A Prospective, Randomized, Double-Blinded Trial Comparing Acetaminophen, Ibuprofen, and Oxycodone for Pain Management After Hand Surgery

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abstract

The goal of this study was to evaluate 3 common oral analgesics—oxycodone (OXY), ibuprofen (IBU), and acetaminophen (ACE)—for pain management following carpal tunnel release (CTR) and trigger finger release (TFR) surgery. Outcome measures were pain scores, capsule consumption patterns, and satisfaction. Carpal tunnel or trigger finger patients indicated to undergo primary, unilateral release received 10 capsules of either OXY (5 mg), IBU (600 mg), or ACE (500 mg) postoperatively. Medications were distributed in a randomized fashion, with both surgeons and patients blinded to the selected analgesic. Postoperatively, patients recorded pain level each day using a 0 to 10 visual analog scale, the number of capsules taken each day, and any adverse effects experienced. Medication distribution among the 188 patients completing the study was 62 OXY, 64 IBU, and 62 ACE. Surgical distribution was 76 TFR, 61 endoscopic CTR, and 51 open CTR. Overall, the mean total number of capsules consumed from postoperative days 0 through 5 for OXY, IBU, and ACE was 3.2, 4.0, and 3.1, respectively ($P>.05$). Mean worst daily pain score for the OXY, IBU, and ACE groups was 2.9, 2.5, and 2.5, respectively ($P<.05$). On subgroup analyses by procedure type, the only difference was found in the open CTR group, with the highest daily pain scores noted in the OXY group ($P<.05$). Nine of the 11 patients experiencing an adverse reaction also came from the OXY group. There were no reoperations or allergic reactions in any group. In this study, no clinically significant difference in pain experience or capsule consumption based on postoperative opioid vs nonopioid medication was identified. Adverse events were highest in the OXY group. In lieu of opioids, the authors suggest prescribing nonopioids first following TFR and CTR surgery. In addition, they advise prescribing 5 to 10 or fewer pills postoperatively regardless of the analgesic selected. [*Orthopedics*. 2019; 42(2):110-115.]

Pain management after orthopedic surgery can affect patient outcomes, safety, and overall satisfaction.[1-3] Although sufficient pain control can improve patient satisfaction and recovery, current literature indicates that opioid analgesics are often prescribed in excess following surgery.[4-7] Moreover, the Centers for Disease Control and Prevention reported that in 2016 alone, prescription opioids were involved in more than 17,000 overdose deaths in the United States.[8] Additionally, the "opioid crisis" has placed a significant financial burden on society that continues to worsen.[9]

The purpose of this study was to assess the effectiveness of 3 different types of pain medications (oxycodone [OXY]—an opioid, ibuprofen [IBU]—a nonsteroidal anti-inflammatory drug, and acetaminophen [ACE]—a nonopioid analgesic) for the treatment of pain following isolated mini-open and endoscopic carpal tunnel

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release (CTR) and trigger finger release (TFR), which are common hand surgeries. The null hypothesis was that there would be no difference in reported pain experience and/or capsule consumption after these surgeries relative to the postoperative analgesic prescribed.

Materials and Methods

This prospective, randomized controlled, double-blinded, noninferiority study received institutional review board approval (**Figure 1**). It involved 2 board-certified and hand surgery fellowship-trained orthopedic surgeons (A.M.I., J.L.M.), each of whom performed CTR and TFR surgery under only local anesthesia without sedation at outpatient surgical centers. The study followed the Consolidated Standards of Reporting Trials guidelines. An analysis of a subset of the carpal tunnel patients enrolled in this study was published previously.[10] This article represents the culmination of the study with all 188 carpal tunnel and trigger finger patients included.

At their clinic visit prior to surgery, all patients scheduled to have a primary, unilateral TFR or CTR under local anesthesia only who were 18 years or older were given the option to participate in the study. After each participant provided formal written informed consent, individual demographics and operative details were saved in a secured research file that was only accessible to the unblinded research coordinator (J.G.G.). Exclusion criteria were bilateral surgical procedures; simultaneous operations involving bone and/or soft tissues; the use of sedation and/or general anesthesia during surgery; a history of allergies and/or medical contraindications to lidocaine, epinephrine, or any of the distributed analgesics (OXY, IBU, or ACE); preoperative exposure to opioids; not speaking English; and pregnancy.

