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ORIGINAL ARTICLE

A Randomized Controlled Trial of Intraarticular Ropivacaine for Pain Management Immediately Following Total Knee Arthroplasty

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Abstract Total knee arthroplasty (TKA) is a commonly performed procedure for the treatment of end-stage arthritis of the knee. Pain control following TKA is difficult to manage in some patients. We examined the use of a postoperative intraarticular injection of 100 mL of 0.2% (200 mg) ropivacaine in a double-blind, prospective, placebo-controlled pilot study to evaluate its use as a pain control modality. All patients received general anesthesia. Postoperatively, patients were placed on intravenous patient-controlled analgesia with morphine. The ropivacaine group showed an early trend in lower visual analog scale (VAS) scores when compared with the placebo group. Patients receiving ropivacaine used a similar amount of narcotics compared with the placebo group. Intraarticular ropivacaine used for pain control after TKA demonstrated no statistically significant difference in lowering VAS scores or narcotic usage; therefore, intraarticular ropivacaine as a single modality is not recommended for effective pain management.

Keywords total knee arthroplasty · ropivacaine · intraarticular injection · pain control · randomized controlled trial

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Each author certifies that his or her institution has approved the reporting of these cases, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participating in the study was obtained.

Level of evidence: 1A SR (with homogeneity*) of RCTs

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Introduction

Total knee arthroplasty (TKA) is a successful procedure for painful arthritic degeneration of the knee. Approximately 534,000 primary total knee arthroplasties and 37,000 revisions were performed in 2006 [1]. While technical improvements have been made in the implant materials, the surgical approaches, and the use of navigation, pain control continues to be a problem postoperatively for many patients. The American Pain Society has termed pain as the "fifth vital sign," and the United States Congress has called 2001–2010 the Decade of Pain Control and Research. All of these are efforts to address patients pain and suffering.

Modalities such as cryotherapy, electrical stimulation, patient-controlled analgesia (PCA), regional anesthesia, pre-emptive analgesia, and intraarticular or peri-articular injections have been used with varying success [2–7]. Other studies have evaluated the use of femoral with or without sciatic nerve blocks, using both single-injection techniques and indwelling catheters [5, 8, 9]. In the literature, many protocols using local anesthetics have shown a reduction in postoperative pain following joint arthroplasty [5, 8–10]. Additionally, many "cocktails" have been used intra- or perioperatively to help alleviate postoperative pain with mixed results. Lombardi et al. used a mixture of bupivacaine, epinephrine, and morphine and demonstrated lower pain scores in the post-anesthesia care

unit (PACU) [11]. Busch et al. demonstrated that the use of a mixture of ropivacaine, ketorolac, epimorphine, and epinephrine significantly reduced patient-controlled analgesia usage at 6 hr and significantly lowered visual analog scale (VAS) in the PACU at 4 hr [4].

Pain after TKA has been addressed with the use of intraarticular injections. At our institution, a prior study evaluating the efficacy of a postoperative intraarticular injection of bupivacaine demonstrated a trend toward lower VAS scores and narcotic usage [3]. One other study has shown a trend toward lower pain scores after an intraarticular injection of bupivacaine following TKA [2]. In studies comparing intraarticular anesthetics after knee arthroscopy, ropivacaine has been shown to provide pain relief similar to bupivacaine as indicated by decreased pain scores and narcotic usage [12, 13]. Ropivacaine is a local anesthetic of the amino amide class and is similar to bupivacaine with regard to onset of action and duration of sensory block. However, ropivacaine has been shown to have less cardio- and neuro-toxicity [14] and less vasodilation [15] than bupivacaine.

We have been searching for ways to combat patients postoperative pain following TKA that decreases the use of narcotics, which have multiple side effects. Our purpose was to evaluate a simple intraarticular injection of ropivacaine to define its efficacy in postoperative pain management. We wanted to determine if this was an efficacious modality to add to a multimodality protocol for postoperative management. Our hypothesis for this pilot study was that an intraarticular injection of ropivacaine at the time of surgery with general anesthesia would decrease pain as measured by VAS scores and narcotic consumption during each 6-hr interval of the first 24 postoperative hours when compared with a saline placebo injection. Finally, we wished to assess if the length of the PACU stay and patient satisfaction with the pain management would differ between the ropivicaine and placebo-treated patients.

