Continuous Peripheral Nerve Blocks

Is Local Anesthetic Dose the Only Factor, or Do Concentration and Volume Influence Infusion Effects as Well?


ABSTRACT

Background: The main determinant of continuous peripheral nerve block effects—local anesthetic concentration and volume or simply total drug dose—remains unknown.

Methods: We compared two different concentrations and basal rates of ropivacaine—but at equivalent total doses—for continuous postoperative pain control following total knee arthroplasty.

Results: Quadriceps MVIC for patients receiving 0.1% ropivacaine (n = 28) declined by a mean (SE) of 64.1% (6.4) versus 68.0% (5.4) for patients receiving 0.4% ropivacaine (n = 24) between the preoperative period and the day after surgery (95% CI for group difference: -8.0–14.4%; P = 0.70). Similarly, the groups were found to be equivalent with respect to secondary endpoints.

Conclusions: For continuous postoperative lumbar plexus blocks, local anesthetic concentration and volume do not influence nerve block characteristics, suggesting that local anesthetic dose (mass) is the primary determinant of perineural infusion effects.

What We Already Know about This Topic

❖ Whether the main determinant of continuous peripheral nerve block effects is local anesthetic concentration and volume or simply total drug dose is unknown

What This Article Tells Us That Is New

❖ After hip arthroplasty, patients with continuous lumbar plexus nerve blocks required the same milligram per hour of ropivacaine in a dilute (0.1%) solution as in a concentrated one (0.4%) and had the same degree of motor block.

❖ Over these concentrations and conditions, lower ropivacaine concentration did not result in less motor block.

Continuous peripheral nerve blockade involves the percutaneous insertion of a catheter directly adjacent to a nerve. The catheter is then infused with local anesthetic resulting in potent, site-specific analgesia (among other
benefits) that lasts well beyond the normal duration of a single-
injection nerve block.1,2 However, one well-recognized side ef-
effect is muscular weakness,3 particularly undesirable in the con-
tinuous psao compartment and femoral nerve blocks that affect
quadriiceps femoris function required for ambulation. Con-
erising that these perineural infusions are often provided for an-
algnesia after hip and knee surgical procedures in elderly
patients,5,6 and in this patient population a fall may prove cat-
atrophic, it is imperative that any risks be minimized.

Because quadriiceps femoris weakness is associated with
significant functional disability8 and an increased risk of falls in
elderly patients,9 it is postulated that any nerve block-
induced muscular weakness is best minimized during peri-
nearal local anesthetic infusion.10 Many different local anes-
thetic concentration and basal-rate combinations have been
proposed: for ropivacaine alone, concentrations have in-
cluded 0.1%,11 0.15%,12 0.2%,13 0.25%,14 0.3%,15 and
0.4%.16 However, optimizing infusion characteristics is dif-
ficult, given that it is currently unknown whether the
primary determinant of continuous peripheral nerve
block effects is simply total drug dose (mass) or whether
local anesthetic concentration or volume exert an addi-
tional influence.

We therefore tested the hypothesis that providing ropiva-
caine at different concentrations and rates (0.1% at 12 ml/h vs.
0.4% at 3 ml/h)—but at an equivalent total basal (12 mg/h)
and patient-controlled bolus doses (4 mg)—produces compa-
rable effects when used in continuous posterior lumbar plexus
blocks after hip arthroplasty. The primary endpoint was the
difference in maximum voluntary isometric contraction
(MVIC) of the quadriiceps the morning after surgery compared
with the preoperative MVIC, expressed as a percentage of the
preoperative MVIC. Secondary endpoints included hip adduc-
tor and hip flexor MVIC changes, sensory changes in the fem-
oral nerve distribution, hip range-of-motion, ambulatory abil-
ity, pain scores, and ropivacaine consumption.

Materials and Methods

Enrollment

The local Institutional Review Board (University of Califor-
nia San Diego, San Diego, CA) approved all study proce-
dures. The trial was prospectively registered at clinicaltrials.
gov (NCT00912873). Patients offered enrollment included
adults (≥18 yr) scheduled for primary, unilateral hip arthro-
plasty via a 15–25-cm curvilinear lateral skin incision cen-
tered over the greater trochanter (either hip resurfacing or
hip replacement) who desired a continuous posterior lumbar
plexus block for postoperative analgesia. Exclusion criteria
included a history of opioid dependence or abuse, current
chronic analgesic therapy (daily use > 20 mg oxycodone-
equivalent opioid use within the 2 weeks before surgery and duration of use > 4 weeks), allergy to study medications,
known hepatic or renal insufficiency/disease, peripheral neu-
ropathy of the surgical extremity, body mass index > 40
kg/m², pregnancy, or incarceration.

