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ORIGINAL RESEARCH REGIONAL ANESTHESIA

A comparative study between femoral nerve block and intravenous ketamine for pain management during positioning for spinal anesthesia in elderly patients with femur fracture

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Abstract

Background & objective: Spinal anesthesia (SA) is preferred for fractured femur surgery but it requires proper positioning which is often very difficult to achieve due to pain. Different methods have been used to control the pain during patient positioning, but the results are inconsistent about the superiority of one over the other. We compared femoral nerve block (FNB) and intravenous ketamine for pain control during positioning for SA in elderly patients with femur fracture.

Methodology: A total of 66 patients above 60 y of age were randomly divided into two equal groups; FNB group to receive ultrasound guided FNB with 15-20 ml of bupivacaine 0.25% and ketamine group to receive IV ketamine 0.25 mg/kg. Assessment of VAS scores during positioning before SA was done. Rescue analgesia for pain during positioning was achieved by inj fentanyl IV, and after the surgery by inj morphine IV. Postoperative VAS scores, calculation of total morphine consumption during the first 24 h and any complications were recorded.

Results: The VAS score during positioning was lower in FNB group compared to ketamine group ($P < 0.001$). This was evident by lower recorded doses of pre-spinal rescue fentanyl. FNB group showed better postoperative analgesia, less morphine consumption and less complications.

Conclusion: FNB provided better analgesia during positioning for spinal blockade in fractured femur patients. Furthermore, FNB was associated with less adverse effects, better postoperative analgesia and less opioid consumption.

Trial Registry: PACTR202112605652525.

Abbreviations: SA - Spinal anesthesia; FNB - Femoral nerve block; NSAIDS - Nonsteroidal anti-inflammatory drugs; VAS - Visual Analog Scale

Key words: Pain; Spinal anesthesia; Femoral nerve block; Ketamine; Femur surgery

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1. Introduction

Patients with fractures are always scared of pain. The psychological and clinical impacts of pain are numerous.[1] Femur fracture commonly occurs following trauma in elderly patients and central neuraxial block especially spinal anesthesia (SA) is preferred for such cases.[2] The favorable physiological effects of the sympathetic blockade such as decreased blood loss, higher leg blood flow, intense pain alleviation and reduced cardiopulmonary and thromboembolic morbidity, explain the superiority of SA over general anesthesia.[3]

Proper positioning during SA is a must for a successful procedure, but extreme pain and need to stabilize the limb are obstacles for an ideal position for this procedure.[2, 4] Different methods, like intravenous fentanyl, ketamine, femoral nerve block (FNB) or fascia iliaca block, have been used to control the pain during positioning. Results are inconsistent regarding the efficiency of FNB over intravenous analgesia. Some studies showed the superiority of FNB, [5, 6] while others showed no benefit of FNB over intravenous opioids.[7, 8]

Poor pain control in elderly patients can lead to delirium which is associated with delayed return of functional status, higher mortality, and poor postoperative functional outcomes. Also, opioid abuse within the elderly population increases susceptibility to illness and impaired recovery. Fascia iliaca compartment block and FNB are considered safe, can be easily performed in elderly patients and decrease the need of opioids with good postoperative analgesia.[9] In addition to pain control, FNB also shortens functional recovery time and hospital stay with less adverse effects when compared to epidural or intravenous analgesia.[10]

Ketamine is an intravenous anesthetic that works by blocking N-methyl-D-aspartate (NMDA) receptors in the central nervous system. In low-dose, it showed analgesic benefit in orthopedic surgery among with cardiorespiratory stability.[11] Ketamine also has a role in managing postoperative pain, decreasing opioid use and postoperative nausea and vomiting.[12]

We compared the analgesic effect of FNB and low dose intravenous ketamine for pain management in patients with femur fracture during positioning for SA due to the scarcity of studies comparing them.

2. Methodology

The study was a randomized prospective comparative study conducted from January 2020 to November 2021 at Ain Shams University Hospitals. Written informed consent was obtained from all patients. Sixty-six patients aged above 60 y, ASA-I and II, scheduled for fractured femur surgery. Patients were randomized into two equal groups by a computer-generated random numbers table, each consisting of 33 patients and received one of the following: ultrasound guided FNB with 15-20 ml of bupivacaine 0.25% (Group F) or intravenous analgesic ketamine dose (0.25 mg/kg) (Group K).

