Efficacy of Celecoxib for Early Postoperative Pain Management in Hip Arthroscopy: A Prospective Randomized Placebo-Controlled Study

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Purpose: To determine whether 400 mg of celecoxib administered 1 hour before hip arthroscopy surgery would reduce pain, provide reduction in overall narcotic consumption, and lead to more rapid discharge from recovery rooms. **Methods:** Ninety-eight patients were randomized to either the celecoxib group (n = 50) or the placebo group (n = 48). An a priori power analysis was done set to detect a difference of 0.50 on the visual analog scale (VAS), based on the senior author's preference. The number of patients planned for recruitment was rounded up to 100 to allow for flexibility in the study. Inclusion criteria were any patient at least 18 years old who underwent hip arthroscopy surgery performed by the senior author. All patients had less than Tönnis grade 2 arthritis. Exclusion criteria were allergy to sulfa-based drugs, prior adverse reaction to celecoxib, or patients who were on chronic narcotics for whom alternative pain management regimens were arranged before surgery. Randomization was performed on a 1:1 basis in blocks of 10 using sealed envelopes stating celecoxib or placebo. One hour before surgery, all patients received either 400 mg celecoxib or placebo. Patients were evaluated using a VAS preoperatively, immediately postoperatively, and at 1 and 2 hours postoperatively. Time from the operating room to "ready for discharge" and number of morphine equivalents of narcotic medication required in the postanesthesia care unit were recorded. **Results:** Age and preoperative VAS were similar between the celecoxib and placebo control group, with average ages of 34.2 ± 11.9 and 35.8 ± 11.6 ($P = .27$) and preoperative VAS of 2.1 ± 2.06 and 2.3 ± 1.98 ($P = .29$), respectively. The celecoxib group had 26 females and 24 males, whereas the placebo group had 29 females and 19 males ($P = .42$). The most common surgical procedures were labral repair (31 patients in the celecoxib group and 29 patients in the placebo group), and labral repair with acetabular osteoplasty (13 patients in the celecoxib group and 11 patients in the placebo group). There were no significant differences in procedures performed between the 2 groups ($P > .05$). At 1 hour postoperatively, patients who received celecoxib had a lower pain score that was statistically significant compared with the placebo group (4.6 vs 5.4, $P = .03$). There was a significant difference in discharge time between patients who received celecoxib and the control group (152.9 minutes vs 172.9 minutes, $P = .04$). There was no significant difference found in morphine equivalents consumed in the postanesthesia care unit between the 2 groups (15.3 vs 15.4, $P = .48$). **Conclusions:** A preoperative dose of 400 mg of celecoxib led to statistically significantly reduced patient-reported pain on the VAS in the acute postoperative period after hip arthroscopy surgery, though the difference is not likely clinically significant. There was a significantly shorter time to discharge in patients who received celecoxib versus placebo. **Level of Evidence:** Level I, randomized controlled trial.

Over the past decade, hip arthroscopy has become increasing prevalent for addressing hip pain in younger patients.[1,2] Although arthroscopic hip surgery has significantly less morbidity compared with open procedures to treat similar pathology,[3] postoperative pain continues to be an evolving domain with no strict guidelines. Prolonged hospital stays, delayed recovery, poor outcomes, and greater consumption of health care resources may be the result of inadequate perioperative pain management.[4,5]

Celecoxib has the distinct properties of rapid absorption, high oral bioavailability, and preferential distribution into inflamed tissue.[6] In addition, COX-2

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The authors report the following potential conflicts of interest or sources of funding: M.A.T. receives support from Smith & Nephew, Saunders/Mosby-Elsevier, and Arthrex.

Received June 1, 2016; accepted January 3, 2017.

