Comparing the Efficacy of Postoperative Pain Control Between Intravenous Parecoxib and Oral Diclofenac in ACL Reconstruction

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Background: A nonsteroidal anti-inflammatory drug such as oral diclofenac is normally used to relieve postoperative pain after anterior cruciate ligament reconstruction (ACLR), but most patients continue to have moderate-to-severe pain that disturbs their rehabilitation. Some orthopaedists prefer to use intravenous (IV) parecoxib for postoperative pain control.

Purpose: To compare the efficacy of IV parecoxib and oral diclofenac for postoperative pain control in ACLR.

Study Design: Cohort study; Level of evidence, 3.

Methods: We retrospectively collected and analyzed postoperative pain in patients who underwent both single- and double-bundle ACLR; pain was reported on a 10-point visual analog scale (VAS; 10 = worst pain). After the operation, each patient was given either IV parecoxib twice a day or oral diclofenac 3 times a day, and all patients received paracetamol 6 times per day for 24 hours postoperatively. If the patient complained of moderate or severe pain (VAS >3) after surgery, 3 mg of morphine would be given intravenously every 3 hours and 1 mg of morphine as a rescue analgesic every 1 hour for 24 hours postoperatively. Postoperative VAS and morphine consumption were recorded every 4 hours for 24 hours. Data were analyzed using paired *t* test, analysis of variance, and chi-square test.

Results: Overall, 161 patients were included in this study, of whom 47 received IV parecoxib and 114 received oral diclofenac. The mean VAS scores at 4 and 8 hours postoperatively were 3.5 and 3.4, respectively, in the parecoxib group, and 4.4 and 4.7, respectively, in the diclofenac group. The parecoxib group had significantly lower mean VAS than the diclofenac group at 4 hours ($P = .047$) and 8 hours ($P = .005$), and the mean cumulative morphine consumption in the parecoxib group was significantly lower than in the diclofenac group at all time points ($P < .05$) except 4 hours postoperatively.

Conclusion: This study found that IV parecoxib was more effective than oral diclofenac in controlling postoperative pain and resulted in lower postoperative morphine consumption within the first 24 hours after ACLR.

Keywords: anterior cruciate ligament; arthroscopic surgery; postoperative pain; reconstruction

Arthroscopic anterior cruciate ligament reconstruction (ACLR) is one of the most common operations in sports medicine. Even though this operation is a minimally invasive procedure, many patients suffer moderate-to-severe postoperative pain. The pain varies depending on individual factors, such as pain perception,[24] pain toleration,[15] intra-articular diseases, and operative procedure, but regardless of the particulars, such pain is an obstacle to early postoperative rehabilitation and affects the patient's satisfaction concerning his or her operation.

In our country and institution, the standard pain modalities in ACLR are spinal block alone, or spinal block combined with either femoral nerve block or adductor canal block, which control postoperative pain for 2 to 4 hours. After the surgery, a combination of analgesic methods, including nonsteroidal anti-inflammatory drugs (NSAIDs) and/or an opioid, can be used to control postoperative pain. The NSAID acts to decrease the inflammation process after surgery by inhibiting cyclooxygenase (COX), an enzyme produced after surgery.[5,12] NSAIDs are divided into nonselective COX-2 inhibitors, selective COX-2 inhibitors and specific COX-2 inhibitors. The advantages of nonselective COX-2 inhibitors are that they are inexpensive and have high efficacy.

There have been many studies evaluating the efficacy of intravenous (IV) and oral NSAIDs for postoperative pain control, and all reported that both had better results in postoperative pain reduction than placebo in either open or minimally invasive surgery.[4,20] There are many types of IV and oral NSAIDs. In Thailand, both IV parecoxib and oral diclofenac are used commonly for postoperative pain

The Orthopaedic Journal of Sports Medicine, 9(10), 23259671211041660
DOI: 10.1177/23259671211041660

control, depending on a patient's decision concerning the different associated costs.

To our knowledge, to date there have been no studies evaluating differences in postoperative pain between IV parecoxib and oral diclofenac treatments. The purpose of this study was to evaluate the efficacy of IV parecoxib and oral diclofenac in postoperative pain control after ACLR, a procedure that is common in sports medicine. We hypothesized that patients in the IV parecoxib group would have lower postoperative pain and morphine consumption than those in the oral diclofenac group.