Patient refusal, patients with major spine deformities and severe truncal obesity, patients with coagulopathy and bleeding disorders, infection at the injection site, known allergy to local anesthetics, patients having multiple fractures, patients with pre-existing myopathy or neuropathy, patients with significant cognitive dysfunction, those who received long acting opioids preoperatively, were excluded.

The primary outcome was the assessment of pain control during positioning before SA, using the Visual Analog Scale (VAS). The secondary outcomes were assessment of postoperative pain using VAS score in the first 24 h at intervals, e.g., on arriving in PACU, at 1, 2, 4, 10, 16 and 24 h. Total postoperative opioid (morphine) consumption in the first 24 h and any complications were noted.

All patients were assessed preoperatively and were fasted for 8 h. In the operating room, venous access was established and lactated Ringer's solution was infused @ 10 ml/kg. Standard monitoring of perioperative vital parameters of the patients was done. Before the start of SA, the femoral nerve block was performed or the intravenous ketamine was given according to the patient group allocation.

FNB (Group F):

Under complete aseptic conditions, using a Fuji M-Turbo ultrasound system, the linear high-frequency ultrasound transducer was placed over the femoral crease to visualize the femoral nerve and artery. Before proceeding with the nerve block, skin infiltration with 1 ml of 2% lidocaine was done. An echogenic 22G, 4 inch needle was used for the block. Once the femoral nerve was visualized, the needle was inserted in-plane in a lateral to medial orientation and advanced towards the

nerve. A volume of 15-20 mL of 0.25% bupivacaine was administered around the femoral nerve after negative aspiration to avoid accidental intravascular injection. The spread of drug solution was observed in tissue planes under ultrasound imaging. Assessment of the block was done by pin prick at anterior of thigh and after establishment of sensory block, the patient was positioned to sitting position for SA.

Intravenous ketamine (Group K):

Intravenous 0.25 mg/kg of ketamine was given 2-3 min before positioning, then the patient was positioned to sitting position to receive SA.

Spinal Anesthesia:

SA was performed in the sitting position under complete aseptic conditions using a 25G Quincke needle through L3-L4 or L4-L5 intervertebral space with 2.5 ml of 0.5% heavy bupivacaine and 25 µg fentanyl with injection rate of 0.2 mL/sec (total volume of 3 ml).

After confirm onset of the sensory block by pin prick at anterior, lateral and posterior thigh, the level of the sensory block was documented and surgery was allowed to start.

Rescue analgesia with increments of fentanyl was used and total intraoperative fentanyl was recorded and the surgery time was documented. Patients were observed for any complications e.g., hematoma formation, hypotension, bradycardia, desaturation, nausea, vomiting or any other adverse effect and managed appropriately.

Outcome assessments

Table 1: Comparison of demographic data between the two groups

Demographic data	FNB group (n = 33)	Ketamine group (n = 33)	t/z/x2	p-value
Age (years)	65.9 ± 3.7	66.5 ± 4.2	0.6 ^{t}	0.55
Sex (males)	15 (45.5%)	18 (54.5%)	0.24^{x2}	0.62
ASA (2)	17 (51.5%)	22 (66.7%)	1^{x2}	0.32
Duration of surgery (min)	116.8 ± 10.99	115.7 ± 9.72	0.43^{t}	0.67
Type of fracture (shaft)	16 (48%)	12 (36%)	1.06^{x2}	0.59

Data expressed as mean ± SD, median (IQR), proportion
t = student t test, Z = Mann-Whitney test, x2 = Chi square

Table 2: Comparison between groups as regard pre-spinal data

Parameters	FNB group (n = 33)	ketamine group (n = 33)	t/z/x2	p-value
Pre-spinal time (min)	11 ± 1.48	4.36 ± 1.14	20.4^{t}	**< 0.001***
Pre-spinal fentanyl (no. of patients)	3 (9.1%)	11 (33.3%)	4.4 ^{x2}	**0.035***
VAS during positioning once by the observer	1 (0-2)	2 (2-4)	4.4^{z}	**< 0.001***

