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Effect of Adding Fentanyl to Bupivacaine in Femoral Nerve Block for Post-Operative Pain in Patient Subjected to Total Knee Replacement Guided by Ultrasound

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Abstract

Background: Total knee replacements surgeries are very important to improve mobility and quality of life and usually associated with sever postoperative pain. Femoral nerve block has been studied to improve post-operative pain. Adding adjuvant to local anesthesia (LA) as fentanyl in femoral nerve block could be a method to prolong the duration of the block. The aim of the study was to study the analgesic efficacy fentanyl added to bupivicaine in ultrasound guided femoral nerve block for patients undergoing elective total knee replacements surgeries.

Methods: Sixty patients (ASA I-II) of either sex were scheduled for elective total knee replacements surgeries. Patients were randomly allocated into two groups (30 patients each), to receive ultrasound guided femoral nerve block using; 18 ml bupivicaine 0.25% plus 2 ml normal saline (Group B) versus 18 ml bupivicaine 0.25% plus fentanyl 1 mic (ug) /kg in 2 ml volume (Group B+F). Postoperative pain was assessed over 24 hours using VAS scale plus time of first analgesic request and overall post-operative analgesics consumption were recorded. The intra and post-operative HR, SBP, DBP and MAP were recorded. Any concomitant complications were observed postoperatively.

Results: As regard patient demographic data and ASA grades, we found there were no significant changes between the two groups, as shown in. Patient hemodynamic parameters either intra or post-operative, were comparable in both groups (P. value 0.19). There was a significant decrease in VAS pain scores in group B+F during first day postoperative (P. value 0.00I*) and post-operative analgesic consumption much more decreased in group B+F in comparison to group B (P. value 0.001*). We found that the time of the 1st request of analgesia in group B was (5.13 ± 1.008) hours while it was (11.27 ± 0.9), hours in group B+F after end of operation, the difference between the two group was significant ($p<0.001$).

Conclusion: Ultrasound guided FNB improve post-operative analgesia and the addition of fentanyl to bupivicaine in femoral nerve block prolonged the duration of block and decreased analgesic requirements in patient subjected to total knee replacement surgery.

Keywords: Fentanyl- bupivacaine; Femoral nerve block; Acute post-operative pain; Total knee replacement; VAS score.

List of Abbreviations:

TKA= Total knee arthroplasty

VAS=Visual analogue scale

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US= ultrasonography

LA= Local anesthesia

ASA= American society of anesthesia

FNB= Femoral nerve block

Introduction

Over the last decades, the number of total knee arthroplasty procedures performed has increasing dramatically. Projections suggest that the same trend will continue over the next decades, resulting in a demand of 3.48 million TKAs in 2030 [1-2]. Modern total knee arthroplasty consists of resection of the diseased articular surfaces of the knee, followed by resurfacing with metal and polyethylene prosthetic components. For the properly selected patient, the procedure results in significant pain relief, as well as improved function and quality of life [3]. Importantly pain has been shown to be associated with reduced patient satisfaction and as such is an important metric in the assessment of knee replacement outcomes [4]. Most of elective orthopedic procedures, like TKAs, are performed under regional anesthesia as the patient being often elderly with multiple medical co-morbidities. Furthermore, regional anesthesia has many advantages over general anesthesia, as less hemodynamic and respiratory instability, better postoperative pain control, and less nausea and vomiting [5-6]. But such methods as neuro-axial blocks still invasive method and relatively needs experience [7]. The femoral nerve arises from the dorsal divisions of the ventral rami of L2-4. It descends through Psoas major, emerging from the muscle at the lower part of its lateral border, and passes down between it and Iliacus. It continues beneath the inguinal ligament and enters the femoral triangle, where it splits into an anterior and a posterior division [8].

The application of ultrasound guidance has enabled very close approximation of needle tip to the targeted nerve, and recent studies confirm impact of decreasing concentration and volume on the efficacy of regional blocks [9].