METHODS

This study was a retrospective review of patients' medical records from January 2016 to December 2019. It was approved by the ethics committee of the Faculty of Medicine of Prince of Songkla University. Included in the review were records of patients between 18 and 50 years of age who underwent ACLR. The exclusion criteria were patients who had undergone revision surgery or who had a history of intra-articular knee fracture, previous knee surgery, or an associated injury involving the posterior cruciate ligament or medial/lateral collateral ligament.

Demographic data (age, sex, and body mass index [BMI]), side of operation, surgical procedure (single- or double-bundle ACLR), associated intra-articular injuries such as meniscal injury and/or cartilage injury, concomitant operative surgeries such as meniscal repair, tourniquet time, visual analog scale (VAS) pain scores, and doses of morphine used were recorded with a standard recording form. Patients were evaluated for 24 hours after their surgery to assess their postoperative pain and the amount of morphine used. The postoperative pain VAS and morphine consumption were recorded every 4 hours after the surgery for 24 hours. The VAS was scored on a scale of 0 (no pain) to 10 (worst pain imaginable).

Surgical Procedures

The single-bundle ACLRs were performed by a single experienced orthopaedist (T.B.) in sports medicine. For each procedure, the patient was placed in the supine position with a thigh tourniquet. An oblique incision was made over the pes anserinus. The semitendinosus and gracilis tendons were harvested and used to prepare a 6-strand graft bundle for the reconstruction. An anterolateral portal was created as a viewing portal, and anteromedial and accessory anteromedial portals were created for instrumentation. An arthroscopic examination was performed to assess the intra-articular abnormality. The severity of the injury was then evaluated, and the problem was managed according to the treatment criteria. The centers of the femoral and tibial footprints were used as landmarks to create femoral and tibial tunnels, the size of which depended on the graft size.

The double-bundle ACLRs were done by another orthopaedist (W.P.) experienced in sports medicine. The procedures of graft harvesting and portal creation were the same as in single-bundle reconstructions. The semitendinosus tendon was used to prepare a triple-strand bundle for anteromedial bundle reconstruction, and the gracilis tendon was used to prepare a triple-strand bundle for posterolateral bundle reconstruction. Anteromedial and posterolateral femoral tunnels and 2 tibial tunnels were created based on the footprint of each bundle in the femoral and tibial footprints.

In all procedures, EndoButton (Smith & Nephew Endoscopy) was used for femoral graft fixation and Biosure HA (Smith & Nephew Endoscopy) was used for tibial graft fixation.

Beginning on postoperative day 1, all patients were fitted with a long knee brace locked at full extension and both reconstruction groups began the same rehabilitation protocol, starting with quadriceps exercises and active straight-leg raises.

Analgesic Protocol

Intraoperative Analgesia. In the operating room, the patient was anesthetized by an experienced anesthesiologist using either a combination spinal nerve block with 0.5% heavy Marcaine (Aspen) and adductor nerve block with 0.25% Marcaine or only a spinal nerve block with 0.5% heavy Marcaine. The level of the analgesic block was at least vertebra L2.

Postoperative Analgesia. After the operation, each patient was given either oral analgesia based on diclofenac (25 mg/tablet) 3 times a day or IV parecoxib (40 mg/vial) twice a day (which drug depended on physician preference and patient reimbursement). All patients were given paracetamol (500 mg/tablet) 6 times per day for 24 hours postoperatively. If a patient complained of moderate or greater pain (VAS >3), 3 mg of morphine was given intravenously every 3 hours and 1 mg of morphine as a rescue analgesic every 1 hour. VAS scores were recorded at 0, 4, 8, 12, 16, 20 and 24 hours postoperatively.

Statistical Analysis

Statistical analysis was performed with R Version 3.4.3 (R Foundation for Statistical Computing) with the "epicalc"

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Final revision submitted April 19, 2021; accepted June 8, 2021.

The authors declared that there are no conflicts of interest in the authorship and publication of this contribution. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

Ethical approval for this study was obtained from Prince of Songkla University (REC 63-554-11 -1).

package. Continuous data such as VAS scores, morphine consumption, operative time, and tourniquet time were shown as mean ± SD and compared with the paired *t* test and analysis of variance. Categorical data such as sex, type of ACLR (single or double bundle), associated intra-articular injuries (cartilage injury or meniscal injury), and concomitant intra-articular surgeries (meniscal repair) were compared with the chi-square test. A *P* value of .05 was considered significant.

