Local Infiltration Analgesia Followed by Continuous Infusion of Local Anesthetic Solution for Total Hip Arthroplasty

A Prospective, Randomized, Double-Blind, Placebo-Controlled Study

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Background: We studied the efficacy of local infiltration analgesia in surgical wounds with 0.2% ropivacaine (50 mL), ketorolac (15 mg), and adrenaline (0.5 mg) compared with that of local infiltration analgesia combined with continuous infusion of 0.2% ropivacaine as a method of pain control after total hip arthroplasty. We hypothesized that as a component of multimodal analgesia, local infiltration analgesia followed by continuous infusion of ropivacaine would result in reduced postoperative opioid consumption and lower pain scores compared with infiltration alone, and that both of these techniques would be superior to placebo.

Methods: In this prospective, double-blind, placebo-controlled study, 105 patients were randomized into three groups: Group I, in which patients received infiltration with ropivacaine, ketorolac, and adrenaline followed by continuous infusion of 0.2% ropivacaine at 5 mL/hr; Group II, in which patients received infiltration with ropivacaine, ketorolac, and adrenaline followed by continuous infusion of saline solution at 5 mL/hr; and Group III, in which patients received infiltration with saline solution followed by continuous infusion of saline solution at 5 mL/hr.

All patients received celecoxib, pregabalin, and acetaminophen perioperatively and patient-controlled analgesia; surgery was performed under general anesthesia. Before wound closure, the tissues and periarticular space were infiltrated with ropivacaine, ketorolac, and adrenaline or saline solution and a fenestrated catheter was placed. The catheter was attached to a pump prefilled with either 0.2% ropivacaine or saline solution set to infuse at 5 mL/hr.

The primary outcome measure was postoperative opioid consumption and the secondary outcome measures were pain scores, adverse side effects, and patient satisfaction.

Results: There were no differences between groups in the administration of opioids in the operating room, in the recovery room, or on the surgical floor. The pain scores on recovery room admission and discharge and the floor were low and similar between groups. There were no differences in the incidence of adverse side effects among groups. Patient satisfaction with pain management was similar in all groups.

Conclusions: Local infiltration analgesia alone or followed by continuous infusion of ropivacaine as part of multimodal analgesia provides no additional analgesic benefit or reduction in opioid consumption compared with placebo following total hip arthroplasty.

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

Disclosure: None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. One or more of the authors, or his or her institution, has had a financial relationship, in the thirty-six months prior to submission of this work, with an entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. No author has had any other relationships, or has engaged in any other activities, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

Optimal postoperative analgesia following total hip arthroplasty is important for early participation in the rehabilitation program as well as patient satisfaction[1]. Various techniques have been utilized for postoperative pain control following total hip arthroplasty including epidural analgesia, peripheral nerve blockade, and systemic and neuraxial opioids[2-4]. Although these methods provide good pain control, they are associated with either weakness of lower-extremity muscles interfering with early walking or opioid-related side effects such as nausea, vomiting, urinary retention, constipation, ileus, sedation, and respiratory depression.

Infiltration of the surgical wound with high-volume local anesthetic solution has gained popularity as an alternative method of providing pain control after total hip arthroplasty[5]. The advantage of local infiltration analgesia is the ability to provide pain control without interfering with lower-extremity motor strength, thereby allowing early mobilization of patients[6]. However, the duration of local infiltration analgesia is limited to a few hours of postoperative relief as the infiltrated local solution is reabsorbed from the surgical site. To prolong the analgesia, catheters can be placed in the periarticular space and soft tissue and can be bolused with local anesthetic solution; however, intermittent dosing may lead to gaps in analgesia. The use of local infiltration analgesia combined with continuous infusion of local anesthetic solution through the wound catheters to maintain the analgesia has been advocated[7,8].

