Local Infiltration Analgesia and Other Multicomponent Techniques to Improve Postoperative Outcome—Are We Comparing Oranges and Apples?

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Wound infiltration with local anesthetics for perioperative and postoperative pain management has been receiving considerable attention in recent years. Administration of local anesthetics at the surgical site seems to be a rational approach to reduce afferent nociceptive input from the source of surgical pain. Local anesthetics can inhibit local inflammatory response to injury, which sensitizes nociceptive receptors and contributes to pain and hyperalgesia. The technique provides potent, site-specific analgesia and can be used widely because of its simplicity, safety, and low cost. It can be used alone or in combination with other regional techniques and/or analgesic modalities as an important opioid-sparing component of multimodal strategy for treating postoperative pain.

Single-dose local anesthetic infiltration in the surgical wound is effective, but analgesia lasts only a few hours and has a questionable role in major surgery.[1] This has led to the study of several modifications such as wound catheter infusions[2]; high-volume local anesthetic infiltration[3]; use of adjuvants such as epinephrine, clonidine, and steroids[4]; or use of alternatives to local anesthetics such as diclofenac[5] and capsaicin.[6] The search for ultra long-acting local anesthetics to eliminate the need for catheter techniques has been ongoing for many years.[7]

A recent modification of the technique is high-volume local infiltration analgesia (LIA), as developed by Kerr and Kohan[3] for lower extremity joint replacement surgery. The LIA approach consists of high-dose intraoperative infiltration of the entire surgical area with a combination of ropivacaine, ketolorac, and epinephrine. Infiltrations are performed 1 layer at a time as the surgery progresses. This is combined with intra-articular catheter for analgesic top-up allowing the blockade to last as long as 36 hours. Thrombosis prophylaxis consists of aspirin for 6 weeks. Postoperative pain relief is provided by a combination of acetaminophen (paracetamol), ibuprophen 400 mg every 4 hours, and 10 mg intravenous morphine as needed. After 36 hours, transdermal buprenorphine is administered if necessary. All surgeries in Kerr and Kohan's report were performed by a single surgeon, and all anesthesia and pain management conducted by a single anesthesiologist. Postoperative mobilization is started 3 to 5 hours after surgery. In this case series of 325 patients, more than half of those undergoing hip or knee replacement could be discharged on the first postoperative day, with most of the remaining patients being discharged the day after. Mean time to independent mobility was less than 25 hours for the entire cohort and 20 hours for patients undergoing total knee replacement. Postoperative pain scores were low, and very few thromboembolic events were noted.[3]

The LIA technique has achieved widespread acceptance by orthopedic surgeons especially in the Scandinavian countries,[8] the United Kingdom,[4,9] and Australia.[3,10] The 2010 annual report of the Swedish Knee Arthroplasty Register showed that the use of LIA has increased steadily and, in 2009, was used in 75% of all TKA surgeries in the country; a catheter was left in the knee joint in 40% of these patients.[11] Most of the recent literature is from Denmark,[12–15] Sweden,[16,17] and Norway[18]; however, none of these studies have been able to replicate the 1- to 2-day discharge times reported by the originators of LIA. The discharge times are in the range of 3 to 5 days, which is still considerably shorter than the 6- to 10-day hospitalization that was common until recently.[3,4,13] A comprehensive research program as a joint venture between Scandinavian clinics has been proposed to address questions such as the role of surgical technique, thromboembolism prophylaxis routines, choice of analgesic drugs, fast-track (FT), multimodal mobilization protocols, and intra-articular top-up requirements.[8]

In this issue of *Regional Anesthesia and Pain Medicine*, Lunn et al[19] report on a study that evaluated the role of intraoperative LIA in patients undergoing total hip arthroplasty (THA). In this

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Accepted for publication June 12, 2011.
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ISSN: 1098-7339
DOI: 10.1097/AAP.0b013e318228e295

placebo-controlled study, the authors did not find any benefit to LIA if patients received a multimodal analgesic regimen. They conclude "Intraoperative high-volume LIA with 0.2% ropivacaine provided no additional reduction in acute pain after THA when combined with a multimodal oral analgesic [regimen] consisting of acetaminophen, celecoxib and gabapentin. Acceptable acute postoperative pain relief was achieved with oral analgesic regimen, and LIA is not recommended in THA."[19] These results are at odds with those reported in 2 other Danish studies of LIA in THA.[12,13] In the study of Andersen et al,[12] use of LIA was associated with reduced pain up to 2 weeks postoperatively. In addition, patients required less analgesics and were more satisfied. Furthermore, LIA resulted in less joint stiffness and better function 1 week postoperatively. In the other study, LIA was compared with epidural analgesia. Local infiltration analgesia was associated with good pain relief, less adverse effects due to avoidance of epidural analgesia, better walking ability, and a 2-day shorter hospital stay.[13] In patients undergoing TKA, LIA was superior to femoral block in one study[15] and to epidural in another.[18]

Why are results of this study so different from those of the other 2 Danish THA studies? The answer seems to lie in the details of the LIA technique. The original LIA concept is a multimodal strategy to improve postoperative outcome. In addition to infiltration of local anesthetic, it includes extensive preoperative patient education, minimal invasive surgery, accelerated rehabilitation protocol, and home care. Local infiltration analgesia itself is a 5-step process using a "moving needle" technique to avoid depositing a large volume of drug intravascularly. The drug combination consists of 0.2% ropivacaine (maximum dose 300 mg) + 30 mg ketorolac + 10 μg/mL epinephrine. Step 1: injection of solution into all exposed tissues after completion of acetabular surgery. Step 2: injection after insertion of femoral component. Step 3: insertion of catheter with tip anterosuperior to the joint. Step 4: injection into subcutaneous tissues before skin closure. Step 5: injection of 10 to 15 mL of solution in the catheter after wound closure. The technique also involves injection of 15 mL of the solution into the catheter 15 to 20 hours postoperatively and another 35 mL as the catheter is withdrawn so as to anesthetize all tissue planes. The LIA technique studied by Lunn et al differs considerably from that described originally. The differences are as follows:

1) The intra-articular catheter was omitted, thus depriving the patients of possible benefits of prolonged analgesia from the top-up doses that have been reported by others,[3,12,13] including reduced pain up to 2 weeks postoperatively.[12]
2) Intra-articular ketolorac was omitted because patients received a single dose of oral celecoxib preoperatively. The authors state that both routes of administration are equianalgesic, but this is not supported by recent literature, wherein studies show that local wound infiltration of diclofenac is more effective than intravenous administration[5] and that intra-articular administration of ketolorac is considerably more effective than intravenous administration.[18]
3) Minimal invasive surgery technique was not used.
4) Lunn et al's study was only an 8-hour study. It is conceivable that the postoperative pain peaked after 8 hours. Andersen et al have reported that they could not evaluate leg-raising pain in their THA patients until 8 hours postoperatively because of spinal bupivacaine.[12] The benefits of LIA can be expected to be more apparent after the residual effects of preoperative analgesics and spinal anesthesia have dissipated.
5) Pressure bandage and ice pack on the wound area were omitted. The Kerr and Kohan technique includes compression, cooling, and splinting of the injection site. Ice packs are applied for the first 4 hours postoperatively.[3] Compression bandage has been shown to improve LIA benefits in TKA patients.[20]
6) The multimodal analgesic regimen described by Lunn et al is only a single preoperative oral administration of acetaminophen combined with celecoxib and gabapentin. After surgery, pain was treated with opioids only, sufentanil in postanesthesia care unit and oxycodone thereafter; this cannot be considered as multimodal analgesia. There is no consensus regarding the definition of multimodal analgesia, but the single-dose preoperative combination used by the authors is not the criterion standard in clinical practice, and typically, the selected multimodal drug combination is continued well into the postoperative period for maximum opioid-sparing benefit. The current recommendations for perioperative use of gabapentin are somewhat contradictory. Meta-analyses have shown gabapentin as an effective analgesic, its use is supported by the Australian and New Zealand College of Anaesthetists latest evidence-based recommendations, the main concern being dose-related sedation.[21] However, the PROSPECT working group does not recommend perioperative use of gabapentin because of lack of evidence-based, procedure-specific evidence in THA patients.[22]
7) Lunn et al did not record the adverse effects of their analgesic drugs, which would have been helpful to know the "costs" of including gabapentin in the recommended multimodal strategy. The length of hospital stay was 3 to 4 days, which is longer than the 1 to 2 days reported by the originators of the LIA technique.