Methods

After approval by the Human Subjects Committee, all patients scheduled for elective primary unilateral TKA were approached and were enrolled from our preoperative history and physical clinic.

Patients were included if they were 18 years of age or older, had signed the informed consent to participate in the study, and were scheduled to undergo unilateral elective primary TKA. Patients were excluded if they had a known allergy or hypersensitivity to any local anesthetic of the amide type, had a history of prior infection or prior joint surgery (other than arthroscopy), required the use of a regional, spinal, or epidural anesthetic perioperatively, required the use of any MAOI, tryptalines, or imipramine type of antidepressant medication pre- and postoperatively, had evidence of abuse of legal or illicit drugs, consumed more than three alcoholic beverages per 24-hr period, had a history of chronic pain (e.g., fibromyalgia, complex regional pain syndrome, neuropathy), or had a history of cardiac disease requiring special monitoring or the use of antiarrhythmic medications.

All patients received general anesthesia and were placed on enoxaparin postoperatively for deep venous thrombosis (DVT) prophylaxis. No drains were used. All patients had the procedure performed through an anterior midline incision by one of the two senior authors. (C. W. C., S. N. C.)

Forty-eight patients signed the informed consent and completed this study. Each group contained 24 patients. The mean age, BMI, ratio of males to females, and diagnosis were similar between groups (Table 1). Patients were randomized via a computer-generated randomization schedule into a ropivacaine injection group or a saline placebo group. Anesthesiologists, surgeons, PACU staff, and floor nurses were blinded to which injection was given. One operating room nurse opened the envelope and prepared the injection sterilely for use at the end of the case. At the end of each procedure with the tourniquet still inflated, the capsule was closed with interrupted non-absorbable suture. One hundred milliliters of either normal saline or 0.2% (200 mg) ropivacaine was injected with an 18-gauge needle into the intraarticular capsule after closure. The subcutaneous tissue and skin were then closed, dressings were applied, and the tourniquet was deflated.

Patients were given intravenous pain medication in the PACU postoperatively for pain control. Patients were placed on PCA morphine for continued pain control prior to transfer to the nursing unit. Though narcotic usage was not standardized, intraoperative, PACU, and postoperative narcotic usage was recorded for 24 hr. Equianalgesia was established by conversion of all narcotics to dose-equivalent (DE) units based on 10 mg of morphine equality [16]. Patients were followed with a VAS to record pain levels at 0 (in PACU), 6, 12, and 24 hr after surgery. The VAS consists of a 10-cm line with 0 representing no pain and 10 representing worst possible pain. All patients were instructed on the use of the VAS, and a baseline VAS score was recorded preoperatively. At completion of the study, patients were given a global pain questionnaire asking how well their pain was controlled and if they would recommend the pain treatment they received to others.

A power analysis using historical data determined that 46 patients (23 in each group) would be needed to detect a 40% reduction in narcotic usage (DE) at 24 hr postoperatively between the ropivacaine and placebo groups with an alpha level of 0.05 and 80% power. A smaller

Table 1 Demographic and clinical characteristics of patients in the ropivacaine and placebo groups are provided at the time of total knee arthroplasty

Characteristics	Ropivacaine group N=24	Placebo group N=24	P value
Male/female	5/19	7/17	0.51
Diagnosis osteoarthritis/ rheumatoid arthritis	22/2	22/2	1.00
Age, years	70.5	71.2	0.82
BMI	31	29	0.24
Blood loss, ml	65	66	0.91
Tourniquet time, min	92	95	0.57
Surgery side (right/left)	10/14	14/10	0.25

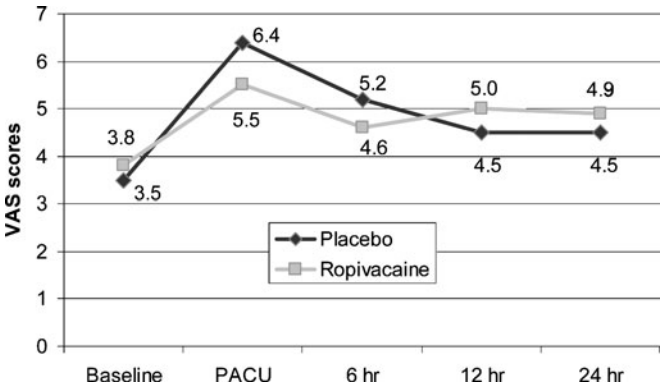

Fig. 1. Mean visual analog scale (VAS) scores are presented at individual time points (0=no pain; 10=worst pain possible)