This study was designed to study the efficacy of local infiltration analgesia alone or a combination of local infiltration analgesia with continuous catheter infusion of local anesthetic solution at the surgical site after total hip arthroplasty as part of a comprehensive multimodal analgesia protocol. The hypothesis was that local infiltration analgesia with continuous infusion of local solution would result in lower pain scores and opioid consumption compared with local infiltration analgesia alone and both these techniques would be superior to patient-controlled analgesia with opioids. The primary outcome measure was postoperative opioid consumption, and the secondary outcome measures were pain scores, adverse side effects (nausea, vomiting), and patient satisfaction with analgesic protocol.

Materials and Methods

In this institutional review board-approved, prospective, double-blind, placebo-controlled study, 105 patients gave written informed consent from December 2009 to April 2011. The study was registered with ClinicalTrials.gov (NCT01409278). Exclusion criteria included an age of less than eighteen years or more than eighty years and a history of neurological disease, neuropathy, diabetes, pregnancy, chronic opioid use, or allergy to local anesthetic or other medications used in the study. Patients were randomized into three groups with use of randomization tables by a study coordinator and the allocation sequence was placed in serially numbered sealed envelopes (Fig. 1). Group I included patients who received an infiltration with an admixture of 0.2% ropivacaine (50 mL), ketorolac (15 mg), and adrenaline (0.5 mg) followed by a continuous infusion of 0.2% ropivacaine at 5 mL/hr for forty-eight hours. Group II included patients who received an infiltration with 0.2% ropivacaine (50 mL), ketorolac (15 mg), and adrenaline (0.5 mg) followed by a continuous infusion of normal saline solution at 5 mL/hr. Group III consisted of infiltration with normal saline solution of 50 mL followed by infusion of normal saline solution at 5 mL/hr.

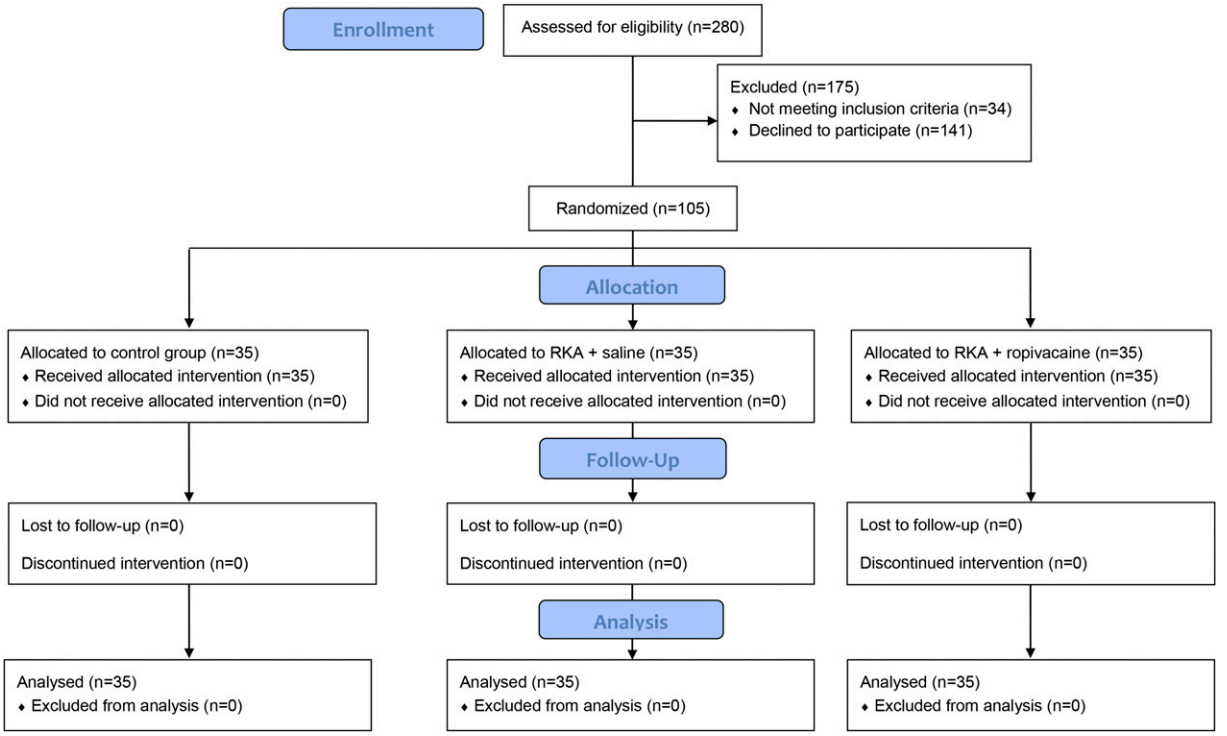

Fig. 1

Consolidated Standards of Reporting Trials (CONSORT) flow diagram. RKA = ropivacaine, ketorolac, adrenaline.