Local anesthetic (LA) drugs represent one of the most important classes of drug in peri-operative care and do not have the adverse effects of systemically administered opioids and adding adjuvant to local anesthesia (LA) as; dexamethasone, opioids, clonidine, and ketamine to femoral nerve block could be a method to prolong the duration of the block, improve the quality of nerve blocks and decrease LA doses [10]. Fentanyl has been added to local anesthetics, with many advantages; increase the success rate of sensory blockade and prolongation of analgesic effects with minimal systematic side effects [11]. The aim of this study was to study effects of adding fentanyl to levo-bupivicaine in ultrasound guided femoral nerve block on the severity of postoperative pain in patients undergoing total knee replacement.

Patients and Methods

This study was designed as a prospective randomized clinical trial and was conducted in Assuit university hospitals, after obtaining local ethical committee approval and written consent from all included patients. Sixty patients (ASA I-II), aged between 18 to 60 years old were scheduled for total knee replacement surgery were enrolled in our study from March 2017 till March 2018. Exclusion criteria were as following: allergy to local anesthetic solutions or fentanyl, patient refusal, coagulopathy, polytrauma and end organ failure. One day before surgery, preoperative data were collected as; demographic data, medical history, physical examination and routine laboratory investigations. The night before surgery, all patients were taught how to evaluate their own pain intensity using the Visual Analogue Scale (VAS), scored from 0-10 (where 0= no pain and 10=worst pain imaginable.

All patients were randomly assigned into two groups (30 patients each) by using opaque sealed envelopes containing computer generated randomization schedule, the opaque sealed envelopes are sequentially numbered that were open before application of anesthetic plan. After shifting the patient to the induction room, ECG, pulse oximeter, non-invasive blood pressure monitors were attached. Peripheral venous line was established and an infusion of lactated ringers' solution was started.

- Group B (No. =30): ultrasound guided femoral nerve block before spinal anesthesia was done for each patient using (18 ml of 0.25% bupivacaine + 2 ml saline to reach total volume 20 ml).
- Group B+F (No. =30): ultrasound guided femoral nerve block before spinal anesthesia was done for each patient using (18 ml of 0.25% bupivacaine + 1mic/kg fentanyl diluted in 2 ml saline to reach total volume 20 ml).

Subarachnoid block was performed in all patients in both groups, in the sitting position under complete aseptic technique and infiltration of 2 ml lidocaine 1%, in targeting inter-vertebral space (L4-L5 or L5-S1). Disposable Quincke-type cutting needle (25 G) was used. The subarachnoid space was identified by spontaneous reflux of CSF, then inject 3 ml of 0.5% hyperbaric bupivacaine. Patients were immediately placed in the supine position without tilting the operating table. Anesthesia was considered satisfactory when there was loss of cold sensitivity from lower limbs to the umbilicus, tested with an alcohol swab. Heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure were recorded as following; before femoral nerve block (baseline), after block and before spinal anesthesia, immediately after spinal anesthesia, and every 5 minutes till end of surgery.

Technique of ultrasound guided femoral nerve block:

Under complete aseptic technique and in the supine position, the skin over the femoral crease was identified and the transducer was positioned to visualize the femoral artery and/or nerve. If the nerve was not immediately apparent lateral to the artery, tilting the transducer proximally or distally often helps to image and highlight the nerve from the rest of the iliopsoas muscle and the more superficial adipose tissue. In doing so, an effort should be made to identify the iliopsoas muscle and its fascia as well as the fascia lata to avoid injection underneath a wrong fascial sheath that.

Once the femoral nerve was identified, a skin wheal of local anesthetic (3 ml) was made on the lateral aspect of the thigh 1 cm away from the lateral edge of the transducer. The needle was inserted in-plane in a lateral-to-medial orientation and advanced toward the femoral nerve. Needle passage through the facsimilia was often felt as a "pop" sensation.