A major problem with multicomponent strategies to improve postoperative outcome is the lack of standardized and internationally accepted definitions, which make the evaluation and comparison between studies difficult. This applies not only to LIA but also to multimodal analgesia techniques and to multimodal, FT, enhanced recovery protocols. A review of literature on multimodal analgesia by a group of pain experts showed the difficulty of a meaningful evaluation because of numerous permutations of analgesic agents and techniques used in the literature. The expert group therefore restricted itself to a combination of 3 classes of the most commonly used analgesics, namely, opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen. Even then, the evidence for analgesic benefits was unimpressive.[23] The group had to reject 21 of 26 articles on multimodal analgesia because of a confusing combination of analgesia drugs and techniques. The only beneficial effect was seen with NSAID-based multimodal analgesia when multidose NSAIDs were used, and evidence for other combinations was limited. Thus, based on the literature review, the expert group concluded "Despite much rhetoric about combining multiple analgesic techniques to provide multimodal analgesia, only limited evidence suggests that this approach will improve pain control or perioperative outcomes."[23] Many questions about multimodal analgesia need to be addressed; these include the following: (1) How many drugs or techniques can be combined before it becomes unsafe or impractical? (2) Which is the most appropriate combination for a particular surgical procedure? (3) Are all components equally effective? (4) What are the risks of adverse effects when different drugs are combined? (5) Is multimodal analgesia cost-effective? In short, the concept of multimodal analgesia to reduce or eliminate opioids is attractive, but the lack of an accepted definition with consequent difficulty in drawing conclusions from published studies has

resulted in unclear signals. This also applies to the study by Lunn et al.

Multimodal, FT, enhanced recovery protocols have also been promoted to improve postoperative outcomes. Indeed, LIA is considered a good example of an FT strategy.[8] Such protocols have been proposed for a variety of surgical procedures,[24] with FT programs for colorectal surgery being perhaps the most studied.[25] Again, the lack of an accepted definition makes the picture rather confusing. In the literature, a large number of FT protocols have been recommended. The number of evidence-based components for FT protocols for colorectal surgery range from 10[26] to 20 or more.[27,28] Enhanced recovery and shorter hospital stay has been claimed with the use of all FT protocols when compared with "traditional care." To complicate matters, traditional care as the comparator also has a large variation of components. Furthermore, traditional care has evolved over the years, and many components of FT protocols such as omission of drains, early removal of nasogastric tube, early feeding, and mobilization are now incorporated into "modern" traditional care.[29] A systematic review of enhanced recovery, FT programs concluded that despite current enthusiasm for implementation of such protocols, there are few supportive data available in the literature.[29] Another meta-analysis showed that the inclusion of epidural analgesia in FT protocols, considered crucial by some,[25] does not lead to shorter duration of hospital stay despite improved pain relief and decrease in ileus in the postoperative period.[30] Not surprisingly, there is no evidence to support the use of epidural technique when colorectal surgery is performed by the increasingly more common laparoscopic approach.[31,32] Again, the main problem with such FT protocols is the lack of consensus regarding the essential components.

Thus, impressive reduction of hospital stay has been demonstrated without increasing morbidity with LIA for lower limb replacement surgery and FT protocols for colorectal (and other) surgeries. However, the role of individual components including analgesia regimens remains unclear. Therefore, it is difficult to distinguish which one of the multiple components may have played a more critical role in influencing the measured parameters.[33] Hardly any 2 protocols for multicomponent treatments are similar, and all components are being tested at once and in combination.[18,33,34] Several authors have commented on the problem of drawing meaningful conclusions when multicomponent treatments are used for LIA,[18,34] for multimodal analgesia techniques,[23] and for FT, enhanced-recovery protocols[29] because of the difficulty in determining whether any of the protocol components had an independent influence on outcome. A clear definition of what constitutes a multimodal, FT program with an accepted list of interventions and well-defined end points would go a long way toward removing the current confusion. All potentially ambiguous end points should be strictly defined before the start of a trial with a standardized discharge protocol.[35] Algorithms of essential and less essential interventions would also be helpful.

Some of the coauthors in the study by Lunn et al have also been involved in systematically evaluating a few of the other components of LIA technique; the current study is an extension of this impressive effort. In the acknowledgments section of their article, Lunn et al thanked Drs. Kerr and Kohan for teaching them the LIA technique, although the technique they have used bears little resemblance to that described by Kerr and Kohan. Thus, the authors' conclusion that the LIA technique cannot be recommended for THA seems premature. They have provided important information about 1 aspect of LIA, that is, that single-dose intraoperative infiltration with local anesthetic is ineffective for the first 8 hours after THA. More such studies are necessary to evaluate why it has been difficult to replicate Kerr and Kohan's impressive outcome results for THA and TKA and, in particular, to confirm if the catheter technique can indeed provide long-term analgesia as demonstrated by others. Although LIA is a relatively new technique, the many reported modifications and variations are already causing confusion and could be one reason for different lengths of hospital stay and other outcomes.[8–18,34] Again, a clear definition of what constitutes LIA would be welcome.

Despite its name, the original LIA technique is not just infiltration of local anesthetic, it is a multicomponent optimization package. Focus on analgesia alone is unlikely to give conclusive answers as has been shown with FT protocols for colorectal surgery, where improvements are more likely to be multifactorial.[35]

Local infiltration analgesia is a major recent development in lower extremity joint replacement surgery and has changed orthopedic practice in many institutions. The recent US Food and Drug Administration warning about the risk of chondrolysis with intra-articular infusions of local anesthetics[36] does not apply to LIA because all cartilage is removed during THA and TKA, and the intra-articular catheter is used for only 1 or 2 bolus administrations. Although many studies are necessary to address the multiple unresolved questions, there is enough evidence to suggest that this promising technique is here to stay, and orthopedic surgeons are unlikely to return to pre-LIA days. However, before such studies are undertaken, a good start to avoid the prevailing confusion would be to agree on a clear definition of multicomponent treatments such as LIA, multimodal analgesia, and multimodal FT protocols so that we can compare oranges with oranges.

REFERENCES

1. Möiniche S, Mikkelsen S, Wetterslev J, Dahl JB. A qualitative systematic review of incisional local anaesthesia for postoperative pain relief after abdominal operations. *Br J Anaesth*. 1998;81:377–383.
2. Liu SS, Richman JM, Thirlby RC, Wu CL. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: a quantitative and qualitative systematic review of randomized controlled trials. *J An Coll Surg*. 2006;203:914–932.
3. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Ortop*. 2008;79:174–183.
4. Scott N. Wound infiltration for surgery. *Anaesthesia*. 2010;65:67–75.
5. Lavand'home PM, Roelants F, Waterloos H, De Kock MF. Postoperative analgesic effects of continuous wound infiltration with diclofenac after elective caesarean section. *Anesthesiology*. 2007;106:1220–1225.
6. Aasvang EK, Hansen JB, Malmström J, et al. The effect of wound instillation of a novel purified capsaicin formulation on postherniotomy pain: a double-blind, randomized, placebo-controlled study. *Anesth Analg*. 2008;107:282–291.
7. Pedersen JL, Lilleso J, Hammer NA, et al. Bupivacaine in microcapsules prolongs analgesia after subcutaneous infiltration in humans: a dose-finding study. *Anesth Analg*. 2004;99:912–918.
8. Röstlund T, Kehlet H. High-dose local infiltration analgesia after hip and knee replacement—what is it, why does it work, and what are the future challenges? *Acta Orthop*. 2007;78:159–161.
9. Busch CA, Whitehouse MR, Shore BJ, MacDonald SJ, McCalden RW, Bourne RB. The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. *Clin Orthop Relat Res*. 2010;468:2152–2159.