Preoperative Management

All participants provided written, informed consent before
any study procedures. Before surgery, subjects had baseline
endpoints measured (endpoint details provided below) by a
single physical therapist (L.K.M.). Subjects were then placed
in the lateral decubitus position with the operative hip up.
Intravenous fentanyl and midazolam were titrated for patient
comfort. The area that would be subsequently covered by the
catheter dressing and tape was prepared with chlorhexidine
gluconate and isopropyl alcohol (ChloraPrep One-Step, Medi-
Flex Hospital Products, Inc., Overland Park, KS) and
then shaved with a surgical hair clipper, if necessary. After
sterile preparation (additional ChloraPrep One-Step) and
draping, a local anesthetic skin wheal was raised at the needle
entry point similar to previously described landmarks.4 With
the bevel-directed caudad, a 102- or 152-mm, 18-gauge,
insulated needle (Contiplex, B. Braun Medical, Inc., Bethle-
hem, PA) was inserted with the long axis perpendicular to the
skin. This needle was connected to a nerve stimulator (Stimu-
pulse-DIG, B. Braun Medical, Inc.) initially set at 1.2 mA, 0.1
ms, and 2 Hz. With gentle aspiration applied to aid in identifi-
cation of a penetrated vessel, the needle was redirected, as
needed, until quadriiceps contractions and patellar motion were
elicited with a stimulating current of 0.20–0.40 mA.

Subsequently, 15 ml of D₂/W was injected in divided
doses. The standard multiforice perineural catheter that
came packaged with the needle was replaced with a similar
catheter with only a single orifice at its tip (B. Braun Medical
Inc.). The catheter was advanced 1 cm past the needle tip and
the needle withdrawn over the catheter. If the catheter met
resistance at the needle tip, the catheter tip was left at the
needle tip location and the needle withdrawn over the catheter.
In both cases, the catheter was inserted an additional 2 cm while
holding the needle stationary once the needle tip had been with-
drawn at least 3 cm from its original location. The injection port
was attached to the catheter and the catheter secured with sterile
liquid adhesive, an occlusive dressing, tape, and an anchoring
device on the ipsilateral shoulder.17

Fifteen milliliters of 2% mepivacaine with epinephrine (5
µg/ml) was slowly injected via the catheter with gentle aspi-
ration every 3 ml. Catheter placement was considered suc-
cessful if, within 15 min, the patient experienced a decreased
sensation to cold temperature over the ipsilateral distal thigh
dehiscence, and weakness upon knee extension. Patients with a suc-
cessful nerve block had their catheters replaced or were with-
drawn from the study.

Randomization

Remaining patients were randomized to one of the two treat-
ment groups—ropivacaine 0.1 or 0.4%—in blocks of four,
stratified by hip arthroplasty procedure (either total or resur-
fac ing) using computer-generated tables available only to the
Investigational Drug Service. The basal rate and patient-con-
trolled bolus volume depended on the treatment group (table 1). Although the basal rate and bolus volume differed for each concentration, the total dose of local anesthetic was the same for all patients. A portable electronic infusion pump (Pain Pump 2 Blockaid, Stryker Instruments, Kalamazoo, MI) was filled with study infusate and programmed by investigational pharmacists and delivered to the operating room of each subject. Although patients were not specifically informed of their ropivacaine concentration, the infusion pumps that were accessible to subjects revealed enough information that subjects should not be considered masked to treatment group.

Intraoperative Management

Patients were administered a standardized general anesthetic using inhaled sevoflurane, nitrous oxide, and oxygen during surgery. The ropivacaine infusion was initiated via the perineural catheter before the end of surgery, with the exact time recorded for study purposes. Intravenous fentanyl (25 μg/kg) was administered in the operating room of each subject. Although patients were not specifically informed of their ropivacaine concentration, the infusion pumps that were accessible to subjects revealed enough information that subjects should not be considered masked to treatment group.

