Reports of Investigation

Femoral nerve block and ketorolac in patients undergoing anterior cruciate ligament reconstruction

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Purpose: The primary objective was to evaluate the analgesic effectiveness of femoral nerve block and ketorolac following ACL reconstruction. The secondary objective was to examine their effects on recovery milestones.

Methods: Prior to standard general anesthesia, 90 patients were randomized into three groups of preoperative treatment: 1) femoral nerve block (15 mL bupivacaine 0.5%) and 1 mL normal saline *iv* (FNB group); 2) placebo femoral nerve block (15 mL normal saline) and 30 mg (1 mL) ketorolac *iv* (KT group); 3) placebo femoral nerve block (15 mL normal saline) and 1 mL normal saline *iv* (PL group). Postoperatively, pain was assessed by visual analogue score, demand and consumption of morphine via patient-controlled analgesia pump. The times for patients to tolerate oral fluid, food, sit up, ambulate and void were also noted.

Results: Morphine consumption within one hour, three hours and until POD 1 in the FNB group was lower than the PL group (7 ± 6, 11 ± 9, 27 ± 23 mg *vs* 13 ± 5, 20 ± 9, 49 ± 28 mg respectively), whereas only that within one hour in the KT group was lower than the PL group. Pain score was lower in FNB and KT groups in the first postoperative hour than in the PL group ($P < 0.05$). There were no differences among the three groups in the times to meet recovery milestone and discharge criteria.

Conclusion: Femoral nerve block provides superior analgesia than placebo for ACL reconstruction but was insufficient to facilitate early recovery.

Objectif : D'abord, évaluer l'efficacité analgésique du blocage du nerf fémoral et de l'administration de kétorolac à la suite d'une reconstruction du ligament croisé antérieur (LCA). Ensuite, examiner leurs effets sur les étapes de la récupération.

Méthode : Avant l'anesthésie générale standard, 90 patients ont été répartis en trois groupes : 1) blocage du nerf fémoral (15 mL de bupivacaïne 0,5 %) et 1 mL de solution salée *iv* (groupe BNF); 2) un placebo du blocage du nerf fémoral (15 mL de solution salée) et 30 mg (1 mL) de kétorolac *iv* (groupe KT); 3) un placebo du blocage nerveux (15 mL de solution salée) et 1 mL de solution salée *iv* (groupe PL). La douleur postopératoire a été évaluée selon l'échelle visuelle analogue, la demande et la consommation de morphine au moyen d'une pompe d'analgésie contrôlée par le patient. On a aussi noté le moment de la prise de liquide et de nourriture, le moment où le patient pouvait s'asseoir et marcher et celui de la première miction.

Résultats : La consommation de morphine pendant la première heure, les trois premières heures et jusqu'à la fin du premier jour postopératoire a été plus faible dans le groupe BNF que dans le groupe PL (7 ± 6, 11 ± 9, 27 ± 23 mg *vs* 13 ± 5, 20 ± 9, 49 ± 28 mg respectivement), mais ce n'est que pendant la première heure qu'elle a été plus faible dans le groupe KT *vs* PL. La douleur a été moins intense dans les groupes BNF et KT que dans le groupe PL pendant la première heure postopératoire ($P < 0,05$). Il n'y a pas eu de différence intergroupe quant au moment des différentes étapes de la récupération et de la conformité aux critères de sortie.

Conclusion : Le blocage du nerf fémoral fournit une analgésie supérieure au placebo dans le cas d'une reconstruction du LCA, mais ne permet pas une récupération plus rapide.

