Efficacy of Anti-inflammatory Treatment Versus Rescue Analgesia After Arthroscopic Partial Meniscectomy in Nonarthritic Knees

A 3-Arm Controlled Study

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Background: There is currently no consensus regarding the appropriate treatment for postoperative pain after arthroscopic partial meniscectomy (APM). Prescribing a mild non–anti-inflammatory protocol of rescue analgesia may be sufficient to avoid the side effects of opioids or anti-inflammatories.

Purpose/Hypothesis: The purpose was to compare the efficacy of pain reduction after APM in nonarthritic knees using betamethasone or celecoxib as anti-inflammatory analgesics versus acetaminophen or tramadol as rescue analgesics. The hypothesis was that there is no advantage for anti-inflammatories in achieving postoperative immediate pain relief after APM in nonarthritic knees compared with a simple nonopioid treatment.

Study Design: Cohort study; Level of evidence, 2.

Methods: This 3-arm controlled study evaluated postoperative pain levels and analgesic consumption in patients who underwent primary APM (under general anesthesia) at a single institution from December 2018 to December 2019. Patients were prospectively divided into 3 treatment groups: (1) betamethasone injection at the end of the procedure, (2) oral celecoxib prescription, or (3) neither treatment (control). All groups were instructed to take supplementary acetaminophen as needed. Patients were also allowed to take tramadol as needed to evaluate the need for opioids. At postoperative weeks 1, 2, and 3, patients completed the Knee injury and Osteoarthritis Outcome Score (KOOS) Pain subscale, and results were compared between time points and groups.

Results: A total of 99 patients were included in the treatment groups: betamethasone group (32 patients), celecoxib group (30 patients), and control group (37 patients). At baseline, there were no statistically significant differences between the groups in age, sex, body mass index, level of activity, comorbidities, or surgical findings. KOOS Pain scores improved at every time point for all 3 groups ($P < .001$), and no differences in scores were observed among groups. The consumption of acetaminophen or tramadol as rescue analgesia throughout the follow-up period was negligible among groups.

Conclusion: During the first 3 postoperative weeks after APM in nonarthritic knees, pain was efficiently controlled by betamethasone or celecoxib; however, pain was also efficiently controlled by minimal consumption of acetaminophen with negligible use of tramadol. Therefore, acetaminophen could be prescribed as an effective first-line postoperative analgesic after APM.

Keywords: arthroscopy; meniscectomy; pain; NSAIDs; steroids

Arthroscopic partial meniscectomy (APM) is considered the standard of care for torn menisci in appropriate selective indications.[8] Postoperative pain control after APM is essential to enhance recovery and early return to daily activities. Current analgesic regimens often include various combinations of corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and nonopioid and opioid medications.[5,14,16,21,22] No consensus has been published so far regarding pain management after APM for nonarthritic knees. As APM is a simple outpatient procedure, it may be that the mildest rescue analgesia protocol is sufficient. Moreover, with the appropriate protocol, surgeons may be able to avoid the side effects of using steroids, NSAIDs, and opioids. Publications regarding the

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current opioid epidemic in the United States recommend reduction of postoperative opioid analgesic prescriptions in orthopaedic surgery.[18,20]

Betamethasone, celecoxib, acetaminophen, and tramadol are 4 drugs that represent different groups of analgesia and are commonly used after arthroscopic knee procedures. Betamethasone is a synthetic glucocorticoid with metabolic, immunosuppressive, and anti-inflammatory activities.[11,23] Celecoxib is a COX-2 selective NSAID.[19] Acetaminophen is frequently used for mild to moderate pain relief,[29] but its mechanism of action is not completely understood. Tramadol is an opioid medication for more severe pain; it induces analgesic effects through a variety of different targets on the noradrenergic system, serotoninergic system, and opioid receptor system.[27]

Guidelines from national professional societies agree in general that the overall first choice for analgesia in any type of musculoskeletal pain is acetaminophen. If the symptoms are not controlled, then NSAIDs should be considered next.[17] The potential gastrointestinal, cardiovascular, and renal risks of NSAIDs must be weighed against the potential benefits in each individual and should be used at the lowest effective dose for the shortest possible duration.[9] The aim of this study was to compare the efficacy of pain reduction and analgesic consumption after APM in nonarthritic knees using betamethasone or celecoxib as anti-inflammatory treatment versus acetaminophen or tramadol as non–anti-inflammatory rescue analgesics. The hypothesis was that there is no advantage for betamethasone or celecoxib in achieving postoperative immediate pain relief after APM in nonarthritic knees compared with a simple nonopioid treatment.

METHODS

Study Design and Participants

This institutional review board–approved study was an analysis of prospectively collected patient-reported outcome measures from December 2018 to December 2019. This comparative observational study evaluated postoperative pain levels and analgesic consumption in patients undergoing primary, arthroscopic meniscectomy at a single institution.