Data expressed as mean ± SD, median (IQR), proportion.
**t = student t test, Z = Mann-Whitney test, x2 = Chi square, p < 0.05*

Table 3: Comparison between groups as regard sedation scores

Sedation scores	FNB group (n = 33)	ketamine group (n = 33)	Z	p-value
Baseline RSS	2 (1-2)	2 (1-2)	0.5	0.6
RSS after intervention	2 (2-2)	3 (2-4)	4.15	**< 0.001***
RSS after 20 min	2 (2-2)	2 (1.75-2)	0.58	0.56

*Data expressed as median (IQR)., Z = Mann-Whitney test, FNB = femoral nerve block; *p < 0.05*

Quantitative relief of pain was assessed using VAS score by a blind observer during positioning of the patient to sitting position (VAS position) to administer SA. A single blind observer asked to mark the pain level by the patient on the line between the two endpoints. Rescue doses of IV fentanyl were given when VAS position was ≥ 4, increments of 50 µg fentanyl (0.5 µg/kg) and modified Ramsay Sedation Score (RSS) was assessed and recorded before and after intervention and after 20 min intraoperative. The pre-spinal time (the time between performing FNB or giving IV ketamine and starting the SA) was recorded.

Postoperative pain was assessed at fixed intervals. Postoperative pain and opioid consumption were assessed by using VAS score. The duration of postoperative analgesia was measured from starting the spinal time till the first rescue analgesia.

Complications were observed and recorded for the first 24 h.

Statistical Analysis

Sample size was calculated using the STATA program, setting alpha error at 5% and power at 80%, results from a previous study showed that the mean VAS score in IV analgesia at positioning was 8.03 while for femoral nerve block it was 6.53 with an estimated common standard deviation of 2. Based on this, a sample size of 33 patients in each group were needed, taking in account 20% dropout rate.

Data were analyzed using Statistical Package for Social Science (SPSS) version 22.0., Quantitative data were expressed as mean ± SD or median (IQR) when

indicated. Qualitative data were expressed as frequency and percentage. The following tests were used: Independent-samples t-test, Chi-square (X^2) test and Mann Whitney U test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the P < 0.05 was considered significant.

Table 4: Comparative complications between the groups

Complication	FNB group (n = 33)	ketamine group (n = 33)	X^2	p-value
Hypotension	12 (36.4%)	10 (30.3%)	0.07	0.79
Desaturation	3 (9.1%)	11 (33.3%)	4.4	**0.035***
Bradycardia	*0 (0%)*	*0 (0%)*	*0.015*	**1**
Nausea / vomiting	*2 (6.1%)*	*6 (18.2%)*	*1.2*	*0.26*

*Data expressed as proportion, X2 = Chi-square; *p < 0.05*

Table 5: Comparative postoperative VAS in the groups

VAS score	FNB group (n = 33)	Ketamine group (n = 33)	Mann-Whitney test	
			z	p-value
PACU	0 (0-0)	0 (0-0)	0	1
1 h	1 (0-1)	3 (2-3)	6.6	**< 0.001***
2 h	2 (1-2)	3 (3-4)	5.8	**< 0.001***
4 h	3 (3-4)	4 (3-4)	0.72	0.47
10 h	4 (3-4)	3 (3-4)	0.66	0.5
16 h	4 (3-4)	4 (3-4)	0.07	0.9
24 h	4 (3-4)	4 (3-4)	0.25	0.8

*Data expressed as Median (IQR): Inter quartile range; *p < 0.05*

3. Results

Both groups were comparable regarding demographic data, e.g., age, ASA status, gender, duration of surgery and the type of the fracture and no significant statistical differences was found between the groups (Table 1).

Pre-spinal time was prolonged significantly in FNB group. Pre-spinal fentanyl consumption was more in ketamine group than in FNB group. VAS score was significantly higher in ketamine group during positioning (Table 2).

Ramsay Sedation Score (RSS) in the two groups at baseline was equivalent,

but after intervention, ketamine group showed significantly higher sedation score. After 20 min of intervention RSS became insignificant between the two groups (Table 3).