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ARTHROSCOPIC anterior cruciate ligament (ACL) reconstruction is a procedure that can be performed as an ambulatory procedure if effective postoperative analgesia can be achieved. After this procedure, 10% of patients report severe pain, mostly in the first two days after surgery.[1,2] The average dose of morphine or equivalent required for the first 24 hr ranges from 50 to 80 mg.[1,3] An effective analgesic regimen is required to optimize the control of pain and to facilitate earlier hospital discharge. Although both non-steroidal anti-inflammatory drugs (NSAIDs) and femoral nerve block have been reported to be effective in pain control following ACL reconstruction,[4,5] these modalities have not been examined and compared in a randomized, double-blind and control manner. The design of this study was primarily to evaluate the analgesic effectiveness of femoral nerve block and ketorolac, an NSAID, in the postoperative pain control following ACL reconstruction. Our secondary objective was to examine the effects of femoral nerve block and ketorolac on recovery milestones.

Methods

With approval from the institutional human ethics committee, informed consent was obtained from 90 ASA physical status I and II patients between 18 and 60 yr of age who were scheduled to undergo elective arthroscopic ACL reconstruction surgery. Patients with a known history of allergy or sensitivity to NSAIDs, local anesthetics, or morphine; a history of opioid abuse; or chronic pain other than that related to the site of surgery were excluded from the study, as were those with an inadequate understanding of English.

Patients were studied using a prospective, double-blind, controlled design. They were randomized by a computer-generated list into femoral nerve block (FNB), ketorolac (KT), or placebo (PL) groups. Preoperatively, patients in the FNB group received femoral nerve block with 15 mL bupivacaine 0.5% and 1 mL normal saline *iv*. Patients in the KT group received femoral nerve block with 15 mL normal saline and 30 mg (1 mL) ketorolac *iv*. Patients in the PL group received both the placebo femoral nerve block and intravenous normal saline injection. All study medications in equivalent volumes were prepared by the pharmacy. Neither the anesthesiologists involved in the anesthesia, the nurses, nor the research assistants involved in the care and assessment of patients were aware of the type of medication used for each patient.

Femoral nerve block was performed preoperatively in the postanesthesia care unit (PACU). Midazolam, 1 to 3 mg *iv*, was administered for anxiolysis before the performance of the block. The femoral nerve was located with the aid of a nerve stimulator, using a regional block needle, and the proximity of the nerve was demonstrated by movement of the patella caused by the contraction of quadriceps femoris muscle. Study medication was injected once the contraction could be maintained with current as low as 0.3 mA. When the femoral nerve block was done, 1 mL of study medication was administered intravenously. All patients received standardized general anesthesia. Anesthesia was induced with 2-3 $mg \cdot kg^{-1}$ propofol and fentanyl (up to a total of 1.5 $\mu g \cdot kg^{-1}$) *iv*. Anesthesia was maintained with nitrous oxide 65% in oxygen and isoflurane (up to 2% end-tidal (ET) concentration), with patients breathing spontaneously through a laryngeal mask airway. If the mean arterial blood pressure or heart rate was >20% above the preoperative baseline values despite isoflurane 2% ET, additional fentanyl, 25 µg bolus, was administered.

At the end of the operation, no intra-articular bupivacaine was administered. After the removal of the laryngeal mask, the patient was transferred to the PACU. Morphine, administered via a patient-controlled analgesia (PCA) pump, was started with the setting of bolus dose from 1.5 mg, lockout interval of five minutes, and four-hour maximum of 40 mg. Pain was assessed by using a self-rated visual analog score (VAS) ranging from 0 to 10, where 0 = no pain and 10 = worst possible pain. In the first 15 min in the PACU, the patient could receive additional morphine (2 mg every five minutes; up to 6 mg over 15 min) administered by a nurse if the VAS was ≥5. The patient was then transferred to the ward for overnight stay. Once patients tolerated fluid well, PCA morphine was stopped and patients were switched to acetaminophen with 30 mg codeine every four hours as requested. No additional NSAID was given throughout the hospital stay.

Demographic characteristics of patients, intraoperative anesthetic management (amount of propofol and fentanyl given), and the type of ACL graft used were documented. A baseline pain score was assessed preoperatively, before the administration of femoral nerve block.