TABLE 1
Comparison of Patient Characteristics Between the Parecoxib and Diclofenac Groups[a]

Characteristic	IV Parecoxib (n = 47)	Oral Diclofenac (n = 114)	*P*
Age, y	31.7 ± 9.1	30.6 ± 9.6	.477
Body mass index, kg/m^2	24.7 ± 3.4	24.8 ± 3.4	.784
Side			≥.999
Right	24 (51.1)	58 (50.9)	
Left	23 (48.9)	56 (49.1)	
Level of spinal block			≥.999
T10-T12	28 (59.6)	70 (61.4)	
L1-L2	19 (40.4)	44 (38.6)	
Additional adductor canal block	24 (51.1)	53 (46.5)	.339
ACLR type			.98
Single bundle	17 (36.2)	41 (36.0)	
Double bundle	30 (63.8)	73 (64.0)	
Tourniquet time, min	96.1 ± 19.9	96.8 ± 23.5	.848
Associated injury			>.05
Medial meniscus	23 (48.9)	71 (62.3)	
Lateral meniscus	24 (51.1)	51 (44.7)	
Cartilage	16 (14)	3 (6.4)	
Concomitant surgery			>.05
Medial meniscal repair	14 (29.8)	47 (41.2)	
Lateral meniscal repair	10 (21.3)	18 (15.8)	

[a]Data are reported as mean ± SD or n (%). ACLR, anterior cruciate ligament reconstruction; IV, intravenous.

RESULTS

Participants

Overall, 161 patients were included in the study (144 men and 17 women); 47 patients received IV parecoxib (parecoxib group) and 114 patients received oral diclofenac (diclofenac group). Single-bundle ACLR was performed on 58 patients and double-bundle reconstruction on 103 patients. The demographic data of all patients (Table 1) showed no statistically significant differences in baseline characteristics (sex, BMI, side of operation, tourniquet time, associated intra-articular injuries and concomitant intra-articular surgeries) between the study groups.

VAS Scores

The patients in the parecoxib group had lower mean VAS scores at all measurement times, from immediately to 24 hours postoperatively (Figure 1). The mean VAS scores in both groups increased from immediately to 8 hours postoperatively, after which they all decreased. The mean VAS scores at 4 and 8 hours postoperatively were 3.5 and 3.4, respectively, in the parecoxib group, and 4.4 and 4.7, respectively, in the diclofenac group. The parecoxib group

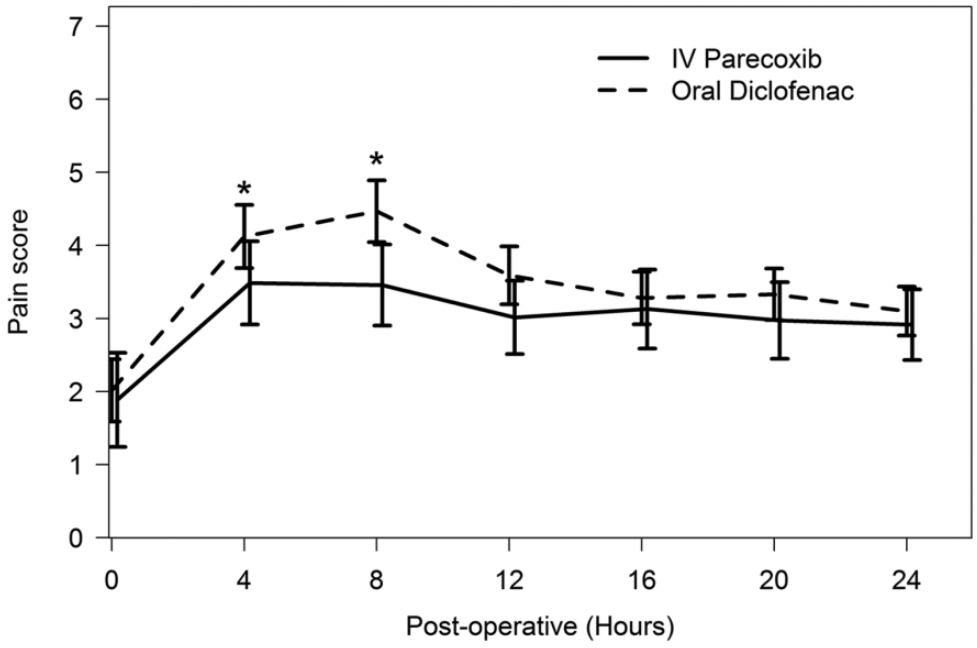

Figure 1. Comparing mean visual analog scale scores for pain between the parecoxib and diclofenac groups during the first 24 hours postoperatively. *Statistically significant difference between groups ($P < .05$). IV, intravenous.