TABLE I Opioids Administered

Time	Group I* (N = 35)	Group II* (N = 35)	Group III* (N = 35)	P Value
Intraoperatively				
Fentanyl *(μg)*	100 (0 to 200)	100 (50 to 300)	100 (0 to 200)	0.99
Hydromorphone *(mg)*	0.8 (0 to 2.0)	1.1 (0 to 2.4)	1.0 (0 to 2.0)	0.36
Recovery room				
Hydromorphone *(mg)*	0.8 (0 to 3.0)	0.6 (0 to 4.0)	0.8 (0 to 4.0)	0.30
Orthopaedic floor				
Cumulative hydromorphone *(mg)*	3.4 (0 to 12.4)	2.6 (0 to 10.6)	3.0 (0 to 12.8)	0.82

*The values are given as the median with the minimum and maximum values in parentheses.

All patients were premedicated with celecoxib (200 mg) (Pfizer) and pregabalin (50 mg) (Pfizer) as per our protocol one hour before surgery; general anesthesia was administered for the surgery. Intraoperatively, fentanyl and hydromorphone were used as deemed necessary by the anesthesia care team. The surgeons infiltrated the joint capsule, all exposed muscle and tissue, the fascia lata, and subcutaneous tissue with 50 mL of ropivacaine, ketorolac, and adrenaline or normal saline solution based on group assignment. Before wound closure, a fenestrated (10-cm) soaker catheter was placed deep to the iliotibial band with the tip anterior to the joint, exiting the skin distal and anterior to the incision. The catheter was connected to a prefilled disposable pump (PainPump 2; Stryker Instruments, Kalamazoo, Michigan; or Autofuser; Moog Medical Devices, Salt Lake City, Utah) that infused either 0.2% ropivacaine at 5 mL/hr in patients in Group I or normal saline solution in patients in Groups II and III at a constant rate of 5 mL/hr.

In the recovery room after emergence from anesthesia, the admission pain score on a verbal numerical pain rating scale (in which 0 points denote no pain and 10 points denote worst pain) was noted and if patients were in pain, intravenous hydromorphone was titrated to patient comfort (a pain score of ≤4); the amount of hydromorphone administered in the recovery room and the pain scores on discharge from the recovery room were recorded. Prior to discharge from the recovery room, all patients were placed on an intravenous patient-controlled analgesia pump with hydromorphone (0.2 mg) available every ten minutes for breakthrough pain. On the surgical floor, the patients continued to receive a regimen of celecoxib (200 mg) every twelve hours, pregabalin (50 mg) every twelve hours, and acetaminophen (975 mg) every six hours orally; the total amount of hydromorphone self-administered by the patients for forty-eight hours with the patient-controlled analgesia and pain scores every four hours for forty-eight hours were recorded. If patients were asleep at the time of pain assessment, a numerical pain rating score of 0 was recorded. Patients, surgeons, anesthesiologists, recovery room nurses, and floor nurses were all blinded to group assignment. The catheter was removed with use of sterile precautions after forty-eight hours. After catheter removal, patients were asked to rate their pain control as being poor, fair, good, or excellent.

All patients were on a standardized physical therapy protocol. For thromboprophylaxis, all patients received enoxaparin (40 mg) subcutaneously once daily, in addition to venous foot pumps that were in place and functioning at all times when patients were not walking. Patients did not undergo routine postoperative ultrasound screening for deep vein thrombosis. All patients received perioperative antibiotics consisting of cefazolin (2 g) intravenously within thirty minutes prior to incision, followed by 1 g intravenously every eight hours for two more doses with no patient receiving antibiotics after twenty-four hours postoperatively.