Each patient was provided with 1 of the following analgesics postoperatively: OXY (5 mg), IBU (600 mg), or ACE (500 mg). In each case, the medication chosen was determined using a computerized random number generator. A compounding pharmacy prepared all 3 medications, with each serial-numbered prescription bottle containing 10 capsules of one of the chosen analgesics. Capsules were indistinguishable from one another. Patients were instructed to take 1 capsule every 6 hours as needed for pain.

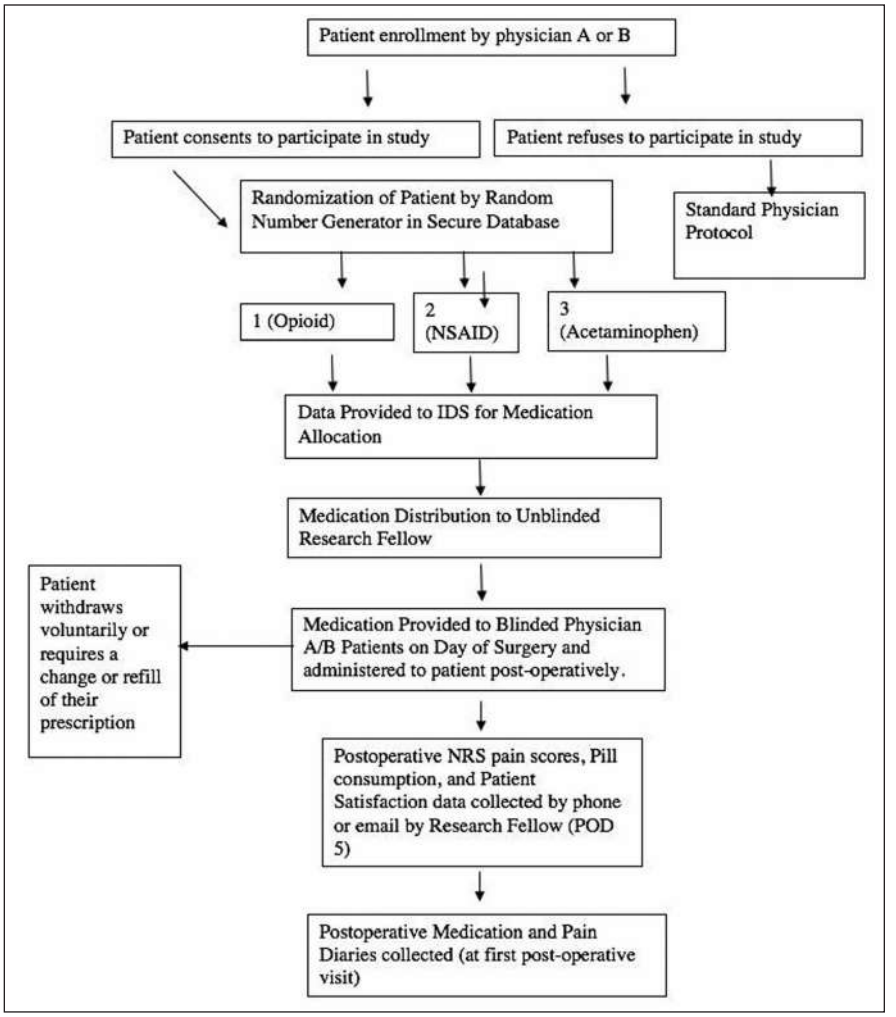

Figure 1: Procedures flow diagram. Abbreviations: IDS, investigational drug services; NRS, numeric rating scale; NSAID, nonsteroidal anti-inflammatory drug; POD, postoperative day.

All formulated medications were stored in a locked cabinet in the research suite. The allocated medications were distributed by the unblinded research coordinator, who provided them to the blinded physician for dispersal to the blinded patient on the day of surgery. In addition, the unblinded research coordinator maintained a drug accountability log for all distributed analgesics throughout the duration of the study. After receiving their assigned medication on the day of surgery, all patients were given a 6-day pain diary to maintain from the day of surgery through postoperative day 5.

