Effect of adding fentanyl to bupivacaine in femoral nerve block for post-operative pain in patient subjected to total knee replacement guided by ultrasound

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 bupivacaine 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 mcg/ kg in 2 ml volume (Group BF). 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 LF during first day postoperative (P. value 0.001*) and post-operative analgesic consumption much more decreased in group LF in comparison to group F (P. value 0.001*). We found that the time of the 1st request of analgesia in group L was (5.13±1.008) hours while it was (11.27±0.9), hours in group LF 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 bupivacaine 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

Abbreviations: TKA: total knee arthroplasty; VAS: visual analogue scale; US: ultrasonography; LA: local anesthesia; ASA: american society of anesthesia; FNB: femoral nerve block

Femoral nerve block has been studied to decrease post operative analgesics consumption and diminish length of hospital stay. However, several studies have raised the concern that femoral nerve block may delay patient ambulation and increase the risk of falls during the postoperative period.6 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.5 Local anesthetic (LA) drugs represent one of the most important classes of drug in perioperative 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 bupivacaine 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, poly-trauma 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 patients using (18ml of 0.25% bupivacaine + 2ml saline to reach total volume 20 ml).

Group BF (No.=30); ultrasound guided femoral nerve block before spinal anesthesia was done for each patients using (18 ml of 0.25% bupivacaine + 1 µ/ 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 iliopectos muscle and the more superficial adipose tissue. In doing so, an effort should be made to identify the iliospectos muscle and its fascia as well as the fascia lata to avoid injection underneath a wrong fascial sheet 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 fascia iliaca 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 paracetamol 1 gm/8 hours as multimodal analgesia, and all patients were observed for 24 hours for the following parameter;

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

Secondary outcomes were;

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

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

Statistical analysis

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 (χ²) 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:

a) Group B (18 ml of 0.25% bupivacaine + 2 ml saline)

b) Group BF (18ml of 0.25% bupivacaine + 1 µ/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 Table 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 significant decrease in VAS pain scores in group BF during first day postoperative (P. value 0.001*) (Table 3) and post operative analgesic consumption much more decreased in group BF 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.
Effect of adding fentanyl to bupivacaine in femoral nerve block for post-operative pain in patient subjected to total knee replacement guided by ultrasound


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 BF: 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 groups.

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

Group B: Bupivacaine group; Group BF: 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 1** Comparison of demographic data among studied two groups

<table>
<thead>
<tr>
<th>Group</th>
<th>No=30</th>
<th>Group BF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53.07±6.8</td>
<td>54.27±5.8</td>
<td>0.47</td>
</tr>
<tr>
<td>Sex</td>
<td>No percent%</td>
<td>No percent%</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 23.3</td>
<td>8 26.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Female</td>
<td>23 76.7</td>
<td>22 73.3</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>72.47±8.18</td>
<td>73.53±7.64</td>
<td>0.58</td>
</tr>
<tr>
<td>Weight</td>
<td>166.1±7.5</td>
<td>169.7±7.01</td>
<td>0.06</td>
</tr>
</tbody>
</table>

In Table 1 & 2

Group BL: Bupivicaine group, Group BF: Bupivicaine plus Fentanyl

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.

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

<table>
<thead>
<tr>
<th>ASA:</th>
<th>No percent%</th>
<th>No percent%</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>14 46.7</td>
<td>16 53.3</td>
<td>0.6 NS</td>
</tr>
<tr>
<td>Grade II</td>
<td>16 53.3</td>
<td>14 46.7</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Group</th>
<th>No=30</th>
<th>Group BF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD 2 Hours</td>
<td>1.6±0.62</td>
<td>1.7±0.75</td>
<td>0.23</td>
</tr>
<tr>
<td>Mean±SD 4 Hours</td>
<td>3.7±1.337</td>
<td>1.93±0.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean±SD 6 Hours</td>
<td>3.7±1.76</td>
<td>1.8±0.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean±SD 8 Hours</td>
<td>2.26±0.69</td>
<td>2.17±0.69</td>
<td>0.58</td>
</tr>
<tr>
<td>Mean±SD 10 Hours</td>
<td>3.63±2.025</td>
<td>3.07±1.41</td>
<td>0.6</td>
</tr>
<tr>
<td>Mean±SD 12 Hours</td>
<td>5.32±0.922</td>
<td>4.16±1.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean±SD 14 Hours</td>
<td>3.17±1.46</td>
<td>1.86±0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean±SD 16 Hours</td>
<td>2.06±0.86</td>
<td>1.6±0.67</td>
<td>0.024</td>
</tr>
<tr>
<td>Mean±SD 20 Hours</td>
<td>1.87±0.73</td>
<td>1.8±0.8</td>
<td>0.73</td>
</tr>
<tr>
<td>Mean±SD 24 Hours</td>
<td>1.67±0.711</td>
<td>1.67±0.711</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Statistically significant difference, P<0.05

* P value between two the groups.

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

<table>
<thead>
<tr>
<th>Group</th>
<th>No=30</th>
<th>Group B+F</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st dose Hours</td>
<td>5.13 ± 1.008</td>
<td>11.27 ± 0.9</td>
<td>&lt;0.0015</td>
</tr>
</tbody>
</table>

Group B: Bupivicaine group; Group BF: 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.

**Discussion**

This study showed that preemptive addition of 1 mic/kg Fentanyl to 18 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. A lot of authors find that postoperative pain is inadequately treated in more than one third of all TKA procedures and many clinical trials confirm that a high quality postoperative pain management must be performed to reduce the risk of postoperative acute adverse effects such as pulmonary dysfunction and chronic adverse effect as delayed recovery, hospital discharge and chronic pain.14,15

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.14,15 We get many benefits from using ultrasound in this study as; facilitates more rapid block onset and prolong block duration, with the added advantages of a decrease in drug dosage and a reduction in the incidence of local anaesthetic toxicity.16,17 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 18,19 and can be performed more easily and safely than neuro-axial block.20

Comparing between opioids that were added as adjuvants 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.21,22 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.22,23 However, previous clinical trial has compared between LAs in terms of their practical potency it compared the analgesic efficacy of ropivacaine and levo-bupivacaine, and concluded that local tissue infiltration with bupivicaine was more effective than ropivacaine in reducing the post-operative pain associated with abdominal surgeries.21,24

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). Supravacular 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 were recorded. The results obtained show that the addition of fentanyl (50mcg) 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.25

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 100 μg fentanyl. Group 3 patients received 40 mL of 1.5% lidocaine with 1:200,000 epinephrine plus 100 μg fentanyl IV. Addition of 100 μg 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 100 μg fentanyl IV.26

The same concept in a study by Karakaya et al.27 and Kaniyil et al.28 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.29,30

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 bupivacaine in femoral nerve block prolonged the duration of block and decreased post-operative analgesic requirements in patient subjected to total knee replacement surgery.

References


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