10. Stringer BW, Singhania AK, Sudhakar JE, Brink RB. Serum and wound drain ropivacaine concentrations after wound infiltration in joint arthroplasty. *J Arthroplasty.* 2007;22:884–892.
11. The Swedish Knee Arthroplasty Register. *Annual Report 2010*. Available at: http://www.nko.se/English. Accessed May 20, 2011.
12. Andersen LJ, Poulsen T, Krogh B, Nielsen T. Postoperative analgesia in total hip arthroplasty: a randomized double-blinded, placebo-controlled study on preoperative and postoperative ropivacaine, ketolorac, and adrenaline wound infiltration. *Acta Orthop*. 2007;78:187–192.
13. Andersen KV, Pfeiffer-Jensen M, Haraldsted V, Söballe K. Reduced hospital stay and narcotic consumption, and improved mobilization with local and intraarticular infiltration after hip arthroplasty: a randomized clinical trial of an intraarticular technique versus epidural infusion in 80 patients. *Acta Orthop*. 2007;78:180–186.
14. Andersen KV, Bak M, Christensen BV, Harazuk J, Pedersen NA, Söballe K. A randomized, controlled trial comparing local infiltration analgesia with epidural infusion for total knee arthroplasty. *Acta Orthop*. 2010;81:606–610.
15. Toftdahl K, Nikolajsen L, Haraldsted V, Madsen F, Tönnesen EK, Söballe K. Comparison of peri- and intraarticular analgesia with femoral nerve block after total knee arthroplasty: a randomized clinical trial. *Acta Orthop*. 2007;78:172–179.
16. Essving P, Axelsson K, Kjellberg J, Wallgren Ö, Gupta A, Lundin A. Reduced hospital stay, morphine consumption, and pain intensity with local infiltration analgesia after unicompartmental knee arthroplasty. A randomized double-blind study of 40 patients. *Acta Orthop*. 2009;80:213–219.
17. Essving P, Axelsson K, Kjellberg J, Wallgrem Ö, Gupta A, Lundin A. Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. A randomized double-blind study of 48 patients. *Acta Orthop*. 2010;81:354–360.
18. Spreng UJ, Dahl V, Hjall A, Fagerland MW, Raeder J. High-volume local infiltration analgesia combined with intravenous or local ketorolac + morphine compared with epidural analgesia after total knee arthroplasty. *Br J Anaesth*. 2010;105:675–682.
19. Lunn TH, Husted H, Solgaard S, et al. Intraoperative local infiltration analgesia for early analgesia after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. *Reg Anesth Pain Med*. 2011;36:424–429.
20. Andersen LÖ, Husted H, Otte KS, Kristensen BB, Kehlet H. A compression bandage improves local infiltration analgesia in total knee arthroplasty. *Acta Orthop*. 2008;79:806–811.
21. MacIntyre PE, Schug SA, Scott DA, Visser EJ, Walker SM. Working Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. *Acute Pain Management: Scientific Evidence*. 3rd edition. Melbourne, Australia: ANZCA & FPM; 2010.
22. Procedure-specific recommendations for the management of postoperative pain after total hip arthroplasty—a literature review by PROSPECT Group. Available at: www.postoppain.org/frameset.htm. Accessed April 15, 2011.
23. Rathmell JP, Wu CL, Sinatra RS, et al. Acute post-surgical pain management: a critical appraisal of current practice. *Reg Anesth Pain Med*. 2006;31:1–42.
24. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. *Ann Surg*. 2008;248:189–198.
25. Carli F, Kehlet H, Baldini G, et al. Evidence basis for regional anesthesia in multidisciplinary fast-track surgical pathways. *Reg Anesth Pain Med*. 2011;36:63–72.
26. Andersen ADG, McNaught CE, Macfie J, et al. Randomized clinical trial of multimodal optimization and standard perioperative care. *Br J Surg*. 2003;90:1497–1504.
27. Maessen J, Dejong CHC, Hausel J, et al. A protocol is not enough to implement an enhanced recovery programme for colorectal resection. *Br J Surg*. 2007;94:224–231.
28. King PM, Blazeby JM, Ewinds P, et al. Randomized clinical trial comparing laparoscopic and open surgery for colorectal cancer within an enhanced recovery programme. *Br J Surg*. 2006;93:300–308.
29. Wind J, Polle SW, Fung Kon Jin PH, et al. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg*. 2006;93:800–809.
30. Marret E, Remy C, Bonnet F. Meta-analysis of epidural analgesia versus parenteral opioid analgesia after colorectal surgery. *Br J Surg*. 2007;94:665–673.
31. Levy BF, Tilney HS, Dowson HMP, Rockall TA. A systematic review of postoperative analgesia following laparoscopic colorectal surgery. *Colorectal Dis*. 2010;12:5–15.
32. Bonnet F, Camu F, and PROSPECT Working Group. Procedure-specific recommendations for pain management after colon resection (2009 update). Available at: http://www.postoppain.org. Accessed May 20, 2011.
33. Pour AE, Parvizi J, Sharkey PF, Hozack WJ, Rothman RH. Minimally invasive hip arthroplasty: what role does patient preconditioning play? *J Bone Joint Surg Am*. 2007;89:1920–1932.
34. Dahl JB, Möiniche S. Relief of postoperative pain by local anaesthetic infiltration: efficacy for major abdominal and orthopedic surgery. *Pain*. 2009;143:7–11.
35. Gatt M, Anderson ADG, Reddy BS, Hayward-Sampson P, Tring IC, MacFie J. Randomized clinical trial of multimodal optimization of surgical care in patients undergoing major colonic resection. *Br J Surg*. 2005;92:1354–1362.
36. US Food and Drug Administration Alert. *Information for Health Care Professionals—Chondrolysis Reported With Continuously Infused Local Anesthetics (Marketed as Bupivacaine, Chloroprocaine, Lidocaine, Mepivacaine, Procaine and Ropivacaine)*. November 13, 2009. Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm190302.h. Accessed May 20, 2011.

Intraoperative Local Infiltration Analgesia for Early Analgesia After Total Hip Arthroplasty

A Randomized, Double-Blind, Placebo-Controlled Trial

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Background and Objectives: High-volume local infiltration analgesia (LIA) is widely applied as part of a multimodal pain management strategy in total hip arthroplasty (THA). However, methodological problems hinder the exact interpretation of previous trials, and the evidence for LIA in THA remains to be clarified. Therefore, we evaluated whether intraoperative high-volume LIA, in addition to a multimodal oral analgesic regimen, would further reduce acute postoperative pain after THA.

Methods: Patients scheduled for unilateral, primary THA under spinal anesthesia were included in this randomized, double-blind, placebo-controlled trial receiving high-volume (150 mL) wound infiltration with ropivacaine 0.2% with epinephrine (10 μg/mL) or saline 0.9%. A multimodal oral analgesic regimen consisting of slow-release acetaminophen 2 g, celecoxib 400 mg, and gabapentin 600 mg was instituted preoperatively. Rescue analgesic consisted of oral oxycodone. Pain was assessed repeatedly the first 8 hrs after surgery using the 100-mm visual analog scale. The primary end point was pain during walking (5 m) 8 hrs after surgery. Secondary end points were pain at rest, pain on 45 degrees of passive flexion of the hip with the leg straight, and cumulative consumption of oxycodone.

Results: A total of 120 patients were included. Pain during walking (median [interquartile range] [95% confidence interval]) was low in the ropivacaine versus the placebo group (20 [14–38] [0–93] vs 22 [10–40] [0–83]) and did not differ significantly ($P = 0.71$). Consumption of rescue oxycodone (5 mg [0–10 mg] [0–24 mg] vs 10 mg [0–15 mg] [0–29 mg]) did not differ ($P = 0.45$).

Conclusions: Intraoperative high-volume LIA with ropivacaine 0.2% provided no additional reduction in acute pain after THA when combined with a multimodal oral analgesic regimen consisting of acetaminophen, celecoxib, and gabapentin and is therefore not recommended.

(*Reg Anesth Pain Med* 2011;36: 424–429)

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Accepted for publication January 12, 2011.

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The study was supported with a grant from The Lundbeck Foundation, Hellerup, Denmark.

Abstracts have been selected for oral presentation and best free paper competition at the Danish Orthopaedic Society, Annual Meeting (October 2010) and Danish Society of Anesthesia and Intensive Care Medicine, Annual Meeting (November 2010).

The authors have no conflicts of interest.

