Parenteral Parecoxib Provides a Similar Reduction in Opioid Requirement to Single-Shot Sciatic Nerve Block after Total Knee Arthroplasty when Combined with Continuous Femoral Nerve Block

Nuj Tontisirin MD*,
Theerawat Chalacheewa MD*, Suwimolwadee Saipimpong MD*,
De QH Tran MD, FRCPC§, Roderick J Finlayson MD, FRCPC§

** Department of Anesthesiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
§ Montreal General Hospital, Department of Anesthesia, McGill University, Montreal, Canada

Objective: *Continuous femoral nerve blockade has become an accepted modality in the management of pain after total knee arthroplasty (TKA); however, posterior knee pain can be problematic and often requires additional analgesia. The present study compared the use of parenteral parecoxib to single-shot sciatic block for this purpose.*

Material and Method: *After the Ethic Review Board gave approval, adults undergoing TKA were randomly divided into 3 groups. Group 1 (Gr-F+S) received single-shot sciatic nerve block (SNB) with 0.25% bupivacaine 25 ml in addition to continuous femoral analgesia (CFA) (0.125% bupivacaine 7 ml/h); group 2 (Gr-F+P) received parenteral parecoxib 40 mg q 12 hours with CFA; and group 3 (Gr-F) received only CFA. Assessments were performed at 0, 6, 12, and 24 hours post op. and included the following variables: NRS (numerical rating score) at rest, morphine use, time to first analgesic dose and side effects.*

Results: *Seventy-eight patients were enrolled, with 26 participants in each of the 3 groups. There was no inter-group difference in pain score (NRS). However, morphine requirements in the first 24 hours were significantly increased in Gr-F (17±12 mg) when compared to Gr-F+S (10±7 mg) and Gr-F+P (9±5 mg) ($p<0.001$). There was no difference in time to first analgesic dose, side effects or patient satisfaction.*

Conclusion: *Parenteral parecoxib and single-shot SNB both significantly reduced morphine requirements when used in combination with femoral nerve blockade after TKA.*

Keywords: *Parecoxib, Total knee arthroplasty, Sciatic nerve block*

J Med Assoc Thai 2017; 100 (1): 57-63
Full text. e-Journal : *http://www.jmatonline.com*

The total knee arthroplasty (TKA) is a common orthopedic procedure, but the high incidence of moderate to severe postoperative pain (up to sixty percent) remains problematic[1]. Adequate postoperative analgesia can promote not only early return to function but can also reduce adverse events[2]. Continuous peripheral nerve blocks have become increasingly popular because they reduce opioid consumption and related side effects[3]. A recent consensus statement supported the use of continuous lumbar plexus or femoral nerve block in addition to systemic analgesics for pain control after TKA[4]. Some studies, however, have found that this regimen cannot provide adequate pain control, particularly for posterior knee pain. Weber et al. described the use of supplemental sciatic nerve blocks (SNB) to address this pain[5,6]. This approach has been controversial, because of the possible masking of a sciatic nerve injury related to the surgery, or even an evolving compartment syndrome. An alterna-

Correspondence to:
Tontisirin N, Ramathibodi Hospital, Department of Anesthesiology, 270 Rama VI road, Ratchatewi, Bangkok 10400, Thailand.
Phone: +66-2-2011513
E-mail: doctornuj@gmail.com, nuj.ton@mahidol.ac.th

tive analgesic would therefore be valuable.Parecoxib, a parental Cyclooxygenase-2 (COX-2) inhibitor, is known to have opioid-sparing effects and has been shown to be well tolerated while improving range of motion after TKA[7-9]. Moreover, the effect of parecoxib on kidney function is transient[10] and associated with cardiovascular thromboembolic events and gastrointestinal side effects similar to placebo[11-13]. The aim of the present study was to compare the analgesic efficacy of single-shot SNB to intravenous parecoxib as an adjuvant to the continuous femoral nerve analgesia in postoperative pain control after TKA in effect on morphine consumption.

Material and Method

After ethical review board approval, seventy-eight adults undergoing unilateral TKA were recruited in a prospective randomized single-blinded controlled study. After providing written and informed consent, all participants were allocated randomly by a computer-generated table into 1 of 3 study groups. Group 1 F+S (Gr F+S) received single-shot sciatic nevae block SNB in addition to continuous femoral analgesia (CFA); group 2 F+P (Gr F+P) received intravenous parecoxib 40 mg every 12 hours for 24 hours together with CFA; and group 3 F (Gr F) received only CFA.