Intraoperative vital signs were comparable between the two groups, there was no statistical difference as regards to hypotension, bradycardia and nausea and vomiting,

but in desaturation was higher in ketamine group than in FNB group, and the difference was statistically significant (Table 4).

The two groups were comparable as regards to postoperative pain control, VAS score was used to assess pain post operatively and used at regular interval (at PACU, after 1, 2, 4, 10, 16 and 24 h). The femoral group showed better pain control with significant difference at 1 and 2 hours postoperatively but at PACU and after 4 hours till 24 hours there was no statistical difference between the two groups (Table 5).

Agitation Sedation Scores (RASS) showed no significant difference spaced every 6 hours (Table 6). between two groups over 24 h.

Postoperative time to request analgesia was significantly more in FNB group. Postoperative opioid (morphine) consumption was much lower in FNB group (Table 7).

4. Discussion

SA is the most favored technique of anesthesia for fractured femur surgeries.[2] Positioning of these patients to receive spinal anesthetic is usually associated with severe pain and many intravenous agents have been tried to relieve it.[13,4,5] FNB and intravenous ketamine, both have been used to relieve pain for positioning during SA;

FNB may also provide extended postoperative analgesia.[2]

In support of our results regarding superiority of FNB over ketamine, previous studies stated that FNB provided better analgesia during positioning than intravenous fentanyl for central neuraxial block. [2, 5, 6] Moreover the patient satisfaction score was better in the FNB group. Another study compared 60 patients as regard the analgesic effect provided by FNB, IV fentanyl and low dose IV ketamine before positioning for central neuraxial block in patients undergoing surgery for lower limb fractures. It was the only study found by us comparing FNB and ketamine. In this study FNB with 1% lignocaine appeared to provide better analgesia than IV fentanyl and IV low dose ketamine (0.1mg/kg). However, IV low dose ketamine appears to alter the pain scores to clinically comfortable levels for the patient in a quick and non-invasive way, and so can be preferred in cases where patients refuse to give consent or have contraindications for FNB.[14]

Table 6: Comparison between groups as regard RASS.

RASS	FNB group (n = 33)	Ketamine group (n = 33)	X^2	p-value
PACU	0 (0-0) Range (-1-1)	0 (0-0) Range (-1-1)	0.8	0.39
6 h	0 (0-0) Range (0-1)	0 (0-0) Range (-1-1)	0.68	0.49
12 h	0 (0-0) Range (0-1)	0 (0-0) Range (0-1)	0	1
24 h	0 (0-0) Range (-1-1)	0 (0-0) Range (0-1)	0 0.6	1 0.55

Data expressed as Median (IQR): Inter quartile range.

Table 7: Comparative postoperative analgesia between the groups

Parameter	FNB group (n = 33)	Ketamine group (n = 33)	t	p-value
Time to request analgesia (min)	356.36 ± 80.6	227.27 ± 46.86	7.9	**< 0.001***
Postoperative morphine consumption (mg)	3.88 ± 0.86	7.42 ± 0.79	17.45	**< 0.001***

Data expressed as mean ± SD. t = student t test, FNB = femoral nerve block.
**p < 0.05*

However, Lamaroon *et al.*, couldn't find any difference or analgesic benefit of FNB over IV fentanyl for patient positioning before spinal block. They evaluated 64 patients who received either two doses of IV fentanyl 0.5 µg/kg with a 5-min interval between doses or FNB using 30 mL of 0.3% bupivacaine (a mixture of 20 mL of bupivacaine 0.5% and 10 mL of normal saline 0.9%). They found that both techniques can provide similar pain relief prior to positioning of patients with fractured femur for spinal block. In both groups, pain scores 15 min after analgesia

and during positioning from the supine to lateral position were not significantly different.[8] Reasons may be due to; first, the 15-min interval before positioning may not be enough to reach the peak analgesic effect of bupivacaine as the average time of the block may reach up to 30 min.[15,16] Second, they used nerve stimulation for the block while ultrasound guided blocks showed more success rates, earlier onset and longer duration of analgesia.[17] Third, they used lateral position during performing SA. There is more chance for overriding of fracture segments in lateral position but it requires minimum flexion, which could have improved patient discomfort.