Once the needle tip is witnessed adjacent (either above, below, or lateral) to the nerve, and after careful aspiration, 1 to 2 mL of local anesthetic was injected to confirm the proper needle placement. When injection of the local anesthetic did not appear to result in a spread close to the femoral nerve, additional needle repositions and injections may be necessary. In post-operative period, all patients received ketorlac 30 mg every 12 hours and raracetamol 1 gm / 8 hours as multimodal analgesia, and all patients were observed for 24 hours for the following parameter;

-VAS- for pain measurement at regular intervals as primary outcome.

Secondary outcomes were;

-HR and MAP were recorded every 4 hours, for 24 hours.

-Any concomitant complications, if happened, as (infections, hematoma or paresthesia) or side effects as (nausea; vomiting, pruritus or respiratory depression).

Statistical Analysis

The required sample size was calculated using Epi Info software version 7 (CDC, 2012) ®. We used VAS as the primary outcome and therefore, it was estimated that minimum sample size of 29 patients in each study group would a chive a power of 80% to detect an effect size of 0.8 in the outcome measures of interest, assuming a type I error of 0.05. All analyses were performed with the SPSS 21.0 ® software. Categorical variables were described by number and percent (N, %), where continuous variables described by mean and standard deviation (Mean, SD). Continuous variables were compared by the t test two-tailed t test. Categorical variables were compared using the chi-square ($\chi 2$) and Fisher's exact tests (if required). To compare between continuous variables, we used t-test. P. value considered significant if < 0.05 at confidence interval 95% and the level of significance was accepted if the P value < 0.05.

Results

Our study included 60 patients who were planned for elective total knee replacement surgery. Patients were randomized into two groups:

- Group B (18 ml of 0.25% Levo-bupivacaine + 2 ml saline)
- Group B+F (18ml of 0.25% Levo-bupivacaine + 1mic/kg fentanyl diluted with saline to reach total volume 20 ml

As regard patient demographic data and ASA grades, we found there were no significant changes between the two groups, as shown in (Tables 1-2). Patient hemodynamic parameters either intra or post-operative, were comparable in both groups (figure 1-4) (P. value 0.19). There was a

Table 1: Comparison of demographic data among studied two groups.

	Group B No=30		Group B+F No=30		P-Value
Age	53.07±6.8		54.27±5.8		**0.47 NS**
Sex	No	percent%	No	percent%	
Male	7	23.3	8	26.7	**0.5NS**
Female	23	76.7	22	73.3	
Height	72.47±8.18		73.53±6.74		**0.58 NS**
Weight	166.1±7.5		169.7±7.01		**0.06 NS**

Table 2: Comparison of two groups according to ASA grades, Total No=60.

	Group B No=30		Group B+F No=30		P-Value
ASA:	No	percent%	No	percent%	
Grade I	14	46.7	16	53.3	**0.6 NS**
Grade II	16	53.3	14	46.7	

Group B = Bupivicaine group, Group B = Bupivicaine plus Fentanyl group
Data expressed as (Mean ± SD), number and percentage (%).
ASA: American society of anesthesiologists
P. value < 0.05 considered statistically significant.
Between two groups no significant changes regarding patient's characteristics or ASA grade.

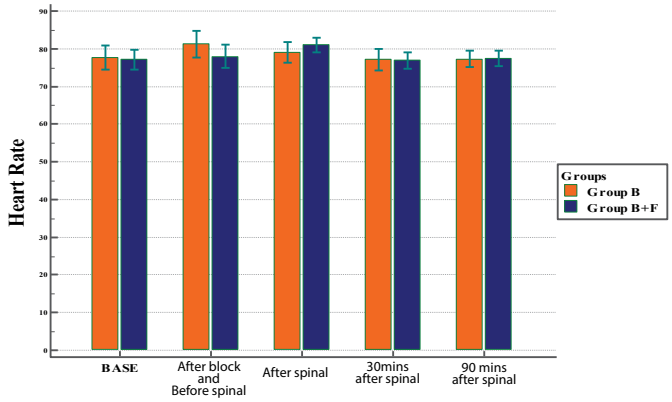

Figure 1: Comparison of Heart rate parameters between the two groups.