Exclusion criteria were: infection at the planned site of skin puncture, coagulopathy, known allergy to local anesthetics, and inable to operate the patient-controlled analgesia device (PCA). Patients with relative contraindications to intravenous parecoxib, such as coronary artery disease, cerebrovascular disease, asthma and severe renal function impairment, were also excluded.

Femoral nerve catheterization was performed preoperatively as follows. The femoral artery was identified, and an 18-gauge, 50-mm Tuohy needle with a stimulating catheter (StimuLong Sono system, Pajunk® Medical Technologies, Geisingen, Germany) was connected to a nerve stimulator and inserted at the level of the inguinal crease 1.5 cm lateral to the femoral artery in a cephalad direction at a 45 degree angle to the skin. After achieving quadriceps muscle movement at 0.5 mA, a stimulating catheter (Stimulong Sono, Pajunk Medical Technologies, Geisingen, Germany) was advanced 5 cm through the needle while maintaining quadriceps movement at 0.5 mA. After negative aspiration, 20 ml of 0.25% bupivacaine was injected, and a continuous infusion of 0.125% bupivacaine at 7 ml/h was started postoperatively in the post-operative anesthesia care unit (PACU).

In Gr F+S, after femoral nerve catheterization was performed, patients were repositioned in a lateral position, and sciatic block was performed. The needle (Plexolong Naniolin cannula facette 19G*100 mm; Pajunk® Medical Technologies, Geisingen, Germany) was connected to a nerve stimulator and inserted in the subgluteal area at the midpoint between the greater trochanter and the ischial tuberosity. The sciatic nerve was identified by eliciting dorsiflexion or plantar

Table 1. Demographic data

Demographic data	Group F +S	Group F + P	Group F	*p*-value
Age (yr) mean (min-max)	68 (54-78)	69 (57-80)	71 (51-80)	0.29
Male: Female (n)	3:23	0:26	3:23	1.00
Weight (kg) mean (min-max)	62 (48-80)	61 (43-74)	61 (39-90)	0.93
Height (cm) mean (min-max)	154 (144-165)	154 (145-167)	154 (142-184)	0.94
ASA-PS: II/III/IV (n)	5/20/1	7/18/1	8/17/1	1.00
Operative time (min)	93 (80-102)	94 (88-105)	93 (85-103)	0.11

ASA-PS; TheAmerican Society of Anesthesiologists Physical Status Classification

Table 2. Pain intensity (numerical rating scale; NRS) in first 24 hour

Group	Numerical rating scale; mean (min-max)			
Postoperative hr	0 hr	6 hr	12 hr	24 hr
Group F+S	0 (0-4)	3.5 (0-10)	3 (0-6)	3 (0-10)
Group F+P	0 (0-8)	5 (0-10)	3.5 (0-9)	3 (0-5)
Group F	0 (0-8)	5 (0-10)	3 (0-10)	3 (0-10)
p-value	0.34	0.35	0.93	0.15

Table 3. Side effects

Side effects	Nausea		Vomiting		Itching		Numbness	
	n	%	n	%	n	%	n	%
Group F+S	14	54	7	27	1	4	5	19
Group F+P	13	50	10	38	2	8	8	31
Group F	15	58	12	46	1	4	5	19
p-value	0.86		0.36		0.77		0.50	

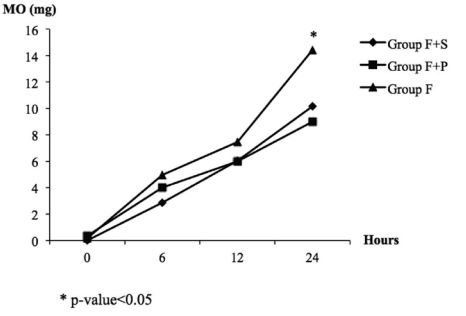

Fig. 1 Cumulative morphine consumption in first 24 hours postoperatively.

flexion of the foot, and the current was then reduced to 0.4-0.5 mA. After negative aspiration, 25 ml of 0.25% bupivacaine was injected. Success of both the femoral and sciatic blocks were confirmed before proceeding to the spinal block.

All patients received a spinal anesthesia at the L3-4 or L4-5 (lumbar spine 3-4 or 4-5) interlaminar space with 14 mg of isobaric bupivacaine[4]. The anesthetic level and operative time were recorded. Intraoperative sedation was given based on patient demand using midazolam or propofol.