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0749-8063/16466/$36.00

http://dx.doi.org/10.1016/j.arthro.2017.01.016

inhibitors like celecoxib may also prevent heterotopic bone formation, which has been implicated as a sequelae of hip arthroscopy.[7] One recent study showed that 200 mg of celecoxib administered 1 hour preoperatively in patients with spinal anesthesia led to improved pain at 12 and 24 hours postoperatively and higher physical composite scores at the same time points.[8]

The purpose of this prospective randomized, double-blinded controlled study was to determine whether 400 mg of celecoxib administered 1 hour before hip arthroscopy surgery would reduce pain, provide reduction in overall narcotic consumption, and lead to more rapid discharge from recovery rooms. We hypothesized that patients who received preoperative celecoxib would experience less pain in the immediate postoperative period compared with patients who received placebo. We additionally hypothesized that patients who received preoperative celecoxib would require less narcotic pain medication in the immediate postoperative period, and would be ready for discharger from the postanesthesia care unit (PACU) earlier than patients who received placebo.

Methods

After ethics approval by the Institutional Review Board at our institution, 119 patients who underwent hip arthroscopy surgery for femoroacetabular impingement between February 2013 and June 2015 were approached on the day of surgery for this study. This study was registered with www.clinicaltrails.gov (registration number NCT02779166; registration date May 13, 2016). An a priori power analysis was done set to detect a difference of 0.50 on the visual analog scale (VAS), based on the senior author's (M.A.T.) preference. The number of patients planned for recruitment was rounded up to 100 to allow for flexibility in the study. This was an effectiveness trial based on routine clinical practice at our intuition.

The study design was a double-blinded randomized controlled trial where both the surgical team and the patient were blinded from the treatment they received. Inclusion criteria were any patient at least 18 years old who underwent hip arthroscopy surgery performed by the senior author. All patients had less than Tönnis grade 2 arthritis. Exclusion criteria were allergy to sulfa-based drugs, prior adverse reaction to celecoxib, or patients who were on chronic narcotics for whom alternative pain management regimens were arranged before surgery. Randomization was performed on a 1:1 basis in blocks of 10 using sealed envelopes stating celecoxib or placebo. Randomization was performed by a third party, assuring that all research personnel as well as the patients were blinded to the treatment group. All patients underwent general endotracheal intubation for surgery and no nerve blocks were used. All surgeries were performed supine on a hip distractor table. At 1 hour before hip arthroscopy surgery, all patients received 2 pills containing either a lactose-based placebo in both pills or 200 mg celecoxib in each pill, for a total dosage of 400 mg celecoxib. The dose of 400 mg of celecoxib was chosen because it was previously used for perioperative pain management in knee arthroscopy, as reported by Ekman et al.[9] All patients then underwent hip arthroscopy performed by the senior author and were subsequently taken to the recovery room and discharged from the surgery center on the day of surgery.

Patient demographics, including age, gender, and specific procedures performed during hip arthroscopy surgery, were collected from the medical record. Patients were evaluated preoperatively on the day of surgery using the VAS for pain. The pain scale was administered verbally, and patients were asked the questions, "Please rate your current pain level on a scale from 0 to 10 with 0 indicating no pain and 10 being the worst pain imaginable." Pain scores were measured immediately on leaving the operating room and at 1 hour and 2 hours postoperatively using the VAS. Pain medication was administered to all patients based on a normal protocol in the PACU, and included acetaminophen-hydrocodone tablets for mild or moderate pain and intravenous hydromorphone for severe pain. Time from leaving the operating room to the point that the patient met our institutional criteria for discharge (based on a 20-point nursing score) was also reported. Furthermore, total narcotic consumption in the postoperative care unit was calculated in morphine equivalents.

Statistical Analysis

Patient outcomes were analyzed using a 1-tailed Student's *t*-test. Significance was defined as $P < .05$. The 1-tailed *t*-test was used in this study because our interest was to determine whether patients who received celecoxib had superior scores than those who did not. Because only one side of the distribution was of concern, a 2-tailed test was not used.

