
Critique author: Linda Metzger 7-31-15

Design: Randomized clinical trial

Objective: To compare two modalities of postoperative pain management which included a combined femoral and sciatic nerve block with periarticular injection as part of a multimodal pain protocol after total knee arthroplasty (TKA) with respect to pain, narcotic use, quadriceps function and length of stay, and peripheral nerve complications.

Population /sample size/setting:

- A total of 160 patients who presented for unilateral TKA were recruited sequentially at the Mayo Clinic in Phoenix, Arizona for this study (89 females, 71 males, mean age 68 years, mean BMI 31), and randomized into 2 groups in a one-to-one ratio resulting in 79 patients in the peripheral nerve block group (PNB) and 81 patients in the periarticular injection group (PAI).
- Study design was a randomized controlled trial.
- Inclusion criteria included patients 18 to 79 years of age with a weight between 50 and 125 kg. and who presented for unilateral TKA.
- Exclusion criteria included prior knee surgery using a peripheral nerve block or periarticular injection, an allergy to any of the medications used, renal insufficiency, or those taking regular narcotic medications before surgery (≥ 20 mg/day of morphine equivalent for >7 days).

Methods/Interventions/Outcome Measures:

- Allocation was concealed by storing the treatment allocation schedule on a randomization web site that indicated the treatment assignment after recording the subject’s identifier.
- The PNB group received a continuous femoral nerve block with an indwelling catheter and a single-shot sciatic nerve block. This technique includes preprocedure sedation with midazolam and fentanyl, identification of the femoral nerve by landmarks or ultrasound, further localization by a nerve stimulator, and subsequent infiltration of 30 mL 0.5% ropivacaine. The infusion by the femoral catheter was discontinued on the morning of postoperative day 2.
- Patients in the PAI group received a periarticular injection cocktail, based on three weight categories, of ropivacaine, epinephrine, ketorolac, and morphine sulphate with normal saline added to bring the volume to 120 mL.
- All surgical procedures were performed in a standardized manner for all patients.
- Preoperatively all patients received the same combination of oral medication.
  Postoperatively all patients were prescribed scheduled analgesic medications as well as standardized narcotics for breakthrough pain.
- The primary outcome measure was the patient’s postoperative pain score on the afternoon of postoperative day 1. This pain score was measured at rest on a linear analog scale from...
0 to 10 points before the patient’s afternoon physical therapy session on the day after surgery (postoperative day 1).

- The secondary outcomes included pain scores measured at rest at other standardized times during hospitalization, self-reported feeling of nausea (scale from 0 to 10 with 0 = no nausea and 10 = extreme nausea), return of quadriceps function assessed as quadriceps extensor lag and ability to straight-leg raise, narcotic use, length of hospital stay, and peripheral nerve complications related to either the peripheral nerve block or injection assessed at 6-week follow-up.

- Estimated sample size was 75 patients per group yielding a power of 80% (a = 0.05) to detect a difference of 1 point (0.5 SD) on the primary outcome measure of pain.

- Data were analyzed according to intent-to-treat principle.

- A subgroup analysis was also performed on patients who received the allocated treatment as per the planned protocol.

Results:

- Baseline characteristics displayed no significant differences between the 2 treatment groups.

- The mean pain score on the afternoon the day after surgery (main outcome measure) did not differ between the two groups (PNB group 2.9, PAI group 3.0, 95% CI = -0.8 to 0.6, p = 0.76). The per-protocol subgroup analysis yielded similar results.

- Mean pain scores taken at three other times points on the day after surgery (postoperative day 1) were also similar between groups.

- On the day of surgery, significantly fewer patients reported pain in the PNB group than in the PAI group on arrival in the patient’s room and on the evening of the day of surgery. All other recorded times had no significant differences in pain scores between the two groups.

- Narcotic consumption intraoperatively and on the day of surgery was significantly lower in the PNB group than in the PAI group (intraoperative: PAI group, 23.6 mg morphine equivalents, PNB group: 17.4, 95% CI = -9.1 to -3.3, p<0.001); day of surgery: PAI group 11.7 mg morphine equivalents, PNB group, 4.6 mg, 95% CI = -10.6 to -3.6, p<0.001). The mean narcotic dose did not differ between groups after the day of surgery.

- The incidence of nausea did not differ between groups on the day of surgery or the day after surgery. The incidence of nausea was slightly higher in the PNB group than in the PAI group on the second day after surgery.

- Quadriceps function was significantly lower in the PNB group than in the PAI group. Fewer patients in the PNB group were able to perform a straight-leg raise, with or without extensor lag, during the first 2 days after surgery. On the morning of day 1, 19 (24%) of the PNB group could perform a straight-leg raise versus 63 (79%), (95% CI = -0.67 to -0.41, p<0.001) in the PAI group. By the afternoon of postoperative day 2, for those remaining in the hospital, quadriceps function no longer differed between the two groups.

- Mean length of stay was 0.4 days longer in the PNB group than in the PAI group (2.84 days PNB and 2.44 days PAI group; 95% CI, 0.1 to 0.7; p = 0.02).

