Chan EY, Fransen M, et al. Femoral nerve blocks for acute postoperative pain after knee replacement surgery. Cochrane Database of Systematic Reviews 2014, Issue 5. Art #CD009941

Study type: Meta-analysis of randomized clinical trials

Study question: Do femoral nerve blocks at the time of total knee replacement reduce pain and opioid use compared to patient-controlled opioid analgesia and other pain control treatments during the time the patient is in the hospital?

PICOS:

- Patient population: adults undergoing total knee replacement (TKR) surgery
- Intervention: Femoral nerve block (FNB) inserted preoperatively, operatively, or postoperatively, either single shot or continuous infusion
- Control intervention: Non-FNB analgesia, either patient-controlled analgesia (PCA) with intravenous opioid, epidural analgesia, local infiltration analgesia, or oral analgesic medication
- Outcomes: Primary outcomes were pain on movement and pain at rest, as well as serious adverse events
    - Secondary outcomes included opioid consumption, physical function (such as range of motion), patient satisfaction with analgesia during the hospital stay, and others
- Study types: Randomized trials; quasi-randomized trials (such as those using alternation) and observational studies were excluded

Study selection:

- Databases for literature search included MEDLINE, EMBASE, CINAHL, ISI Web of Science, and the Cochrane Central Register through January 2013
- Two authors independently screened articles for inclusion and assessed quality for risk of bias with criteria of random sequence generation, allocation concealment, blinding of patients/personnel, blinding of outcome assessment, completeness of outcome data, selective reporting of outcomes, and intention-to-treat analysis for primary outcomes
- Most treatment effects were estimated in terms of standard mean differences, in which the difference in outcome (such as pain) is reported as how many standard deviations separate the treatment groups
    - 0.2 to 0.5 SD is a small effect; 0.5 to 0.8 SD is a moderate effect, and 0.8 SD or greater is a large effect

- The authors assumed that the treatment effects would be heterogeneous between studies, and planned for all meta-analyses to use a random effects model

Results:

- The search led to a review of 87 full text articles, of which 45 RCTs with 2710 participants were selected for inclusion
- A large number of analyses were performed, many of them on the basis of single studies, but the principal analyses had enough studies to combine the results of different studies of the same intervention
    - FNB with or without PCA opioid versus PCA opioid for pain at rest and pain on movement at 24 hours
    - FNB versus epidural analgesia for pain at rest and on movement at 24 hours
    - FNB versus infiltration analgesia
    - FNB versus oral analgesia
    - Continuous versus single shot FNB
- Many meta-analyses showed significant heterogeneity between studies, but the source of heterogeneity was a matter of large versus moderate or small effect sizes, not in the direction of the effect; that is, the combined studies almost all agreed on the direction of the effect, and differed with respect to its magnitude
- For FNB versus PCA opioid on pain at rest at 24 hours, 19 studies with 1066 participants demonstrated lower pain (0.72 SD) with FNB; at 48 hours, data from 17 studies with 957 patients demonstrated lower pain (0.64 SD) with FNB
    - For FNB plus PCA opioid versus PCA opioid alone, 15 studies with 771 participants demonstrated less pain with FNB (0.67 SD)
    - For FNB without PCA opioid versus PCA opioid, 5 studies with 295 participants also demonstrated less pain with FNB (0.93 SD)
    - A similar pattern was seen with pain with movement
    - For opioid consumption at 24 hours, 20 studies with 1152 participants demonstrated that FNB reduced opioid use by 14.74 IV morphine equivalents; the effect at 48 hours was similar (14.53 IV morphine equivalents)
- For FNB versus epidural analgesia, no difference in pooled pain scores at rest or with movement were demonstrated in the first 72 hours using 6 studies with 328 participants
    - FNB and epidural analgesia did not demonstrate statistically significant differences in opioid use at 24 or 48 hours
- For FNB versus local infiltration with agents such as ropivacaine and ketorolac, pooled results did not show differences between FNB and local analgesia when results from 4 studies with 216 participants were combined
    - No differences were found with respect to opioid consumption either

- For FNB versus oral analgesia, only one study with 62 participants was included; it compared FNB with oral hydrocodone/acetaminophen with oral hydrocodone/acetaminophen alone, and found that the pain scores were lower with FNB plus hydrocodone/acetaminophen (3 VAS points at 24 hours and 2 VAS points at 48 hours); because only a single study was included and no pooling of data was possible, raw VAS differences rather than standardized mean differences were reported
- For continuous FNB versus single-shot FNB, pooled data from 4 studies with 272 participants showed less pain at rest with continuous FNB at 24 hours (0.62 SD); at 48 hours, the difference in favor of continuous FNB was 0.96 SD
    - Opioid use was also lower with continuous FNB in 3 trials with 236 participants; at 24 hours, the difference was 13.8 mg morphine equivalent; at 46 hours, the difference was 14.6 morphine equivalents
- Some sensitivity analyses were done in which study quality features were assessed
    - Allocation concealment was adequate in some studies and not in others; however, the comparisons of FNB with other interventions was robust to this feature
    - Blinding was also adequate in some studies more than in others; however, although the effect sizes in favor of FNB were slightly smaller with adequate blinding, the results remained robust to this analysis

Authors' conclusions:

- Following total knee replacement, FNB is superior to PCA opioid, whether FNB is or is not accompanied by PCA opioid in reducing pain at rest and with movement
- FNB and epidural analgesia did not differ significantly with respect to analgesic effectiveness
- Continuous FNB was superior to single shot FNB for postoperative analgesia
- Effectiveness beyond 72 hours is not known because of a lack of data
- The heterogeneity of effect sizes probably arose from differences in drug concentrations, supplemental analgesics, and different local anesthetics, among other factors
- FNB, in particular continuous FNB, is likely to be favored over PCA opioid
- More research needs to be done in comparing FNB with local anesthetic infiltration, since the potential for cardiac toxicity is a matter of concern with infiltration of anesthetics

Comments:

- While the meta-analysis is very lengthy and makes a large number of subgroup comparisons, the principal results are less complex and favor FNB over PCA opioid for pain control following total knee replacement

- Publication bias is briefly discussed with results in Appendix 10
    - Its interpretation is that there were 19 studies of FNB versus PCA opioid analgesia for pain at rest at 24 hours, with an effect size of 0.72 SD in favor of FNB (a moderate to large effect size); the fail-safe N of 60 means that there would need to be 60 unpublished trials of comparable size but with null results (where FNB and PCA were equally effective) to reduce the pooled effect size to a clinically unimportant value of 0.2 SD (the cutoff for declaring a small effect)
        - The next line in Appendix 10 means that there were 9 studies with a low risk of bias for the same issue, and these had a pooled effect size of 0.54 SD in favor of FNB; it would require 18 unpublished and unbiased studies to reduce this to a trivial effect size of 0.2 SD

Assessment: High quality meta-analysis supporting evidence that FNB reduces postoperative pain from total knee replacement more effectively than patient-controlled opioid intravenous analgesia, and that total opioid use in the immediate postoperative period is also lower with FNB than with PCA opioids