All study patients were seen in clinic by their surgeon within 2 weeks of their procedure. At this first postoperative visit, patients returned their pain diary and remaining blinded medication. In the pain diary, patients recorded their worst pain experienced each day using a 0 to 10 visual analog scale (VAS), which has been previously validated.[11] In a separate sec-

Table 1

Patient Demographics by Group

Group	No. of Patients	Mean Age (Range), y	Sex Distribution, F/M, No. (%)
Open CTR and OXY	19	60.9 (29-84)	13 (68.4)/6 (31.6)
Open CTR and IBU	18	63.4 (19-88)	8 (44.4)/10 (55.6)
Open CTR and ACE	14	62.3 (45-88)	6 (42.9)/8 (57.1)
Endo CTR and OXY	19	61.1 (50-74)	8 (42.1)/11 (57.9)
Endo CTR and IBU	16	59.6 (40-79)	10 (62.5)/6 (37.5)
Endo CTR and ACE	26	58.8 (32-74)	13 (50.0)/13 (50.0)
Open TFR and OXY	24	57.3 (42-72)	15 (62.5)/9 (37.5)
Open TFR and IBU	30	62.7 (30-94)	20 (66.7)/10 (33.3)
Open TFR and ACE	22	58.7 (35-86)	15 (68.2)/7 (31.8)

Abbreviations: ACE, acetaminophen; CTR, carpal tunnel release; F, female; IBU, ibuprofen; M, male; OXY, oxycodone; TFR, trigger finger release.

tion of the diary, patients recorded the number of capsules they consumed each day from the day of surgery through postoperative day 5 and any adverse events they experienced. Subsequently, a brief questionnaire containing the following 3 questions was administered in the office to assess patient satisfaction: (1) Were the 10 painkillers provided after surgery an adequate amount? (2) Were the painkillers strong enough to manage the pain after surgery? (3) Were the painkillers too strong for managing the pain after surgery? Response options, on a Likert scale, were strongly agree, agree, neutral, disagree, or strongly disagree.

Demographics were analyzed using descriptive statistical analysis. In addition, single-factor analysis of variance was used to determine if differences in discrete variables (daily pain VAS scores and the number of capsules consumed each postoperative day) between randomized medication groups reached statistical significance. Independent *t* tests were used during subanalyses between groups, and post hoc tests were used when appropriate. Significance was set at $P<.05$.

To detect a 1-capsule difference in consumption and/or a 0.5-unit difference as measured on an 11-point numeric rating scale for pain, the authors determined that 60 patients per medication cohort (180 total) would be necessary using a beta of 80%. After some degree of attrition was accounted for, 197 patients undergoing primary, unilateral CTR or isolated TFR under local anesthesia alone were enrolled in the study. When grouped by type of surgical procedure, 72 patients underwent TFR, 68 patients underwent endoscopic CTR, and 57 patients underwent mini-open CTR. The allocations ratio was 1:1:1.

Results

Patients were enrolled from March 2017 through May 2018 and followed for 2 weeks postoperatively. Of the 197 patients enrolled, medication distribution was as follows: 65 patients received OXY, 65 patients received IBU, and 67 patients received ACE. Nine patients exited the study based on protocol. In 8 cases (4 patients receiving ACE, 3 patients receiving OXY, and 1 patient receiving IBU), the patient contacted the office for a stronger medication. One patient in the ACE group was excluded after developing a wound infection after TFR that required a return to the operating room. Although 7 patients (3 patients receiving ACE, 2 patients receiving OXY, and 2 patients receiving IBU) disclosed taking a different pain medication during the study period, they were maintained in the study based on the intention-to-treat principle. Specifically, 1 patient discontinued the blinded pain medication (ACE) and independently started taking IBU. Two patients (1 receiving IBU and 1 receiving ACE) later opted out of the study and took over-the-counter medications and/or medications prescribed elsewhere for a previous surgery. Four patients (2 receiving OXY, 1 receiving IBU, and 1 receiving ACE) did not follow the study directions and supplemented their analgesic with different medications during the study period.

