A state-of-the-art pain protocol for total knee replacement

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Abstract
Total knee replacement is acknowledged as a successful and durable operation, but recovery from this surgery is often lengthy and painful. A great deal of attention has recently been directed at enhancing this recovery, most of which has focused on improvements in perioperative pain control. Various protocols have been suggested. This article discusses a pain management program that uses local infiltration analgesia with a specific “cocktail” which, when combined with an oral multimodal pain regimen, has led to excellent patient satisfaction and a substantially shorter length of stay.

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Introduction
Total knee replacements (TKRs) are known to be very successful procedures that are often associated with lengthy and painful recoveries. Great strides have been made in the last several years in minimizing patient discomfort and enhancing their recovery. Less invasive surgical approaches, more selective soft tissue balancing, improved patient education, and perhaps instrument and implant design have all contributed to an overall easier recovery for a patient undergoing TKR. However, improvements in pain control deserve the greatest credit for the more rapid recoveries that are now being seen [1].

Options for postoperative pain control include patient administered narcotics, epidural anesthetics, and spinal anesthetics with adjuncts such as long-acting morphine and peripheral nerve blocks (with and without catheters). These concepts are widely used, but there are reports of multiple side effects secondary to parenteral opioids and problems associated with motor blockade after nerve blocks, which can lead to delays in rehabilitation [2-4].

Because of dissatisfaction with the aforementioned modalities, the concept of a multimodal pain protocol, along with preemptive analgesia, has gained wide acceptance as a means of controlling pain after TKR. Most multimodal pain protocols currently include some combination of anti-inflammatories, nonnarcotic medications, and limited narcotic use. Perhaps the most important component of a multimodal pain protocol is the use of local infiltration analgesia (LIA). This article focuses on the use of a periarticular LIA combination technique.

Office tip
This comprehensive pain protocol after TKR has been very successful in my practice (Table 1).

Discussion
Modern pain protocols were developed as a result of both surgeon and patient recognition that advances were needed to improve patient recovery after TKR. The concepts of preemptive analgesia and multimodal pain protocols are commonly used. LIA is an important component of a multimodal protocol.

Since Kerr and Kohan [5] published one of the earliest reports of the benefits of an LIA pain protocol in 2008, a growing body of literature has supported this concept, along with a multimodal oral regimen that includes preemptive analgesics, and many studies have reported substantial improvements in patient recoveries with this regimen after TKR [2,5-9]. LIA offers several advantages over peripheral blocks, including the fact that they can be administered by the orthopaedic surgeon directly into the locally traumatized...
tissues, they do not require a particular skill set, and, importantly, they do not cause motor blockade, which enables patients to be more active earlier. The ability to avoid or limit the use of narcotics has many advantages for the patient.

Various “cocktails” have been suggested for the local injections. Most include a long-acting local anesthetic along with epinephrine and other additives such as opioids or ketorolac, corticosteroids, and various antibiotics [10-13]. Although little scientific data exist to help delineate the most effective combination, a prospective, randomized, double-blinded study to evaluate the efficacy of several ingredients in a periarctic “cocktail”—ropivacaine, epinephrine, ketorolac, and clonidine—that had been used for an LIA was undertaken [14]. The study showed that, overall, patient pain control was highest and functional outcome was enhanced when all 4 of the ingredients were combined. The particular mixture that was evaluated included ropivacaine 0.5% (49.25 mL), epinephrine 0.5 mg (0.5 mL), ketorolac 30 mg (1 mL), clonidine 80 mcg (0.8 mL), and sterile water (48.45 mL) for a total of 100 mL. The hospital pharmacist mixed the ingredients and delivered them in a sterile container each day for the day’s cases. The stability and sterility of this mixture at 48 hours was tested by an independent laboratory. In addition to having been shown to be effective in decreasing patient pain and enhancing earlier function, this mixture has the advantage that the ingredients are inexpensive (total estimated cost, $46) and easily available and, therefore, could be used in most centers.