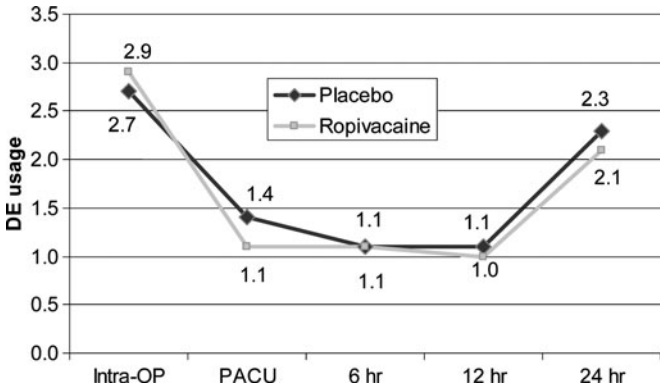

Fig. 3. Mean narcotic usage at individual time points expressed in mean dose equivalents (DE), where 1 DE=10 mg of morphine

sample size was required to detect a 40% reduction in VAS pain scores, so the larger of the two was used (DE) in order to provide sufficient power for both endpoints.

Data were analyzed using SPSS version 13.0 (Chicago, IL). After checking for normal distribution of the data, independent *t* tests were used to analyze the differences in VAS pain scores and DE units between groups. To establish a group's mean VAS score for an interval of time encompassing two or more timepoints, the grand mean of patients' individual mean VAS scores for that interval was calculated. To establish a group's mean DE usage for an interval of time, the mean of patients' individual cumulative narcotic usage for that interval was calculated. A Chi-square test and Fisher's exact test were used to analyze the differences between groups for items on the global pain questionnaire. Demographic and baseline data were analyzed using independent *t* tests for continuous data and Chi-square test for categorical data to determine if any differences between groups existed. All statistical tests were two-tailed and the alpha level was set at 5%.

Results

Adverse events were recorded for the patients in each group. Nine patients (38%) in the ropivacaine group reported nausea while 11 patients (46%) in the placebo group reported nausea. Two patients in the ropivacaine group developed respiratory depression. One documented proximal DVT occurred in the ropivacaine group. No distal DVT, pulmonary embolus, infections, or wound healing complications occurred in either group.

Mean VAS during the first 24 hr after surgery ranged from 4.5 to 6.4 (Fig. 1). There was no difference in the VAS scores recorded between the two groups for any of the individual time points or for the total mean postoperative and post-PACU time intervals (Fig. 2).

No differences were found between groups in narcotic consumption as reflected by mean DE usage for any of the individual time points (Fig. 3) or for total mean cumulative DE usage (from intraoperative through 24 hr), postoperative (from PACU through 24 hr), or post-PACU mean cumulative usage (from 6 through 24 hr; Fig. 4). We stratified the ropivacaine and placebo groups by age and weight to assess whether these variables could be confounding the relationship between treatment and total mean cumulative DE usage. Neither variable was found to affect DE usage.

The duration of the PACU stay was similar between groups. Mean time spent in the PACU for the ropivacaine and placebo groups was 2 hr, 6 min, and 2 hr, 22 min (P=0.32), respectively. Based on the global pain questionnaire admin-

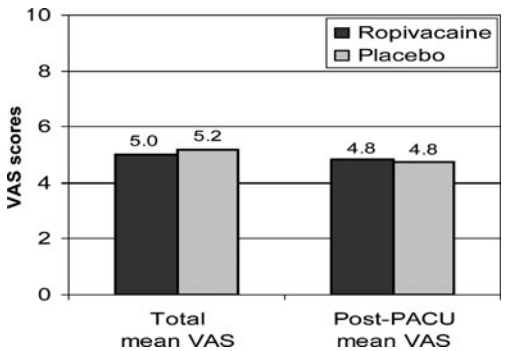

Fig. 2. Mean visual analog scale (VAS) scores presented for intervals of time (0=no pain; 10=worst pain possible). Each score represents the grand mean of the patients' individual mean VAS scores for that interval. The total mean VAS score includes PACU through 24 hr and the post-PACU mean VAS score includes 6 through 24 hr