The sample size estimation was based on a previous study that reported a range of a mean reduction (and standard deviation) in morphine consumption from 43.3 ± 24.7 mg to 28.5 ± 18.9 mg, a mean difference (and standard deviation) of 14.8 ± 5.5 mg, in patients who received local infiltration analgesia compared with controls over the first twenty-four hours following total hip arthroplasty[9]. This dose of morphine was converted to an equianalgesic dose of hydromorphone for power analysis because hydromorphone is primarily used in our institution (the conversion factor is 10-mg morphine is equal to 2-mg hydromorphone). A total sample of 105 subjects (thirty-five subjects in each group) would be required to detect a similar difference in opioid consumption with use of the Tukey-Kramer pairwise multiple comparison test in hydromorphone use between groups at a two-sided 5% significance level and a power of 95%. Analysis of variance (ANOVA) was used for the between-group comparison of parametric continuous variables and the Kruskal-Wallis test was used for nonparametric variables. The chi-square or Fisher exact test was used to compare categorical data. Outcome assessments for multiple measurements (narcotic consumption) were analyzed as summary measures. Data are presented as the mean and the standard deviation or as the median with the minimum and maximum values. Categorical variables are presented as the count with the corresponding percentage. Significance was set at $p < 0.05$. The analyses were executed with use of SPSS for Windows, version 18.0 (SPSS, Chicago, Illinois).

Source of Funding

There was no external funding for this study.

Results

Demographic characteristics were similar between groups (see Appendix). There was no significant difference ($p = 0.36$) among groups in the amount of hydromorphone administered intraoperatively (Table I); the median (and minimum and maximum values) was 0.8 mg (0 to 2.0 mg) for Group I, 1.1 mg (0 to 2.4 mg) for Group II, and 1.0 mg (0 to 2.0 mg) for Group III. There was also no significant difference ($p = 0.99$) among groups in the amount of fentanyl administered intraoperatively (Table I); the median (and minimum and maximum values) was 100 μg (0 to 200 μg) for Group I, 100 μg (50 to 300 μg) for Group II, and 100 μg (0 to 200 μg) for Group III. In the recovery room, similar amounts ($p = 0.30$) of hydromorphone were given to patients in each group; the median (and minimum and maximum values) was 0.8 mg (0 to 3.0 mg) for Group I, 0.6 mg (0 to 4.0 mg) for Group II, and 0.8 mg (0 to 4.0 mg) for Group III. In addition, similar amounts ($p = 0.82$) of hydromorphone were self-administered by patients with patient-controlled analgesia pumps over the first forty-eight hours postoperatively; the median (and minimum and maximum values) was 3.4 mg (0 to 12.4 mg) for Group I, 2.6 mg (0 to 10.6 mg) for Group II, and 3.0 mg (0 to 12.8 mg) for Group III (Table I,

TABLE II Overall Patient Rating of Pain Management

Rating	Group I*† (N = 35)	Group II*† (N = 35)	Group III*† (N = 35)	P Value‡
Excellent	27 (79)	21 (63)	25 (75)	0.22
Good	7 (20)	12 (34)	7 (20)	0.20
Fair	1 (3)	1 (3)	2 (6)	0.79
Poor	0 (0)	0 (0)	0 (0)	—

*The values are given as the number of patients, with the percentage in parentheses. †One patient had an unknown rating in this group. ‡The p value is given per rating among the groups. The cumulative p value for all groups is 0.44.

Fig. 2). The pain scores on admission and discharge from the recovery room and on the surgical floor were similar between groups (Fig. 3).

Postoperative nausea was reported by three patients (9%) in Group I, four patients (11%) in Group II, and one patient (3%) in Group III. One patient (3%) in Group III reported experiencing heartburn and indigestion and one patient (3%) in Group I reported light-headedness. There were no significant differences in the incidence of adverse side effects among groups (p = 0.20). Patient satisfaction with postoperative pain control was similar between groups (p = 0.44) (Table II).