Results

Twenty-one patients were excluded because of patient refusal (n = 9), reported allergy to sulfa drugs (n = 7), prior patient-reported adverse reaction to celecoxib (n = 2), and postoperative pain regimens that had been arranged preoperatively in consultation with pain management service (n = 3). Ninety-eight patients were available for randomization. Fifty were randomized to receive 400 mg of celecoxib and 48 were randomized to receive placebo (Fig 1). Table 1 states the surgical procedures performed in each group. There were no significant differences in procedures performed between the 2 groups ($P > .05$).

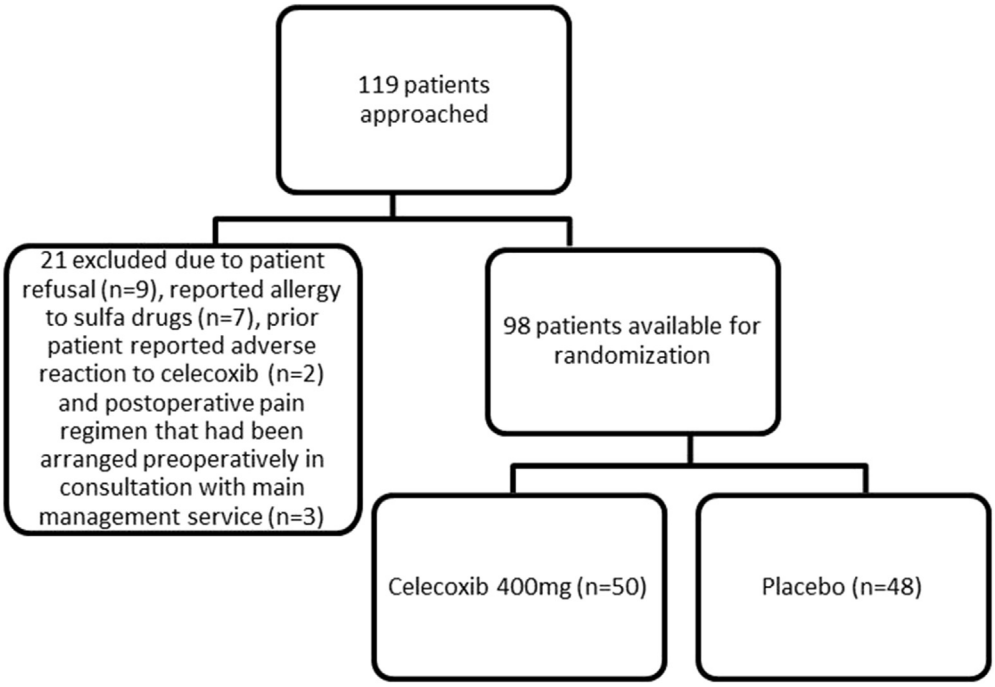

Fig 1. Consolidated Standards of Reporting Trials diagram. Patient randomization and exclusions.

Age and preoperative VAS were similar between the celecoxib and placebo control group, with average ages of 34.2 ± 11.9 and 35.8 ± 11.6 ($P = .27$) and preoperative VAS of 2.1 ± 2.06 and 2.3 ± 1.98 ($P = .29$), respectively. The celecoxib group had 26 females and 24 males, whereas the placebo group had 29 females and 19 males ($P = .42$). There was no significant difference in operative time (mean 95.4 ± 20.2 minutes in the celecoxib groups vs 95.8 ± 17.3 minutes in the placebo group, $P = .91$). There was also no significant difference found in morphine equivalents consumed in the PACU between the 2 groups (mean 15.3 mg vs 15.4 mg, $P = .48$).

At 1 hour postoperatively, patients who received celecoxib had a lower pain score, which was statistically significantly different compared with the placebo group (4.6 ± 1.91 vs 5.4 ± 1.92 after 1 hour, $P = .03$). At 2 hours postoperatively, the mean VAS in the celecoxib group was 4.1 ± 1.75 versus 4.9 ± 1.98 in the placebo group ($P = .06$) (Fig 2). There was a significant difference in discharge time between patients who received celecoxib and the control group. An average decrease of 20 minutes from the time into the recovery room until discharge was noted for patients who received celecoxib versus placebo (152.9 minutes vs 172.9 minutes, $P = .04$) (Table 2). There were no surgical complications and no perioperative complications related to celecoxib. Monitored complications related to celecoxib included cardiovascular thrombotic events, myocardial infarction, stroke, and severe gastrointestinal upset.