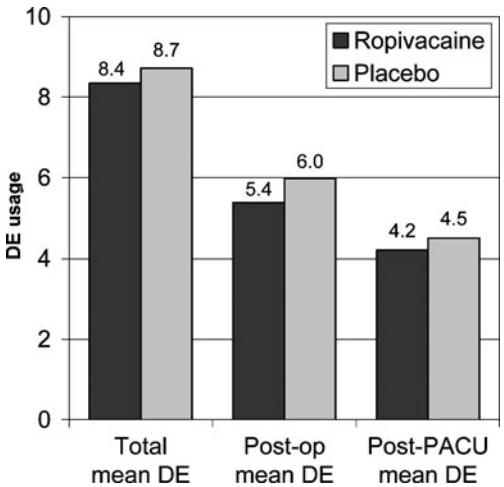

Fig. 4. The mean of patients' individual cumulative narcotic usage, expressed as dose equivalent (DE) units, is presented for intervals of time(1 DE=10 mg of morphine). The total mean DE includes cumulative narcotic usage from intraoperative through 24 hr, postoperative includes PACU through 24 hr and post-PACU includes 6 through 24 hr

istered at the end of the study, pain control was considered good to excellent by 63% of the ropivacaine group versus 59% of the placebo group (P=0.81). Of the ropivacaine group, 82% would recommend their pain control treatment in contrast to 81% of the placebo group (P=0.64).

Discussion

Healthcare has had a renewed interest in pain control during the postoperative management of surgical patients. Many studies have examined a complex protocol of different types of anesthesia, blocks, or cocktails. Although many combinations are reported as successful, discerning which medications are having the most effect on postoperative pain control is difficult. We wanted to effectively look at one pain control adjunct to examine the patients' response to that adjunct in the management of postoperative pain. The most effective pain management protocol would be to use the most effective drugs in a minimal amount to both control pain and limit potential side effects.

This study has limitations. We were not able to demonstrate a statistically significant difference between groups but a study with a larger sample size might be able to detect a smaller between-group difference in outcomes. Other limitations of the study may be the use of general anesthesia and anesthesiologist dosing of intraoperative narcotics. Since no defined drug or drug dosing was specified for the patients in the operating room, the amount of narcotics given by the anesthesiologist differed from physician to physician during the study. Better control might have been obtained by using one narcotic and having a weight-based calculation for the anesthesiologists to follow during the study for administration of narcotics.

At the time of our study, our routine practice was neuraxial anesthesia for bilateral TKA and general anesthesia for most unilateral TKA. Many institutions are now using regional or selective nerve blocks such as femoral with or without sciatic blocks as we now do. Our renewed interest in postoperative pain control has resulted in our added use of selective nerve blocks plus preoperative and postoperative “cocktails,” which consist of a combination of narcotic and non-narcotic pain medications and anti-inflammatories. In this study, we were examining the effect of one facet of pain control.

A strength of the study was the use of general anesthesia, as the use of regional blocks would obscure the true effectiveness of an intraarticular injection. We also used PCAs for postoperative pain control to limit factors unrelated to ropivacaine or placebo effectiveness that could influence a VAS score (e.g., increased pain at a given time due to a delay in narcotic administration prior to the VAS measurement).

We did not examine blood levels of ropivacaine as part of our protocol. Many previous studies have examined ropivacaine blood levels, and they did not show toxic levels after intraarticular injections [4, 12, 14, 17]. We did not, therefore, feel it necessary to monitor blood levels post-injection.

Other studies using ropivacaine along with other intraarticular medications have shown improvements in postoperative pain control [4]. Improvement in pain control may be due to the combinations of anesthetics and opioids [2, 4, 6, 11]. Another factor may be the addition of epinephrine, which may prolong the effect of all medications due to vasoconstriction [4]. Another variable is the use of intraarticular injection versus adding capsular injections into the tissues, as used in other studies. Our study did not incorporate tissue infiltration of the capsule, which might have added additional pain control [2, 11].

