Multimodal Nonopioid Pain Protocol Provides Equivalent Pain Versus Opioid Control Following Meniscus Surgery: A Prospective Randomized Controlled Trial

Toufic R. Jildeh, Kelechi R. Okoroha, M.D., Noah Kuhlmann, B.S., Austin Cross, B.S., Muhammad J. Abbas, B.S., and Vasilios Moutzouros, M.D.

Purpose: To assess the effectiveness of a nonopioid pain regimen in controlling postoperative pain as compared with a traditional opioid pain control following primary meniscectomy or meniscal repair. **Methods:** Ninety-nine patients undergoing primary meniscectomy or meniscal repair were assessed for participation. A prospective randomized control trial was performed in accordance with the Consolidated Standards of Reporting Trials 2010 statement. The 2 arms of the study included a multimodal nonopioid analgesic protocol and a standard opioid regimen with a primary outcome of postoperative pain level (visual analog scale) for the first 10 days postoperatively. Secondary outcomes included patient-reported outcomes, complications, and patient satisfaction. Randomization was achieved using a random-number generator. Patients were not blinded. Data collection was done by a blinded observer. **Results:** Eleven patients did not meet the inclusion criteria, and 27 declined participation. A total of 61 patients were analyzed with 30 randomized to the opioid regimen and 31 randomized to the nonopioid regimen. Patients receiving the nonopioid regimen demonstrated noninferior visual analog scale scores compared with patients who received opioid pain medication ($P > .05$). No significant differences were found in preoperative (opioid: 58.9 ± 7.0; nonopioid: 58.2 ± 5.5, $P = .724$) or postoperative (opioid: 59.8 ± 6.5; nonopioid: 54.9 ± 7.1, $P = .064$) Patient-Reported Outcomes Measurement and Information System Pain Interference Short Form scores. No difference was found in recorded side effects between both groups at any given time point: constipation, nausea, diarrhea, upset stomach, and drowsiness ($P > .05$). **Conclusions:** This study found that a multimodal nonopioid pain protocol provided equivalent pain control and patient outcomes following primary meniscus surgery while having an equivalent side effect profile. All patients reported satisfaction with their pain management without requiring emergency opioid analgesia. **Level of Evidence:** Level I, prospective randomized controlled trial.

With the declaration of pain as the fifth vital sign in patients, there has been increased attention on treating acute and chronic pain. Increased opioid prescriptions have added to the opioid abundance and dependence in the United States. Currently, Americans find themselves in an opioid epidemic, and in 2017, the opioid epidemic was declared a national emergency in the United States.[1] Opioid prescriptions increased from 76 million in 1990 to a peak of 255 million in 2012, with a 6-fold increased death toll between 1990 and 2017.[2,3] The US population accounts for 4.6% of the world population but represents approximately 80% of global opioid consumption.[4] In a recent study, musculoskeletal pathology ranked as the second leading category associated with an initial opioid prescription, which in turn led to sustained opioid use.[5] Postoperative pain has proven to be one of the most challenging aspects of patient care for orthopaedic surgeons, and surgeons are uniquely positioned to exert a positive effect on the current epidemic.

Arthroscopic meniscus surgery is the most common orthopaedic surgery, and meniscectomy and meniscal repair

From Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A. (T.R.J., N.K., A.C., M.J.A., V.M.) and Mayo Clinic, Department of Orthopaedic Surgery, Rochester, Minnesota, U.S.A. (K.R.O.).

The authors report that they have no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received September 14, 2020; accepted February 25, 2021.

Address correspondence to Toufic R. Jildeh, M.D., Department of Orthopaedic Surgery, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, U.S.A. E-mail: touficjildeh@gmail.com

0749-8063/201570/$36.00

https://doi.org/10.1016/j.arthro.2021.02.043

represent prime targets for reduction of postoperative opioid use.[6] Attempts have been made to reduce the overall opioid burden for these surgeries. Most notably, Daniels et al.[7] found that most patients undergoing arthroscopic partial meniscectomy achieve satisfactory pain control with nonopioid pain management. In addition, many studies have employed multimodal analgesia to decrease postoperative opioid burden following many surgical procedures.[8-10] The usage of multimodal analgesia allows for effective pain control through targeting pain receptors at multiple points of the nociceptive pathway. Recently, a multimodal nonopioid pain regimen suggested adequate pain control following common sports procedures with few to no breakthrough opioid medication, but no multimodal pain regimen has been able to eliminate the need for opioid pain medication.[11]

The purpose of this randomized controlled trial was to assess the effectiveness of a nonopioid pain regimen in controlling postoperative pain as compared with a traditional opioid pain control following primary meniscectomy or meniscal repair. We hypothesized that our nonopioid protocol would demonstrate no significant difference in postoperative pain control compared with a standard opioid regimen. Our secondary hypothesis was that patients in the nonopioid cohort will experience a reduced side effect profile when compared with patients in the opioid cohort.

Methods

This study was designed as a randomized controlled trial with 2-week follow-up. The Consolidated Standards of Reporting Trials statement was followed to conduct this prospective, observer-blinded, randomized controlled trial[12] (Fig 1). The hypothesis was formulated prior to collection of data. The study was reviewed and approved by our institutional review board (IRB No. 12318) and was registered at ClinicalTrials.gov (NCT03820193).