Discussion

The results of this double-blinded randomized controlled trial of 400 mg of celecoxib versus placebo administered preoperatively for pain management after hip arthroscopy surgery showed a benefit of celecoxib in decreasing pain at 1 hour postoperatively and also in leading to a significantly shorter time to discharge. Celecoxib showed no benefit in decreasing the amount of narcotic requirements in the PACU.

Perioperative use of celecoxib has previously been shown to be beneficial in enhancing pain control in other areas of orthopaedic surgery. In the knee arthroscopy literature, Ekman et al[9] showed that a dose of 400 mg of celecoxib administered 1 hour before surgery as well as a dose of 200 mg of celecoxib at the first request for pain medication postoperatively

Table 1. Hip Arthroscopy Procedures Performed

Procedure	Number of Patients: Celecoxib Group	Number of Patients: Placebo Group	*P* Value
Labral repair	31	29	>.99
Labral debridement	2	2	>.99
Labral reconstruction	1	0	>.99
Labral repair with acetabular osteoplasty	13	11	.82
Revision labral repair	1	2	.61
Labral repair with acetabular chondroplasty	2	2	>.99
Labral repair with femoral head chondroplasty	0	2	.24

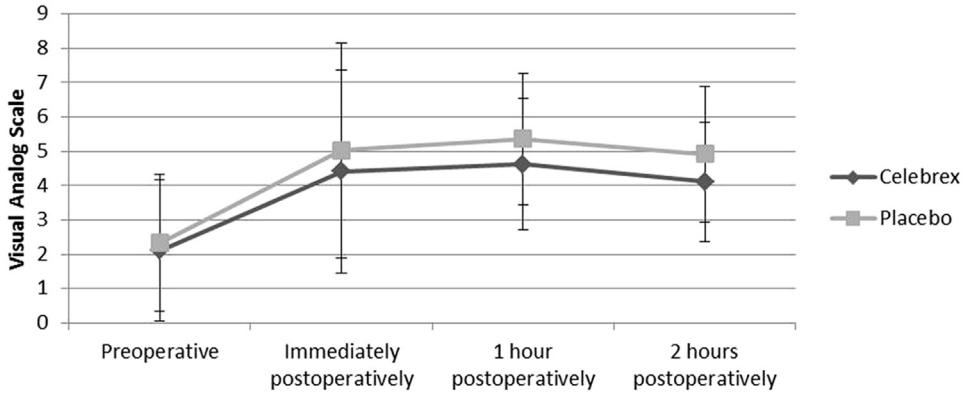

Fig 2. Visual analog scale scores during the study period.

reduced the consumption of opioid medication and also reduced the incidence of opioid-related adverse events in the early postoperative period for patients undergoing knee meniscectomy. Similarly, studies of pain management after knee arthroplasty have shown a benefit of celecoxib administered shortly before and after surgery for reducing pain and opioid consumptions and increasing knee range of motion.[10] Known severe side effects of celecoxib include cardiovascular thrombotic events, myocardial infarction, and stroke, severe GI upset[11]; however, none of these were found in the present study.

Our study noted a difference in VAS of 0.73 between the intervention and placebo groups at 1 hour postoperatively. Although this difference was statistically significant, it falls below the minimal clinically important difference that has been noted in prior studies. Previous studies have cited a difference of 1.0 to 1.3 in VAS on a 10-point scale to be clinically significant.[12-15] Although celecoxib did lead to statistically lower pain scores at 1 hour after surgery, the difference was small and lower than the previously cited minimal clinically important difference for the VAS. This indicates that celecoxib alone may not have a clinically significant effect on decreasing pain after hip arthroscopy surgery, but celecoxib may be useful in conjunction with other pain management strategies. Celecoxib may be a safe adjunct for pain control, leading to ease of discharge and improved pain scores, but not as an alternative to postoperative pain control as a whole.