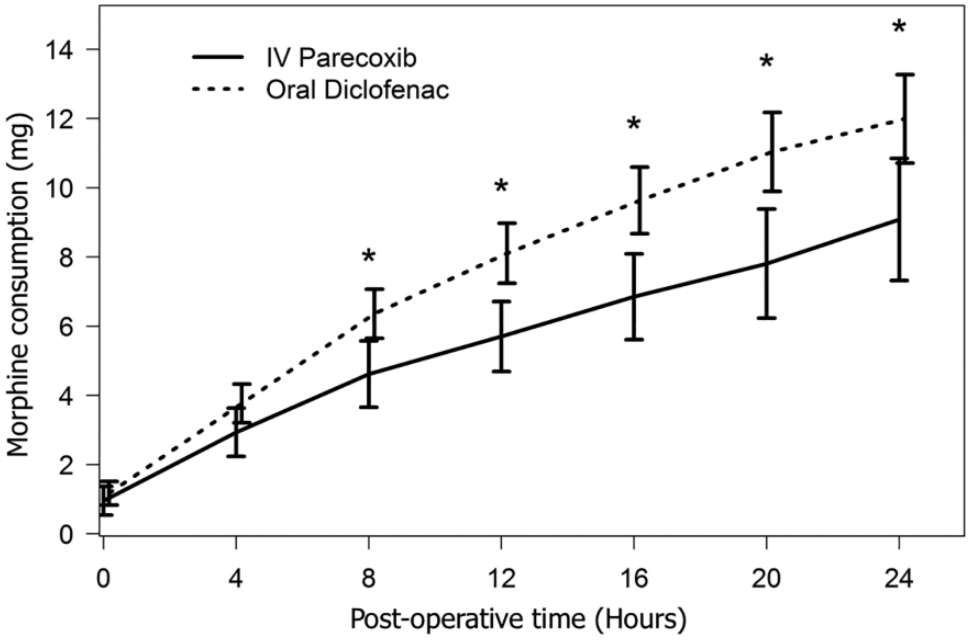

Figure 2. Comparing mean cumulative morphine consumption between the parecoxib and diclofenac groups during the first 24 hours postoperatively. *Statistically significant difference between groups ($P < .05$). IV, intravenous.

had significantly lower mean VAS scores than the diclofenac group at 4 and 8 hours postoperatively.

Morphine Consumption

The mean cumulative doses of morphine given to the 2 groups is shown in Figure 2. The mean cumulative morphine consumption in the parecoxib group was statistically significantly lower than in the diclofenac group at 8, 12, 16, 20, and 24 hours postoperatively ($P = .007$, .002, .001, .002, and .013, respectively).

DISCUSSION

ACLR is one of the most common procedures in sports medicine, and, as with most surgical procedures, there is postoperative pain. This study found that patients given IV parecoxib after ACLR had significantly lower mean pain VAS scores at 4 and 8 hours postoperatively compared with patients given oral diclofenac. In addition, the mean cumulative morphine consumption was significantly lower in the parecoxib group than in the diclofenac group at all time points except 4 hours postoperatively.

Postoperative pain management is one of the most important factors affecting the early stages of postoperative rehabilitation and the patient's satisfaction with the surgery.[10,19,26] The surgeon can decrease postoperative pain by using preemptive analgesia,[4] combined general and regional anesthesia, combined regional analgesia (spinal nerve block and femoral nerve block or adductor canal block), and postoperative analgesia (IV NSAIDs, IV patient-controlled analgesia, oral NSAIDs, oral gabapentin, or oral acetaminophen).[1,6,7,14,18,20,27] Regional anesthesia, of which the main choices are spinal nerve block, femoral nerve block, and/or adductor canal block, is used more commonly than general anesthesia in orthopaedic surgery,[13] especially in ACLR.