ISSN: 1098-7339
DOI: 10.1097/AAP.0b013e3182186866

Increasing focus has been made on optimizing pain management after total hip arthroplasty (THA) as a prerequisite for early recovery and rehabilitation. Epidural analgesia and peripheral nerve blockade provide good pain control,[1–3] but both techniques may have inherent risk of partial motor blockade, potentially delaying early postoperative mobilization.

Local infiltration analgesia (LIA) was introduced by Kerr and Kohan.[4] The technique covers a systematic intraoperative infiltration of a high-volume analgesic mixture (ropivacaine, ketorolac, and epinephrine) into the surgical wound along with subsequent postoperative injections through an intra-articular placed catheter. Although their study was a nonrandomized, noncontrolled, cohort study with several interventions included, because of the short length of stay, the simplicity, and the apparent safety, the LIA technique has gained widespread acceptance and is frequently used as part of a multimodal pain management strategy after THA.

Three randomized studies evaluating the effect of LIA in THA have been published, all reporting superior analgesia in the LIA group.[5–7] However, some methodological inadequacies hinder sufficient interpretation, and consequently, the evidence for the analgesic effect of LIA in THA is questionable.[8] In particular, an LIA mixture combining ropivacaine and ketorolac applied in the previous studies (but without a nonsteroidal anti-inflammatory drug [NSAID] for controls) makes the interpretation of the local anesthetic component and the LIA technique difficult. Thus, the analgesic benefit observed might be due to an analgesic effect of NSAID rather than an effect of the LIA per se.[8,9]

Therefore, the purpose of this randomized, double-blind, placebo-controlled trial was to clarify, whether intraoperative high-volume LIA with ropivacaine 0.2% combined with a simple multimodal oral analgesic regimen consisting of acetaminophen, celecoxib and gabapentin, would further reduce acute pain after primary, unilateral THA. The primary end point was pain during walking 8 hrs after surgery.

METHODS

Patients and Design

The trial was approved by the local research ethics committee (De Videnskabsetiske Komitéer for Region Hovedstaden, Hillerød, Denmark) and the Danish data protection agency and registered at www.clinicaltrails.gov (no. NCT00968955). Oral and written informed consent was obtained from all patients, and the study was carried out in accordance with the principles of the Helsinki Declarations. The CONSORT recommendations for reporting randomized controlled clinical trials was followed.[10]

Patients scheduled for elective, unilateral, primary THA by 1 of 3 orthopedic surgeons at Hvidovre University Hospital (from

September 2009 to March 2010) and by 1 of 2 orthopedic surgeons at Hørsholm Hospital (from November 2009 to June 2010), older than 18 years, and familiar with the Danish language were screened for inclusion in the study. Exclusion criteria were alcohol and medical abuse, daily use of strong opioids (morphine, fentanyl, hydromorphone, ketobemidone, methadone, nicomorphine, oxycodone, and pethidine) or glucocorticoids, body mass index (BMI) higher than 40 kg/m^2, allergies to local anesthetics, pregnancy or breast-feeding, diabetic neuropathy, rheumatoid arthritis, and neurological or psychiatric diseases potentially influencing pain perception. The design was a 2-center, prospective, randomized, double-blind, placebo-controlled trial.

Randomization and Blinding

One hundred twenty patients were randomly assigned to 2 groups of 60. A random allocation sequence concealed in 120 consecutively numbered, opaque, sealed envelopes determining active treatment or placebo was computer-generated by a project nurse not otherwise involved in the trial. The envelopes were opened on the morning of surgery, and the trial drug was prepared by an anesthetist not otherwise involved with data collection. The envelopes were divided between the 2 hospitals, and no stratification was made. Trial participants, care providers, and data collectors were all blinded to the allocation throughout the study.

Study Parameters

The primary end point was pain during walking with a walking aid (5 m) 8 hrs after surgery. Secondary end points were pain at rest (supine), pain on 45 degrees of passive flexion of the hip with the leg straight, and cumulative consumption of oxycodone 8 hrs after surgery. Pain during walking was assessed 4 and 8 hrs postoperatively and pain at rest and on hip flexion 2, 4, 6, and 8 hrs postoperatively using the 100-mm visual analog scale (VAS) (0 mm indicating no pain and 100 mm indicating worst pain imaginable). The investigator asked the patients at each time point: "Please show me how much pain you have right now on the VAS, where the lower limit indicates no pain and the upper limit indicates worst pain imaginable." Complications occurring during hospitalization were registered.

Study Intervention

Local infiltration analgesia was performed intraoperatively using ropivacaine 0.2% (AstraZeneca, Södertälje, Sweden) with epinephrine (10 μg/mL) or saline 0.9% (placebo). A total volume of 150 mL was injected using a systematic technique ensuring uniform delivery to all tissues incised and instrumented during the surgery.[4] The first 50 mL was systematically injected in the periacetabular tissues after reaming of the acetabulum and before insertion of the acetabular component. After insertion of the femoral component, another 50 mL was injected in the cut rotators and the gluteus muscles and the proximal part of the iliotibial tract. Finally, 50 mL was systematically injected in the subcutaneous layers. The subcutaneous injections (in case of allocation to ropivacaine) were without epinephrine to minimize the risk of subcutaneous blister formation.[4] No intra-articular catheter was placed, and no postoperative injections were administered.

Anesthesia, Surgery, and Analgesia

Anesthesia, surgery, and analgesia were standardized for all patients. Thus, interventions were fixed for all but the modality under investigation. Surgery was performed under lumbar spinal anesthesia with 12.5 mg of isobaric bupivacaine (0.5%) and optional sedation with propofol (1–5 mg/kg per hour) by 1 of 5 surgeons all specialized in arthroplasty and the LIA technique. They agreed on a similar surgical and LIA technique before the study. Cefuroxime 1.5 g and tranexamic acid 1 g were administered intravenously. Intraoperative fluid therapy was standardized and consisted of saline 0.9% 5 mL/kg per hour and colloid (Voluven; Fresenius Kabi AB, Uppsala, Sweden) 7.5 mL/kg per hour.[11] Total hip arthroplasty was performed using a standard posterior approach without the use of minimally invasive surgical techniques. Drains were not used. Prostheses were Bimetric with Ringloc-cup or Magnum-cup (Biomet-Merck, Inc, Warsaw, Ind) or CLS Spotorno with Trilogy-cup (Zimmer, Inc, Warsaw, Ind).

A multimodal oral analgesic regimen consisting of slow-release acetaminophen 2 g, celecoxib 400 mg, and gabapentin 600 mg was instituted 1 to 2 hrs preoperatively. Rescue analgesics (administered if VAS >50 at rest) consisted of sufentanil 5 μg intravenously in the postanesthesia care unit (PACU) and subsequently, oral oxycodone 5 mg. Patients followed a well-defined, fast-track rehabilitation regimen and were discharged to their homes according to functional discharge criteria.[12]

Statistical Analyses

The estimated sample size for the primary effect variable was calculated based on the results from a pilot study (n = 10), where average pain during walking (5 m) 8 hrs after primary, unilateral THA was found to be 28 mm with an SD of 22 mm. A total sample of 120 patients would allow the detection or rejection of a 50% reduction in pain in the ropivacaine group compared with the placebo group at a 2-sided 5% significance level with a power of 90% and 15% dropouts.

Continuous numeric variables were assessed for normality of distribution (Kolmogorov-Smirnov). Depending on whether variables were normally distributed (only the case for age, BMI, and duration of surgery), they are presented as mean with range, and otherwise as median with interquartile range (IQR). Categorical variables are presented as count with percentage, and tests for significant differences between groups were done with the χ^2 test. The Mann-Whitney rank sum test was used for comparison between groups because pain data were not normally distributed and no meaningful transformation could be performed (many values = 0 and skew was very positive).[13] Subsequent Bonferroni adjustment for repeated measurements was applied. In addition, summarized (cumulated) pain was calculated for each of the 3 pain assessments by adding up pain scores from the different time points (2–8 hrs). Data analyses were conducted using SPSS for windows, version 12.0 (SPSS, Inc, Chicago, Ill). $P < 0.05$ was considered statistically significant.

RESULTS

One hundred twenty patients were included, and all received their allocated intervention (Fig. 1). Baseline demographic and perioperative characteristics of study patients are shown in Table 1. Groups were comparable. Pain hindering walking (5 m) was not different to a significant degree between the 2 groups (count [%], ropivacaine vs placebo: 7 patients [0.12] vs 2 patients [0.03], $P = 0.08$) (Fig. 1). For secondary end points (pain at rest and pain on passive hip flexion), data were only missing once (1 patient in the ropivacaine group was asleep 8 hrs postoperatively).