After the 9 patients detailed previously were removed, the remaining 188 patients completed the study, with 62 receiving OXY, 64 receiving IBU, and 62 receiving ACE. The mean age was 60 years (range, 19-94 years; SD, 12.1 years). There were 108 female and 80 male participants (**Table 1**).

A subanalysis of the TFR group (**Figure 2**) found that the mean worst daily pain VAS scores were 2.5, 2.5, and 2.3 for the OXY, IBU, and ACE groups, respectively ($P>.05$). The mean total numbers of capsules taken during the study period were similar (OXY, 2.7; IBU, 3.2; and ACE, 3.4) ($P>.05$).

A subanalysis of the endoscopic CTR group (**Figure 3**) showed no significant difference in mean daily pain VAS scores (OXY, 2.8; IBU, 2.7; and ACE, 2.7) ($P>.05$). The mean total numbers of capsules consumed from the day of surgery through postoperative day 5 by endoscopic CTR patients in the OXY, IBU, and ACE groups were 2.9, 4.3, and 2.5, respectively, and no statistical difference was detected ($P>.05$).

A subanalysis of the open CTR group (**Figure 4**) showed a significant difference in mean daily pain VAS scores (OXY, 3.5; IBU, 2.5; and ACE, 2.1) ($P<.05$). Post hoc

1-tailed independent *t* tests also confirmed significantly greater mean daily pain VAS scores in the OXY group compared with the 2 other groups ($P<.05$). No significant difference was detected between the IBU and ACE groups ($P>.05$). The mean total numbers of capsules consumed from the day of surgery through postoperative day 5 by open CTR patients in the OXY, IBU, and ACE groups were 4.1, 4.9, and 3.9, respectively, and no statistical difference was detected ($P>.05$).

Mean daily pain VAS scores did not differ significantly among the 3 surgical groups (TFR, 2.5; endoscopic CTR, 2.7; and open CTR, 2.7) ($P>.05$). Single-factor analysis of variance of the mean total number of capsules consumed from the day of surgery through postoperative day 5 for the 3 groups showed a significant difference (TFR, 3.1; endoscopic CTR, 3.1; and open CTR, 4.3) ($P<.05$). Post hoc 1-tailed independent *t* tests confirmed significantly greater capsule consumption in the open CTR group compared with the endoscopic CTR and TFR groups ($P<.05$). No significant difference was detected between the TFR and endoscopic CTR groups ($P>.05$).

Throughout the study period, the mean worst daily pain VAS scores (0 to 10 scale) for patients in the OXY, IBU, and ACE groups were 2.9, 2.5, and 2.5, respectively ($P<.05$). Post hoc 1-tailed independent *t* tests confirmed significantly greater mean daily pain VAS scores in the OXY group compared with the IBU and ACE groups ($P<.05$). There were no significant differences in mean daily pain VAS scores between the IBU and ACE groups. The mean total numbers of capsules consumed from the day of surgery through postoperative day 5 for the OXY, IBU, and ACE groups were 3.2, 4.0, and 3.1, respectively ($P>.05$). There was no statistically significant difference between groups.

Of the 188 patients completing the study, 11 (6%) experienced an adverse reaction to their assigned medication. Nine patients in the OXY group (15%) had an adverse reaction. Seven experienced nausea, 1 experienced mild pruritus, and 1 experienced constipation. One patient in the ACE group (1.6%) reported an episode of diarrhea after taking the medication. One patient in the IBU group (1.6%) experienced an episode of dizziness.

A subanalysis of satisfaction data indicated that the groups were similar. Most of the patients reported that 10 capsules were an adequate amount and that the provided medication was strong enough. When surveyed whether the provided pain medication was too strong, patients overwhelmingly disagreed (**Table 2**).