Eligible patients were at least 18 years of age and were scheduled for surgical arthroscopic meniscectomy without osteoarthritis (ie, Kellgren-Lawrence grade <2 on preoperative weightbearing radiographs[13]). Exclusion criteria were allergy or intolerance to one of the study drugs and patients who had cruciate ligament reconstruction, meniscal repair, concurrent osteotomy, patellar realignment, infection, surgery for synovial disease, or ipsilateral previous knee surgery. Enrolled patients were informed regarding their postoperative pain treatment and consented to be interviewed during the study period.

Interventions

Before surgery and after completion of all baseline measurements, participants were divided into 3 groups (betamethasone, celecoxib, control). The betamethasone group was treated by injection of betamethasone suspension (10 mg dipropionate and 4 mg sodium phosphate) at the end of the arthroscopic procedure. The celecoxib group was prescribed 200 mg celecoxib 2 times per day for the first 10 days. The control group did not have either the betamethasone injection or celecoxib prescription. All 3 groups were instructed to take supplementary analgesia (rescue treatment) as needed using a dose of oral acetaminophen (up to 3 g/day) or oral tramadol (up to 200 mg/day). All drug types and quantities used were recorded at each time point during follow-up. Patients were not restricted to using only their prescribed study medication; if they chose to use an outside over-the-counter (OTC) analgesic, the type and quantity of the medication was recorded at each time point throughout the study. Surgeries under general anesthesia were done 3 times per week, and so each of the 3 treatment groups was randomly (but not blindly) assigned to one of the weekdays.

Preoperative Evaluation

All preoperative evaluations and operations were performed and reported by 3 senior orthopaedic surgeons (B.H., L.Y., M.K.) who work together in an academic sports medicine regional referral center. Preoperative data included patient details, patient history, Charlson Comorbidity Index,[4] Tegner activity scale,[28] and pain subscale of the Knee injury and Osteoarthritis Outcome Score (KOOS).[24]

Surgical Technique

Surgery was performed under general anesthesia with the patient in a supine position. None of the patients were treated by nerve blocks. A leg holder and tourniquet were placed around the thigh of the affected leg. Standard anterolateral and anteromedial knee portals were used. Diagnostic arthroscopy was performed to evaluate and

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TABLE 1
Patient Preoperative and Operative Characteristics[a]

	Overall	Betamethasone Group	Celecoxib Group	Control Group	*P* Value
No. of patients	99	32	30	37	
Age, y	47.5 ± 12.5	47.1 ± 11.4	48.8 ± 12	46.9 ± 13.9	.8
Sex, female/male	35/64	14/18	9/21	12/25	.4
Side, right/left	49/50	17/15	15/15	17/20	.9
Height, cm	171.9 ± 9.1	169.8 ± 9.3	171.8 ± 8.6	173.7 ± 9.1	.2
Weight, kg	83.4 ± 13	81.3 ± 15	83.5 ± 10.7	85.1 ± 12.9	.5
Body mass index, kg/m^2	28.2 ± 4	28.2 ± 4.6	28.4 ± 4	28.2 ± 3.6	>.99
Tegner activity scale	4 ± 1.9	4.3 ± 1.9	3.9 ± 1.8	3.8 ± 2.1	.6
Knee injury, yes/no	44/55	14/18	11/19	19/18	.4
Charlson Comorbidity Index	0.2 ± 0.5	0.2 ± 0.4	0.2 ± 0.6	0.3 ± 0.6	.6
Meniscal tear, medial/lateral/both	78/8/13	27/2/3	23/2/5	28/4/5	.5
Tear type, bucket handle/complex/radial/root	11/55/30/3	1/19/11/1	6/15/9/0	4/21/10/2	.5
Cartilage damage, ICRS/compartments	1.8/0.9	1.8/0.8	1.8/0.9	1.8/0.9	.9

[a]Data are shown as mean ± SD. ICRS, International Cartilage Repair Society.

document abnormal findings of the menisci (tear type and laterality), ligaments, and cartilage (graded from 0 to 4 according to the International Cartilage Repair Society classification[2]). Meniscal tears were trimmed until a stable rim was reached. All patients were discharged from the hospital on the day of surgery and were given instructions for gradual self-rehabilitation by illustrated handouts, which were translated from the "Knee Arthroscopy Exercise Guide" at OrthoInfo.aaos.org.[15]

Outcome Measures

The primary outcome measure was the KOOS Pain subscale. A secondary outcome was analgesic weekly cumulative consumption during the first 3 weeks after surgery. Patients were contacted by independent observers through telephone calls at the first, second, and third postoperative weeks. All complications during the follow-up were recorded.