For the first 8 hrs after surgery, pain was low for all pain assessments (pain during walking, pain at rest, and pain on passive hip flexion) at all time points investigated, and no significant difference between the ropivacaine and placebo groups was seen (Fig. 2). No significant difference in summarized pain (added pain scores) for each of the 3 pain assessments (walking $P = 0.11$, rest $P = 0.84$, passive hip flexion $P = 0.52$) was

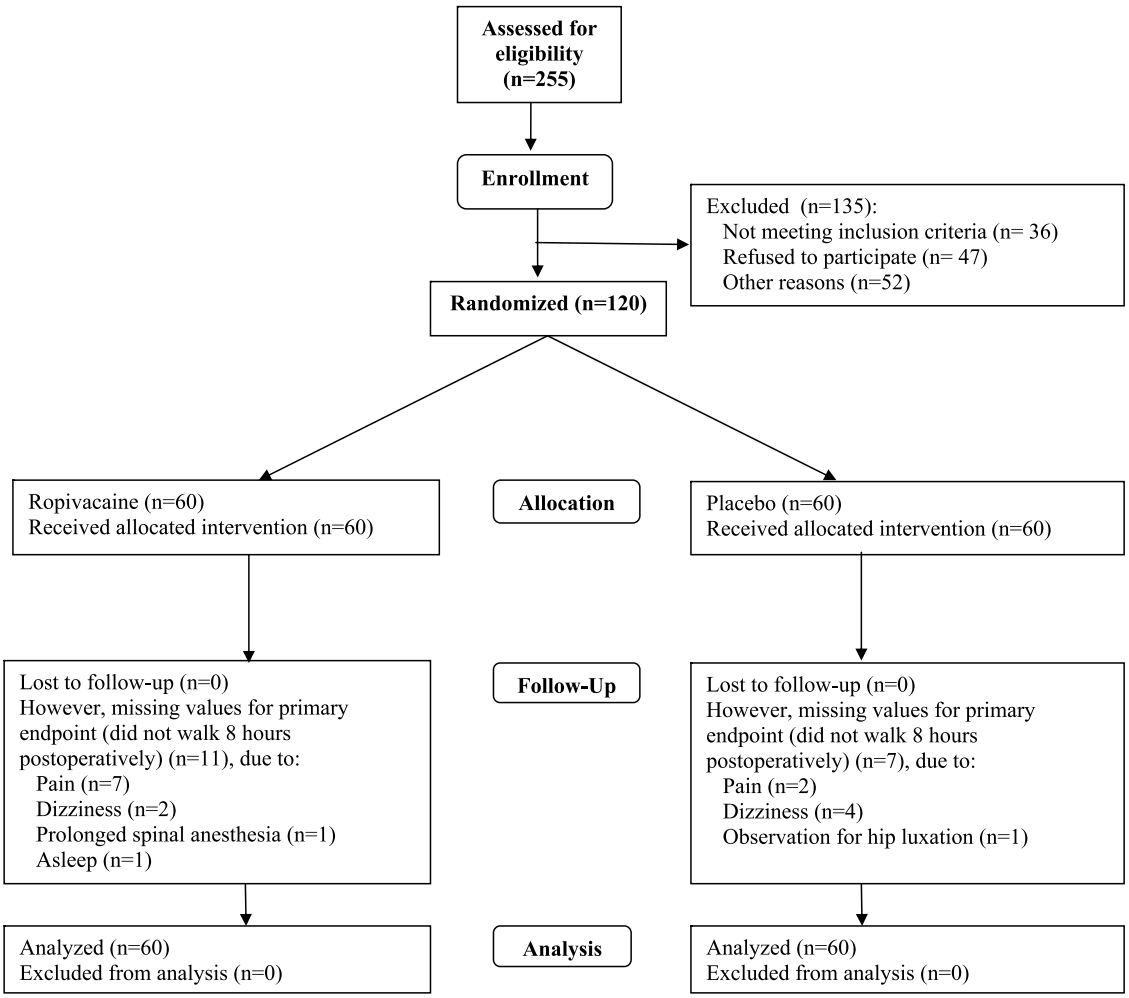

FIGURE 1. Flow of patients through the study.

TABLE 1. Baseline Demographic and Perioperative Characteristics of Study Patients

Variable	Ropivacaine (n = 60)	Placebo (n = 60)
Patient characteristics		
Age, y	67 (47–82)	67 (35–87)
Sex, male/female	27/33 (45/55)	21/39 (35/65)
BMI, kg/m^2	27 (19–40)	27 (17–40)
ASA, I/II/III	18/37/5 (30/62/8)	14/43/3 (23/72/5)
Smoking, yes/no	9/51 (15/85)	17/43 (28/72)
Perioperative data		
Hospital, HvH/HH	25/35 (42/58)	24/36 (40/60)
Duration of surgery, min	49 (25–84)	51 (25–110)
Prosthesis, BR/BM/ST	17/8/35 (28/13/58)	19/5/36 (32/8/60)

Data are expressed as mean (range) or count (%) where appropriate.

ASA indicates American Society of Anesthesiologists physical status; BR, Bimetric with Ringloc-cup; BM, Bimetric with Magnum-cup; HH, Hørsholm Hospital; HvH, Hvidovre University Hospital; ST, CLS Spotorno with Trilogy-cup.

observed. Furthermore, no significant difference was observed in cumulative consumption of oxycodone for the first 8 hrs postoperatively (median [IQR] [95% confidence interval], ropivacaine vs placebo: 5 mg [0–10 mg] [0–24 mg] vs 10 mg [0–15 mg] [0–29 mg], $P = 0.45$), in number of patients having sufentanil in PACU (count [%], ropivacaine vs placebo: 5 patients [0.08] vs 13 patients [0.22], $P = 0.07$ [range, 0–30 mg]), or in length of stay (median [IQR], 3 nights [2–3] in both groups, $P = 0.86$).

One patient in the placebo group developed computed tomographic scan verified cerebral infarction after surgery. A patient in the ropivacaine group had quadriceps muscle palsy, and electromyography suggested that the complication was due to an intraoperative local mechanical injury on the femoral nerve rather than related to the ropivacaine infiltration because the nerve injury was limited to the branches innervating the quadriceps muscle.

A post hoc power analysis yields a power of 93% for the primary end point, pain during walking 8 hrs after surgery (mean [SD], ropivacaine vs placebo: 28 [23] vs 26 [21]).

DISCUSSION

This randomized, double-blind, placebo-controlled trial demonstrated that intraoperative high-volume LIA with ropivacaine 0.2% provided no additional reduction in acute pain after