Although no publications have been identified that demonstrate differences attributable to the method of injection, experience has shown that the technique of injection is also an important aspect of LIA. The goal is to deliver as much of the fluid as possible into the tissues, where it will be most effective. Using smaller needles, such as 22 gauge, is the best choice, and using control syringes (that allow for aspiration before injection and are also more comfortable for the hand) are helpful when injecting in areas of potential danger such as the posterior midline of the knee. Using 2 syringes allows the nurses to draw up the syringe as the surgeon is injecting and keeps the process moving. Multiple, small, slow injections are most effective. Aiming to deliver the injection into the areas that are known to be most sensitive, such as the periosteum, the posterior capsule, and the fat pad, is crucial. One should see an actual elevation of the periosteum off the femur to ensure that that tissue has been injected. One should aim to cover the entire surgical site, but it has been found that the skin incision needs the least amount (usually 10–15 mL).

Currently, an identical combination is used in each patient regardless of age, weight, and diagnosis. No nerve palsies nor any cases of intravascular injection have been identified, nor have any issues with skin healing, even with epinephrine in the mixture.

Although the LIA composition and method of delivery are the most important considerations in a comprehensive pain control (and rehabilitation) protocol, several other aspects are also essential to keep the patient comfortable: a supplemental multimodal pain program, control of nausea and vomiting, and limiting bleeding. Currently, the favored supplemental program consists of a nonsteroidal anti-inflammatory drug, acetaminophen, gabapentin, ketorolac, and a limited amount of short-acting oral narcotics, which work synergistically. Control of nausea and vomiting is accomplished with intravenous hydrocortisone sodium succinate for most patients, with liberal use of ondansetron as needed. The use of tranexamic acid has been extremely effective in limiting blood loss, bruising, and the need for transfusions and has been shown to be cost-effective [15,16]. There are several protocols for the use of this medication, but currently the regimen favored is 1 g intravenously at the time of incision and an additional 1 g at the time of skin closure for all patients, regardless of weight, unless the patient has a contraindication to the use of an antifibrinolytic.

### Table 1

| Medication by time point | Dose | Route | Frequency | Notes |
|--------------------------|------|-------|-----------|-------|
| **Preoperative**         |      |       |           |       |
| Celecoxib                | 400 mg | Oral  | 1 Dose | If allergic, meloxicam 15 mg may be substituted |
| Aprepitant               | 40 mg | Oral  | 1 Dose | For female patients with a history of PONV |
| Scopolamine transdermal patch | 1 mg | Transdermal | 1 Dose | For patients with a history of PONV |
| **Intraoperative**       |      |       |           |       |
| Ropivacaine              | 5 mg/mL (49.25 mL) | Intra-articular | 1 Dose | Local infiltrative analgesia; normal saline added to medications to total 100 mL; delivered with 22-gauge needle into periosteum of femur and tibia, as well as posterior capsule and arthroteny; minimal injection needed in skin incision |
| Ketorolac                | 30 mg/mL (1 mL) | Intra-articular | 1 Dose | |
| Epinephrine              | 1 mg/mL (0.5 mL) | Intra-articular | 1 Dose | |
| Clonidine                | 0.1 mg/mL | Intra-articular | 1 Dose | |
| **Postoperative**        |      |       |           |       |
| Ondansetron              | 4 mg | Intravenous | 1 Dose every 8 h | As needed for nausea |
| Solu-Cortef              | 100 mg | Intravenous | 1 Dose every 8 h | For 24 h |
| Oxycodone                | 5 mg | Oral | 1-2 Tablets every 4 h | As needed |
| Acetaminophen            | 1000 mg | Oral | 1 Tablet 3 times a day | Maximum 3 g/day |
| Celecoxib                | 400 mg | Oral | Once daily | |
| Tramadol                 | 50 mg | Oral | 1 Dose every 6 h | As needed; maximum 300 mg/day |
| Neurontin                | 300 mg | Oral | 1 Dose every 6 h | As needed |
| Ketorolac                | 30 mg | Intra-articular | 1 Dose | As needed for breakthrough pain |
| Hydromorphone            | 0.5 mg | Intra-articular | 1 Dose every 6 h | As needed |
| **Discharge**            |      |       |           |       |
| Celecoxib                | 400 mg (200 mg) | Oral | Once daily | 400 mg for 2 wk postoperatively (reduce dose to 200 mg for an additional 2 wk) |
| Hydrocodone              | 5/325 mg | Oral | 1-2 Tablets every 4 h | As needed |
| Gabapentin               | 300 mg | Oral | 1 Dose every 6 h | As needed |
| Zolpidem                 | 5-10 mg | Oral | 1 Dose every 4 h | As needed |

