Postoperative Analgesia for Total Knee Replacement: Comparing between Pre-and Postoperative "3-in-1" Femoral Nerve Block

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Background: *Total Knee Replacement (TKR) produces severe postoperative pain. Pre- and postoperative single-shot "3-in-1" Femoral Nerve Block (FNB) were reported to improve analgesia and reduce morphine consumption post TKR.*
Objective: *To find out the most beneficial time for injection of single shot "3-in-1" FNB for TKR between preoperative and postoperative in a prospective controlled trial.*
Material and Method: *In a Randomized, double-blind Controlled Trial (RCT), 48 patients undergoing TKR received either pre- or postoperative "3-in-1" FNB using 30 mL of bupivacaine 0.25% after a standardized general anesthesia. Morphine consumption, Numeric Pain-Rating Scale (NPRS) at rest and during movement, tension in the back of the knee, nausea/vomiting, pruritus, sedation, and respiratory depression at 1, 4, 24 and 48 hr after TKR were compared.*
Results: *There were no significant differences in 48-hr morphine consumption [46.5 (20.0) vs 45.0 (23.6) mg, p = 0.809], NPRS both at rest and during movement, tension in the back of knee, nausea/vomiting, pruritus, sedation, and respiratory depression at any time during 48-hr postoperative TKR between groups.*
Conclusion: *Preoperative single-shot "3-in-1" FNB using 30 mL of bupivacaine 0.25% is not better than postoperative single-shot "3-in-1" FNB using the same drug in postoperative pain and morphine reduction in patients undergoing elective TKR under general anesthesia.*

Keywords: *Analgesia, Total knee replacement, "3-in-1" Femoral nerve block, Bupivacaine, RCT*

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Postoperative pain after Total Knee Replacement (TKR) is a serious concern. Sixty-six percent of patients have severe pain on movement up to 48 hr after the operation[1]. It inhibits early effective physiotherapy, the most influential factor for good postoperative knee rehabilitation[2]. Multi-modal pain therapy (balanced analgesia) is recommended for the treatment of postoperative pain[3]. For TKR, the techniques are epidural analgesia with local anesthetics and/or narcotics[4], lumbar plexus blockade[5,6], intravenous Patient-Controlled Analgesia (PCA)[7], addition of Non Steroidal Anti-Inflammatory Drug (NSAID)[8] etc.

At the beginning of the last century, Crile was among the first who introduced the concept of treating pain prior to its onset: preemptive analgesia[9,10]. It was later defined as an antinociceptive treatment that prevents establishment of altered processing of afferent input, which amplifies postoperative pain. According to the theory of central sensitization, a painful stimulus can lead to sensitization of dorsal horn neurons[11,12], which results in subsequent hypersensitivity to low-intensity stimuli (central hypersensitization). Theoretically, preemptive analgesia should be very effective for controlling postoperative pain and decreasing subsequent narcotic use. However, conclusion of its

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advantage is still controversial[13-16]. Positive results occurred when performed on local or nerve blocks for some types of surgery such as laparoscopic cholecystectomy[13] or appendectomy[14] and, TKR[17,18], etc.

Single shot "3-in-1" Femoral Nerve Block (FNB) was reported to be effective for postoperative analgesia after TKR when performed either preoperative (preincisional)[17] or the immediate postoperative (post-incisional) period[1,19]. In combination with subarachnoid anesthesia, the postoperative "3-in-1" FNB lasts for at least 8 hr[19]. However, no study has compared the effect of preoperative to postoperative "3-in-1" FNB for postoperative analgesia after TKR. Whether preoperative FNB is better due to preemptive effect or postoperative block is better because of longer postoperative duration of analgesia is still unknown.

The aim of the present study was to compare the 48-hr postoperative PCA morphine used and pain between preoperative and postoperative single shot "3-in-1" FNB for TKR in a prospective, double-blind, Randomized, Controlled Trial (RCT), to find out the most beneficial time for injection.

Material and Method

After approval by the institutional ethics committee and written informed consent was obtained, 48 ASA physical status I-III patients scheduled for elective unilateral TKR under General Anesthesia (GA) were included in the present study. Exclusion criteria were coagulation abnormality, local infection, sepsis, allergy to local anesthetics and/or opioids, age < 40 or > 80 yr, weight < 40 or > 90 kg, preexisting neurological deficit, severe liver impairment, creatinine $\geq$ 1.7 mg/dl or inability to quantify pain scales or to use a PCA device.