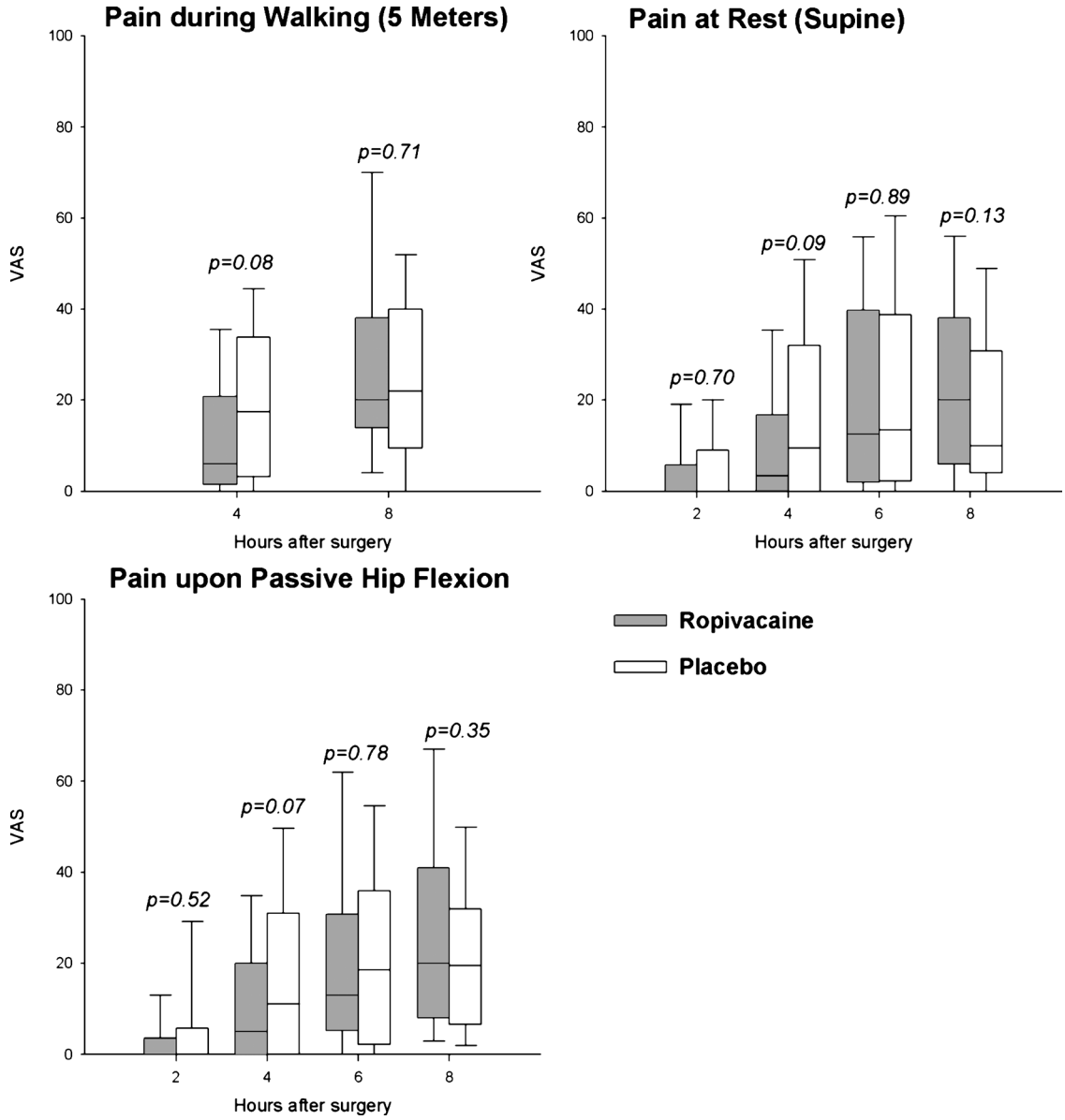

FIGURE 2. Pain 2 to 8 hrs after surgery. Horizontal lines indicate medians, boxes indicate IQRs, and whiskers indicate 5th to 95th percentiles. No statistically significant differences between groups were observed in any end point (Mann-Whitney rank sum test, with subsequent Bonferroni adjustment for repeated measurements).

THA when combined with a multimodal oral analgesic regimen. Furthermore, no significant reduction in consumption of rescue oxycodone was achieved.

Our findings are in contrast to previous results from randomized trials in the orthopedic literature, all reporting superior analgesia in the LIA group.[5–7] Reduced pain (20–96 hrs postoperatively) and opioid requirement (96 hrs postoperatively) were reported when intraoperative and postoperative LIA was compared with continuous epidural analgesia.[5] When intraoperative and postoperative LIA was compared with saline infiltration, a reduction in pain (up to 2 weeks postoperatively) and opioid requirement (96 hrs postoperatively) was reported.[6] Finally, reduced pain (in PACU) and opioid requirement (24 hrs postoperatively) were reported when intraoperative LIA was compared with no infiltration.[7] However, some methodological problems hinder the exact interpretation of these trials. First, NSAID was not administered in the control group in any of the 3 trials,[5–7] making the interpretation of the local anesthetic component and the LIA technique in particular difficult[8]; second, 1 trial was not blinded, and pain not sufficiently assessed/reported[5]; third, 1 trial was not placebo-controlled, and the surgeon was not blinded[7]; and fourth, in 2 trials, administration of morphine in LIA versus control groups was unmatched.[5,7]

Because an intraoperative catheter was not applied, we did not evaluate the effect of repeated postoperative LIA injections. The role of catheter administration and its placement and type is unknown, and we consider in keeping with results from a recently published trial[14] that a significant analgesic effect of postoperative injections is unlikely, when it is not observed with the systematic intraoperative infiltration.

In contrast to previous trials, we omitted ketorolac from the LIA-mixture because celecoxib was included in the comprehensive multimodal oral analgesic regimen. The analgesic benefit of LIA previously reported in THA[5–7] might be due to an analgesic effect of NSAID in combination with a less comprehensive multimodal oral analgesia. This assumption is based on the results from the present study in combination with previous results indicating that NSAID provides analgesia whether administered locally or systemically and probably without important difference.[9]

Our study might be limited by pain scores a little less than 30 mm in both groups, which challenge the demonstration of an intervention effect.[15,16] However, because LIA is already widely used in THA, our aim was to clarify if LIA in addition to a simple multimodal oral analgesic regimen would reduce acute postoperative pain additionally. Furthermore, the large sample size made the trial sufficiently powered ensuring final evaluation. At the same time, our study does not exclude that intraoperative LIA may have a minor, short-lasting analgesic effect with a less comprehensive oral analgesic regimen or in selected patients (high pain responders).

It may also be argued that the absent effect of LIA may be explained by a continuous effect of the spinal anesthesia. However, a small dose of bupivacaine was used, which should not have prolonged analgesic effects.[17]

The results from the present study illustrate that a simple multimodal oral analgesic regimen with acetaminophen, celecoxib, and gabapentin provides sufficient analgesia with acceptable low opioid requirements in opioid naive patients after THA, and it emphasizes the need for procedure-specific trials because LIA might be effective in other procedures.[8] In our opinion, the applied multimodal oral analgesic regimen seems effective, simple, and easy and may be preferable compared with more invasive techniques. However, further data are required on the specific role of gabapentin regarding efficacy and adverse effects, especially the concerns about sedation in older patients[18,19] (we did not measure sedation level). Although acceptable immediate postoperative pain relief after THA was achieved in opioid-naive patients with a simple multimodal oral nonopioid analgesic regimen in this study, higher pain scores have been reported by other investigators.[1,20] This difference may relate to study design (basic analgesic regimen and duration of follow-up) or surgical technique. Therefore, further studies in subacute and late postoperative recovery and rehabilitation are needed.[21] In this context, it remains noteworthy that not only pain but also multiple factors may limit ambulation ability and other functional recovery parameters.[1] In future pain trials, the effects of long-duration administration of simple oral analgesics on long-term outcome need to be studied. Moreover, continuous low-dose peripheral nerve blockade[1,22,23] and systemic administration of high-dose glucocorticoids[24,25] may play important roles because they may be provided on an ambulatory basis, thereby possibly prolonging their benefits. However, potential risks of motor adverse effects resulting in delayed mobilization or falls[26] and risk of deep infection,[25] respectively, need to be clarified. Finally, these modalities need to be evaluated against the efficacy, safety, and costs of other evidence-based components of multimodal analgesia.[3]

In conclusion, intraoperative high-volume LIA with ropivacaine 0.2% provided no additional reduction in acute pain after THA when combined with a multimodal oral analgesic regimen consisting of acetaminophen, celecoxib, and gabapentin. Acceptable acute postoperative pain relief was achieved with the oral analgesic regimen, and LIA is not recommended in THA.

ACKNOWLEDGMENTS

The authors thank Research Nurse Susan Randall, Hørsholm Hospital, Denmark, for helpful assistance with data collection and Dr. Henning Erik Holm, Hørsholm Hospital, Denmark, for implementation of the standardized anesthetic procedure. Furthermore, we acknowledge assistance from Dr. Kerr and Dr. Kohan, St. Luke's Hospital, Australia, in teaching us the technique of high-volume infiltration analgesia, and Steen Ladelund, Clinical Research Centre, Hvidovre University Hospital, Denmark, for helpful advice regarding the statistical method.