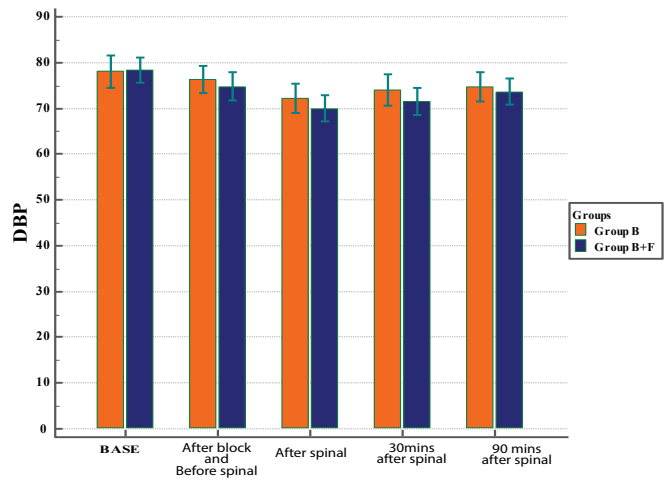

Figure 2: Comparison of Mean blood pressure parameters between the two groups.

Group B =Bupivicaine group, Group B+F =Bupivicaine plus Fentanyl group, Mean blood pressure by mmgh, HR= heart rate by beat/minutes, Data expressed as (Mean ± SD) and number / percentage (%).
P. value < 0.05 considered statistically significant.
Between two groups no significance was found regarding hemodynamic parameters.

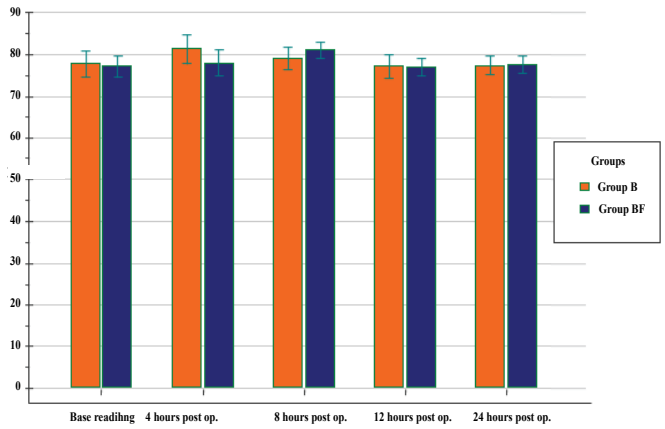

Figure 3: Comparison of post-operative Heart rate between the two group.

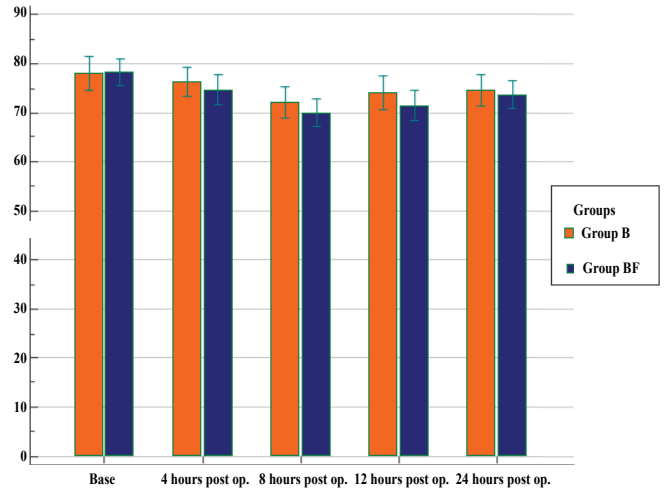

Figure 4: Comparison of post-operative mean blood pressure between the two groups.

Group B =Bupivicaine group, Group B+F =Bupivicaine plus Fentanyl group, Mean blood pressure by mmgh, HR= heart rate by beat/minutes, Data expressed as (Mean ± SD) and number / percentage (%).
P. value < 0.05 considered statistically significant.
Between two groups no significance was found regarding hemodynamic parameters.