Postoperative Management

In addition to the ropivacaine perineural infusion initiated in the operating room and continued at least through postoperative day 2, all patients were provided oral acetaminophen (975 mg every 6 h), celecoxib (200 mg every 12 h), and sustained-release oxycodone (OxyContin, 10 mg every 12 h). For breakthrough pain, patients were instructed to depress the bolus button on their pump and wait 15 min for the effect. Rescue opioid and route of administration were titrated to pain severity using a numeric rating scale (NRS) of 0–10, with 0 equal to no pain and 10 being the worst imaginable pain; mild pain (NRS < 4): oral oxycodone 5 mg, moderate pain (NRS 4–7): oral oxycodone 10 mg, and severe pain (NRS > 7): intravenous morphine sulfate was titrated to a respiratory rate of 12–14 just before emergence.

Sensory Effect

We evaluated femoral nerve tolerance to transcutaneous electrical stimulation with the same quantitative procedure as the one described previously. Electrocardiogram pads were placed over the proximal patella and quadriceps tendon, and attached to a nerve stimulator (Model NS252; Fisher & Paykel, Auckland, New Zealand). The current was increased from 0 mA until subjects described mild discomfort at which time the current was recorded as the tolerated level and the nerve stimulator turned off.

Ambulatory Ability

We evaluated ambulatory ability using the 30-m walking test and 6-min walk test. The 30-m walking test simply measures the amount of time it takes patients to ambulate 100 ft. After patients ambulated 100 ft, they were instructed to continue walking and the total distance covered in the first 6 min was recorded as the result of the 6-min walk test. Patients were allowed to slow or stop and rest during the walk but were...
asked to resume walking as soon as they felt they were able to. The maximum ambulatory distance was also recorded.

**Hip Range-of-Motion**

We evaluated hip range-of-motion using standard goniometry for passive hip flexion with patients in the supine position before ambulation. A maximum of 90° was permitted to decrease the risk of femoral head dislocation.

**Pain**

We evaluated all pain measurements using the 0–10 NRS. Pain scores were recorded immediately after physical therapy, every 4 h (except when patients were sleeping), and when patients requested analgesics.

**Statistical Analysis**

Sample size calculations were centered around our primary hypothesis that differing the concentration (0.1 vs. 0.4%) while providing an equal total dose of ropivacaine through a psoas compartment catheter after hip arthroplasty has no impact on the percentage of quadriceps muscle strength retained the morning after surgery compared with preoperative strength (expressed as a percentage of the preoperative MVIC). We considered a difference of 15% points to be clinically relevant because a 10% side-to-side strength difference is common, yet functionally unnoticeable in healthy individuals. With an SD of each group of 17 (based on unpublished data, Brian Ilfeld, M.D., M.S., San Diego, California, March 2008) and assuming a two-sided type I error protection of 0.05 and a power of 0.80, approximately 21 patients in each group were required (StatMate 2.0; GraphPad Software, San Diego, CA). To allow for a larger SD than anticipated or potential drop-out, we randomized 25 subjects per group.

Because the aim of the study was to evaluate equivalency (because of a proposed hypothesis of no group effect), standard inferential statistics used to demonstrate statistically significant nonzero effects do not strictly apply. Instead, we used the method described by Armitage et al. for equivalency trials, whereby we conclude equivalency if the 95% confidence interval falls within the prespecified range, i.e., 8.0 to 14.4%; 0.35). Because the confidence interval falls within the prespecified range, we found that the effect of the two concentrations on quadriceps MVIC was equivalent.

**Secondary Endpoints**

The 95% confidence intervals for the estimated group differences in quadriceps femoris (fig. 1), hip adductor (fig. 2), or tolerance of transcutaneous electrical stimulation in the cutaneous distribution of the femoral nerve (fig. 4) all fell within prespecified tolerances and were therefore deemed equivalent. The amount of ropivacaine delivered was 13.0 (0.8) mg/h for patients receiving 0.1% ropivacaine compared with 13.2 (0.9) mg/h for patients receiving 0.4% ropivacaine (P = 0.83). Total intravenous morphine equivalents were 26 (3) and 26 (4) mg for patients receiving 0.1 and 0.4%, respectively (P = 0.35). There was no statistically significant difference between groups in any of the additional secondary endpoints (table 3). There were no patient falls in either treatment group, and no patient required a decrease in their basal infusion rate because of quadriceps weakness.

### Table 2. Demographic, Anthropometric, and Surgical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine 0.1% (n = 26)</th>
<th>Ropivacaine 0.4% (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>53 (3)</td>
<td>52 (4)</td>
</tr>
<tr>
<td>Sex (female/male)</td>
<td>11/15</td>
<td>9/15</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172 (2)</td>
<td>171 (2)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>80 (3)</td>
<td>77 (3)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27 (1)</td>
<td>26 (1)</td>
</tr>
<tr>
<td>Procedure (total arthroplasty/resurfacing)</td>
<td>17/9</td>
<td>16/8</td>
</tr>
<tr>
<td>Surgery duration, min</td>
<td>132 (7)</td>
<td>132 (7)</td>
</tr>
</tbody>
</table>

Values are reported as mean (SE) or number of subjects.