Between February 2019 and January 2020, 91 patients who presented to 2 fellowship-trained sports surgeons and were scheduled for primary arthroscopic meniscectomy or meniscal repair were screened for study eligibility. The inclusion criteria consisted of patients aged older than 16 years and patients undergoing primary arthroscopic meniscectomy or meniscal repair. Patients were excluded if they had a significant history of substance abuse, peptic ulcer disease, recent or current pregnancy, intolerance or allergy to any study medication, renal impairment or dysfunction, same-joint surgery for any reason within the previous year, use of blood thinner medication, gastrointestinal bleeding, use of opioid medication within 3 months of surgery, or if they were undergoing revision surgery. Studies have shown that patients using opioids preoperatively demonstrated sustained opioid use postoperatively, and opioid-naive patients were selected to limit confounders.[13-15] All concomitant cartilage procedures were recorded (Table 1).

A secure computer database was used to store data of patients included in the study. Following surgical discussion, patients consented for participation were randomly assigned to either an opioid or a nonopioid pain regimen with a 1:1 allocation ratio using adaptive randomization computer software (MD Anderson Cancer Center, Houston, TX). One week before surgical intervention, surgeons were notified by secure e-mail of the patient's group designation for the upcoming week by the project coordinator. The study did not require physician blinding due to patient outcomes being self-reported. Research staff was not involved with the care of the patients and performed enrollment and data collection. Meniscus repair was performed through an all-inside technique.

Intervention

Preoperatively, all patients received onetime doses of the following medications: gabapentin 300 mg, tramadol 50 mg, acetaminophen 975 mg, and celecoxib 400 mg. In addition, an intravenous dose of dexamethasone 8 mg was administrated preoperatively. An intraoperative local infiltration consisting of 150 mg (30 mL) 0.50% ropivacaine, 1 mg (1 mL) epinephrine, and 30 mg (1 mL) ketorolac was evenly injected in 2-mL increments along the subcutaneous incision at portal sites prior to closure using a 20-mL syringe with a 22-gauge, 1-inch needle.

Patients in the nonopioid group received a novel nonopioid multimodal analgesic protocol described previously in the literature.[11] The protocol consisted of multiple nonopioid medications used to alter postoperative pain using various mechanisms. Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) (ketorolac and meloxicam) were used to target the pain cascade and postoperative inflammation, respectively. Gabapentin was used to address neuropathic pain and diazepam to control muscle cramps and spasm. Medication dosage and frequency are described in Table 2.

Patients enlisted in the opioid group were prescribed 40 pills of 5 mg hydrocodone/325 mg acetaminophen and instructed to take 1 to 2 pills orally every 4 to 6 hours as needed (PRN) for moderate to severe postoperative pain.

Patients were then discharged home on the day of surgery per their group designation pain protocol. All patients were encouraged to contact the on-call physician if pain control was unbearable or they were experiencing any side effects or complications. Patients were also given instructional pamphlets on the effects of opioids, ways to effectively manage pain postoperatively, and pain treatment goals following surgery.

Outcomes

All data collection was performed by observers who were blinded to group randomization. Prior to surgery,

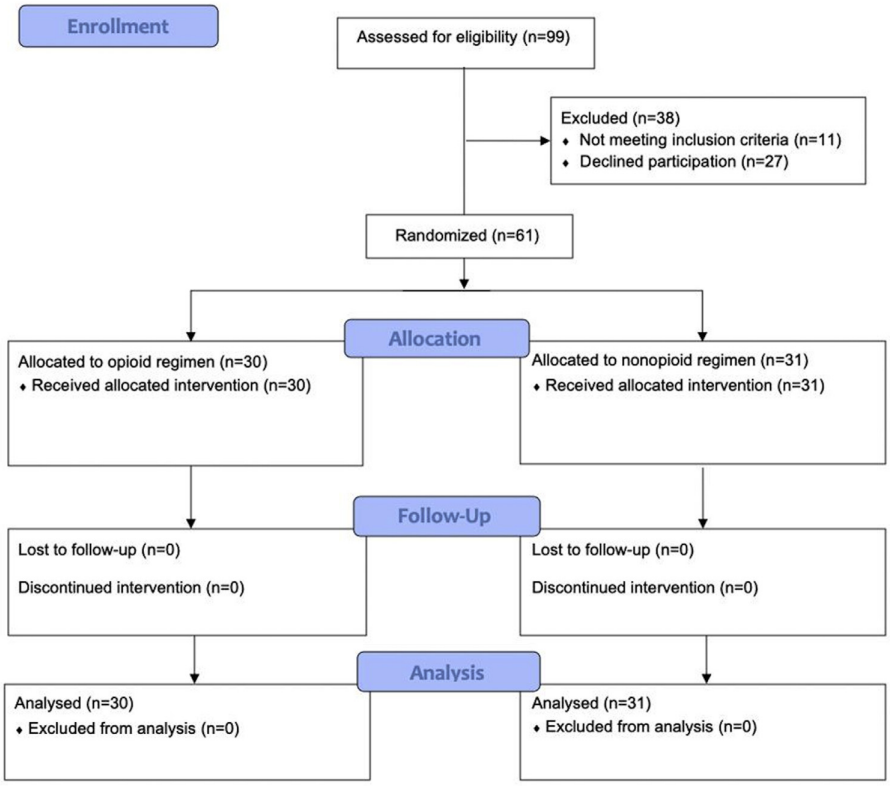

Fig 1. Consolidated Standards of Reporting Trials flow diagram. Patients were excluded if they had a significant history of substance abuse, peptic ulcer disease, recent or current pregnancy, intolerance or allergy to any study medication, renal impairment or dysfunction, same-joint surgery for any reason within the previous year, use of blood thinner medication, gastrointestinal bleeding, use of opioid medication within 3 months of surgery, or if they were undergoing revision surgery.

patients were instructed to complete a Patient-Reported Outcomes Measurement and Information System Pain Interference Short Form (PROMIS PI-SF) questionnaire at the preoperative assessment. Following surgery, a mobile messaging-based outcomes collection software (Mosio, Seattle, WA) was used to collect patient data postoperatively. The software allows patients to submit responses to surveys using numerical text message responses and allows for quick and efficient collection. Surveys were sent to patients 3 times a day for 10 days postoperatively.