Table 3: Comparison of VAS findings among studied groups, Total No=60.

	Group B No=30	Group BF No=30	
	Mean±SD	Mean±SD	*P-Value*
2 Hours	1.6±.62	1.7±0.75	***0.23 NS****
4 Hours	#3.7±1.337	1.93±0.86	***<0.001 S****
6 Hours	#3.7±1.76	1.8±0.84	***<0.001 S****
8 Hours	#2.26±0.69	#2.17±0.69	***0.58 NS****
10 Hours	#3.633±2.025	#3.07±1.41	***0.6 NS****
12 Hours	#5.3±0.922	#4.16±1.74	***<0.001 S****
14 Hours	#3.17±1.46	1.867±0.77	***<0.001 S****
16 Hours	2.067±0.86	1.6±.67	***0.024 S****
20 Hours	1.87±0.73	1.8±.8	***0.73 NS****
24 Hours	1.67±0.711	1.67±.711	***0.1 NS****

statistically significant difference, P<0.05
* P value between two the groups.
# Paired T-Test within the same group.

Table 4: Comparison of 1st Ketorlac dose among studied groups, Total No=60.

	Group B No=30	Group B+F No=30	P-Value
1st dose Hours	5.13 ± 1.008	11.27 ± 0.9	<0.001S

Group B =Bupivacaine group, Group B+F =Bupivacaine plus Fentanyl group, Mean blood pressure by mmgh, HR= heart rate by beat/minutes, Data expressed as (Mean ± SD) and number / percentage (%).
P. value < 0.05 considered statistically significant.

significant decrease in VAS pain scores in group BF during first day postoperative (P. value 0.00I*) (tables 3) and post-operative analgesic consumption much more decreased in group B+F in comparison to group B (P. value 0.001*). We found that the time of the 1st request of analgesia in group B was (5.13 ± 1.008) hours while it was (11.27 ± 0.9), hours in group BF after end of operation, the difference between the two group was significant (p<0.001) as shown in (table 4). In the current study no local anesthetic toxicity, no hematoma or excessive tissue trauma had been developed at the site of injection in both group this result could probably due the guidance of ultrasonography that enabled better visualization of the femoral triangle before injection.

Discussion

This study showed that preemptive addition of 1 mic/kg Fentanyl to 20 mL bupivicaine 0.25% for femoral nerve block guided with ultrasound for total knee replacement surgery resulted in reduction of VAS pain score with longer time till first analgesic requirement. So fentanyl prolong the duration and intensity of local anesthetic and this may be due to direct binding with opioid recptor on the dorsal nerve roots aided with these axonal transport or by diffusing into surrounding tissues and subsequently into the epidural and subarachnoid spaces, it may also have been central opioid receptor mediated after systemic absorption of Fentanyl [12].

Fentanyl could act directly on the nervous system by way of opioid-binding sites or penetration of the nerve membrane and direct action at the dorsal horn, fentanyl may diffuse from the brachial plexus sheath and bind to the opioid receptor of the dorsal horn. Or fentanyl may reach the systemic circulation and potentiate local anesthetic action via central opioid receptor-mediated analgesia [13]. In the current study no local anesthetic toxicity, no hematoma or excessive tissue trauma had been developed at the site of injection in both group this result could probably due the guidance of ultrasonography that enabled better visualization of the femoral triangle before injection.

Heo BH etal.,2016 study, the patients were divided into 2 groups, each with n = 40 in ropivacaine (R) group and n = 42 in R with fentanyl (R+F) group, after operation, the patients in each group received R+F and R alone via a femoral nerve catheter, respectively. they assessed the visual analog scale (VAS) pain immediately before administration (baseline) and at 15, 30, and 60 minutes on post-anesthesia care unit (PACU), and resting and ambulatory VAS score up to 24 hours. The main findings of their study were that femoral nerve catheter infusions of fentanyl with ropivacaine resulted in an insignificant decline in the postoperative VAS score compared to infusions of ropivacaine (except at