During the preoperative visit, patients received a full explanation of numeric pain-rating scale (NPRS, 0-10) and the use of PCA device. All patients received no premedication.

All patients received a standard general anesthesia. Patients were randomly divided into two groups, preoperative and postoperative group.

In the preoperative group, after induction with thiopentone 4-5 mg/kg, a mixture of isoflurane 1-2% and nitrous oxide 66% in oxygen was given to the patient via mask and the "3-in-1" FNB was performed by one of two investigators (PB, SN) who was not involved with subsequent data collection for that patient. Then atracurium 0.5 mg/kg was administered and intubation was performed. Maintenance of anesthesia composed of isoflurane 0.5-3%; nitrous oxide 66% in oxygen and fentanyl 100 ug. The surgery started more than 30 minutes after the "3-in-1" FNB was done and all the patients were extubated at the end of surgery.

In the postoperative group, the patient received the same technique of general anesthesia except for performing the "3-in-1" FNB at the end of surgery before extubation.

The "3-in-1" FNB was performed following the guideline of Winnie et al[20]. The puncture site was located 1-1.5 cm lateral of the femoral artery, approximately 2 cm below the inguinal ligament. The nerve was identified by using a 5-cm insulated needle and nerve stimulator (Stimuplex DIG, B. Brown, Melsungen, Germany). With an initial output of 2 mA, the needle was advanced at an angle of 30-45^{o} to the skin until quadriceps femoris muscle contraction was elicited. Its position was then optimized and considered adequate when the contraction still appeared at an output of < 0.5 mA. After negative aspiration for blood, 30 mL of bupivacaine 0.25% with adrenaline 1:200,000 was injected. Meanwhile compression beneath the puncture site was done to promote dissemination of bupivacaine in the cephalad direction to additionally block both obturator and lateral femoral cutaneous nerves.

During the 48-hr postoperative period, all patients received only intravenous PCA morphine for analgesia. The setting was morphine 0.05 mg/kg loading for the first complaint of pain by the patients then 1 mg /demand with a lockout interval of 6 minutes and 4-hour limit of 30 mg (no background infusion).

Data collection included patient demographics and surgical characteristics, time to the first loading dose of morphine, cumulative morphine consumption, NPRS (0 = no pain, 10 = worst pain) both at rest and during movement, tension in the back of the knee (0 = nil, 1 = mild, 2 = moderate, 3 = severe), associated side effects: vomiting score (0 = nil, 1 = nausea, 2 = vomiting), pruritus (0 = nil, 1 = present), sedation score (0 = awake, 1 = drowsy but response to verbal stimulus, 2 = drowsy but arousable to physical stimulus, 3 = unarousable), respiratory depression (respiratory rate < 10/min). Efficacy assessments were recorded at 1, 4, 24 and 48 hr postoperatively by an investigator who was blinded to the patient's grouping. Patient's decision to use the same technique of analgesia in the future was also assessed at 48-hr postoperatively.

Power analysis from Peng et al[21] indicated that 23 patients per group were required to detect 50% difference in morphine consumption (power 0.8, α = 0.05). Data for operation time, cumulative morphine

consumption and NPRS were compared with Student t-test. The chi-square test was used for tension in the back of the knee, vomiting score, pruritus, sedation score, and respiratory depression. Data were expressed as frequency, mean (SD) or median (range). Significance was determined by a p value < 0.05.

Results

Two groups were comparable with respect to baseline demographics and surgical time (Table 1).

Comparing between the groups, there were no significant differences in median time to the first dose of morphine [62.5 (5-575) vs 62.5 (5-360) min in preoperative and postoperative group, respectively], cumulative morphine consumption at all times of study (Table 2), NPRS at rest (Table 3), and during movement (Table 4). Twenty-three patients in each group had tension in the back of the knee with comparable severity (Table 5). The incidences of side effects were comparable in both groups. Fifteen vs fourteen patients in preoperative and postoperative group, respectively, had nausea and/or vomiting. Especially three vs two cases in preoperative and postoperative group, respectively, had very severe vomiting and required 3 doses of 10 mg of metoclopramide. Five patients in each group had pruritus but needed no treatment. Nineteen vs eighteen patients in the preoperative and postoperative group, respectively, had sedative score 1 or 2. No one had sedative score > 2 or respiratory depression. Patient's decision to use the same technique of analgesia in the future was similar between the groups (87.5 vs 83.4% for the preoperative and postoperative group, respectively, p = 1).