Each day using the mobile-messaging application, patients were asked to report their current pain level using an 11-point ordinal scale (visual analog scale [VAS]) 3 times daily: in the morning (9 AM), afternoon (1 PM), and evening (7 PM). Each evening, patients were then asked to report medical side effects, as well as how many opioid pills were taken in the last 24 hours (if applicable). Opioid consumption was converted to morphine milligram equivalents (MME). At the first postoperative visit (7-10 days), patients also completed the PROMIS PI-SF questionnaires.

The following variables were abstracted from medical records: demographic data (age, sex, body mass index [BMI], and history of diagnosed psychiatric condition), smoking status, anxiety/depression status, workers compensation status, and preoperative opioid chronicity.

Statistical Analysis

The primary outcome of this study was an average daily pain difference of 13 mm on the VAS score, as a previous study demonstrated this difference represents the minimum clinically important difference of the VAS score.[12] Prestudy power analysis, with a power of 80% (β level = .80, α level = .05) revealed that a minimum of 25 patients per group (n = 50) was necessary to properly evaluate the primary hypothesis. All continuous data were described using means, standard deviations, medians, minimums, and maximums. Categorical data were presented using counts and column percentages. Continuous data were compared between groups using the Wilcoxon rank-sum test, and categorical data were compared using χ^2 or Fisher exact text. Univariate Poisson regression

Table 1. Demographic Characteristics of Patients Prescribed Opioid and Nonopioid Protocols for Postoperative Analgesia

Characteristic	Opioid (n = 30)	Nonopioid (n = 31)	*P* Value
Age, mean ± SD, y	48.8 ± 14.1	41.3 ± 16.4	.059
Sex			.837
Male	22 (73)	22 (71)	
Female	8 (27)	9 (29)	
Race			.830
White	17 (57)	16 (52)	
African American	6 (20)	5 (16)	
Hispanic	1 (3)	0 (0)	
Asian	1 (3)	2 (6)	
Other	3 (10)	5 (16)	
Unknown	2 (7)	3 (10)	
Body mass index, mean ± SD, kg/m^2	30.2 ± 6.3	28.5 ± 5.0	.233
Smoker			.613
Yes	7 (23)	9 (29)	
No	23 (77)	22 (71)	
Depression			.671
Yes	3 (10)	2 (6)	
No	27 (90)	29 (94)	
Meniscus repair			1.000
Yes	1 (3)	1 (3)	
No	29 (97)	30 (97)	
Meniscus excision			1.000
Yes	29 (97)	30 (97)	
No	1 (3)	1 (3)	
Chondroplasty			.662
Yes	20 (67)	19 (61)	
No	10 (33)	12 (39)	
Loose body removal			.492
Yes	0 (0)	2 (6)	
No	30 (100)	29 (94)	
Microfracture			1.000
Yes	0 (0)	1 (3)	
No	30 (100)	30 (97)	

Values are presented as number (%) unless otherwise indicated. Bold values denote statistical significance ($P < .05$).

models were used to compare VAS and number of hydrocodone pills between groups, with results displayed using least squares means and 95% confidence intervals. Repeated-measures analyses were performed using mixed models and included the effects of time, group, and the interaction between time and group. Models were then adjusted for using specified variables. Predicted means resulting from the adjusted models were plotted for the outcome variables. Spearman correlation coefficient was used to describe the relationship between the number of hydrocodone pills and pain score. Statistical significance was set at $P < .05$. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

Results

Patient Demographics

Ninety-nine consecutive patients with the primary diagnosis of meniscal tear were assessed for participation in the study. Twenty-seven declined participation and 11 were also excluded in the study due to significant history of substance abuse, peptic ulcer disease, renal impairment, or dysfunction. A total of 61 patients were included in the study for analysis. Thirty patients were randomized to receive opioid analgesia, and 31 patients were randomized to receive nonopioid analgesia. The entire study population had a mean age of 45.0 ± 15.7 years and an average BMI of 29.35 kg/m^2, with males constituting 72% of all participants. No patients were workers compensation claims. No significant differences exist between any of the demographic variables between the 2 cohorts. All demographic characteristics can be visualized in Table 2. Of the 30 patients in the opioid cohort, 43.3% of patients reported discontinuing opioid usage prior to postoperative day 10.