Results

During a 12-month period beginning June 2008, 56 patients were enrolled in this study. Three subjects were withdrawn from the study before catheter insertion (exclusion criteria identified after enrollment but before randomization). Of the remaining 53 subjects, 50 had a psoas compartment perineural catheter successfully inserted per protocol (in three subjects, an evoked motor response could not be elicited at a current <0.5 mA as required by the study protocol). All 50 subjects exhibited a sensory and motor block within 15 min after being given a local anesthetic bolus via the catheter. Subjects were randomized to one of the two treatment groups, and these two groups were similar in demographic, anthropometric, and surgical characteristics (table 2).

**Primary Endpoint**

Quadriceps MVIC for patients receiving 0.1% ropivacaine (n = 26) declined by a mean (SE) of 64.1% (6.4) versus 68.0% (5.4) for patients receiving 0.4% ropivacaine (n = 24) between the preoperative period and the day after surgery (95% CI for the group difference: −8.0 to 14.4%; P = 0.70). Because the confidence interval falls within the prespecified range, we found that the effect of the two concentrations on quadriceps MVIC was equivalent.
Discussion

This investigation provides evidence that local anesthetic concentration and volume do not influence the effects of continuous posterior lumbar plexus nerve blocks. This finding suggests that local anesthetic dose (mass) is the primary determinant of perineural infusion effects. Three previous studies investigated this topic involving popliteal, infraclavicular, and interscalene perineural infusion. However, those reports failed to provide a definitive answer because of two protocol limitations common to all three studies: (1) the primary endpoint—the incidence of an insensate extremity over a 24-h period—lacked objective measurement and had not been previously validated; (2) the number of patient-controlled bolus doses administered was unavailable; therefore, the total hourly local anesthetic dose could not be calculated. This study was specifically designed to correct these weaknesses: (1) the primary outcome variable—quadriceps femoris MVIC—is a validated, reproducible, objective endpoint; (2) the total hourly local anesthetic consumption was available from the portable electronic infusion pumps. There are additional dose-response studies involving continuous peripheral nerve blocks. However, these studies varied either local anesthetic concentration or rate/volume while holding the other constant, resulting in differing drug doses. When both variables were allowed to vary, an equal mass among groups was not required. Our study is thus unique in that it varied both concentration and infusion rate in a static ratio so that the total dose from the basal infusion was comparable in each treatment group and corrected for previous weaknesses in similar studies. This allowed for the first valid examination of the relative importance of local anesthetic dose compared with concentration/volume during perineural infusion.

Clinical Importance

The relative importance of local anesthetic concentration/volume versus dose has significant clinical consequence, given the wide range of local anesthetic concentrations the investigators have used for perineural infusion. The issue has particular importance for lower extremity perineural in-
fusions. Although inhibition of pain fibers is the primary goal for postoperative continuous peripheral nerve blocks, currently available local anesthetics approved for clinical use decrease other afferent (e.g., nonpain-related sensory and proprioception) and efferent (e.g., motor) nerve fibers as well, resulting in undesirable side effects such as muscular weakness. There is growing evidence that lower extremity continuous peripheral nerve blocks may increase the risk of patient falls, although to what degree the perineural local anesthetic infusion was a contributing factor in these cases remains unknown because the studies were neither designed nor powered to detect such (presumably) rare complications. Nonetheless, patient falls during perineural infusion are now being highlighted in the surgical and anesthesiology literature.

Related to the issue of infusion-induced muscle weakness, in a previous study involving continuous femoral nerve blocks after knee arthroplasty, 43% of patients receiving 0.2% ropivacaine at 8 ml/h (vs. 12% of patients receiving perineural saline) required a decrease in their basal infusion rate because of quadriceps weakness limiting ambulation.3

This suggests that an initial basal rate of 8 ml/h is too high for many patients when using 0.2% ropivacaine. However, simply decreasing the concentration of local anesthetic may provide insufficient analgesia, as reported in an excellent dose–response study. A great deal of further research is required to both maximize the benefits of perineural local anesthetic infusion while concurrently minimizing the associated risks. Although the results of this study are the most definitive to date regarding the issue of the relative importance of local anesthetic dose versus concentration/volume during perineural infusion, these data should be viewed as a reference point to help design future clinical trials.

