence interval of 95% and power of 0.8, a minimum of 32 patients were required per group. Adding 10% for drop out and data loss, a sample size of 35 was taken in each group.

Data was entered in excel, filtered, coded and further analysed using SPSS version 11.5. Mann-Whitney U test was used to compare the nonparametric variables and non-normally distributed parametric variables.

Fischer Exact test was used to compare variables when the expected values in any of the cells of a contingency table were below 5. Probability value was considered significant when $p < 0.05$.

RESULTS

Out of 80 patients accessed for eligibility, 70 patients fulfilled the inclusion criteria. All the 70 patients completed the study (**Fig. 1**). The baseline patient characteristics were comparable between the groups. The mean duration of analgesia with FICB was significantly higher in ropivacaine with morphine adjuvant group compared to ropivacaine alone group (Mean difference -92.71 minutes; 95% CI: -171.95 − -13.47). The mean dosage of rescue analgesics required in first postoperative 24 h was significantly lower in ropivacaine with morphine adjuvant group compared to ropivacaine alone group (Mean difference 14.28 mg; 95% CI: 2.95 − 25.63) (**Table 2**).

The intensity of pain (**Fig. 2**) and sedation score (**Fig. 3**) remained statistically comparable at all observation time points between the groups. Satisfaction level was comparable between the two groups (**Table 3**).

DISCUSSION

The present study has shown that morphine added to ropivacaine for FICB significantly prolongs the duration of analgesia following femoral fracture surgeries with reduced 24-hour postoperative analgesic requirement.
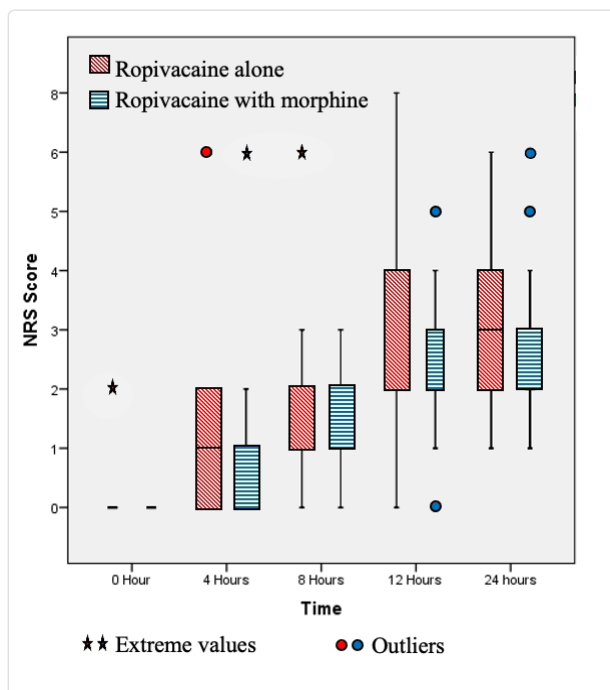
Figure 2: Comparison of NRS between two groups at various time points
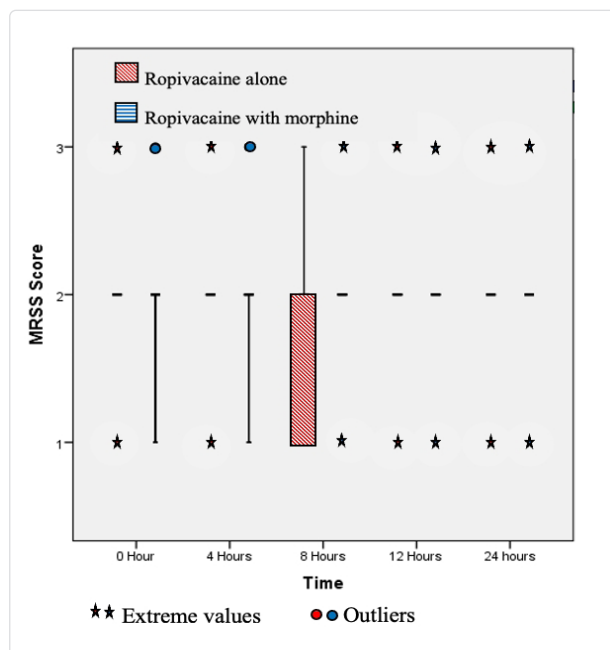

Figure 3: Comparison of MRSS between two groups at various time

In patients receiving morphine as an additive to ropivacaine for FICB in our study, the postoperative analgesia was prolonged by about 90 minutes. This finding is further supported by reduction in tramadol requirement in patient receiving ropivacaine and mor-

phine for FICB.