The spinal nerve block is the most common method in our country, but this technique is contraindicated in patients with elevated intracranial pressure (usually because of intracranial mass), coagulopathy, or infection at the site of the procedure.[16] The advantages of the spinal nerve block are decreased immediate postoperative pain, a lower number of doses of postoperative morphine required, and fewer and less severe adverse effects such as nausea and vomiting.[17] Although the spinal nerve block has some effect on decreasing postoperative pain,[13,17] the analgesic effect wears off rapidly postoperatively and further pain control is often required, for which NSAIDs have been shown to have good efficacy in postoperative pain reduction.[2,4,6,7,14,20,28]

Postoperative NSAIDs can be given to the patient by either oral or IV routes. Peng et al[20] compared IV ketorolac with IV saline and found that the ketorolac was superior to saline in postoperative pain control. In 3 studies that examined oral NSAIDs, the drugs oral ibuprofen, ketorolac, and etoricoxib were found to be more effective in postoperative pain control than oral placebo.[4,6,7] In Thailand, most patients undergoing ACLR are young adults or adults and are commonly given oral diclofenac to control postoperative pain, but some of these patients are still forced to delay the start of postoperative rehabilitation because of moderate or severe pain. Several studies have evaluated the efficacy of IV parecoxib, which is used widely to relieve postoperative pain, in cases of total

knee arthroplasty[2,14,28]; all found that it had high efficacy in postoperative pain control and was also associated with reduced morphine consumption.[2,28]

The current study was designed to compare the efficacy of IV parecoxib and oral diclofenac; we found that patients who underwent ACLR and given parecoxib had significantly lower mean immediate postoperative VAS scores (at 4 and 8 hours), and mean cumulative morphine consumption was also significantly lower at 8, 12, 16, 20, and 24 hours. We believe that IV parecoxib relieved postoperative pain more effectively than oral diclofenac because the onset time and peak effect of IV parecoxib are shorter than for oral diclofenac. The half-lives of IV parecoxib and oral diclofenac are 22 minutes and 2 hours, respectively.

The results from this study can be applied to manage postoperative pain in patients with ligament reconstruction in either a 1-day surgery or limited-resource setting.[21,25] The aims of these settings are to use minimal resources while achieving the highest efficacy. We suggest the IV parecoxib should be begun immediately after finishing the operation followed by an oral NSAID such as diclofenac because we found that IV parecoxib initiated immediately resulted in significantly lower mean VAS scores at 4 and 8 hours postoperatively.

Even though NSAIDs are efficacious in postoperative pain control, some surgeons avoid NSAIDs because of reported adverse effects on strengthening and tendon healing. In biomechanical studies on animals, IV parecoxib, celecoxib, indomethacin, and ibuprofen were given to rats and rabbits and the strengthening and tendon healing effects were evaluated.[3,8,9,22,23] These studies found that the strengthening and tendon healing in the treated animals was lower than in the placebo groups. However, although NSAIDs affected the strengthening and tendon healing in these animal studies, a clinical study in humans found that receiving NSAIDs did not affect healing after ACLR. Ge et al[11] evaluated knee stability (measured with an anterior drawer test, Lachman test, pivot-shift test, and KT-2000 arthrometer) and functional outcomes (using the International Knee Documentation Committee Questionnaire, Lysholm score, and Tegner scale) by comparing patients receiving celecoxib or tramadol, and they found no significant differences between the 2 groups in knee stability and functional outcomes at 1-year follow-up.

There were some limitations to this study. First, this was a retrospective study, thus there was a chance of selection bias between the parecoxib and diclofenac groups. However, we believe this potential bias was minimal at best, as there were no statistically significant differences in the demographic data between the 2 groups. Second, many factors can affect postoperative pain, such as preoperative psychological status, that we did not evaluate in this study. However, no patient in our study was taking preoperative opioid medications. Third, the pain scores were assessed with the patient only in the resting position, and we did not evaluate the patients' pain during rehabilitation, which is an important factor for timely recovery.

CONCLUSION

This study found that IV parecoxib was more effective than oral diclofenac in controlling postoperative pain at all time points, and significantly at 4 and 8 hours; the parecoxib group also had lower mean morphine consumption at all time points within the first 24 hours after ACLR.

ACKNOWLEDGMENT

The authors sincerely thank Boonsin Tangtrakulwanich of the Orthopedics Department and Nannapat Pruphetkaew of the Epidemiology Unit, Faculty of Medicine, for providing methodological and statistical supports; and David Patterson for his linguistic support.

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