Statistical Analysis and Sample Size

Baseline differences between the 3 groups were assessed by either univariate analyses of variance for continuous variables or the chi-square test for categorical variables. Pain score differences for each group were assessed by paired Student *t* test. A minimal clinically important change of 8 to 10 points is considered appropriate for the KOOS Pain score. A 10-point change was used as the cutoff indicating recovery.[6] The enrollment of 30 participants per treatment group (considering dropouts) was estimated to provide a power of 80% to detect a between-group difference of 10 ± 13 points in the KOOS Pain score, at a type 1 error rate of 5%. A *P* value less than .05 was considered statistically significant.

RESULTS

Baseline details for all study participants are shown in Table 1. A total of 102 patients met the inclusion criteria during the study period. Three patients were not included because of communication problems. Final data analysis included 99 patients divided into 3 regimen prescription groups: betamethasone group (32 patients), celecoxib group (30 patients), and a control group (37 patients).

TABLE 2
Pre- and Postoperative KOOS Pain Scores[a]

	Betamethasone Group	Celecoxib Group	Control Group	*P* Value
Day of surgery	51.6 ± 10.5	54.8 ± 14.5	54.4 ± 16.8	.2
Postoperative day 7	71.7 ± 6.7	67.9 ± 15.8	68.5 ± 13.8	.8
Postoperative day 14	78.1 ± 11	66.9 ± 14.8	65.4 ± 17.4	.05
Postoperative day 21	76.1 ± 15.2	70.8 ± 12.6	78.7 ± 11.6	.2

[a]Data are shown as mean ± SD. KOOS, Knee injury and Osteoarthritis Outcome Score.

There were no statistically significant differences at baseline between the study groups in age, sex, body mass index, level of activity, comorbidities, and surgical findings. The betamethasone group had only 1 patient with a bucket-handle tear type. No patient experienced severe adverse events during the study period.

Effect of Treatment on Short-Term Knee Pain

Table 2 compares the effect of treatment among all groups on KOOS Pain scores at postoperative days 7, 14, and 21. The KOOS Pain score improved at every time point in all groups ($P < .001$), and there were no significant differences in scores between groups.

The consumption of acetaminophen and tramadol as rescue analgesia throughout the follow-up period was minimal and similar among groups (Table 3). There was a statistically significant observation at postoperative day 14, when patients in the control group did not consume acetaminophen.

There was no difference among groups in the consumption of nonprescribed OTC analgesics (Table 4). Most

TABLE 3
Postoperative Acetaminophen and Tramadol Cumulative Consumption[a]

	Betamethasone Group	Celecoxib Group	Control Group	*P* Value
Postoperative day 7				
Acetaminophen	0.7 ± 1.6	1.2 ± 2.3	2 ± 3.7	.3
Tramadol	0	0.3 ± 0.4	0.3 ± 0.5	.05
Postoperative day 14				
Acetaminophen	0.2 ± 0.6	1.3 ± 2.1	0	.01
Tramadol	0.1 ± 0.2	0.1 ± 0.2	0.1 ± 0.2	>.99
Postoperative day 21				
Acetaminophen	0.2 ± 0.6	0.9 ± 1.5	0	.1
Tramadol	0	0.1 ± 0.3	0	.3

[a]Data are shown in grams as mean ± SD.

TABLE 4
Postoperative Over-the-Counter Analgesic Cumulative Consumption (Dipyrone, Ibuprofen, Etodolac)[a]

	Betamethasone Group	Celecoxib Group	Control Group	*P* Value
Postoperative day 7				
Dipyrone	0.3 ± 0.7	0	0.3 ± 1.4	.3
Ibuprofen	0.1 ± 0.4	0	0.1 ± 0.4	.3
Etodolac	0	0.1 ± 0.3	0.1 ± 0.4	.4
Postoperative day 14				
Dipyrone	0.4 ± 0.9	0.1 ± 0.3	0.1 ± 0.2	.1
Ibuprofen	0.1 ± 0.5	0.1 ± 0.2	0.1 ± 0.2	.6
Etodolac	0	0.2 ± 0.7	0.2 ± 0.7	.5
Postoperative day 21				
Dipyrone	0.3 ± 1	0	0.3 ± 1	.7
Ibuprofen	0.2 ± 0.6	0.4 ± 1	0	.2
Etodolac	0	0.2 ± 0.7	0	.3

[a]Data are shown in grams as mean ± SD.

patients among the different groups did not consume any pain medication at the last follow-up.

DISCUSSION

The most important finding of the present study was that short-term pain relief after APM was achieved efficiently with or without anti-inflammatory treatment, with negligible consumption of rescue analgesics.

Several studies have documented the efficacy of nonopioid oral medications after arthroscopy.[1,7] A recent study by Pham et al[21] highlighted the fact that the majority of patients who undergo a partial meniscectomy are overprescribed opioids for postoperative pain that could otherwise be effectively controlled with simple analgesics. The results of the present study support their conclusion.