Postoperative Analgesia: Opioid vs Nonopioid Regimens

There were no significant differences in the reported VAS pain scores between the opioid and nonopioid cohorts (Fig 2). When accounting for confounding

Table 2. Multimodal Nonopioid Pain Regimen

Postoperative Days 1-5			
Morning	Noon	Afternoon	Evening
- Ketorolac 10 mg	- Ketorolac 10 mg	- Ketorolac 10 mg	- Ketorolac 10 mg
- Gabapentin 300 mg	- Gabapentin 300 mg	- Gabapentin 300mg	- Diazepam 5 mg
- Diazepam 5 mg	- Diazepam 5 mg	- Diazepam 5 mg	
- Acetaminophen 1,000 mg	- Acetaminophen 1,000 mg	- Acetaminophen 1,000 mg	
Postoperative Days 6-14			
Morning	Afternoon	Evening	
- Meloxicam 7.5 mg	- Meloxicam 7.5 mg	- Diazepam 5 mg	
- Diazepam 5 mg	- Diazepam 5 mg	- Acetaminophen 1,000 mg	
- Acetaminophen 1,000 mg	- Acetaminophen 1,000 mg		

Preoperative per os (PO) regimen: PO celecoxib 400 mg, acetaminophen 975 mg, gabapentin 300 mg, tramadol 50 mg, dexamethasone 8 mg intravenous. Intraoperative local infiltration analgesia: 150 mg (30 mL) ropivacaine, 30 mg (1 mL) ketorolac, and 1 mg (1 mL) epinephrine. Gabapentin weaning began on postoperative day 6 in the following manner: 300 mg in the morning and 300 mg in the evening on days 6 to 7, 300 mg in the morning on days 8 to 9, and discontinuation on day 10.

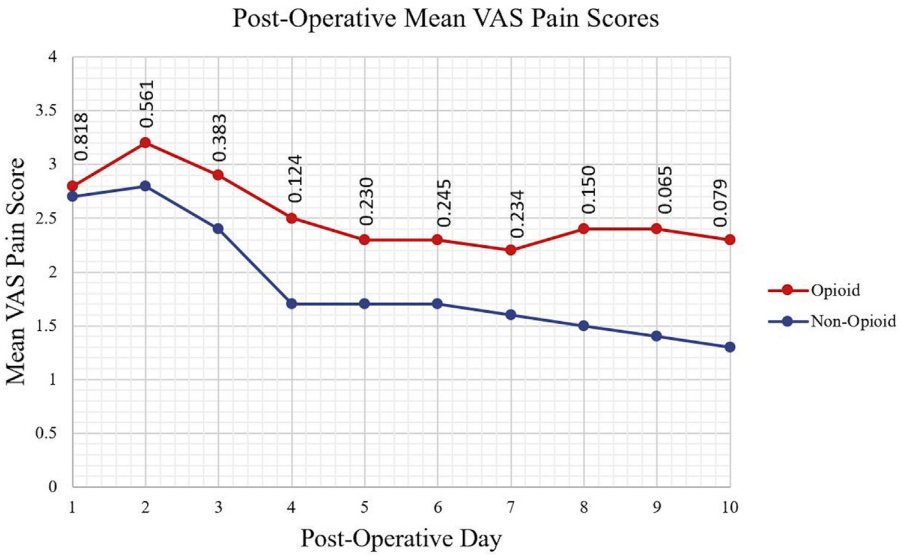

Fig 2. Mean visual analog scale (VAS) pain score of the opioid and nonopioid groups for the first 10 postoperative days. Patients in the nonopioid group reported noninferior pain control compared with the opioid group. Bold values denote statistical significance ($P < .05$).

variables with measured mixed models, there were no significant differences found in preoperative (opioid: 58.9 ± 7.0; nonopioid: 58.2 ± 5.5, $P = .724$) or postoperative (opioid: 59.8 ± 6.5; nonopioid: 54.9 ± 7.1, $P = .064$) PROMIS-PI scores (Fig 3). Mean pain levels were predicted using VAS scores and repeated-measures mixed models and showed no significant difference between the opioid and nonopioid groups (Fig 4). Measured mixed models demonstrated that opioid consumption was highest in the first 3 postoperative days (POD 1: 1.6 ± 1.4 pills, 8.2 ± 7.2 MME; POD 2: 1.8 ± 1.9 pills, 9.1 ± 9.7 MME; and POD 3: 1.6 ± 1.9 pills, 7.8 ± 9.5 MME) and lowest on postoperative days 6, 7, and 10 (POD 6: 0.9 ± 1.7 pills, 4.3 ± 8.3 MME; POD 7: 0.8 ± 1.8, 3.8 ± 8.9 MME; POD 10: 0.9 ± 1.7, 4.5 ± 8.3 MME) among the group receiving opioid analgesia (Fig 5).

A Pearson correlation did not find any significant findings between age, sex, BMI, race, workers compensation, presence of meniscus repair, loose body removal, or microfracture and VAS pain score (Table 3). Pearson correlations did return significance between presence of a chondroplasty and VAS pain score on postoperative days 8 and 9. A Pearson correlation failed to show significance between presence of meniscus repair, loose body removal, chondroplasty, or microfracture and MME at every postoperative day ($P > .05$).