Postoperative care was started at time zero, which was the time the patient arrived in the PACU. All patients received CFA with infusion of 0.125% bupivacaine 7 ml/h, in addition to acetaminophen 1,000 mg orally every 6 hours and intravenous morphine PCA (IVAC-PCA machine, CareFusion®, San Diego, California, USA) with a 1 mg bolus and lockout interval of 5 minutes for the first 24 hours. In Gr F+P, patients were given parecoxib 40 mg intravenously at time zero and 12 hours later.

Only one assessor (SS), who blinded to patients' group, visited all participants at 6, 12, and 24 hours after time zero and assessed pain scores at rest using the NRS (numerical rating scale; 0 = no pain, 10 = maximum pain). Morphine consumption and side effects such as nausea/vomiting, itching and weakness, were also evaluated. Serious side effects such as respiratory depression, congestive heart failure and acute renal failure were recorded. The catheters and PCA were left beyond the study period for at least 24 hours more or until the patients had mild pain (NRS <4) with oral analgesics or when intravenous fluid was discontinued.

Sample size calculation

The sample size was calculated using nQuery Advisor version 6.01. The result showed that 21

patients per group was a sufficient number to detect a difference in Visual Analog Scale (VAS) of 13/100[14] with a power of 80% and type I error of 0.05. However, we included 20% more patients to make up for possible lost, as a result, the total sample size was 26 patients in each group.

Statistical analysis

Data analysis was performed using SPSS for Windows version 11.5. Normality was first tested using the Kolmogorov–Smirnov test, and data were then analyzed using the one-way analysis of variance (ANOVA) or Fisher's exact test (demographic data), ANOVA and t-test (morphine requirement), Kruskal-Wallis test and Mann-Whitney test (NRS) or Chi-square test (side effects).

Results

Seventy-eight participants were enrolled in the present study. There were no differences in demographic data between groups, including age, gender, body weight, height, the American Society of Anesthesiologists Physical Status Classification (ASA-PS) and operative time (Table 1, Fig. 1).

Gr F+S showed the lowest pain level at most time points, although there was no significant difference in pain scores at the 24 hours between the groups (Table 2). Morphine consumption in the first 24 hours was significantly higher in Gr F (17±12 mg) than in Gr F+S (10±7 mg) or Gr F+P (9±5 mg) (p = 0.00) (Fig. 2); there was no difference between Gr F+S and Gr F+P. Gr F showed rapidly increasing morphine requirements during the 12-24 hour postoperative period.

The time to first analgesic dose in Gr F+S (6±2 h) and Gr F+P (6±2 h) was longer than that in Gr F (3±2 h) (p = 0.47), but this difference was not statistically significant.

Gr F showed a higher incidence of vomiting, but this difference was not statistically significant. There were no differences in other side effects, including nausea, itching and numbness (Table 3). No serious side effects related to opioids (respiratory depression) or parecoxib (neurological or cardiac events, impaired renal function) were noted. No complications occurred that were related to peripheral nerve blockade. Patient satisfaction was equally high in all groups.

Discussion

In patients with continuous femoral analgesia after TKA, parenteral parecoxib and SNB both similarly reduced postoperative morphine requirements in the first 24 hours, without producing additional side effects.

Parenteral parecoxib has been used in combination with opioids to provide postoperative analgesia after orthopedic surgery. In vivo, it can reduce the inflammatory response[15] and inhibit the release of excitatory amino acids such as glutamate[16]. Clinically, parecoxib reduces opioid consumption, pain intensity at rest and the need for rescue analgesics[12,17-19], it also showed a similar side-effect profile to placebo after hip and spine surgery. Potential concerns regarding the use of parecoxib include the risk of renal, gastrointestinal and cardiovascular complications. For instance, Keppert reported that renal function was transiently affected in elderly patients undergoing orthopedic surgery[10]. However, Stoltz RR found that parecoxib was safe and well tolerated in healthy elderly subjects with a decreased risk of gastroduodenal mucosal injury compared to ketorolac[13], and Nussmeier found that parecoxib and placebo were both associated with the same incidence of cardiovascular and thromboembolic events after non-cardiac surgery[11]. In our study, we did not detect any adverse events in the parecoxib group, although patients with risk factors had been excluded. Contraindications to the use of parecoxib include the presence of severe renal dysfunction, active peptic ulceration or gastrointestinal bleeding, and a history of allergic reactions to aspirin, Non-steroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors or sulfonamides[20].