REFERENCES

1. Ilfeld BM, Ball ST, Gearen PF, et al. Ambulatory continuous posterior lumbar plexus nerve blocks after hip arthroplasty: a dual-center, randomized, triple-masked, placebo-controlled trial. *Anesthesiology.* 2008;109:491–501.
2. Choi PT, Bhandari M, Scott J, Douketis J. Epidural analgesia for pain relief following hip or knee replacement. *Cochrane Database Syst Rev.* 2003;CD003071.
3. Fischer HB, Simanski CJ. A procedure-specific systematic review and consensus recommendations for analgesia after total hip replacement. *Anaesthesia*. 2005;60:1189–1202.
4. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop*. 2008;79:174–183.
5. Andersen KV, Pfeiffer-Jensen M, Haraldsted V, Soballe K. Reduced hospital stay and narcotic consumption, and improved mobilization with local and intraarticular infiltration after hip arthroplasty: a randomized clinical trial of an intraarticular technique versus epidural infusion in 80 patients. *Acta Orthop*. 2007;78:180–186.
6. Andersen LJ, Poulsen T, Krogh B, Nielsen T. Postoperative analgesia in total hip arthroplasty: a randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration. *Acta Orthop*. 2007;78:187–192.
7. Busch CA, Whitehouse MR, Shore BJ, MacDonald SJ, McCalden RW, Bourne RB. The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. *Clin Orthop Relat Res*. 2010;468:2152–2159.
8. Dahl JB, Moiniche S. Relief of postoperative pain by local anaesthetic infiltration: efficacy for major abdominal and orthopedic surgery. *Pain*. 2009;143:7–11.
9. Romsing J, Moiniche S, Ostergaard D, Dahl JB. Local infiltration with NSAIDs for postoperative analgesia: evidence for a peripheral analgesic action. *Acta Anaesthesiol Scand*. 2000;44:672–683.
10. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA*. 2001;285:1987–1991.
11. Holte K, Kristensen BB, Valentiner L, Foss NB, Husted H, Kehlet H. Liberal versus restrictive fluid management in knee arthroplasty: a randomized, double-blind study. *Anesth Analg*. 2007;105:465–474.
12. Husted H, Holm G, Jacobsen S. Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: fast-track experience in 712 patients. *Acta Orthop*. 2008;79:168–173.
13. Altman DG, Bland JM. Parametric v non-parametric methods for data analysis. *BMJ*. 2009;338:a3167.
14. Chen DW, Hsieh PH, Huang KC, Hu CC, Chang YH, Lee MS. Continuous intra-articular infusion of bupivacaine for post-operative pain relief after total hip arthroplasty: a randomized, placebo-controlled, double-blind study. *Eur J Pain*. 2010;14:529–534.
15. Breivik H, Borchgrevink PC, Allen SM, et al. Assessment of pain. *Br J Anaesth*. 2008;101:17–24.
16. Mathiesen O, Jacobsen LS, Holm HE, et al. Pregabalin and dexamethasone for postoperative pain control: a randomized controlled study in hip arthroplasty. *Br J Anaesth*. 2008;101:535–541.

17. Pitkänen M. Spinal (subarachnoid) blockade. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbough PO. *Neural Blockade in Clinical Anesthesia and Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.
18. Buvanendran A, Kroin JS, la Valle CJ, Kari M, Moric M, Tuman KJ. Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial. *Anesth Analg*. 2010;110:199–207.
19. Tiippana EM, Hamunen K, Kontinen VK, Kalso E. Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. *Anesth Analg*. 2007;104:1545–1556.
20. Marino J, Russo J, Kenny M, Herenstein R, Livote E, Chelly JE. Continuous lumbar plexus block for postoperative pain control after total hip arthroplasty. A randomized controlled trial. *J Bone Joint Surg Am*. 2009;91:29–37.
21. Nikolajsen L, Brandsborg B, Lucht U, Jensen TS, Kehlet H. Chronic pain following total hip arthroplasty: a nationwide questionnaire study. *Acta Anaesthesiol Scand*. 2006;50:495–500.
22. Ilfeld BM, Mariano ER, Girard PJ, et al. A multicenter, randomized, triple-masked, placebo-controlled trial of the effect of ambulatory continuous femoral nerve blocks on discharge-readiness following total knee arthroplasty in patients on general orthopaedic wards. *Pain*. 2010;150:477–484.
23. Ilfeld BM, Gearen PF, Enneking FK, et al. Total hip arthroplasty as an overnight-stay procedure using an ambulatory continuous psoas compartment nerve block: a prospective feasibility study. *Reg Anesth Pain Med*. 2006;31:113–118.
24. Kardash KJ, Sarrazin F, Tessler MJ, Velly AM. Single-dose dexamethasone reduces dynamic pain after total hip arthroplasty. *Anesth Analg*. 2008;106:1253–1257.
25. Lunn TH, Kristensen BB, Andersen LO, et al. Effect of high-dose preoperative methylprednisolone on pain and recovery after total knee arthroplasty: a randomized, placebo-controlled trial. *Br J Anaesth*. 2011;106:230–238.
26. Ilfeld BM, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. *Anesth Analg*. 2010;111:1552–1554.

Wound Infiltration—Apples, Oranges, or Fruit Cocktail?

Accepted for Publication: 2 November 2011

To the Editor:

I read with interest the editorial on wound infiltration for lower-limb arthroplasty by Dr Rawal[1] that accompanies an article by Lunn et al[2] showing no benefit from wound infiltration for total hip arthroplasty. Dr Rawal seems to suggest that the transition of the technique of wound infiltration for hip arthroplasty from the original technique, as described by Kerr and Kohan[3] via a systematic series of prospective randomized clinical trials within an established enhanced recovery program, has resulted in poorer clinical outcomes and that clinicians should not abandon wound infiltration via a catheter for this operation.

The article by Lunn et al is, I believe, the latest—and largest (n = 120)—in a series of prospective randomized clinical trials performed to elucidate the mechanisms, benefits, and improved clinical outcomes associated with local infiltration analgesia (LIA). I would like to highlight the following points.

1. Importantly, the same systemic nonopioid analgesia was used in both groups, which has not always been done before[4]; doing so allows a more accurate assessment of the analgesic technique under investigation: LIA.
2. Kerr and Kohan's[3] consecutive series has had a major impact on the subsequent development of orthopedic enhanced recovery programs. However, their consecutive audit of 325 patients was not prospective, randomized, blinded, or placebo controlled, and their patients were preselected. As Kerr and Kohan[3] state, the "patient population was therefore from a more privileged group in the community, with greater access to resources and support than may be found in the general population."
3. I cannot find published data to support Dr Rawal's assertion that intra-articular ketorolac provides considerably better analgesia than intravenous. Indeed, Kerr and Kohan correctly acknowledge that "the literature is equivocal as to its efficacy." Statistical, but not "considerable," clinical differences in pain scores have been demonstrated with ketorolac in LIA versus systemic administration in knee replacement.[4] Other orthopedic studies comparing intra-articular or systemic nonsteroidal anti-inflammatory drug have also not been able to demonstrate clinically relevant analgesic differences.[5] I agree with Dr Rawal that interpretation of published randomized studies on LIA for total hip arthroplasty is hindered by several limitations in methodology, but this is particularly relevant to the analgesic regimens being different between the control and LIA groups, especially the use of ketorolac only in the LIA groups.[6]
4. Of the 325 patients in the Kerr and Kohan study, only 54 patients underwent total hip arthroplasty, and their mean length of stay was 4.3 (SD, 6.1) days (range, 1–27 days)—not 1 to 2 days as suggested by the editorial. Thus, Lunn et al[2] have a shorter length of stay, but this outcome parameter is more likely to be a result of organizational improvements within an enhanced recovery program than LIA itself.[5]
5. I do not understand the comment on later analgesic effects of LIA. When an intraoperative infiltration is not demonstrably effective for the first 8 hours, how does it then become effective later?

In summary, I hope Dr Rawal's editorial has not unintentionally confused readers by mixing comments between total hip arthroplasty and total knee arthroplasty studies, multimodal analgesia, and the concept of fast-track surgery. His conclusion that we may be comparing "apples with oranges" appears to be based on "cherry" picking data that have resulted in a "fruit salad" cocktail. In contrast, as has been seen many times in clinical practice, the initial positive observations with LIA have had to be modified based on subsequent results from well-performed randomized, double-blind, placebo-controlled, procedure-specific studies.

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The author declares no conflict of interest.