Until additional data are available, practitioners may want to consider steps that may minimize the risk of falls, including minimizing the dose/mass of local anesthetic; providing limited-volume patient-controlled bolus doses that allow for a decreased basal dose without compromising analgesia in...
some cases\textsuperscript{41,42}—although not all\textsuperscript{13}; using a knee immobilizer and walker/crutches during ambulation\textsuperscript{96}; and educating physical therapists, nurses, and surgeons of possible continuous peripheral nerve block–induced muscle weakness and necessary fall precautions. Of note, in one study involving continuous posterior lumbar plexus blocks, local anesthetic dose (mass) is the primary determinant of perineural infusion effects.

### Study Limitations

Subjects and nearly all investigators were not masked to treatment group. Yet, it is unlikely that patients had a bias toward one concentration. In addition, endpoint measurements were performed by a physical therapist masked to treatment group assignments. Furthermore, the current finding that local anesthetic dose and not concentration or volume influences the effects of continuous posterior lumbar plexus blocks may not be applicable to other anatomic catheter locations.\textsuperscript{29–31}

In summary, for continuous posterior lumbar plexus blocks, local anesthetic concentration and volume do not influence nerve block characteristics. This finding suggests that local anesthetic dose (mass) is the primary determinant of perineural infusion effects.

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### References


5. Ilfeld BM, Le LT, Meyer RS, Mariano ER, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, Berry LF, Spadoni EH, Gearen PF: Ambulatory continuous femoral nerve blocks decrease time to discharge readiness after tricompartment total knee arthroplasty: A randomized, triple-

### Table 3. Secondary Endpoints (All Values Postoperative Day 1, Unless Otherwise Noted)

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine 0.1%</th>
<th>Ropivacaine 0.4%</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulation 30 m, min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>4.6 (0.3)</td>
<td>5.3 (0.2)</td>
<td>0.41</td>
</tr>
<tr>
<td>Afternoon</td>
<td>4.0 (0.3)</td>
<td>3.6 (0.3)</td>
<td>0.56</td>
</tr>
<tr>
<td>6-Min walking test, m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>107 (17)</td>
<td>90 (11)</td>
<td>0.82</td>
</tr>
<tr>
<td>Afternoon</td>
<td>182 (35)</td>
<td>155 (23)</td>
<td>0.91</td>
</tr>
<tr>
<td>Total ambulation, m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>136 (23)</td>
<td>119 (16)</td>
<td>0.95</td>
</tr>
<tr>
<td>Afternoon</td>
<td>223 (43)</td>
<td>214 (36)</td>
<td>0.81</td>
</tr>
<tr>
<td>Total ambulatory duration, min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morning</td>
<td>6.1 (0.7)</td>
<td>6.2 (0.6)</td>
<td>0.83</td>
</tr>
<tr>
<td>Afternoon</td>
<td>6.9 (0.6)</td>
<td>7.4 (0.8)</td>
<td>0.93</td>
</tr>
<tr>
<td>Hip flexion, degrees</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>88 (3)</td>
<td>90 (3)</td>
<td>0.60</td>
</tr>
<tr>
<td>Morning</td>
<td>69 (4)</td>
<td>67 (3)</td>
<td>0.41</td>
</tr>
<tr>
<td>Afternoon</td>
<td>75 (3)</td>
<td>78 (3)</td>
<td>0.51</td>
</tr>
<tr>
<td>Mean resting pain (NRS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average dynamic pain (NRS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>4.8 (0.4)</td>
<td>5.2 (0.4)</td>
<td>0.35</td>
</tr>
<tr>
<td>Morning</td>
<td>3.8 (0.4)</td>
<td>3.8 (0.4)</td>
<td>0.97</td>
</tr>
<tr>
<td>Afternoon</td>
<td>3.2 (0.4)</td>
<td>2.9 (0.3)</td>
<td>0.49</td>
</tr>
<tr>
<td>Worst dynamic pain (NRS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>7.6 (0.4)</td>
<td>8.0 (0.4)</td>
<td>0.60</td>
</tr>
<tr>
<td>Morning</td>
<td>6.2 (0.5)</td>
<td>6.5 (0.5)</td>
<td>0.76</td>
</tr>
<tr>
<td>Afternoon</td>
<td>4.3 (0.4)</td>
<td>5.0 (0.6)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Values are reported as mean (SE).

NRS = Numeric Rating Scale of pain.
Dose, Concentration, and Volume for CPNB


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