Wegener reported that single-injection SNB could reduce severe pain on the day of surgery, and continuous SNB reduced moderate pain during mobilization in the first 2 postoperative days[14]. Cappelleri also found that continuous SNB improved analgesia, decreased morphine use, and facilitated early rehabilitation compared to single-injection SNB in patients undergoing TKA and lumbar plexus block[21].

Our study found that SNB improved analgesia in the first 6 hours and reduced opioid consumption in the first 24 hours by forty percent, although opioid related side-effects were not reduced. Although our sample size had not been calculated to detect

differences in side effects, these findings echo those of similar studies[21-22]. SNB does, however, increase the technical burden for anesthesia providers, requiring both additional time and skill. Thus, because parecoxib was associated with a similar reduction in opioid use, this treatment could represent a less resource-intensive option.

The present study included similar surgical techniques performed by the same 2-3 orthopedic surgeons for all patients. We did not measure pain with motion because in our hospital, most patients had tight-bandage (Jones bandage) and they were not allowed to perform knee mobilization in first 24 hour. Therefore, we decided to focus on the use of analgesics to control the resting pain. The limitations of our study included the lack of functional outcomes such as the degree of knee flexion because no knee flexion was allowed in this period. The sample size was also insufficient to detect differences in parecoxib side effects. However, future studies with larger patient populations may be able to detect these differences. A previous study[13] showed that continuous sciatic infusion provided longer postoperative pain control and greater morphine reduction up to 48 hours when compared to single-shot SNB. However, we decided not to perform continuous sciatic infusion due to concerns for patient accidental falls, as all patients received continuous femoral infusions.

Conclusion

Parecoxib provides similar effect as a single-shot SNB in reducing morphine requirement in patients with continuous femoral nerve blockade after TKA. It may be considered as an alternative in the management of postoperative pain after TKA.

What is already known on this topic?

The continuous femoral nerve analgesia is commonly used for post-operative control after total knee arthroplasty as showed in the recent recommendation from ESRA (European Society of Regional Anesthesia and pain therapy). However, its efficacy is limited to control only anterior part of the knee. The posterior knee pain is still problematic. Sciatic nerve analgesic has been less popular since it causes weakness and limits patient's mobility. Intravenous morphine has been used to control posterior knee pain, however, it has side effects such as dizziness, nausea, vomiting and urinary retention. An alternative for posterior knee pain management is still lacking.

What is this study adds?

This study showed the efficacy of intravenous parecoxib which can reduce morphine requirement as same as sciatic nerve analgesia. It might be used to control posterior knee pain after total knee arthroplasty in addition to continuous femoral analgesia.

Acknowledgement

The authors wish to thank the Faculty of Medicine Ramathibodi Hospital for supporting facilities and instruments of the present research. Also, we deeply thank Ms. Rojnarin Komonhirun forher advice on data analysis.

Potential conflicts of interest

The authors have no commercial, proprietary, or financial interest in the products or companies described in this article.

References

1. Singelyn FJ, Deyaert M, Joris D, Pendeville E, Gouverneur JM. Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. Anesth Analg 1998; 87: 88-92.
2. Napier DE, Bass SS. Postoperative benefits of intrathecal injection for patients undergoing total knee arthroplasty. Orthop Nurs 2007; 26: 374-8.
3. Chelly JE, Greger J, Gebhard R, Coupe K, Clyburn TA, Buckle R, et al. Continuous femoral blocks improve recovery and outcome of patients undergoing total knee arthroplasty. J Arthroplasty 2001; 16: 436-45.
4. Fischer HB, Simanski CJ, Sharp C, Bonnet F, Camu F, Neugebauer EA, et al. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total knee arthroplasty. Anaesthesia 2008; 63: 1105-23.
5. Tierney E, Lewis G, Hurtig JB, Johnson D. Femoral nerve block with bupivacaine 0.25 percent for