Postoperatively, an investigator assessed the patient without knowing the type of analgesia the patient had received. In the PACU, a pain score was measured when the patient was stable and oriented. The number of patients complaining of nausea and requiring an anti-emetic (dimenhydrinate) was documented. Anti-emetics were not given routinely but were available on request or for observed nausea and vomiting. The amount of morphine administered and the demand from the PCA pump were also measured. All these measurements were repeated at 15-min intervals until the

patient was discharged from PACU, and then every 30 min until the patient reached a Postanesthesia Discharge Score (PADS) of 9.[6]

Postoperative recovery was evaluated by using the following criteria: 1) orientation time (time until the patient was oriented to person, place, and time); 2) time from PACU admission to first request for postoperative analgesic medication; 3) time to reach an Aldrete score of 9 (the Aldrete score was recorded every 15 min); 4) total amount of morphine and dimenhydrinate administered; 5) time to tolerate oral fluid and solid food intake; 6) time to sit up; 7) time to ambulate; 8) time to void; and 9) time to reach a PADS of 9.

The demographic data, dose of anesthetic, amount of morphine and the time to reach various recovery milestones were analyzed with Krushal-Wallis test followed by post-hoc pairwise comparison. The pain score (VAS) was analyzed by repeated measure of analysis of variance (ANOVA) while the number of patients requiring oral analgesic, anti-emetic medication or with nausea by the Fisher exact test. $P \leq 0.05$ was considered significant. All data were recorded as mean ± SD.

Sample size calculation was based on the data obtained from the previous study[a] on a similar surgical population in which the postoperative pain score was 51 ± 25. Assuming a type I error of 0.05 and type II error of 0.2, 30 patients would be required in each group to detect a reduction of 33% in pain score.

Results

Five patients were excluded from the study: three patients received only diagnostic arthroscopy without ACL reconstruction, one patient admitted to a history of opioid abuse in the postoperative period, and another patient was excluded because of an anesthesia protocol violation.

There were no differences among the study groups in age, sex, weight, height, ASA physical status, duration of surgery, type of graft used or total amount of propofol and fentanyl administered intraoperatively (Table I).

The time to request the first analgesic was longer in the KT and FNB groups than in the PL group with no difference between KT and FNB group (Table II). The total morphine consumption and PCA attempts within one hour, three hours and before discharge on postoperative day 1 were lower in the FNB group than in the PL group ($P < 0.05$). In the KT group, only the morphine consumption within the first hour was lower than in the PL group and the rest of morphine consumption was not different from the FNB or PL groups (Table II). Baseline VAS scores for pain were similar among the three study groups. In the first hour, they were lower in the FNB and KT groups than in the PL group, with no difference between the FNB and KT groups (Figure). The number of patients requiring postoperative analgesia (acetaminophen with 30 mg codeine) was similar among the three groups.

The number of patients requiring dimenhydrinate in the PACU and those with nausea within one hour and three hours in the postoperative period were similar in the three groups (Table II). Time in the PACU, time to reach PADS 9, time to sit up, to ambulate, to drink, to eat and to void were not different among the groups (Table III).

TABLE I Demographic characteristics, details of surgery and dose of anesthetic agent

	FNB (n=29)	*KT (n=28)*	*PL (n=28)*
Age (yr)	31 ± 9	30 ± 8	32 ± 7
Height (cm)	175 ± 10	175 ± 9	173 ± 11
Weight (kg)	78 ± 15	85 ± 17	77 ± 16
Body Mass Index ($kg \cdot m^{-2}$)	26 ± 4	27 ± 4	26 ± 3
Sex (M/F)	19 / 10	23 / 6	20 / 7
ACL graft HS/BPT/AL	22/3/4	12/8/8	15/8/8
ASA class I/II	26 / 3	27 / 2	24 / 3
Duration of surgery (min)	78 ± 19	81 ± 19	81 ± 20
Propofol (mg)	243 ± 82	216 ± 45	246 ± 78
Fentanyl (μg)	135 ± 58	149 ± 46	137 ± 53

Values are presented as mean ± SD.

FNB, femoral nerve block group; KT, ketorolac group; PL, placebo group.