- Postoperative sensory changes or peripheral nerve injury, mainly as a dysesthesia, assessed at 6 weeks follow-up were significantly more common in the PNB group than in
the PAI group. Twelve percent (9 of 77) of patients in the PNB group experienced sensory change versus one percent (1 of 79) in the PAI group (p = 0.009). No motor changes were observed in either group.

- The type of postoperative pain management may also have played a role in another postoperative adverse event, accidental falls. Three patients in the PNB group and no patient in the PAI group fell postoperatively, but this difference was not significant. (p = 0.12).

Authors’ conclusions:

- Patients receiving periarticular injections had similar pain scores, shorter lengths of hospital stay, less likelihood of peripheral nerve dysesthesia, but greater narcotic use on the day of surgery compared with patients receiving peripheral nerve blocks. Periarticular injections provide adequate pain relief, are simple to use, and avoid the potential complications associated with nerve blocks.
- Both modalities of postoperative pain management showed beneficial effects and no significant difference between treatment groups was found on the primary outcome measure of pain.
- Strengths of this study include its randomized design, and standardized patient care medications, surgical procedure, and postoperative therapy protocols. It was adequately powered and relatively homogeneous. Patients with prior knee surgery or who were narcotic-tolerant were excluded. Patient evaluations conducted at 6 weeks follow-up beyond the hospitalization for any neurologic complications related to the surgery were another strength of the study.
- One limitation of the study was the inability to blind patients and staff to the treatment arms that each patient received, because the presence of the femoral catheter and neurological changes expected from peripheral blocks make it obvious as to which group the patients were allocated.
- The only complication that was statistically different between the two groups was neuritis. Nine patients (12%) in the PNB group versus one (1%) in the PAI group reported sensory changes 6 weeks postoperatively. These changes were typically described as a dysesthesia in the distribution of the nerve.
- Another limitation of the study was that patients’ pain was evaluated at rest and not with activity. It might be expected that both groups would have proportionally higher pain with activity and hence no difference between the groups.
- Since length of hospital stay data was calculated from the medical records and not necessarily when the patient was deemed ready for discharge, this result may present some bias. Randomization should eliminate any bias regarding length of stay data, because all patients had the same postoperative physical therapy protocol.
- Another limitation was that the study was not powered to identify certain rare events such as falls. A larger sample may have shown significance in the trend of more falls in the peripheral nerve block group.
- Although the study found a statistically shorter length of stay (almost a half day less) in the PAI group, this may not translate into significant savings because the majority of cost is incurred early in the hospital stay for joint replacement.
Based on the results of this study, the authors now use periarticular injections in combination with scheduled analgesic medications instead of peripheral nerve blocks with multimodal medications for routine pain management after knee arthroplasty.

Comments:

- The primary outcome of the pain score on the afternoon of postoperative day 1 was chosen because it was felt that the periarticular injection would have lost all or the majority of its effect by this time and therefore this would reflect a “truer” evaluation of differences between the two methods. Even with using this “truer” time point for evaluation, the results still indicated no difference in pain scores between the 2 groups.
- Despite similar pain scores, narcotic use intraoperatively and on the day of surgery was greater in the PAI group. The increased intraoperative use in this group of patients may be related to the lack of local anesthetic blockade during the surgery.
- This study found that pain scores did not differ between the two groups for the primary outcome, even though pain scores were statistically higher the day of surgery in the PAI group compared to the PNB group. The differences between the two groups at those time points were less than 1 point, thus unlikely to be clinically relevant.
- Not surprisingly, the return of quadriceps function was slower in the PNB group. The earlier return of quadriceps function in the PAI group allowed patients to be mobilized faster and resulted in nearly a half day less length of hospital stay.
- Even though it was not possible to blind patients or staff to each patient’s treatment allocation during assessments taken during the patient’s hospital stay, it is unclear if the assessors at the 6-week follow-up evaluating postoperative sensory changes and peripheral nerve injury, mainly as a dysesthesia, were blinded to treatment assignment. This outcome could be susceptible to detection or assessment bias if outcome assessors were not blinded.
- Twelve percent of patients in the PNB group experienced postoperative sensory changes or peripheral nerve injury, mainly as a dysesthesia, 6 weeks after surgery. Only one percent experienced these complications in the PAI group. This is truly an adverse event caused by the PNB, and by itself warrants a no-recommendation.
- Periarticular injections provide comparable pain management to peripheral nerve blocks, are simpler to administer, are less costly, allow for a sooner return to quadriceps function, avoid the sensory dysesthesia seen in a small number of patients with nerve blocks, and result in a slightly reduced length of hospital stay.

Assessment:

- This adequate study provides some evidence that periarticular injections provide comparable pain relief to femoral sciatic nerve blocks as part of postoperative pain management in patients after total knee arthroplasty, but peripheral nerve blocks have a higher rate of peripheral nerve dysesthesia 6 weeks after surgery.