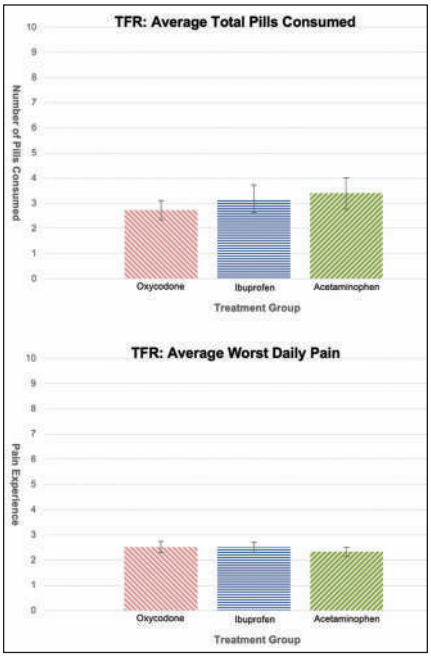

Figure 2: A subanalysis of the capsule consumption and pain experience in the trigger finger release (TFR) group.

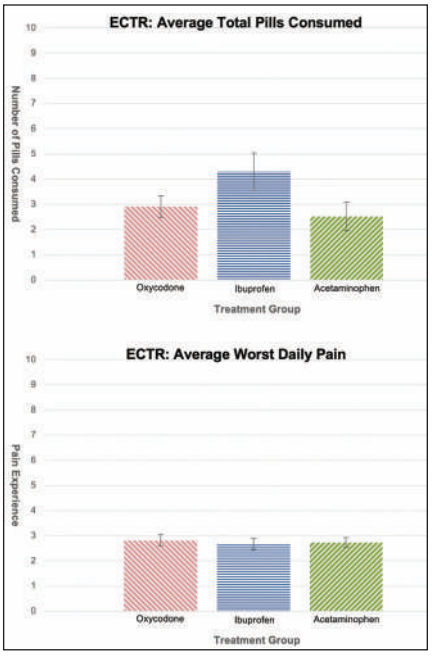

Figure 3: A subanalysis of the capsule consumption and pain experience in the endoscopic carpal tunnel release (ECTR) group.

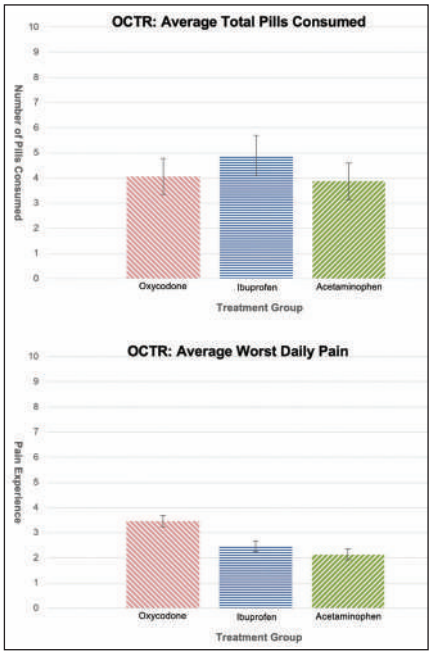

Figure 4: A subanalysis of the capsule consumption and pain experience in the open carpal tunnel release (OCTR) group.

Discussion

Safe but effective postoperative pain management is a challenge facing not only orthopedics but all surgical specialties.[12] Common surgeries performed by both orthopedic and plastic surgeons include CTR and TFR.[13,14] Current evidence indicates that patients are being overprescribed opioids at the rate of 2 to 3 times their usage after these surgeries.[15-17] Therefore, the goal of this study was to determine the optimal pain medication and number of pills that should be prescribed in the period