Our study did not demonstrate any significant decrease in pain levels or narcotic usage in the first 24 hr after surgery. An intraarticular injection is simple to administer and has limited potential side effects. The use of ropivacaine may help alleviate postoperative pain and might be more beneficial as a part of a more intensive pain protocol that may include preoperative medications and additional neuraxial blockade. Although intraarticular ropivacaine has been shown to be efficacious in other studies as a portion of a cocktail, we do not recommend intraarticular ropivacaine alone for control of postoperative pain following TKA using general anesthesia.

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References

1. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. 2006 National Hospital Discharge Survey. Available at: http://www.cdc.gov/nchs/nhds.htm. Accessed Oct 7, 2009.
2. Badner NH, Bourne RB, Rorabeck CH, et al. Intra-articular injection of bupivacaine in knee-replacement operations. Results of use for analgesia and for preemptive blockade. J Bone Joint Surg Am. 1996; 78: 734–738.
3. Browne C, Copp S, Reden L, et al. Bupivacaine bolus injection versus placebo for pain management following total knee arthroplasty. J Arthroplasty. 2004; 19: 377–380.
4. Busch CA, Shore BJ, Bhandari R, et al. Efficacy of periarticular multimodal drug injection in total knee arthroplasty. A randomized trial. J Bone Joint Surg Am. 2006; 88: 959–963.
5. Hebl JR, Kopp SL, Ali MH, et al. A comprehensive anesthesia protocol that emphasizes peripheral nerve blockade for total knee and total hip arthroplasty. J Bone Joint Surg Am. 2005; 87 Suppl 2: 63–70.
6. Ritter MA, Koehler M, Keating EM, et al. Intra-articular morphine and/or bupivacaine after total knee replacement. J Bone Joint Surg Br. 1999; 81: 301–303.
7. Walker RH, Morris BA, Angulo DL, et al. Postoperative use of continuous passive motion, transcutaneous electrical nerve stimulation, and continuous cooling pad following total knee arthroplasty. J Arthroplasty. 1991; 6: 151–156.
8. Pham Dang C, Gautheron E, Guilley J, et al. The value of adding sciatic block to continuous femoral block for analgesia after total knee replacement. Reg Anesth Pain Med. 2005; 30: 128–133.
9. Chelly JE, Greger J, Gebhard R, et al. Continuous femoral blocks improve recovery and outcome of patients undergoing total knee arthroplasty. J Arthroplasty. 2001; 16: 436–445.
10. Ben-David B, Schmalenberger K, Chelly JE Analgesia after total knee arthroplasty: Is continuous sciatic blockade needed in addition to continuous femoral blockade? Anesth Analg. 2004; 98: 747–749, table of contents.

11. Lombardi AV, Jr., Berend KR, Mallory TH, et al. Soft tissue and intra-articular injection of bupivacaine, epinephrine, and morphine has a beneficial effect after total knee arthroplasty. Clin Orthop Relat Res. 2004; 125–130.
12. Convery PN, Milligan KR, Quinn P, et al. Efficacy and uptake of ropivacaine and bupivacaine after single intra-articular injection in the knee joint. Br J Anaesth. 2001; 87: 570–576.
13. Marret E, Gentili M, Bonnet MP, et al. Intra-articular ropivacaine 0.75% and bupivacaine 0.50% for analgesia after arthroscopic knee surgery: A randomized prospective study. Arthroscopy. 2005; 21: 313–316.
14. Knudsen K, Beckman Suurkula M, Blomberg S, et al. Central nervous and cardiovascular effects of I.V. infusions of ropivacaine, bupivacaine and placebo in volunteers. Br J Anaesth. 1997; 78: 507–514.
15. Wienzek H, Freise H, Giesler I, et al. Altered blood flow in terminal vessels after local application of ropivacaine and prilocaine. Reg Anesth Pain Med. 2007; 32: 233–239.
16. Drug facts and comparisons. 60th edn. St Louis, MO: Lippincott Williams & Wilkins 2006.
17. Bianconi M, Ferraro L, Traina GC, et al. Pharmacokinetics and efficacy of ropivacaine continuous wound instillation after joint replacement surgery. Br J Anaesth. 2003; 91: 830–835.