Table 1. Baseline demographic characteristics and surgical time

	Preoperative group	Postoperative group
Number	24	24
Age (yr)*	70.2 (5.3)	66.2(8.3)
Weight (kg)*	60.4 (8.0)	61.1 (9.3)
Gender (F/M)	18/6	20/4
ASA physical status I/II/III	0/19/5	3/20/1
Surgical time (min)*	133.1 (38.1)	148.5 (46.8)#

* Age, weight, surgical time data are mean (SD)
# p value = 0.217

Table 2. Cumulative morphine consumption (mg) [mean (SD)]

Period (hr)	Preoperative group	Postoperative group	p value
0-1	3.6 (3.2)	3.9 (3.3)	0.774
0-4	9.9 (5.8)	10.5 (7.2)	0.720
0-24	31.1 (14.9)	30.3 (16.4)	0.871
0-48	46.5 (20.0)	45.0 (23.6)	0.809

Discussion

The knee is supplied by the femoral, lateral femoral cutaneous, obturator and sciatic nerves. The relative contribution made by conduction block of each of these nerves to postoperative analgesia is unclear. Allen et al[19] reported no improvement of analgesic efficacy from addition of a sciatic nerve block to the FNB. They suggested that sciatic innervation of the posterior knee is a relatively minor contribution to

Table 3. Numeric pain-rating scale at rest [mean (SD)]

Time (hr)	Preoperative group	Postoperative group	p value
1	6.3 (3.6)	6.4 (3.0)	0.866
4	4.0 (2.9)	3.7 (3.1)	0.772
24	3.6 (2.8)	3.3 (2.5)	0.702
48	2.3 (2.2)	2.6 (2.5)	0.626

Table 4. Numeric pain-rating scale during movement [mean (SD)]

Time (hr)	Preoperative group	Postoperative group	p value
1	6.7 (3.6)	7.2 (2.7)	0.558
4	5.2 (3.1)	4.9 (3.2)	0.746
24	6.3 (2.9)	6.4(2.8)	0.842
48	4.0 (2.9)	4.8(3.4)	0.389

Table 5. Incidence vs severity of tension in the back of the knee (no. of cases)

	Preoperative group	Postoperative group
Tension in the back of the knee	23	23
Mild	0	2
Moderate	9	7
Severe	14	14

postoperative pain after TKR. However, Hirst et al [22] postulated that the sciatic nerve also provides a major contribution to the innervation of the knee as the reason why FNB is insufficient to significantly reduce morphine requirements or improve analgesia beyond the recovery room in their study since all the patients who received a "3-in-1" FNB complained of pain in the back of the knee. The finding in the present study supported this concept, because most (44 from 48) patients still experienced moderate to severe tension in the back of the knee and moderate pain during movement on the 1st postoperative day. Furthermore, Lang et al[23] have also demonstrated that, despite complete cutaneous anesthesia of the knee provided by combined sciatic and "3-in-1" FNB, patients may still complain of severe pain when the knee joint is entered.

From recent clinical trials and systematic reviews, the definition of preemptive has been redefined as treatment that[24] prevents establishment of central sensitization caused by incisional and inflammatory injuries. It starts before incision and covers both the period of surgery and the initial postoperative period which may be $\geq$ 12-48 hr, depending on the type of surgery. By this definition, preemptive means "preventive" and not simply "before" incision. An insufficient afferent block cannot be preemptive, even if it is administered before the incision. The criteria specific for preemptive analgesia are verification of block sufficiency and degree of initial difference in nociceptive response between control and preemptive groups. Five out of six studies[25-30] of neural blockade for preemptive analgesia, with the above criteria, demonstrated that clinically meaningful effects can be observed when the degree of nociceptive blockade is confirmed and the block is extended into the initial postoperative period. In addition, experimental evidence[31] indicates that both central mechanisms and afferent input are needed to maintain pain hypersensitivity. The established postoperative pain hypersensitivity can be reversed by the blockade of afferent input if it is sufficiently prolonged. Studies comparing preincisional with postincisional treatment failed to provide convincing evidence of the value of preemptive analgesia because they had not excluded from comparison the results of central sensitization caused by inflammatory injury that occurs after surgery[32].