30 minutes) and also decreased the mean supplemental analgesic dose. they tested the hypothesis that the addition of an opioid may enhance the analgesic effect of FNB according to a different mechanism to that which underlies the action of local anesthetics. However, they were unable to demonstrate statistically significant differences in VAS scores after TKA at most of the time points. These results are not consistent with our study [14]. We took in our consideration the anatomy of knee region, as the knee is supplied anteriorly by the femoral nerve while posteriorly by the sciatic nerve and the overlap in their innervation of the anterolateral aspect of the knee. Regarding that, many studies noted the little effect of the sciatic nerve contributing to the pain originating from the knee region after TKA and this pain was relieved dramatically after receiving ketorlac 30 mg as in our study [15].

Recently, femoral nerve block (FNB) was reported, in many studies, to be effective for postoperative pain control after TKA as it responsible for most of post-operative pain [16-17] and can be performed more easily and safely than neuro-axial block [18]. Comparing between opioids that was added as adjuvant either morphine or fentanyl, our choice was fentanyl and this is based on the higher lipophilicity of fentanyl that makes it rapid onset of action, lower incidence of side effects, and reduced risk of respiratory depression [19]. Fentanyl prolong the duration and intensity of bupivicaine and this occur by many mechanisms; direct binding with opioid receptor on the dorsal nerve roots, diffusing into surrounding tissues and subsequently into the epidural and subarachnoid spaces or finally, it may also have been central opioid receptor mediated after systemic absorption of fentanyl and potentiate local anesthetic [20].

Agree with our study, a study by Rajkhowa, that included 66 patients, divided into 2 groups, group Ropivacaine (R) and group Ropivacaine Plus Fentanyl (RF). Supraclavicular brachial plexus block was performed in the group R using 0.5% ropivacaine and in group RF received 0.5% ropivacaine plus 50 micrograms fentanyl in brachial plexus block. The onset time of sensory and motor block, duration of sensory and motor block was recorded. The results obtained show that the addition of fentanyl (50 mcg) to ropivacaine 0.5% for brachial plexus blocks significantly prolonged the duration of sensory and motor blockade but delayed the sensory and motor block onset time. Fentanyl used with ropivacaine in this study prolonged the duration of sensory and motor blockade [21].

Also, Nishikawa et al, studied 66 patients divided into three groups for axillary brachial plexus block. Group 1 patients received 40 mL of 1.5% lidocaine with 1:200,000 epinephrine. Patients in Group 2 received 40 mL of 1.5% lidocaine with 1:200,000 epinephrine containing 100μg fentanyl. Group 3 patients received 40 mL of 1.5% lidocaine with 1:200,000 epinephrine c plus 100μg fentanyl IV. Addition of 100μg fentanyl to an axillary brachial plexus block significantly prolonged the onset of analgesia and duration of sensory blockade compared to patients who received 1.5 % lidocaine plus saline or 100μg fentanyl IV [22].

The same concept in a study by Karakaya et al. [23] and Kaniyil,., et al. [24] who concluded that, addition of fentanyl to local anesthetics in brachial plexus block significantly prolonged the duration of analgesia without any significant side effects though it had delayed the onset of block. And these results are consistent with our study.

Previous experimental electrophysiological studies concluded that, opioids might exert a nonspecific action by impairing sodium and potassium conductions or an increase in calcium conduction in the nerve fibers. When injected near neurovascular sheaths, opioids may cause systemic effects by absorption to systemic circulation [25]. The limitations of our study were, small sample size and short term follow up, only for 24 hours. It is possible, for patients to self-report any untoward reaction that can mimic late-onset neuropathy, it was advisable to establish continuous follow-up using survey questionnaires and periodic checking for a longer period.

Conclusion

Ultrasound guided FNB improve post-operative analgesia and the addition of fentanyl to bupivicaine in femoral nerve block prolonged the duration of block and decreased analgesic requirements in patient subjected to total knee replacement surgery.

Declarations

-The authors declare no conflicts of interest.

-The study was done after local ethical committee approval of Assuit university hospitals and written consent from all included patients.

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