Patient-Reported Adverse Events

There were no significant differences between the 2 groups in the number of days patients reported each adverse event, including constipation ($P = .124$), nausea ($P = .979$), diarrhea ($P = .464$), upset stomach ($P = .174$), drowsiness ($P = .572$), and dizziness ($P = .217$) (Table 4). The number of days patients reported no adverse events was also nonsignificant between the groups (opioid: 5.3 ± 3.8; nonopioid: 5.8 ± 3.4, $P = .798$). The most commonly reported adverse events in both groups were constipation (opioid: 1.9 ± 2.9; nonopioid: 0.9 ± 2.0) and drowsiness (opioid: 2.5 ± 3.6; nonopioid: 1.0 ± 1.6). Neither group had any intraoperative or postoperative complications, such as venous thromboembolism, infection, or reoperation. Patients in the nonopioid group reported zero complications in compliance with the medication protocol, no additional need for emergent opioid analgesia, and a 100% satisfaction with pain control. Patients in the opioid group did not require additional opioid analgesic medication.

Discussion

The current study found that pain control and patient satisfaction were no different in patients undergoing meniscal surgery who had either a multimodal nonopioid pain regimen or an opioid pain regimen postoperatively. Pain following meniscus surgery was able to be effectively managed without opioids while maintaining an equivalent side effect profile. Due to the addictive nature of opioids and the dramatic increase in opioid-related deaths in the past 20 years,[16] this study suggests that using a nonopioid multimodal pain control regimen following a primary meniscectomy or meniscal repair is a viable alternative for managing postoperative pain.

There is a paucity of literature evaluating a completely opioid-free pain regimen prospectively in meniscal surgery. Research supporting single-agent alternatives to opioids has offered promise for the elimination of narcotic use in the postoperative window. Carrier et al.[17]

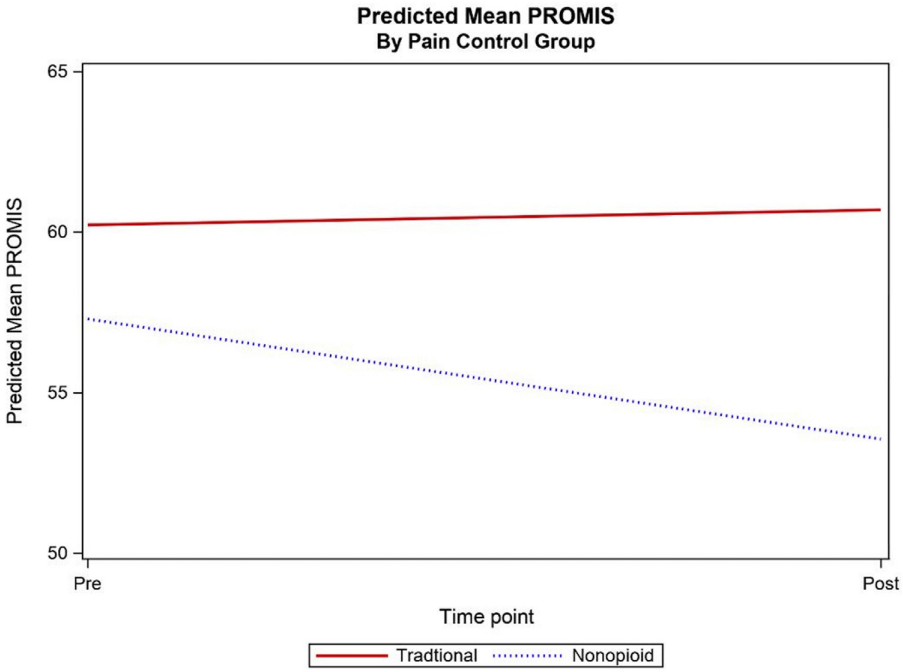

Fig 3. Predicted Patient-Reported Outcomes Measurement and Information System Pain Interference Short Form (PROMIS PI-SF) scores for opioid and nonopioid groups. Nonsignificant differences exist for PROMIS-PI SF scores between the 2 groups while controlling for age, sex, body mass index, depression, and anxiety.

examined patient satisfaction with NSAID use following partial meniscectomy. They examined 34 patients who were prescribed ibuprofen 800 mg postoperatively with a 2-week follow-up and found that 82% of patients did not use any opioids and reported that they were sufficiently satisfied with pain control achieved. In a prospective observational study, Pham et al.[18] examined the postoperative pain control of 77 patients following meniscectomy with oxycodone/acetaminophen alone or ibuprofen plus oxycodone/acetaminophen for