The present study that the time to the first morphine dose was only approximately 1 hr in both groups with moderate pain as mentioned. The possible important factors that explain negative results in the present study are incomplete blockade of the knee as mentioned above and insufficient duration of the blockade. In other words, under general anesthesia, preoperative (preincisional) single shot "3-in-1" FNB cannot prevent establishment of central hypersensitization caused by incisional injury while postoperative (postincisional) single shot "3-in-1" FNB cannot block the established postoperative central hypersensitization caused by inflammatory injury. Even if the authors did not collect data to compare intraoperative serum catecholamine or anesthetic drugs used in the present study, they found that in preoperative group, the patients had less surgical stress and required fewer anesthetic drugs for a period of time at the beginning of the operation than the postoperative group. Therefore, the authors suggest performing "3-in-1" FNB at the preoperative rather than the postoperative period. Furthermore, since approximately 60% of the patients in the present study had morphine causing nausea/vomiting, the authors believe that effective balanced analgesia without intravenous morphine should be superior. Hence, the authors suggest that future studies should compare the effect of complete and prolonged, multimodal (preventive) analgesia to the conventional method for postoperative pain management in TKR and try to decrease the necessity of morphine supplement.

In conclusion, the present study was unable to confirm improvement in analgesia and decreased morphine consumption provided by a preoperative single shot "3-in-1" FNB compared to postoperative block by using 30 mL of bupivacaine 0.25% in patients undergoing elective TKR under general anesthesia.

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การระงับความปวดหลังการผ่าตัดเปลี่ยนเข่า เปรียบเทียบระหว่างการทำ Femoral 3-in-1 block ก่อนและหลังการผ่าตัด

ปวีณา บุญบูรพงศ์, สุปราณี นิรุตติศาสน์, เทวารักษ์ วีระวัฒกานนท์, วรศักดิ์ กียปัจจ์, อนันตโชติ วิมุกตะนันทน์, กุศลศรี ตอเล็บ

***ที่มา**: ความปวดหลังการผ่าตัดเปลี่ยนเข่าเป็นความปวดที่รุนแรงอย่างยิ่ง มีรายงานถึงประสิทธิภาพของการฉีดยาชาที่เส้นประสาท femoral, lateral femoral และ cutaneous โดยการฉีด ครั้งเดียว [single shot "3-in-1" femoral nerve block (FNB)] ว่าช่วยลดความปวดและปริมาณความต้องการยามอร์ฟีนหลังการผ่าตัดเปลี่ยนเข่า ได้เป็นที่น่าพอใจไม่ว่าจะเป็นการฉีดก่อนหรือหลังการผ่าตัด*

***วัตถุประสงค์**: ศึกษาถึงประสิทธิภาพของการลดความปวดและปริมาณมอร์ฟีนที่ใช้หลังการผ่าตัดจากการทำ single shot "3-in-1" FNB เปรียบเทียบก่อนและหลังการผ่าตัด*

***รูปแบบการศึกษา**: ทำการศึกษาแบบ randomized, double-blind control trial ในผู้ป่วย 48 รายที่มาทำการผ่าตัดเปลี่ยนเข่า ซึ่งได้รับการดมยาสลบร่วมกับการทำ "3-in-1" FNB ด้วย 0.25% bupivacaine 30 มิลลิลิตร ก่อนหรือหลังการผ่าตัด*

***การประเมินผล**: บันทึกปริมาณมอร์ฟีนที่ใช้ คะแนนความปวดขณะพักและเคลื่อนไหว ความตึงของกล้ามเนื้อหลังเข่า อุบัติการณ์และความรุนแรงของการเกิดคลื่นไส้อาเจียน อาการคัน ความง่วง และการกดการหายใจ ที่ 1, 4, 24 และ 48 ชั่วโมง หลังการผ่าตัด ปริมาณมอร์ฟีนที่ได้แสดงเป็น mean (SD)*

***ผลการศึกษา**: ไม่พบความแตกต่างอย่างมีนัยสำคัญของปริมาณมอร์ฟีนที่ใช้หลังผ่าตัด 48 ชม [46.48 (19.97) และ 44.95 (23.55) มิลลิกรัม, p = 0.809] คะแนนความปวดทั้งขณะพักและเคลื่อนไหว ความตึงของกล้ามเนื้อหลังเข่า อาการคลื่นไส้อาเจียน อาการคัน ความง่วง และ การกดการหายใจ ในระยะ 48 ชั่วโมง หลังการผ่าตัดเปลี่ยนเข่าระหว่าง 2 กลุ่ม*

***สรุป**: การฉีด single shot "3 in 1" FNB ด้วย 0.25% bupivacaine 30 มิลลิลิตร ก่อนการผ่าตัด ให้ผลไม่แตกต่างกับการฉีดยาหลังผ่าตัด ในการช่วยลดความปวดและมอร์ฟีนที่ใช้หลังผ่าตัดเปลี่ยนเข่า*