Earlier in 2008, A survey for trauma anesthetists was done in the UK to check current practice for the peri-operative anesthetic management for patients with fractured necks of femur. They received 155 replies from 218 questionnaires sent. A large ratio of 75.8% of the received replies preferred regional anesthesia with 95.5% of these using a spinal technique. This was performed with bad side down 45.7%, using ketamine 37.3%, and/or midazolam 41.2%, to aid positioning. Midazolam was the most frequently used, followed by ketamine and propofol when considering analgesia and sedation for positioning patients for SA. The most favorable combination was midazolam and ketamine. Nerve blocks were not used frequently to help with positioning. In 15.1% of patients positioning was done without analgesia or sedation.[7]

In contrary to this survey, more recent studies have shown that nerve block has become more widespread and frequently used for preoperative pain management, [12,18,19] as follows: AA15 members panel with experience in orthopedic trauma and pain management reviewed the literature and developed recommendations on acute orthopedic pain management. The guideline was submitted to the OTA (Orthopedic Trauma Association) for review and was approved in October 2018. The panel recommended that nerve blocks such as femoral nerve or fascia iliaca block should be used in patients with hip fractures once presented to the Emergency Department (high-quality evidence, strong recommendation). Various studies showed that nerve blocks applied in the ED can be performed by trained personal with minimal complications and minimal risks. These blocks are effective when compared to parenteral opioids alone in decreasing the use of opioids, respiratory depression and improving patient's pain in the preoperative period. The technique of nerve block has varied between studies. Some studies used FNB, while others used fascia iliaca block. Most studies recommend that the applied block should be ultrasound guided.[18]

Femoral nerve blocks have showed benefits beyond effective analgesia for hip fracture which are lower incidence of delirium and less hospital stay. Also they can be administered in the emergency department or even as a prehospital setting because of their easy technique.[19]

Another review wanted to consolidate current knowledge that femoral nerve blocks are effective in managing acute pain of hip fractures in elderly. Nerve block decreases the pain intensity with less systemic analgesia and less adverse events.[12]

In our study, the two groups were also compared as regard pain control post operatively as a secondary outcome. The FNB group showed better pain control with significant difference at 1 and 2 hours postoperatively with a p value <0.001. At PACU and after 4 hours till 24 hours there was no statistical difference between the two groups. In support to our results, previous study found that FNB is comparatively better than IV fentanyl when used as preoperative and postoperative analgesic in patients undergoing operations for fractured femur.[20]

Also, as regard to the cumulative 1st 24 hours Morphine consumption in our study, the FNB group showed less Morphine consumption compared to the ketamine group postoperatively with a p value <0.001. In support to our results, previous study found that the patients with fractured neck of fracture who received FNB required less morphine for the next 12 hours after the block.[21]

As regard complications in our study, desaturation was more observed in the ketamine group than the FNB group with a p value 0.035. Sedation was also more in the ketamine group. In support to our results, previous study recorded Oxygen saturation less than 90% during positioning after intravenous Fentanyl.[22]

We also assessed delirium score to detect postoperative delirium whether it would be more with the ketamine group or not but it was not significant. Previous study found that ketamine given intraoperatively does not affect postoperative delirium or pain after major surgeries in elderly patients either using low or high dose.[23]

5. Conclusion

FNB provided better analgesia than ketamine during positioning for spinal blockade in fractured femur patients. Furthermore, FNB was associated with less adverse effects, better postoperative analgesia and less opioid consumption.

6. Limitations

Assessment of pain couldn't be done in sedated patients who received ketamine or additional doses of fentanyl so VAS was assessed by blind observer after performing the intervention.

7. Future scope

Incorporation of femoral nerve blocks into standard clinical practice can improve the quality of care provided to the elderly patients with femur fractures.

8. Ethics approval

This study was approved by the research ethics committee at the faculty of medicine, Ain Shams University (FMASU MD 26a / 2020 / 2021) and registered retrospectively with Pan African Clinical Trial Registry, identifier: PACTR202112605652525.

8. Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

9. Competing interests

The authors declare that there were no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

11. Authors contribution

ME: Conduction of the study work.

HG: Manuscript editing

HS: Literature search

AA: Statistical analysis and review

AG: Literature search.

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