Corticosteroids have been studied as an adjunctive therapy at the time of surgery to decrease pain and reduce analgesic consumption in the early postoperative period after arthroscopic knee procedures.[14,16,22] In contrast to the present study of nonarthritic knees, corticosteroids are often injected into patients with preexisting osteoarthritis because of anticipated prolonged postoperative recovery.[26] Segelman et al[25] conducted a randomized controlled trial to compare an intravenous preoperative injection of 8 mg betamethasone (34 patients) to a placebo (40 patients) for pain reduction after ambulatory arthroscopic meniscectomy. Patients' age and sex were similar to those in the present study. They observed better pain reduction with betamethasone on the first postoperative day, but no differences were found on the third postoperative day.

Another randomized controlled trial was conducted by Koyonos et al[16] to investigate the effectiveness of methylprednisolone injection in patients after they underwent meniscectomy with osteoarthritis of the knee. They found higher outcome scores in the steroid group at 6 weeks but no differences later on. Compared with the present study, Koyonos et al included older patients with osteoarthritis. In the present study, patients injected intraoperatively with betamethasone showed no advantage in pain reduction at the first 3 weeks postoperatively. Corticosteroids should be used cautiously, as there have been reports of an increased risk of postoperative infection in patients receiving intra-articular corticosteroids at the time of surgery.[3] In addition, the lowest efficacious dose of corticosteroids should be used to avoid detrimental effects on articular cartilage.[30]

Two recent studies have evaluated the efficacy of NSAIDs as a nonopioid pain medication after APM. Pham et al[21] enrolled 68 patients with a mean age of 51.2 years. A group of 28 patients were prescribed ibuprofen and compared with a group of 40 patients prescribed oxycodone. They found no significant difference in pain control, satisfaction, or total 1-week opioid use between groups. Daniels et al[5] enrolled 163 patients with a mean age of 48.7 years. Patients were prescribed ibuprofen or acetaminophen and completed a preoperative and 2-week postoperative questionnaire to assess satisfaction with pain management. Patients reported satisfactory postoperative pain control without the use of opioids. The authors suggested that a greater majority of patients undergoing simple knee arthroscopy may be successfully managed with a nonopioid pain medication. This is supported by the results of the present study with the use of celecoxib and acetaminophen.

Onda et al[19] compared the effects of treatment with celecoxib, loxoprofen, and acetaminophen on postoperative acute pain after arthroscopic knee surgery. They found that celecoxib was superior to acetaminophen in pain relief; however, their evaluation included only the first 48 hours postoperatively. Although celecoxib may have a benefit over acetaminophen in pain reduction because of its anti-inflammatory effect, this was not observed in the current study. As with all NSAIDs, the potential gastrointestinal, cardiovascular, and renal risks of celecoxib must be weighed against the potential benefits in each individual. If selected, celecoxib, like all NSAIDs, should be used at the lowest effective dose for the shortest possible duration.[9,10,12] In the present study, some patients consumed NSAIDs that were not prescribed by the protocol. Although the dosages of these nonprescribed NSAIDs were

appropriate, surgeons need to warn patients against the use of multiple NSAIDs types.

There are some limitations to this study. This was a single- rather than multicenter study, with only 3 surgeons involved. The results of our surgical technique and rehabilitation protocol may not reflect the results of other centers. Other centers occasionally use regional nerve blocks, which were not used in this study, but even so, the consumption of rescue analgesics was negligible. In addition, this was a nonblinded study, which may have led to selection bias, yet the final analysis showed no differences in characteristics among the 3 treatment groups. Medication consumption was patient reported, which may not always be accurate. The power analysis in this study was based on changes in the KOOS Pain score and not on analgesic consumption (comparison of pharmacological equivalents). Furthermore, other medications were allowed to be taken, which may have influenced variability between groups. Finally, follow-up questionnaires did not include inquiring about minor drug adverse effects, which may influence their consumption. In future studies, it would be interesting to investigate analgesic consumption during longer postoperative periods beyond the acute inflammatory phase.

This study was designed to evaluate the analgesic efficacy of anti-inflammatories or rescue analgesics shortly after APM in nonarthritic knees. Surgeons can reassure APM candidates beforehand that postoperative pain can be controlled first with simple OTC medications such as acetaminophen. The strengths of this study were its design as a prospective controlled study with no significant differences between the 3 treatment groups in terms of patient characteristics, daily activities, comorbidities, and surgical findings during arthroscopy. In addition, follow-ups were conducted by independent observers.

CONCLUSION

During the first 3 postoperative weeks after APM in nonarthritic knees, pain was efficiently controlled by betamethasone or celecoxib; however, pain was also efficiently controlled by minimal consumption of acetaminophen with negligible use of tramadol. Therefore, acetaminophen could be prescribed as an effective first-line postoperative analgesic after APM.

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