There were no infections. The surgical site was inspected daily. A small amount of serous drainage was commonly seen at the catheter site after its removal, and surrounding tissues were subjectively noted to be slightly edematous. Wound-healing was not impaired. There were seventy-nine patients with anterolateral incisions and twenty-six patients with posterior incisions; an analysis of the distribution of patients among groups revealed

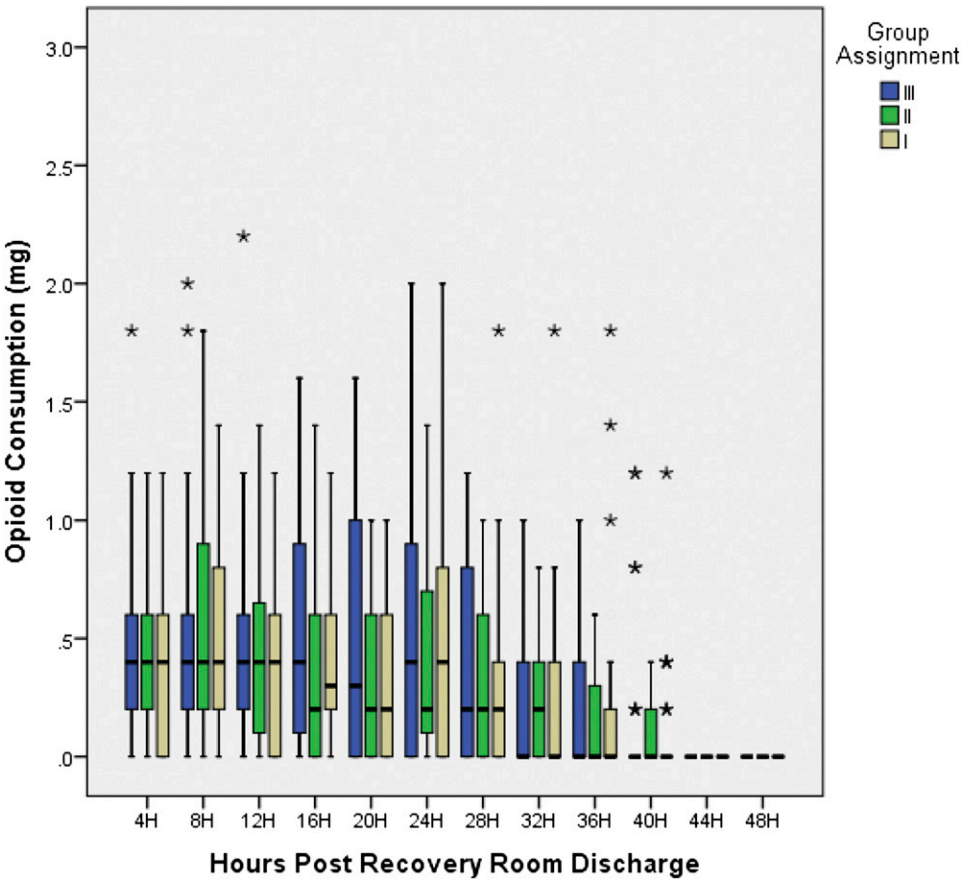

Fig. 2

Box plot showing intravenous patient-controlled analgesia of hydromorphone administered forty-eight hours after discharge from the recovery room. Horizontal lines indicate medians, boxes indicate interquartile range (25th to 75th), whiskers indicate minimum and maximum values, and asterisks indicate outliers. There were no significant differences between groups. NS = normal saline; RKA = ropivacaine (Ropiv), ketorolac, adrenaline.