postoperative analgesia after open knee surgery. Can J Anaesth 1987; 34: 455-8.
6. Weber A, Fournier R, Van Gessel E, Gamulin Z. Sciatic nerve block and the improvement of femoral nerve block analgesia after total knee replacement. Eur J Anaesthesiol 2002; 19: 834-6.
7. Buvanendran A, Kroin JS, Tuman KJ, Lubenow TR, Elmofty D, Moric M, et al. Effects of perioperative administration of a selective cyclooxygenase 2 inhibitor on pain management and recovery of function after knee replacement: a randomized controlled trial. JAMA 2003; 290: 2411-8.
8. Hubbard RC, Naumann TM, Traylor L, Dhadda S. Parecoxib sodium has opioid-sparing effects in patients undergoing total knee arthroplasty under spinal anaesthesia. Br J Anaesth 2003; 90: 166-72.
9. Rasmussen GL, Steckner K, Hogue C, Torri S, Hubbard RC. Intravenous parecoxib sodium foracute pain after orthopedic knee surgery. Am J Orthop 2002; 31: 336-43.
10. Koppert W, Frotsch K, Huzurudin N, Boswald W, Griessinger N, Weisbach V, et al. The effects of paracetamol and parecoxib on kidney function in elderly patients undergoing orthopedic surgery. Anesth Analg 2006; 103: 1170-6.
11. Nussmeier NA, Whelton AA, Brown MT, Joshi GP, Langford RM, Singla NK, et al. Safety and efficacy of the cyclooxygenase-2 inhibitors parecoxib and valdecoxib after noncardiac surgery. Anesthesiology 2006; 104: 518-26.
12. Schug SA, Joshi GP, Camu F, Pan S, Cheung R. Cardiovascular safety of the cyclooxygenase-2 selective inhibitors parecoxib and valdecoxib in the postoperative setting: an analysis of integrated data. AnesthAnalg 2009; 108: 299-307.
13. Stoltz RR, Harris SI, Kuss ME, LeComte D, Talwalker S, Dhadda S, et al. Upper GI mucosal effects of parecoxib sodium in healthy elderly subjects. Am J Gastroenterol 2002; 97: 65-71.
14. Wegener JT, van Ooij B, van Dijk CN, Hollmann MW, Preckel B, Stevens MF. Value of single-injection or continuous sciatic nerve block in addition to a continuous femoral nerve block in patients undergoing total knee arthroplasty: a prospective, randomized, controlled trial. Reg Anesth Pain Med 2011; 36: 481-8.
15. Geng D, Mao H, Wang J, Zhu X, Huang C, Chen L, et al. Protective effects of COX-2 inhibitor on titanium-particle-induced inflammatory osteolysis via the down-regulation of RANK/RANKL. Acta Biomater 2011; 7: 3216-21.
16. Jean YH, Wen ZH, Chang YC, Hsieh SP, Tang CC, Wang YH, et al. Intra-articular injection of the cyclooxygenase-2 inhibitor parecoxib attenuates osteoarthritis progression in anterior cruciate ligament-transected knee in rats: role of excitatory amino acids. Osteoarthritis Cartilage 2007; 15: 638-45.
17. Villasís-Keever MA, Rendón-Macías ME, Escamilla-Núñez A. Systematic review to assess the effectiveness and safety of parecoxib. Acta OrtopMex 2009; 23: 342-50.
18. Jirarattanaphochai K, Thienthong S, Sriraj W, Jung S, Pulnitiporn A, Lertsinudom S, et al. Effect of parecoxib on postoperative pain after lumbar spine surgery: a bicenter, randomized, double-blinded, placebo-controlled trial. Spine (Phila Pa 1976) 2008; 33: 132-9.
19. Lloyd R, Derry S, Moore RA, McQuay HJ. Intravenous or intramuscular parecoxib for acute postoperative pain in adults. Cochrane Database Syst Rev 2009; (2): CD004771.
20. Martinez V, BelbachirA, Jaber A, Cherif K, Jamal A, Ozier Y, et al. The influence of timing of administration on the analgesic efficacy of parecoxib in orthopedic surgery. AnesthAnalg 2007; 104: 1521-7.
21. Cappelleri G, Ghisi D, Fanelli A, Albertin A, Somalvico F, Aldegheri G. Does continuous sciatic nerve block improve postoperative analgesia and early rehabilitation after total knee arthroplasty? A prospective, randomized, double-blinded study. Reg Anesth Pain Med 2011; 36: 489-92.
22. Abdallah FW, Brull R. Is sciatic nerve block advantageous when combined with femoral nerve block for postoperative analgesia following total knee arthroplasty? A systematic review. Reg Anesth Pain Med 2011; 36: 493-8.