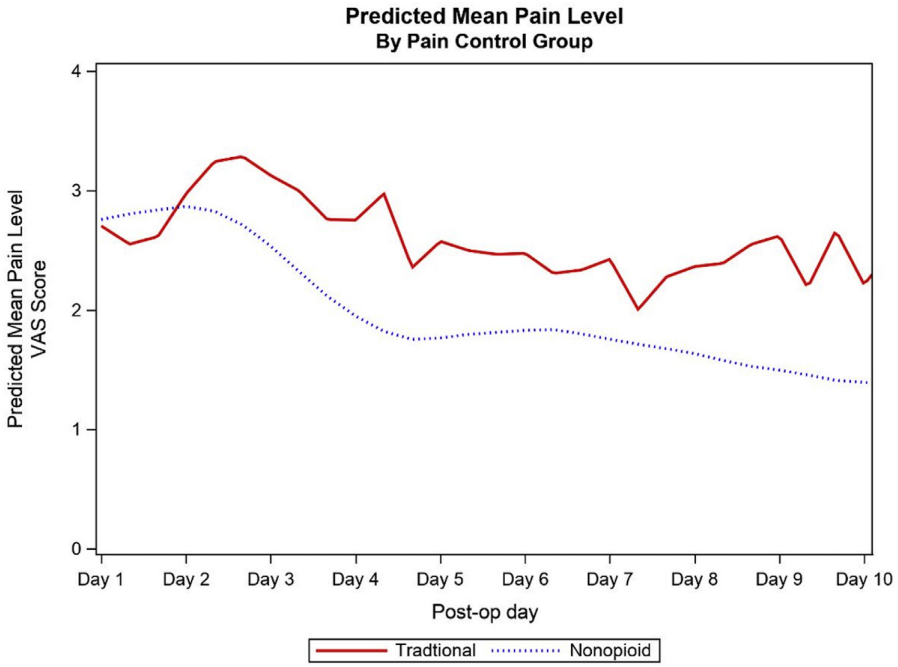

Fig 4. Predicted mean hourly pain levels for opioid and nonopioid groups. Nonsignificant difference exists for pain levels between the 2 groups while controlling for age, sex, body mass index, smoking status, depression, and anxiety. VAS, visual analog scale.

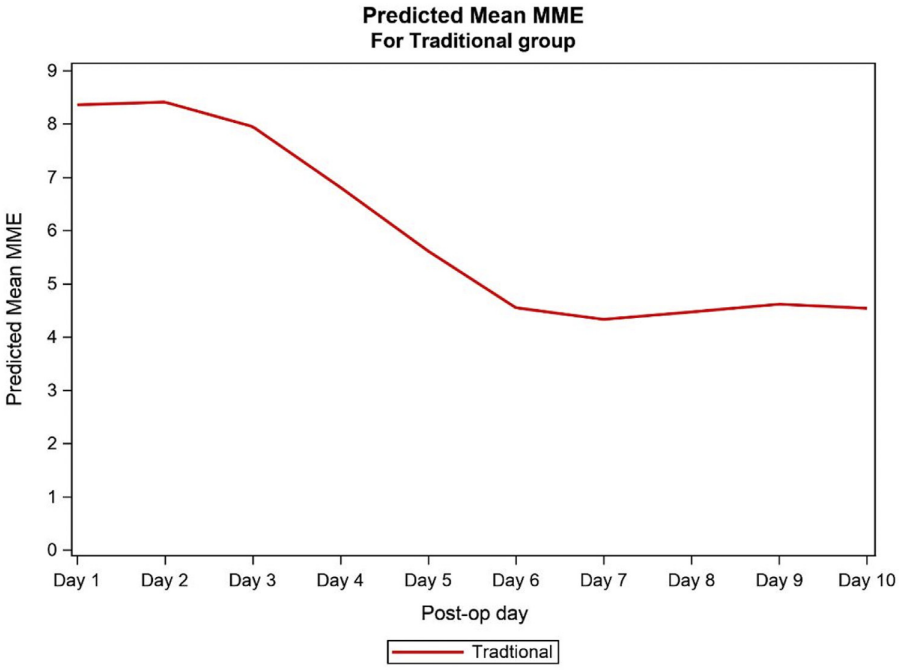

Fig 5. Predicted mean morphine milligram equivalents (MME) for opioid pain control group. Controlling for the effects of age, sex, body mass index, anxiety, and depression, no significant effects were found.

breakthrough pain. The authors found that patients who received NSAIDs and opioids for breakthrough pain had no significant difference in pain level and satisfaction compared with patients who received opioids alone (VAS score 1.8 vs 1.5, $P = .64$, NSAID vs opioid). Furthermore, Pham et al.[18] found in their study that 53% of patients in the opioid group independently chose to forego their opioid medication and used NSAIDs and acetaminophen instead, suggesting that opioids are being overprescribed following meniscal surgery. Drez et al.[19] evaluated 52 patients' pain levels 6 hours after surgery following arthroscopy or arthroscopic meniscectomy in a multicenter, double-blinded randomized, parallel trial. Patients were randomized and received either naproxen sodium or propoxyphene napsylate with acetaminophen (PN/A), and they found that patients taking naproxen had a more rapid decline in the pain intensity differences in the first hour postoperatively as compared with the PN/A group (23.9 vs 10.8, $P = .017$, NS vs PN/A), advocating for the use of NSAIDs after meniscus surgery. Last, Moutzouros et al.[11] performed a case series of 141 patients (49 arthroscopic partial meniscectomy) and examined the postoperative pain control following a multimodal pain regimen. The authors found that 1 week following meniscus surgery, patients reported a mean VAS level of 2.6 ± 2.3, and 45% of all patients required no breakthrough opioids and achieved satisfactory pain control. The present study evaluated patients in a prospective randomized fashion and found no difference in pain score between patients

Table 3. Pearson Correlation Coefficients Between VAS Pain and Intraoperative Procedures

POD	Meniscus Repair	*P* Value	Chondroplasty	*P* Value	Loose Body Removal	*P* Value	Microfracture	*P* Value
1	−0.2111	.8762	−0.11175	.4079	0.12385	.3587	−0.16716	.2139
2	−0.06015	.6688	0.01823	.8969	−0.02843	.8399	−0.16716	.2139
3	−0.02549	.8548	0.07465	.5916	−0.07351	.5973	−0.1748	.2061
4	−0.02674	.8507	0.07446	.5998	−0.00743	.9583	−0.16747	.2354
5	−0.05458	.6979	0.0506	.719	0	1	−0.15288	.2745
6	−0.08687	.5486	0.11821	.4136	0.02896	.8418	−0.15537	.2813
7	−0.14849	.3034	0.22141	.1223	−0.04923	.7342	−0.15949	.2686
8	−0.16219	.2707	**0.31038**	**.0318**	−0.06655	.6531	−0.1536	.2973
9	−0.16004	.272	**0.28769**	**.045**	−0.0108	.4895	−0.15323	.2932
10	−0.17877	.2456	0.20995	.1714	−0.08541	.5815	−0.17387	.259

Bold values denote statistical significance ($P < .05$). Chondroplasty on POD 8 and 9 was found to have a positive correlation with VAS pain.
POD, postoperative day; VAS, visual analog scale.