HS-hamstring, BPT- bone-patella-tendon, AL- allograft

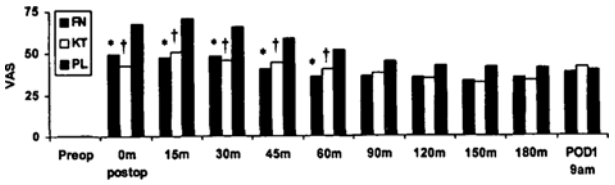

FIGURE Pain scores (VAS) in the postoperative period. FN, femoral nerve block group; KT, ketorolac group; PL, placebo group; POD1, postoperative day 1.

* $P < 0.05$ between the FN and PL groups.

† $P < 0.05$ between the KT and PL groups.

[a] *Rajasingham M, Moote CA, Fowler PJ, et al.* Propofol vs thiopentone and isoflurane anesthesia for cruciate ligament surgery. Anesthesiology 1992; 77: A28.

TABLE II Postoperative analgesia and nausea

	FNB (n=29)	*KT (n=28)*	*PL (n=28)*
Time to first analgesic (min)	16 ± 22*	25 ± 46*	7 ± 5
Morphine within 1 hr (mg)	7 ± 6†	9 ± 7*	13 ± 5
Morphine within 3 hr (mg)	11 ± 9†	17 ± 13	20 ± 9
Morphine until POD1‡ (mg)	27 ± 24*	39 ± 33	49 ± 28
No. of PCA attempts < 1 hr	5 ± 8*	9 ± 11	15 ± 31
No. of PCA attempts < 3 hr	9 ± 11*	19 ± 22	24 ± 32
No. of PCA attempts until POD1‡	20 ± 21*	45 ± 61	56 ± 71
Patients requiring PO analgesic < 1 hr	1	1	0
Patients requiring PO analgesic < 3 hr	1	1	0
Patients requiring PO analgesic until POD1‡	1	2	3
No. of patients requiring dimenhydrinate in PACU	8	7	7
Patients with nausea within 1 hr	12	9	7
Patients with nausea within 3 hr	18	14	15

Values are presented as mean ± SD

FNB, femoral nerve block group; KT, ketorolac group; PL, placebo group.

*$P < 0.05$ compared with PL group in post-hoc pairwise comparison; † $P < 0.001$ compared with PL group in post-hoc pairwise comparison; ‡ Measurement before discharge on postoperative day 1 (POD1)

TABLE III Recovery milestones

Interval in min	*FNB (n=29)*	*KT (n=28)*	*PL (n=27)*
Time in PACU	86 ± 25	84 ± 25	93 ± 33
Time to PADS 9	1045 ± 512	1010 ± 739	1299 ± 605
Sit up	223 ± 324	315 ± 497	287 ± 409
Drink	172 ± 205	124 ± 88	193 ± 205
Eat	499 ± 376	450 ± 382	622 ± 491
Ambulate	995 ± 554	970 ± 616	1174 ± 613
Void	278 ± 170	537 ± 645	488 ± 466

Values are presented as mean ± SD

FNB, femoral nerve block group; KT, ketorolac group; PL, placebo group.

Discussion

Although femoral nerve block is suggested to be effective for postoperative analgesia, this is the first double-blind, randomized placebo-controlled study on the postoperative analgesic efficacy of femoral nerve block in patients receiving ACL reconstruction under general anesthesia. We have shown that femoral nerve block provides superior analgesia and a reduction in postoperative analgesic consumption compared with a placebo group. We also showed that a single intravenous dose of ketorolac preoperatively provides better analgesia and reduced analgesic requirement than placebo only in the first postoperative hour.

