Local Infiltration Analgesia for Pain After Total Knee Replacement Surgery: A Winner or Just a Strong Runner-Up?

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Local infiltration analgesia (LIA) has been introduced recently as a promising step forward in reducing postoperative pain and side effects from analgesics after knee arthroplasty and, so far, with less convincing results after hip artroplasty.[1]

As often with new methods, there is a way to go from the first, enthusiastic, nonblinded case series[2] to evidence-based recommendations for clinical, everyday use.[3,4] This way is paved with some important questions:

1. Does the method work at all?
2. What parts and components of the new method are efficient?
3. How does the method compare to other methods in terms of safety, quality, and cost efficacy?

It is tempting to throw all potential ingredients of a new method into a huge cocktail and show superiority versus controls who receive a stripped and nonoptimal regimen. This may give an answer to question 1, but certainly no or few answers to questions 2 and 3.

In the present issue of the *Journal*, Essving et al. present an interesting study on LIA versus intrathecal morphine for postoperative analgesia after knee artroplasty in bupivacaine spinal anesthesia.[5] The LIA group had less morphine consumption during 0- to 24-hour and 24- to 48-hour periods after surgery, less pain on movement at 24 and 48 hours, less pain at rest on 24 hours, better patient satisfaction at 24 hours, and shorter time to discharge readiness. No differences were demonstrated at 3 days, 1 week, or 3 months after surgery in any variable, including no difference in knee functional outcome.

Thus, the LIA method worked well for the patients in comparison with the simple alternative of a single shot of morphine 0.1 mg added intrathecally. Still, turning to question 2 on important components, we may look closer at the LIA method of Essving et al.:

(a) Multiple injections of local anesthesia in joint structures during the procedure, ketorolac and epinephrine added, whereas the control group receives 0.1 mg morphine intrathecally.
(b) Injection of ketorolac into joint at 21 and 45 hours, saline to control group.
(c) Injection of ropivacaine into joint at 21 and 45 hours, saline to control group.
(d) Injection of epinephrine into joint at 21 and 45 hours, saline to control group.

As to (a), we know that proper local anesthesia in all relevant wound structures pre- or perioperatively during knee replacement is efficient.[6] Also, in a study of hernia repair with complete single-shot bupivacaine infiltration analgesia, Aasboe et al. showed improved pain relief for as much as 1 week after the procedure.[7] Still, such results are to some extent procedure specific, and not reproduced with total knee arthroplasty in the literature. In a study of Andersen et al. on knee arthroplasty, the preoperative ropivacaine infiltration was superior to placebo at 6 hours but not at 24 hours.[6] The success may also have to do with how extensive the local infiltration technique is performed in terms of including all relevant structures, not only the superficial wound.[7] Although intrathecal morphine 0.1 mg in Essving et al.'s study had inferior effect at 24 hours, it may be that the control group would have improved with simple local anesthesia infiltration in the wounds by end of surgery, as is a frequent routine in many hospitals.

As to (b), (c), and (d), we may, as the authors also mention, ask whether things would have been different if the control group received a slow IV dose of ketorolac, ropivacaine, and epinephrine at 21 and 45 hours instead of just saline in the joint. We know that ketorolac[8] and ropivacaine have analgesic effects when given systemically and also that intra-articular administration will result in systemic absorption and systemic effects. We also know that infiltration of saline into the knee joint does have some analgesic effect, mostly as a placebo effect of the injection,[9] but also potentially by pharmacological volume effect per se,[10] tentatively explained by cooling and dilution of inflammatory local proteins.

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The role of epinephrine in the LIA mixture has not been studied. Although epinephrine has an analgesic effect on the spinal α-2 receptors when given epidurally or spinally, there is no documentation on any specific analgesic effect or target mechanism of this drug when used peripherally.[11] Still, epinephrine is probably often included "just in case" because of potential strengthening of the effect of other locally active drugs, because their clearance from the local site is delayed owing to the epinephrine-induced vasoconstriction.

Thus, being the devil's advocate and to summarize: The prolonged (48 hours) analgesic effect from LIA may have been due to a specific effect or may have been a result of the meticulously administered perioperative local anesthesia infiltration and joint bolus, the systemic effects of ropivacaine given twice, and systemic effects of ketorolac given 3 times; none of such systemic effects actually being LIA specific. In addition, the control group was very simple and received just a single-shot spinal and morphine patient-controlled analgesia. This group could have been further improved by adding local anesthetic wound infiltration, as well as regular doses of paracetamol and nonsteroidal anti-inflammatory drugs throughout the perioperative phase.

Still, there is no doubt that in Essving et al.'s study the patients in the LIA group had a better quality of analgesia than did the morphine intrathechal group during their first postoperative 2 days, and these positive results should be used for the rest of our future research and clinical practice. There are data suggesting that ketorolac works better when given locally than systemically,[12] and it is certainly established that local anesthesia does so. Also, clinical impressions suggest that the morning injection the day after surgery seems to have a clear effect on patients in pain, although not shown convincingly in controlled studies.[4,10,13] This may be because control patients in studies usually get a placebo injection and often have low to moderate pain; thus there is not much potential or statistical power for showing improvements for the whole group.

What then are the alternatives to LIA for knee arthroplasty? In terms of "best" pain relief, it is probably hard to beat a well-functioning epidural, as long as the catheter is in place and used for regular top-ups, infusion, or adjustments.[12] Still, the epidural technique does not seem to provide any pain protection or benefits beyond the period of active use, and during this period the technique demands resources and may result in some motor block with subsequent limitations in mobilization and physiotherapy.[12] Furthermore, there are risks of urinary retention and hypotension and very rare, but serious, hematoma formation. Femoral nerve block provides a more limited area and time period of focused pain relief, but includes motor block and carries the rare risk of nerve damage. In a recent study comparing LIA and femoral block for knee arthroplasty, Affas et al. found less movement pain with LIA at 24 hours and therefore recommended it. They also found the LIA less expensive and easier to perform than femoral block.[14] There may also be other blocks for more focused single knee pain relief without motor block, as presented in a recent preliminary report on adductor canal block of the saphenus and obturator nerves.[15]

Finally, we should not forget the more common alternative: multimodal nonopioid pain propylaxis combined with the spinal 0.1 mg morphine. In the expert evidence-based procedure-specific recommendation for knee arthroplasty,[a] the combination of either spinal (without opioid) or general anesthesia with femoral block is recommended as first choice for anesthesia, supplemented with paracetamol, nonsteroidal anti-inflammatory drugs regularly and opioid top-up when needed. The recommendation to avoid intrathecal morphine was based on nausea in a study that used a morphine dose of 0.25 mg[16] and may not be relevant with the 0.1-mg dose as used by Essving et al. Finally, other components of a multimodal drug analgesic strategy for total knee replacement may also include glucocorticoid[17] and gabapentinoid.[18]

In conclusion, the LIA method seems promising as a routine tool for analgesia after total knee replacement. Still, we need more clinical research along 2 important paths to move the LIA concept into its proper clinical place: The first is to test each component individually (keeping the rest unchanged and standardized) in very controlled and standardized conditions, to elucidate that what is working is LIA specific. The second path, that Essving et al. have started on, is to compare LIA with the best potential alternatives used most optimally: intrathecal opioid, epidural analgesia, femoral nerve block, other nerve blocks, or just optimal multimodal analgesia including local anesthesia wound infiltration.

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