Table 4. Reported Adverse Events in Opioid and Nonopioid Pain Groups

Adverse Event	Opioid (n = 30)	Nonopioid (n = 31)	*P* Value
Constipation, d	1.9 ± 2.9	0.9 ± 2.0	.124
Nausea, d	0.3 ± 0.6	0.4 ± 1.2	.979
Diarrhea, d	0.1 ± 0.5	0.0 ± 0.2	.464
Upset stomach, d	0.4 ± 0.7	0.2 ± 0.5	.174
Drowsiness, d	2.5 ± 3.6	1.0 ± 1.6	.572
Dizziness, d	0.0 ± 0.2	0.4 ± 1.3	.217

Values are presented as mean ± SD.

receiving a nonopioid and an opioid pain protocol. This suggests a nonopioid pain regimen can be effective in decreasing narcotic consumption following meniscal surgery in a safe and effective manner. It should be noted that while concerns exist regarding the use of NSAIDs and bone healing, 2 meta-analyses by Kurmis et al.[20] and Marquez-Lara et al.[21] have established there is no high-quality literature supporting NSAID inhibition of tissue healing in the clinical setting.

When managing postoperative pain, it is critical to maximize therapeutic effects while striving to minimize any adverse effects of the drugs that can negatively affect patient experience and their hospital stay. In a prior case series, Moutzouros et al.[11] found that 53.6% of patients reported no adverse effects of their pain regimen, and 23.5% of patients reported they were experiencing drowsiness. The most common reported adverse events in both groups were constipation (opioid: 1.9 ± 2.9; nonopioid: 0.9 ± 2.0) and drowsiness (opioid: 2.5 ± 3.6; nonopioid: 1.0 ± 1.6). In the present study, adverse effects were tracked in real time, and patients were asked to report side effects each day. Our study found no significant difference in constipation, nausea, diarrhea, drowsiness, or dizziness between the opioid and nonopioid protocols. Of note, postoperative narcotic usage is widely known to induce constipation, with up to 60% of patients reporting this effect.[11] Interestingly, the present study demonstrated a nonsignificant decrease in reported constipation postoperatively in the nonopioid cohort when compared with the opioid cohort (0.9 vs 1.9 days, respectively). A future investigation into the incorporation of a bowel regimen could help determine if postoperative constipation can be further minimized following meniscal surgery for patients receiving a nonopioid pain regimen. The incidence of reported constipation in the nonopioid cohort can likely be attributed to the synergistic effect of gabapentin and diazepam, which have both been demonstrated to cause constipation in patients.[22,23] These findings suggest an equivalent side effect profile for the nonopioid regimen with a diminished risk of opioid dependence.

In the initial study evaluating opioid use after meniscus surgery, Moutzouros et al.[11] sent patients home with an adjunct rescue opioid (oxycodone 5 mg), and patients reported a VAS score of 2.6 ± 2.3 while taking 1.6 ± 3.4 oxycodone pills (5.2 ± 11.3 morphine equivalents). In their cohort, patients undergoing meniscus surgery had significantly better pain control than those undergoing rotator cuff repair, labrum surgery, or anterior cruciate ligament reconstruction. In the present cohort, patients reported a VAS score of 1.3 ± 1.3 at an equivalent time (POD 10) without consuming any opioids whatsoever, which was improved from the opioid analgesic cohort (2.3 ± 1.7), although this finding was not statistically significant. This disparity may be attributed to the multimodal nature of the pain protocol, where multiple steps of the nociceptive pathway are targeted, as compared with opioid analgesia where pain is blocked at essentially a singular point. In a comparative study of medial meniscal repair, partial meniscectomy, and intact meniscus following concomitant anterior cruciate ligament reconstruction, Aglietti et al.[24] found that at an average follow-up of 55 months, patients who underwent partial meniscectomies had a significant increase in pain experienced when compared with other groups. Given these findings, in combination with the present study, there is suggestion that pain after meniscus surgery is exceptionally low, particularly when considering that there is no insult to the bony anatomy and that patient's perception of pain may be dependent on how much meniscus is damaged and/or removed. This may allow for alteration of the pain protocol and de-escalation of the multimodal protocol for relatively small meniscal lesions, but more work must be done in meniscus surgery and postoperative pain dynamics.

Limitations

This study is not without limitations. The first limitation is that it was not possible to double blind this study as all patients were informed of their current postoperative treatment. This could have introduced bias-reported pain scores, as could patients opting to not take opioid medication because of the known side effect profile. The second limitation of this study was our inability to measure patient compliance with prescribed medication. This could have introduced bias-reported pain scores, as could patients opting to not take opioid medication because of the known side effect profile. Third, this study was only powered to identify a significant difference in VAS scores between cohorts and was not powered to detect differences in adverse drug effects, function, mental status, postoperative complications, or long-term pain and disability past 10 days postoperatively. A larger sample size would have been required in order to perform a subgroup analysis of psychosocial variables that could have affected pain perception and opioid intake. Twenty-seven patients declined to participate in the study, primarily due to preexisting preferences for postoperative pain control; this represents a potential confounder due to the effect of subject bias. Two patients were found to

require meniscal repair following diagnostic arthroscopy, and it was not possible to exclude these patients due to the stated aim of the study. These patients may potentially confound the level of reported pain control as meniscal repairs may present with higher levels of postoperative pain.