REFERENCES

1. Rawal N. Local infiltration analgesia and other multicomponent techniques to improve postoperative outcome-are we comparing oranges and apples? *Reg Anesth Pain Med*. 2011;36:417–420.
2. Lunn TH, Husted H, Solgaard S, et al. Intraoperative local infiltration analgesia for early analgesia after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. *Reg Anesth Pain Med*. 2011;36:424–429.
3. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop*. 2008;79:174–183.
4. Spreng UJ, Dahl V, Hjall A, Fagerland MW, Raeder J. High-volume local infiltration analgesia combined with intravenous or local ketorolac + morphine compared with epidural analgesia after total knee arthroplasty. *Br J Anaesth*. 2010;105:675–682.
5. Kehlet H, Andersen LO. Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practice. *Acta Anaesthesiol Scand*. 2011;55:778–784.
6. Romsing J, Moiniche S, Ostergaard D, Dahl JB. Local infiltration with NSAIDs for postoperative analgesia: evidence for a peripheral analgesic action. *Acta Anaesthesiol Scand*. 2000;44:672–683.

Reply to Dr. Scott and to Dr. Lunn et al

Accepted for Publication: 6 December 2011

To the Editor:

Thank you for the opportunity to respond to comments by Dr. Scott[1] and Dr. Lunn et al.[2] Contrary to Dr. Scott's assertion, the editorial did not draw any conclusions, negative or positive, about clinical outcomes of the studies he refers to. The main purpose of the editorial was to highlight the lack of accepted definitions of multicomponent interventions, resulting in difficulties in drawing meaningful outcome conclusions.[3]

In the absence of clear definitions and outcome criteria, researchers have used numerous combinations, permutations, and modifications of such interventions, all under the umbrella names of local infiltration anesthesia (LIA), multimodal analgesia, and enhanced recovery programs. Predictably, many studies show conflicting results, as noted in a recent review of 17 randomized LIA studies, where a common feature was the heterogeneity of the study protocols.[4] So the question is: which LIA is the real LIA? Because there is no consensus, the study by Kerr and Kohan,[5] which generated widespread interest by demonstrating impressive reductions in length of stay, should qualify as LIA technique.[6] The study by Lunn et al[6] was cited in the editorial to illustrate the above point, that is, that authors can make major changes in the study design and still call the technique LIA. The study of Lunn et al was well designed, and they may have valid reasons for making the changes, but that is beside the point. Lunn et al are in no position to judge LIA, let alone condemn it, because

they did not study LIA. Because of multiple changes, "their LIA" bears hardly any resemblance to the original. Until a consensus is reached, LIA without catheter cannot be called LIA. Currently, 4 studies (2 randomized controlled trials) show catheter LIA to be very effective for total hip arthroplasty, and 1 study disputes this finding.[7]

Dr. Scott writes, "I cannot find published data to support Dr. Rawal's assertion that intra-articular ketorolac provides considerably better analgesia than IV." He need look no further than the study by Spreng et al[8] referenced in the editorial. In addition to finding LIA (with intra-articular catheter) superior to epidural for TKA (total knee arthroplasty), the study compared LIA using ketorolac and morphine either locally (including intra-articularly) or with IV. It concluded, "…results confirm that local administration of ketorolac and morphine has a specific local effect regarding pain, narcotic consumption, mobilization, and length of stay. These effects were significantly stronger than after giving the same total dose of adjuvants IV."[8] This should qualify as "considerably better" for any clinician, not just "slightly more effective," as suggested by Lunn et al. However, some systemic effect of ketorolac cannot be ruled out; coadministration of morphine is a confounder, and the studied joint was the knee, not the hip. I agree that there is a need for more studies to clarify the role of local nonsteroidal anti-inflammatory drug administration in LIA.

Regarding the comment on later analgesic effects of LIA, that section in the editorial says nothing about a possible later effect of LIA; what it says is that "The benefits of LIA can be expected to be more apparent after the residual effects of preoperative analgesics and spinal anesthesia have dissipated."[3] Lunn et al may dispute this, but even the critics of catheter LIA concede: "This may be explained by the fact that pain treatment with LIA during surgery is highly effective, with an extended postoperative 'hangover' pain-reducing effect, making postoperative treatment with LINFA (administered through catheter into the hip) of minor or no importance."[7] Lunn et al now say their multimodal regimen was administered twice daily for 6 days; this is new information and therefore not relevant to the discussion in the editorial.

In summary, the editorial was not about the pros and cons of individual techniques. It was a call for clearly defined criteria, accepted list of interventions, and well-defined end points for evaluation of multicomponent techniques, such as LIA, multimodal analgesia, and enhanced recovery programs. The study of Lunn et al was taken as an example to emphasize the consequences when the components of the LIA technique are changed, but the name is not. Although literature supports the use of multicomponent interventions to improve outcome, the prevailing lack of accepted definitions has resulted in a mish-mash "fruit cocktail" combination of numerous interventions leading to ambiguous results.[3] Only good-quality, comparative "orange versus orange" studies within the framework of predefined outcome criteria can answer the critical questions, reduce the use of inappropriate and unnecessary interventions, and make multicomponent techniques more cost-effective.

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REFERENCES

1. Scott N. Wound infiltration - apples, oranges or fruit cocktail? *Reg Anesth Pain Med*. 2012;37:233.
2. Lunn T. What is effective (and what is not) when multi component interventions are applied to improve postoperative outcome? *Reg Anesth Pain Med*. 2012;37:232.
3. Rawal N. Local infiltration analgesia and other multicomponent techniques to improve postoperative outcome—are we comparing oranges and apples? *Reg Anesth Pain Med*. 2011;36:417–420.
4. Kehlet H, Andersen LÖ. Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practice. *Acta Anaesthesiol Scand*. 2011;55:778–784.
5. Kerr DR, Kohan L. Local infiltration analgesia: a technique for control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop*. 2008;79:174–183.
6. Lunn TH, Husted H, Solgaard S, et al. Intraoperative local infiltration analgesia after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. *Reg Anesth Pain Med*. 2011;36:424–429.
7. Specht K, Leonhardt JS, Revald P, et al. No evidence of a clinically important effect of adding local infusion analgesia administered through a catheter in pain treatment after total hip arthroplasty. A randomized double-blind and placebo-controlled clinical trial involving 60 patients. *Acta Orthop*. 2011;82:315–320.
8. Spreng UJ, Dahl V, Hjall A, et al. High-volume local infiltration analgesia combined with intravenous or local ketorolac+morphine compared with epidural analgesia after total knee arthroplasty. *Br J Anaesth*. 2010;105:675–682.

Is a Single Sciatic Really Equivalent to a Continuous Sciatic Block for Total Knee Replacement?

Accepted for Publication: 4 November 2011

To the Editor:

We read with interest the recent publication by Wegener et al.[1] We found the study particularly relevant, because the authors' criteria for "discharge readiness" are very similar to those used for discharging patients undergoing total joint replacement at our institution.

As with all studies, the authors likely realize that their proposed conclusions apply only to their specific clinical pathway. Thus, Figure 4 clearly shows that the patients included in this study were not mobilized on the day of surgery and that, on postoperative day 1, the use of continuous sciatic block provided better pain control than either a continuous femoral block alone or a combination of a continuous femoral and a single sciatic block. At our institution, patients undergoing a total knee replacement are actively mobilized starting on the day of surgery. This can be accomplished only if motor function is preserved. A single sciatic block, even using the approach the authors proposed, produces a significant motor block limiting any active mobilization on the day of surgery. In contrast, a continuous sciatic infusion of diluted local anesthetic solution provides the necessary analgesia to allow active mobilization within hours following surgery, and the actual discharge from the hospital, for the majority of patients, is in 2 days or less.[2] At our institution, we favor a continuous femoral (5 mL/hr of bupivacaine 0.06%) and a continuous sciatic (3 mL/hr of bupivacaine 0.03%), with an injection of saline for the placement of the sciatic perineural catheter. Using criteria similar to those described by Ilfeld and Madison,[3] our blocks are performed before surgery, and the time to perform both a continuous femoral and a continuous sciatic is 28 to 33 mins.[4] It is also important to recognize that the use of continuous sciatic blocks offers the advantage of reducing the frequency of postoperative nausea and vomiting, which can limit patient recovery, especially in the case of an accelerated clinical pathway.[5]