Traditional pain management after many orthopaedic procedures has relied heavily on the use of narcotic medications.[16] Narcotic medications can have severe known side effects on the gastrointestinal, respiratory, integumentary, genitourinary, and neurologic systems of the body.[17,18] The use of multimodal pain management, initially introduced over 2 decades ago,[19,20] has led to more effective pain control with fewer side effects of narcotic medications. The goal of multimodal pain management is to target multiple pathways in the pain signaling cascade to minimize pain while also minimizing side effects.[18] Opioids work by binding to specific pain receptors in the brain and spinal cord, whereas nonsteroidal anti-inflammatory drugs including celecoxib work by inhibiting cyclooxygenase production of prostaglandins in the peripheral tissues.[18] Although we were not able to show a decrease in narcotic requirements in patients taking celecoxib in our trial, future studies are needed to examine the role of anti-inflammatory medication in decreasing narcotic requirements after hip arthroscopy surgery.

Our finding of significantly earlier time to discharge in the celecoxib group versus the placebo group may be particularly relevant in the current health care climate. The celecoxib group had on average 20 minutes earlier time to discharge compared with the placebo group. This could have significant implications on staffing needs and workflow in busy hospitals and surgical centers. Facilitating earlier discharge may also benefit patient satisfaction in the perioperative period. Further work is needed to substantiate these hypotheses.

Although this double-blinded randomized controlled trial did find that a single preoperative dose of celecoxib helped to decrease early postoperative pain and may help facilitate earlier discharge, future investigations are

Table 2. Results

	Celecoxib (N = 50)	Placebo (N = 48)	*P* Value
Age, yr	34.2	35.8	.54
Preoperative VAS	2.11	2.33	.29
Minutes from leaving OR until ready for discharge	152.96	172.96	.04
VAS immediately postoperatively	4.41	5.02	.17
VAS 1 h postoperatively	4.63	5.36	.03
VAS 2 h postoperatively	4.11	4.92	.06
Morphine equivalents used in the PACU, mg	15.326	15.419	.48

OR, operating room; PACU, postanesthesia care unit; VAS, visual analog scale.

needed to look into varying doses and regimens of celecoxib use in hip arthroscopy in the perioperative period before recommending it for widespread use, especially given that all medications, including celecoxib, come with potential side effects. Overall, as health care shifts toward using patient satisfaction and length of hospital stay as key quality measures, it will become increasingly important for orthopaedic surgeons to find ways to decrease postoperative pain and facilitate discharge after surgery. Helping patients get home safely and comfortably after hip arthroscopy will help to increase patient satisfaction and may have future consequences on reimbursement.

Limitations

This study is not without limitations. First, this study included no time points after hospital discharge, thus limiting the ability of the study to evaluate the benefit of celecoxib in pain management for hip arthroscopy surgery after discharge from the hospital. Second, PACU staff at our institution continued with routine postoperative pain management during the study period. This routine management typically included administration of narcotic pain medicine when the patient first expressed pain postoperatively. It is possible that stricter guidelines for administration of narcotics could have led to a finding of a difference in narcotic consumption between the celecoxib and placebo groups. Third, this study used a 1-tailed *t*-test for statistical analysis. The 1-tailed *t*-test was used because the study was designed to look at the amount of pain benefit that celecoxib would provide, with the assumption that celecoxib administration would not lead to increased pain. Given this statistical analysis, it is possible that we could have overlooked a worsening effect of celecoxib on pain control, though this is unlikely based on prior studies on the use of celecoxib. Fourth, it is possible that there may have been variability in intraoperative narcotic administration among patients. Although our standard protocol only involves intraoperative narcotic administration during induction, it is possible that some patients received additional intraoperative narcotic medications during surgery, which could have biased results. Finally, differences in medical comorbidities such as obesity and obstructive sleep apnea, as well as differences in exact measurements of hip alpha angle and hip deformities between the 2 groups, were not recorded and may have influenced postoperative pain management and pain control.