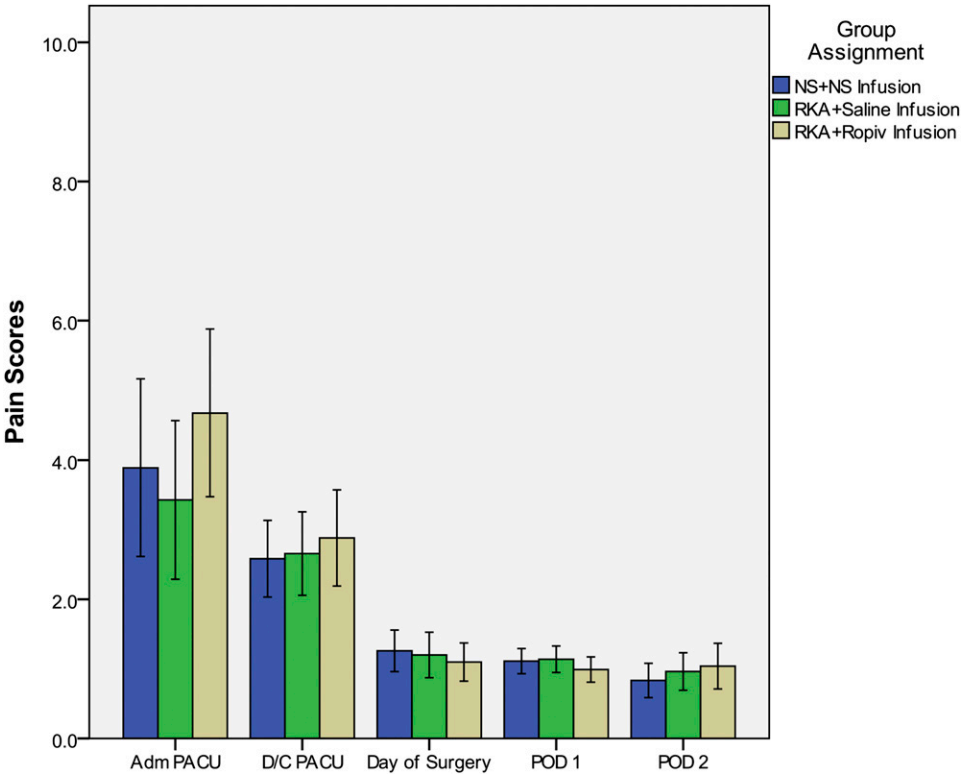

Fig. 3

Bar graph showing pain scores reported on admission (Adm) to the recovery room, discharge (D/C) from the recovery room, and forty-eight hours on the surgical floor. Bars indicate the mean pain scores and the error bars indicate the 95% confidence intervals for these scores. There were no significant differences between groups. POD = postoperative day; RKA = ropivacaine, ketorolac, adrenaline; PACU = post-anesthesia care unit; NS = normal saline; and Ropiv = ropivacaine.

no significant differences in the distribution of patients in the surgical approach ($p = 0.827$).

Discussion

This study demonstrates that local infiltration analgesia alone or local infiltration analgesia followed by continuous infusion of local anesthetic confers no analgesic benefit compared with placebo in patients undergoing total hip arthroplasty when multimodal perioperative pain management is employed. These results are in contrast to previous reports that local infiltration analgesia lowered pain scores and reduced opioid consumption in patients who had undergone total hip arthroplasty[6,10]. The difference in findings could be attributed to a lack of comprehensive multimodal analgesia used in previous studies. In three studies demonstrating improved pain control with local infiltration analgesia, only acetaminophen was used as an adjunct to opioids for postoperative pain[6,10,11]. In contrast, we used a combination of celecoxib, acetaminophen, and pregabalin perioperatively that was continued until the patients were discharged from the hospital. This multimodal analgesic approach provided comparable pain relief in the placebo group with minimal side effects. There is mounting evidence to suggest that using analgesic medications from different pharmacologic classes improves postoperative pain control in patients who have undergone arthroplasty[12]. The opioid-sparing effect of nonsteroidal anti-inflammatory drugs and, specifically, cyclooxygenase-2 inhibitors is well documented in patients who have undergone total hip arthroplasty. However, the use of gabapentinoids for patients undergoing total hip arthroplasty is controversial[13,14]. Clarke et al. showed no incremental analgesic effect with gabapentin in patients undergoing total hip arthroplasty but only two doses of gabapentin were used perioperatively[14]. However, in a randomized controlled study, Mathiesen et al. showed that pregabalin (300 mg) decreased the twenty-four-hour morphine consumption by 51% in patients who had undergone total hip arthroplasty[15]. A reduced dose of pregabalin was used in this study to avoid undue sedation and dizziness in patients who had undergone arthroplasty.