To improve the efficacy of postoperative analgesia, and to avoid the placement of catheters and their complications, opioids are added to local anesthetics in peripheral nerve blocks. The advantages of adding opioids to local anesthetics in peripheral nerve blocks are thought to decrease local anesthetic dose, prolong duration of action and lessen adverse effects when compared to parenteral opioids. Evidence suggests the presence of opioid receptors and their endogenous ligands in the peripheral nervous system. Opioids have effect on modulation of inflammatory pain at this site [14, 15]. Opioid receptors are synthesized and transferred to the nerve terminals at the dorsal root ganglions. When

Table 1: Baseline patient characteristics. Values are presented as number or mean ± SD.

Characteristic	Group	
	Ropivacaine alone (n = 35)	Ropivacaine with morphine (n = 35)
Gender (M/ F)	20/ 15	25/ 10
ASA-PS (I/ II)	23/ 12	28/ 7
Age (y)	47.74 ± 15.70	43.03 ± 12.69
Weight (kg)	57.69 ± 9.83	59.11 ± 9.85
Duration of surgery (min)	105.29 ± 27.30	103.71 ± 32.50

these receptors are stimulated, opioid peptides are activated inside inflammatory cells [16]. The presence of perioperative inflammation also affects the analgesic effects of peripherally applied opioids [19].

Our study showed that the duration of analgesia was prolonged with addition of morphine to ropivacaine in FICB. This was consistent with the findings of a previous study where the addition of morphine to combination lidocaine/ bupivacaine supraclavicular blocks prolonged the median duration of analgesia after internal fixation of upper extremity fractures [21]. Similar were the results obtained by Atef et al., by addition of morphine to bupivacaine in transverse abdominis plane block following inguinal herniorrhaphy [22]. Flory et al demonstrated a prolongation of postoperative analgesia by 30 minutes when they added morphine to bupivacaine plus epinephrine in interscalene block for elective shoulder surgery [23].

In addition to longer duration of postoperative analgesia, addition of morphine to ropivacaine decreased the requirement of postoperative rescue analgesics (62.86 vs 77.14 mg tramadol). This finding was con-

Table 2: Comparison of clinical parameters. Values are presented as mean ± SD.

Parameter	Group		Mann-Whitney U	p-value
	Ropivacaine alone (n = 35)	Ropivacaine with morphine (n = 35)		
Duration of analgesia (min)	541.71 ± 167.57	634.43 ± 164.65	404	**0.01***
Total dose of IV tramadol (mg)	77.14 ± 25.27	62.86 ± 22.17	437	**0.01***

Mann-Whitney U test

Table 3: Comparison of satisfaction level using Likert scale between two groups

Satisfaction level	Group		p-value
	Ropivacaine alone (n = 35)	Ropivacaine with morphine (n = 35)	
1 (Strongly dissatisfied)	0	0	0.17*
2 (Dissatisfied)	12	5	
3 (Neutral)	11	10	
4 (Satisfied)	10	16	
5 (Strongly satisfied)	2	4	

Fisher's exact test

sistent with that of Atef et al., who also demonstrated that total morphine requirements in the first 24 postoperative hours was reduced by addition of morphine to bupivacaine in TAP block after inguinal herniorrhaphy [22]. Significant decrease in postoperative analgesic (tramadol) requirement with addition of morphine to bupivacaine for transversus abdominis plane block after appendectomy has been demonstrated elsewhere [24].

We found that the NRS score for pain was similar between the two groups. This finding was contradictory to that of Atef et al, who showed significant decrease in Visual Analog Pain Scale (VAS) in first 24 postoperative hours by addition of morphine to bupivacaine in TAP block following inguinal herniorrhaphy [22]. But our finding was consistent with that of Ghimire et al., who did not find significant difference in VAS score in two groups of patients receiving bupivacaine and bupivacaine plus morphine in TAP block following appendectomy, and Sternlo et al. who did not find any difference of combination of morphine and bupivacaine for intercostal blocks after biliary surgery [24, 25]

We found no difference in sedation scores in the postoperative period between the two groups. Our study has some limitations. Firstly, we did not study the cost of the procedure. Secondly, despite femur fractures being more common in elderly patients with many comorbidities, we excluded patients above 65 years and those of ASA PS III or greater. This was done because we regarded that elderly patient might not properly comply with NRS scale, which would further affect our results. Thirdly, we did not use patient controlled analgesia for postoperative analgesia, which would be better for pain relief in these patients. Fourthly, we did not measure serum morphine and ropivacaine levels.

CONCLUSION

Under the conditions of our study, morphine as an adjuvant to ropivacaine in ultrasound guided fascia iliaca compartment block as a component of multimodal analgesia prolonged duration of postoperative analgesia with reduced opioid analgesic requirement in patients undergoing femoral fracture surgeries.

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