PONV, postoperative nausea and vomiting.
Summary

The combination of an effective, technically well-delivered LIA, in addition to a multimodal supplemental pain program and the use of tranexamic acid to control bleeding has revolutionized the postoperative recovery after TKR. Patient, nursing, and physical therapist satisfaction is extremely high. For the patient being discharged home (not being transferred to an inpatient rehabilitation center) after TKR, the average in-hospital length of stay has decreased to 1.2 days, with most patients being discharged within 24 hours, and all by 48 hours.

Enhanced pain control and early rehabilitation are desired by patients and surgeons alike. Although there are numerous choices by which to achieve these goals, the above combination has been found to be safe and extremely effective.

References

1. Dalury DF, Lieberman JR, MacDonald SJ. Current and innovative pain management techniques in total knee arthroplasty. J Bone Joint Surg Am 2011;93:1938.
2. 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.
3. 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;87:63.
4. Sharma S, Iorio R, Specht LM, Davies-Lepie S, Healy WL. Complications of femoral nerve block for total knee arthroplasty. Clin Orthop 2010;468:135.
5. 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.
6. Maheshwari AV, Blum YC, Shekhar L, Ranawat AS, Ranawat CS. Multimodal pain management after total hip and knee arthroplasty at the Ranawat Orthopaedic Center. Clin Orthop 2009;467:1418.
7. Muliagi A, Kanna R, Shetty GM, Chavda V, Singh DP. Efficacy of periarticular injection of bupivacaine, fentanyl, and methylprednisolone in total knee arthroplasty: a prospective, randomized trial. J Arthroplasty 2010;25:851.
8. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS. Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections. A prospective randomized study. J Arthroplasty 2007;22:33.
9. Vendittoli PA, Maksimov D, Drolet P, et al. A multimodal analgesia protocol for total knee arthroplasty. A randomized, controlled study. J Bone Joint Surg Am 2006;88:282.
10. Ashraf A, Raut VV, Canty SJ, McLauchlan GJ. Pain control after primary total knee replacement. A prospective randomised controlled trial of local infiltration versus single shot femoral nerve block. Knee 2013;20:324.
11. Kurosaka K, Tsukada S, Seino D, Morooka T, Nakayama H, Yoshida S. Local infiltration analgesia versus continuous femoral nerve block in pain relief after total knee arthroplasty: a randomized controlled trial. J Arthroplasty 2015. http://dx.doi.org/10.1016/j.arth.2015.10.030. Epub ahead of print Oct 30.
12. Spangehl MJ, Clarke HD, Hentz JC, Misra L, Blocher JL, Seamans DP. The Chitranjan Ranawat Award: periarticular injections and femoral & sciatic blocks provide similar pain relief after TKA: a randomized clinical trial. Clin Orthop 2015;473:45.
13. Tsukada S, Waku M, Hoshino A. Postoperative epidural analgesia compared with intraoperative periarticular injection for pain control following total knee arthroplasty under spinal anaesthesia: a randomized controlled trial. J Bone Joint Surg Am 2014;96:1433.
14. Kelley TC, Adams MJ, Mulliken BD, Dalury DF. Efficacy of multimodal periprosthetic analgesia protocol with periarticular medication injection in total knee arthroplasty: a randomized, double-blinded study. J Arthroplasty 2013;28:1274.
15. Gillette BP, Maradit Kremers H, Duncan CM, et al. Economic impact of tranexamic acid in healthy patients undergoing primary total hip and knee arthroplasty. J Arthroplasty 2013;28:137.
16. Georgiadis AG, Muh SJ, Silvertown CD, Weir RM, Laker MW. A prospective double-blind placebo controlled trial of topical tranexamic acid in total knee arthroplasty. J Arthroplasty 2013;28:78.