Conclusions

A preoperative dose of 400 mg of celecoxib led to statistically significantly reduced patient-reported pain on the VAS in the acute postoperative period after hip arthroscopy surgery, though the difference is not likely clinically significant. There was a significantly shorter time to discharge in patients who received celecoxib versus placebo.

References

1. Bozic KJ, Chan V, Valone FH III, Feeley BT, Vail TP. Trends in hip arthroscopy utilization in the United States. *J Arthroplasty* 2013;28:140-143.
2. Montgomery SR, Ngo SS, Hobson T, et al. Trends and demographics in hip arthroscopy in the United States. *Arthroscopy* 2013;29:661-665.
3. Botser IB, Smith TW Jr, Nasser R, Domb BG. Open surgical dislocation versus arthroscopy for femoroacetabular impingement: A comparison of clinical outcomes. *Arthroscopy* 2011;27:270-278.
4. Fortier J, Chung F, Su J. Unanticipated admission after ambulatory surgery—A prospective study. *Can J Anaesth* 1998;45:612-619.
5. Pavlin DJ, Chen C, Penaloza DA, Polissar NL, Buckley FP. Pain as a factor complicating recovery and discharge after ambulatory surgery. *Anesth Analg* 2002;95:627-634. table of contents.
6. Holmes N, Cronholm PF, Duffy AJ III, Webner D. Nonsteroidal anti-inflammatory drug use in collegiate football players. *Clin J Sport Med* 2013;23:283-286.
7. Vasileiadis GI, Sioutis IC, Mavrogenis AF, Vlasis K, Babis GC, Papagelopoulos PJ. COX-2 inhibitors for the prevention of heterotopic ossification after THA. *Orthopedics* 2011;34:467.
8. Zhang Z, Zhu W, Zhu L, Du Y. Efficacy of celecoxib for pain management after arthroscopic surgery of hip: A prospective randomized placebo-controlled study. *Eur J Orthop Surg Traumatol* 2014;24:919-923.
9. Ekman EF, Wahba M, Ancona F. Analgesic efficacy of perioperative celecoxib in ambulatory arthroscopic knee surgery: A double-blind, placebo-controlled study. *Arthroscopy* 2006;22:635-642.
10. Huang YM, Wang CM, Wang CT, Lin WP, Horng LC, Jiang CC. Perioperative celecoxib administration for pain management after total knee arthroplasty—A randomized, controlled study. *BMC Musculoskelet Disord* 2008;9:77.
11. Chan FK, Lanas A, Scheiman J, Berger MF, Nguyen H, Goldstein JL. Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR): A randomized trial. *Lancet* 2010;376:173-179.
12. Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 2001;94:149-158.
13. Hägg O, Fritzell P, Nordwall A, Swedish Lumbar Spine Study Group. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J* 2003;12:12-20.
14. Carragee EJ, Cheng I. Minimum acceptable outcomes after lumbar spinal fusion. *Spine J* 2010;10:313-320.
15. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity

measured on a visual analog scale. *Ann Emerg Med* 2001;38:633-638.
16. Horlocker TT. Pain management in total joint arthroplasty: A historical review. *Orthopedics* 2010;33:14-19.
17. Wheeler M, Oderda GM, Ashburn MA, Lipman AG. Adverse events associated with postoperative opioid analgesia: A systematic review. *J Pain* 2002;3:159-180.
18. Parvizi J, Bloomfield MR. Multimodal pain management in orthopedics: Implications for joint arthroplasty surgery. *Orthopedics* 2013;36:7-14.
19. Wall PD. The prevention of postoperative pain. *Pain* 1988;33:289-290.
20. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesth Analg* 1993;77:1048-1056.