Conclusions

This study found that a multimodal nonopioid pain protocol provided equivalent pain control and patient outcomes following primary meniscus surgery while having an equivalent side effect profile. All patients reported satisfaction with their pain management without requiring emergency opioid analgesia.

References

1. Office HP. *HHS* acting secretary declares public health emergency to address national opioid crisis. HHS press release, 2017.
2. Baker DW. History of The Joint Commission's Pain Standards: lessons for today's prescription opioid epidemic. *JAMA* 2017;317:1117-1118.
3. Centers for Disease Control and Prevention. Drug overdose deaths, 2020. Available at: https://www.cdc.gov/drugoverdose/data/statedeaths.html. Accessed April 28, 2020.
4. Manchikanti L, Fellows B, Ailinani H, Pampati V. Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. *Pain Physician* 2010;13:401-435.
5. Schoenfeld A, Jiang W, Chaudhary M, Scully R, Koehlmoos T, Haider A. Sustained prescription opioid use among previously opioid-naive patients insured through TRICARE (2006-2014). *JAMA Surgery* 2017;152:2.
6. Molina C, Thakore R, Blumer A, Obremskey W, Sethi M. Use of the National Surgical Quality Improvement Program in orthopaedic surgery. *Clin Orthop Relat Res* 2015;473:8.
7. Daniels S, Garvey K, Collins J, Matzkin E. Patient satisfaction with nonopioid pain management following arthroscopic partial meniscectomy and/or chondroplasty. *Arthroscopy* 2019;35:1641-1647.
8. Dahl V, Spreng U, Waage M, Raeder J. Short stay and less pain after ambulatory anteriorcruciate ligament (ACL) repair: COX-2 inhibitor versusglucocorticoid versus both combined. *Acta Anaesthesiol Scand* 2012;56:7.
9. Barber F, Gladu D. Comparison of oral ketorolac and hydrocodone for pain relief after anterior cruciate ligament reconstruction. *Arthroscopy* 1998;14:6.
10. Christophe M, Frédéric A, Bruno G, Daniel S, Marcel C. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. *Anesth Analg* 2005;100:5.
11. Moutzouros V, Jildeh T, Khalil L, et al. A multimodal protocol to diminish pain following common orthopedic sports procedures: can we eliminate postoperative opioids? *Arthroscopy* 2020;36:2249-2257.
12. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med* 2010;152:726-732.
13. Fox LM, Hoffman RS, Vlahov D, Manini AF. Risk factors for severe respiratory depression from prescription opioid overdose. *Addiction* 2018;113:59-66.
14. Zhao S, Chen F, Feng A, Han W, Zhang Y. Risk factors and prevention strategies for postoperative opioid abuse. *Pain Res Manag* 2019;2019:7490801.
15. Anthony CA, Westermann RW, Bedard N, et al. Opioid demand before and after anterior cruciate ligament reconstruction. *Am J Sports Med* 2017;45:3098-3103.
16. Singh GK, Kim IE, Girmay M, et al. Opioid epidemic in the United States: Empirical trends, and a literature review of social determinants and epidemiological, pain management, and treatment patterns. *Int J MCH AIDS* 2019;8:89-100.
17. Carrier C, Garvey K, Brook B, MatzKin B. Patient satisfaction with nonopioid pain management following knee arthroscopic partial meniscectomy and/or chondroplasty. *Orthopedics* 2018;41:5.
18. Pham H, Pickell M, Yagnatovsky M, et al. The utility of oral nonsteroidal anti-inflammatory drugs compared with standard opioids following arthroscopic meniscectomy: A prospective observational study. *Arthroscopy* 2019;35:6.
19. Drez D, Ritter M, Rosenberg T. Pain relief after arthroscopy: Naproxen sodium compared to propoxyphene napsylate with acetaminophen. *South Med J* 1987;80:4.
20. Kurmis AP, Kurmis TP, O'Brien JX, Dalen T. The effect of nonsteroidal anti-inflammatory drug administration on acute phase fracture-healing: a review. *J Bone Joint Surg Am* 2012;94:815-823.
21. Marquez-Lara A, Hutchinson ID, Nunez F Jr, Smith TL, Miller AN. Nonsteroidal anti-inflammatory drugs and bone-healing: A systematic review of research quality. *JBJS Rev* 2016;4:01874474.
22. Witenko C, Moorman-Li R, Motycka C, et al. Considerations for the appropriate use of skeletal muscle relaxants for the management of acute low back pain. *P T* 2014;39:427-435.
23. Lee KJ, Kim JH, Cho SW. Gabapentin reduces rectal mechanosensitivity and increases rectal compliance in patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther* 2005;22:981-988.
24. Aglietti P, Zaccherotti G, Biase P, Taddei I. A comparison between medial meniscus repair, partial meniscectomy, and normal meniscus in anterior cruciate ligament reconstructed knees. *Clin Orthop Relat Res* 1994;307:8.