ประสิทธิภาพของยาพาริค็อกซิบเมื่อให้ทางหลอดเลือดดำ ในการลดปริมาณยาระงับปวดเทียบเท่ากับการฉีดยาชาเฉพาะที่ที่เส้นประสาทไซแอททิค ในการบำบัดปวดหลังผ่าตัดเปลี่ยนข้อเข่าเทียม เมื่อใช้ร่วมกับการให้ยาชาเฉพาะที่ที่เส้นประสาทฟีมอรัลอย่างต่อเนื่อง

นุช ตันติศิรินทร์, ธีรวัฒน์ ชลาชีวะ, สุวิมลวดี สายพิมพ์พงษ์, เดกว่าง เฮียวทราน, รอเดอริค เจ ฟินเลย์สัน

วัตถุประสงค์: *การให้ยาชาเฉพาะที่ที่เส้นประสาทฟีมอรัลอย่างต่อเนื่องหลังผ่าตัดเปลี่ยนข้อเข่า เป็นวิธีที่ได้รับความนิยมในการบำบัดปวดหลังผ่าตัด แต่วิธีดังกล่าวไม่ครอบคลุมการบำบัดปวดทางด้านหลังของข้อเข่าซึ่งต้องใช้ยาระงับปวดกลุ่มอนุพันธ์ฝิ่นในการบำบัด วัตถุประสงค์ของศึกษานี้คือ ศึกษาประสิทธิภาพของยาพาริค็อกซิบ ในการลดปริมาณยาระงับปวดเมื่อเปรียบเทียบกับการฉีดยาชาเฉพาะที่ที่เส้นประสาทไซแอททิค*

วัสดุและวิธีการ: *เมื่อได้รับการอนุมัติจากคณะกรรมการจริยธรรมการวิจัยในคนโรงพยาบาลรามาธิบดีแล้ว ได้ทำการรวบรวมผู้เข้าร่วมวิจัย ได้แก่ ผู้ป่วยที่เข้ารับการผ่าตัดเปลี่ยนข้อเข่าเทียมที่โรงพยาบาลรามาธิบดี ตั้งแต่เดือนมกราคม พ.ศ. 2557 ถึง ธันวาคม พ.ศ. 2557 โดยทุกคนจะได้รับการบำบัดปวดด้วยวิธีการหยดยาชา เฉพาะที่ที่เส้นประสาทฟีมอรัลอย่างต่อเนื่องด้วยบูพิวาเคอีน 0.125 เปอร์เซ็นต์ 7 มล.ต่อชม. ร่วมกับการใช้เครื่องหยดให้ยาแก้ปวดเมื่อต้องการ ผู้เข้าร่วมวิจัยจะถูกแบ่งเป็น 3 กลุ่ม ได้แก่ กลุ่ม 1 ได้รับการบำบัดปวดเพิ่มเติมด้วยวิธีการฉีดยาชาเฉพาะที่ที่เส้นประสาทไซแอททิคด้วยบูพิวาเคอีน 0.25 เปอร์เซ็นต์ 25 มล. กลุ่มที่ 2 ได้รับยาพาริค็อกซิบทางหลอดเลือดดำปริมาณ 40 มก. ทุก 12 ชม. กลุ่มที่ 3 เป็นกลุ่มควบคุม ผู้เข้าร่วมวิจัยจะถูกประเมินที่ 0, 6, 12 และ 24 ชม. หลังผ่าตัด โดยทีมวิจัยที่ไม่ทราบกลุ่มที่ผู้เข้าร่วมวิจัยอยู่ซึ่งจะประเมินระดับความปวด 0 ถึง 10 ขณะพัก ปริมาณยามอร์ฟีนที่ใช้ เวลาที่ใช้ยามอร์ฟีนครั้งแรก และผลข้างเคียงของยามอร์ฟีน*

ผลการศึกษา: *มีผู้เข้าร่วมงานวิจัย 78 คน โดยแบ่งเป็น 26 คนในแต่ละกลุ่ม ไม่พบความแตกต่างในระดับความปวดหลังผ่าตัด แต่พบกว่ากลุ่ม 3 ใช้ปริมาณมอร์ฟีนสูงกว่า (17±12 มก.) กลุ่ม 1 (10±7 มก.) และ 2 (9±5 มก.) อย่างมีนัยสำคัญ ($p<0.001$) ที่ 24 ชม. หลังผ่าตัด ไม่พบความแตกต่างในเวลาที่เริ่มใช้มอร์ฟีน ผลข้างเคียงจากยามอร์ฟีน และความพึงพอใจของผู้เข้าร่วมวิจัย*

สรุป: *การให้ยาพาริค็อกซิบทางหลอดเลือดดำและการฉีดยาชาเฉพาะที่ที่เส้นประสาทไซแอททิค สามารถลดปริมาณการใช้มอร์ฟีนเมื่อใช้ร่วมกับการให้ยาชาเฉพาะที่ที่เส้นประสาทฟีมอรัลอย่างต่อเนื่องในการบำบัดปวดหลังผ่าตัดเปลี่ยนข้อเข่าเทียม*