Favourable results have been reported with the use of femoral nerve block in postoperative pain management of various knee surgeries.[7–9] However, there is a paucity of information regarding the use of femoral nerve block with arthroscopic ACL reconstruction surgery. In one such study, 92% of patients receiving femoral nerve block preoperatively did not require parenteral opioids in the postoperative period.[5] However, it was not a control study. Preliminary data from a recent double-blind, control study showed that there was a reduction in pain score and morphine consumption with the use of femoral nerve block.[10] In that study, combined spinal-epidural anesthesia was used, and fentanyl (100 μg) was administered via epidural before the end of the surgery. In our study, patients received general anesthesia, and no other analgesic modality such as neuraxial opioids, intraarticular local anesthetic or morphine were administered with the femoral nerve block. Nevertheless, femoral nerve block provided effective postoperative pain control and an opioid-sparing effect.

Non-steroidal anti-inflammatory agents are another alternative for the control of postoperative pain following ACL reconstruction.[11] In a study comparing the use of PCA opioids with intermittent administration of ketorolac in ACL reconstruction surgery, ketorolac provided effective analgesia similar to that of PCA opioids postoperatively.[4] Furthermore, side effects such as nausea, vomiting, constipation, and drowsiness were less in the ketorolac group.[4] In our study, the KT group received one single intravenous dose of ketorolac preoperatively. The only benefit shown was better pain score and lower morphine consumption in the first post-operative hour. Given the terminal elimination half-life of ketorolac of approximately five hours, it is expected that the opioid-sparing effect of ketorolac, if any, would occur in the early post-operative period.

Despite the difference in pain control and morphine consumption between the FNB and PL groups, the recovery milestones were not different among the three groups. One possible explanation is that the difference in the amount of analgesic and in side effects from this single-modal approach was not significant enough to facilitate earlier recovery and discharge. The incidence of nausea was similar among the three groups, and pain scores in the FNB and KT groups were lower than those in the PL group only in the immediate postoperative period. With a multimodal analgesic approach, better analgesia can be achieved with concomitant reduction of side effects.[12] This has been shown to result in faster recovery and earlier discharge.[13] Acute pain from ACL reconstruction surgery has three major components: tissue injury, nociceptor sensitization, and activation of a central pathway.[14] The multimodal approach can be exemplified by using local instillation of anesthetic and morphine into the joint, NSAIDs, femoral nerve block, and systemically administered opioids. Since our study was designed to evaluate the analgesic effectiveness of femoral nerve block and ketorolac as the sole analgesic modality in addition to systemic opioids, a combination of analgesic modalities was not considered.

Other possible explanations for the absence of improvement in recovery milestones may be related to the intrinsic design of our study. The times to achieve the recovery milestones were much longer that one would expect for ambulatory surgery. This may be related to the use of intravenous patient-controlled analgesia with morphine as the initial method of analgesia. In our institution, ACL reconstruction is performed on an in-patient basis, and patients stay in the short-stay unit overnight. Although PCA gives an objective assessment of opioid requirement, this is not the practice of choice at our institution and in many other centres for ambulatory patients as this may result in delayed discharge. Furthermore, the nursing staff in this short-stay unit are not aggressive about encouraging patients to start oral intake and ambulate early on the day of surgery.

There are several limitations in our study. The pain score was assessed only at rest. In evaluating the efficacy of a certain analgesic modality in lower limb surgery, pain scores at rest and with movement are equally important. Although pain scores with movement were not measured in our study, a similar study showed that femoral nerve block provided effective analgesia at rest as well as with movement.[10] Another limitation is related to the use of ketorolac. Only one dose of ketorolac was administered in the preoperative period. Thus, the duration of analgesic effect was shorter than that with femoral nerve block. Given the terminal elimination half-life of ketorolac of approximately five hours, the duration of analgesia effect is expected to cover the early postoperative period. If repeated doses of ketorolac had been given in the postoperative period, it is possible that the analgesic benefits of ketorolac could be demonstrated beyond the early postoperative period.

In conclusion, femoral nerve block provides a superior analgesic effect for patients undergoing ACL reconstruction surgery than does placebo. However, when applied alone, femoral nerve block does not facilitate early recovery. A multimodal approach, combining the use of femoral nerve block with NSAIDs, may encourage faster recovery and needs to be further studied.

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