In three recent studies utilizing a similar combination of multimodal medications combined with local infiltration analgesia in patients who had undergone total hip arthroplasty, superior analgesia was not achieved by injecting ropivacaine in the wound or continuously infusing ropivacaine postoperatively[11,16,17]. Lunn et al. reported that infiltration with 150 mL of 0.2% ropivacaine with epinephrine into the surgical site in total hip arthroplasty did not lower postoperative pain or reduce opioid requirements[16]. In another study, Specht et al. found no evidence of improved analgesia in patients who underwent

total hip arthroplasty and received wound infiltration followed by continuous catheter infusion of 0.2% ropivacaine at 5 mL/hr postoperatively[17]. Similarly, Andersen et al. showed no difference in hip pain in patients undergoing bilateral total hip arthroplasty when one hip was infiltrated with ropivacaine while the other was infiltrated with normal saline solution[11]. However, in contradistinction to these studies, we administered general anesthesia to our patients instead of spinal anesthesia for the surgery to eliminate any analgesic gain that may have extended to the recovery room and the early postoperative period from the residual neuraxial block. The pain scores and opioid consumption were similar in the recovery room and the early postoperative period across the groups.

Another reason for dissonance with previously published data is that these reports lacked a rigorous study design that may have led to bias in reporting results[18]. In previously published studies showing superior efficacy of local infiltration analgesia, ketorolac was included in the injectate in the local infiltration analgesia group but not in the control group, confounding the results as the addition of a nonsteroidal anti-inflammatory drug may enhance analgesia[6,9,10,19]. Although we did not include ketorolac in the placebo group, all patients were given celecoxib and acetaminophen orally as part of multimodal analgesia. Similarly, in two studies, morphine was added to the injection solution in the local infiltration analgesia arm with no injection performed in the control group, resulting in unequal opioid administration between groups[9,20]. In our study, the ability to self-administer opioids with patient-controlled analgesia was available to all patients, allowing us to accurately measure opioid intake.

A criticism of our study may be that we used a lower volume of the ropivacaine, ketorolac, and adrenaline solution compared with other investigations, although previous studies have shown the use of injectate volumes ranging from 25 mL to 150 mL[7,16]. Despite injecting three times the volume of 0.2% ropivacaine compared with our study, Lunn et al. failed to show any additional benefit in pain control[16]. Another weakness of our study was that we did not record pain scores related to walking or physical therapy. However, all patients followed a routine and consistent total hip arthroplasty rehabilitation pathway; no significant differences in opioid consumption were noted among groups. We also did not record when patients achieved physical therapy milestones and met discharge criteria. Caution must also be exercised in interpreting pain levels in the control group because a significant placebo effect has been reported when using the normal saline solution injection in orthopaedic surgery[21]. An alternative placement of the catheter may have resulted in different pain outcomes because the local solution would target a different tissue. In addition, a meaningful conclusion could not be made regarding pain associated with the two surgical approaches used in the present study.

Finally, the overall pain scores were so low in these patients who had undergone total hip arthroplasty that our study may have been underpowered to discriminate any difference in pain scores or opioid consumption. Post hoc power calculations indicate that to detect a significant difference among the three treatment groups, 188 subjects would be needed in each group to achieve a power of 0.80 with a two-sided alpha level of 0.05. However, with three recent studies showing similar postoperative pain outcome with local infiltration analgesia and continuous infusion of local anesthetic as part of multimodal analgesia, the confidence in our findings is strengthened.

In conclusion, this study demonstrates that local infiltration analgesia alone or in combination with continuous infusion of local anesthetic does not significantly reduce opioid consumption or lower pain scores in patients who have undergone total hip arthroplasty and receive multimodal medications for postoperative analgesia.

Appendix

eA A table showing patient demographic characteristics is available with the online version of this article as a data supplement at jbjs.org. ■

NOTE: The authors wish to express their appreciation to Ifeoma Inneh, MPH, for patient data management and statistical analysis.

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