Table 2

Patient Satisfaction Data

Medication and Answer Choice	Ten Pills Adequate?	Medication Strong Enough?	Medication Too Strong?
Oxycodone			
Strongly agree	59.7%	43.5%	4.8%
Agree	19.4%	25.8%	4.8%
Neutral	8.1%	8.1%	8.1%
Disagree	3.2%	11.3%	41.9%
Strongly disagree	0%	0%	29%
No data	9.7%	11.3%	11.3%
Ibuprofen			
Strongly agree	51.6%	40.6%	0%
Agree	29.7%	26.6%	1.6%
Neutral	7.8%	14.1%	12.5%
Disagree	1.6%	4.7%	35.9%
Strongly disagree	1.6%	3.1%	39.1%
No data	7.8%	10.9%	10.9%
Acetaminophen			
Strongly agree	58.1%	41.9%	1.6%
Agree	24.2%	27.4%	0%
Neutral	3.2%	12.9%	11.3%
Disagree	1.6%	1.6%	27.4%
Strongly disagree	3.2%	4.8%	46.8%
No data	9.7%	11.3%	12.9%

following these surgeries. To the authors' knowledge, no study has randomly and prospectively evaluated the consumption of nonopioid analgesics compared with opioid analgesics after hand surgery.

These findings challenge the perceived necessity of opioids following CTR and TFR surgeries. In overall pain experience, there was a statistically significant increase in the OXY group compared with the IBU and ACE groups. However, the authors would not consider that difference to be clinically relevant. Moreover, the greatest pain was experienced on day 0 and day 1, with rapid reduction thereafter.

Regarding overall capsule consumption, mean capsule consumption was similar in all groups. Again, the greatest capsule consumption occurred on day 0 and day 1, with a rapid drop off thereafter.

Although previous studies disagree regarding whether open vs endoscopic techniques are more painful postoperatively,[18-20] the authors found that there was statistically significant greater capsule consumption in the open group compared with the endoscopic group ($P<.05$). However, the authors would not consider this small difference to be clinically relevant. The capsule consumption by both groups was consistent with past studies showing that mean opioid consumption following CTR is approximately 4 pills, regardless of type of procedure used.[6,7,21]

Only 10 capsules were prescribed to each group in this study, yet there were only 4 (3 in the IBU group and 1 in the ACE group) refill requests among the 188 participants (2%). None of these requests were from patients who had been receiving OXY. Eight patients requested a stronger pain medication, and 3 of them were receiving OXY. Of the remaining patients, 4 were receiving ACE and 1 was receiving IBU.

Regarding adverse events, 11 patients reported only minor complications. Nine were in the OXY group, and these complications consisted of nausea and itchiness. One patient in the ACE group had diarrhea. There was 1 report of dizziness after consumption of IBU.

The prospective, randomized, double-blinded design of this study makes the findings particularly applicable to clinical practice. This was bolstered by the authors' comparison of 3 commonly used pain medications, including an opioid (OXY), a nonsteroidal anti-inflammatory drug (IBU), and a nonopioid analgesic (ACE). In addition, the inclusion of CTR and TFR cases only—2 of the most common procedures in hand surgery—provided uniformity of analysis. Finally, making the use of sedation and/or general anesthesia during surgery a strict exclusion criterion eliminated their potential impact on the postoperative pain experience and adverse events.

This study had some weaknesses. Eight patients were excluded after contacting the office to request a stronger medication. Technically, these were failures of treatment; ideally, these patients should have still been accounted for. Because this involved patients in various groups (4 in the ACE group, 3 in the OXY group, and 1 in the IBU group), the authors think it is unlikely to have changed the conclusion of the study. Only 1 patient in the IBU group requested a stronger medication, and it is possible that there is some clinical advantage to its preferential use. Next, the results may have been susceptible to bias from a volunteer effect. In addition, it is possible that the study was underpowered to detect subtle differences. However, based on the small differences seen between the groups in both pain experience and capsule consumption, it is unlikely that any such difference would be

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clinically significant. Finally, only soft tissue procedures of the hand were evaluated; therefore, its applicability to non–soft tissue surgeries of the hand is not known but can be anticipated to potentially have similar results.

Conclusion

The authors would recommend ACE and/or IBU rather than OXY following CTR and TFR surgery. If an opioid is prescribed postoperatively, the authors would advise prescribing no more than 5 to 10 pills to avoid inadvertent overprescribing. In addition, they would encourage surgeons to consider extrapolating these study findings that nonopioids may be as effective as opioids for other surgeries. Finally, the authors would encourage the continued investigation of nonopioids and other perioperative pain strategies with the aim of optimizing prescribing for postoperative pain management.

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