Wound Infiltration and Drain Lavage with Ropivacaine After Major Shoulder Surgery

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Subcutaneous infiltration and wound lavage with ropivacaine is an alternative to opioids after major shoulder surgery. However, the efficacy and potential toxicity of this method remain unclear. We therefore evaluated plasma ropivacaine concentrations after shoulder infiltration and wound lavage. We subsequently quantified the efficacy of two ropivacaine concentrations. Patients undergoing major shoulder surgery were anesthetized with alfentanil and propofol. The initial patients (n = 18) received ropivacaine 7.5 mg/mL and ropivacaine plasma concentrations were measured in 15-min intervals. The subsequent 45 patients were randomly assigned to: 1) isotonic saline, 2) 3.75 mg/mL ropivacaine, or 3) 7.5 mg/mL ropivacaine. Ten milliliters of each solution was administered subcutaneously and 20 mL was injected into the wound drain which was clamped for 10 min. Supplemental postoperative pain relief was provided by patient-controlled anesthesia using the opioid piritramid (3.5-mg boluses, 6-min lock-out).

Postoperative pain scores were recorded on a 100-mm visual analog scale for 4 h in the initial patients and for 10 h in the second part of the study. Unbound ropivacaine plasma concentrations peaked after 15 min at 0.08 ± 0.09 μg/mL; the maximum was 0.30 μg/mL, compared with a toxic threshold of 0.6 μg/mL. In the second part of the study, pain scores were significantly lower after 3.75 mg/mL (20 ± 15 mm) or 7.5 mg/mL (10 ± 9 mm) ropivacaine than saline (35 ± 10 mm). Piritramid requirements differed significantly in the three groups, being highest with saline and lowest with ropivacaine 7.5 mg/mL. We conclude that wound infiltration and lavage with 30 mL ropivacaine 7.5 mg/mL after major shoulder surgery resulted in very low pain scores and opioid requirement. Implications: Wound infiltration and lavage with 30 mL ropivacaine 7.5 mg/mL after major shoulder surgery resulted in very low pain scores and opioid requirement.


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Subcutaneous infiltration and wound lavage with ropivacaine is an alternative to opioids after major shoulder surgery. However, the efficacy and potential toxicity of this method remain unclear.
of the required interscalene catheter is relatively tricky. Furthermore, interscalene analgesia is typically accompanied by unwanted motor weakness and occasional serious side effects, such as acute respiratory or cardiac arrest (4,5).

An alternative pain treatment is postoperative wound infiltration and lavage of the surgical drain. Infiltration is considerably easier than catheter insertion and likely to be associated with fewer complications because manipulation of tissue near major nerve trunks during insertion of the interscalene catheter can be avoided. A limitation of subcutaneous wound infiltration and drain lavage is that only long-acting local anesthetics produce sufficient duration of analgesia. Bupivacaine is the classic long-acting local anesthetic and has been used successfully for local infiltration after thyroidectomy and inguinal herniotomy (6). However, large doses of bupivacaine are relatively toxic, and even moderate plasma concentrations can cause catastrophic cardiotoxicity (7).

Ropivacaine, a long-acting amide local anesthetic, is chemically related to bupivacaine but it has less cardiac and central nervous system toxicity (8). This drug acts at sodium channels but additionally binds to the internal entrance of the potassium pore and blocks the channel in an open position (9). Ropivacaine also produces cutaneous vasoconstriction that restricts systemic absorption of the drug and increases its local duration of action (10). Moreover, ropivacaine possesses antiinflammatory activity that may further reduce pain when administered locally (11). Wound infiltration with 100 or 200 mg ropivacaine after inguinal herniotomy, for example, is far more effective than placebo in reducing postoperative pain (12). Furthermore, Petterson et al. (13) recently demonstrated that unbound plasma concentrations after subcutaneous wound infiltration with 375 mg ropivacaine peak near 3 μg/mL which is within the safe range.

Our first goal was to evaluate the systemic absorption of ropivacaine after wound infiltration of the shoulder. The resulting plasma concentrations were compared with the established toxic thresholds for unbound ropivacaine (0.6 μg/mL) (14). Our second goal was to evaluate the analgesic effect of subcutaneous infiltration and wound lavage with ropivacaine after major shoulder surgery. Because the optimal concentration of ropivacaine for shoulder infiltration is unknown, we compared 30 mL of 3.75 mg/mL with 30 mL of 7.5 mg/mL.

**Methods**

After approval of the local Ethics Review Board and written informed consent, we studied a total of 63 patients undergoing elective major orthopedic shoulder surgery. Surgical procedures included anterior shoulder stabilization, rotator cuff repair, and total shoulder replacement. Patients were excluded if they were younger than 18 yr, if their ASA physical status exceeded II, if vasoconstrictor drugs were required for surgery, and if opioids or α2-agonists were administered preoperatively. Furthermore, arthroscopic surgical procedures and revision surgery were excluded.

On the day of surgery, patients were premedicated with 7.5 mg of oral midazolam. A venous catheter was inserted into one hand and an infusion of lactated Ringer’s solution was started. Normothermia was maintained with forced air (Augustine Medical, Inc., Eden Prairie, MN). All patients were anesthetized with 0.02 mg/kg IV alfentanil and 2.0 mg/kg IV propofol. Anesthesia was maintained by continuous infusion of 0.04 mg·kg⁻¹·h⁻¹ alfentanil and 8 mg·kg⁻¹·h⁻¹ propofol. In cases of hemodynamic depression, the propofol dose was reduced in 1 mg·kg⁻¹·h⁻¹ steps. Ventilation was assisted with a laryngeal mask using oxygen in air (inspired oxygen fraction = 0.3).

In the first part of the study (n = 18), a central venous catheter was inserted after induction of anesthesia. At the end of surgery, patients were given 30 mL of 7.5 mg/mL ropivacaine which was administered into the wound by the orthopedic surgeon. Ten milliliters of the solution was injected subcutaneously and 20 mL was injected into the wound drain which was clamped for 10 min. Infusions of alfentanil and propofol were then discontinued.

Central venous blood was sampled for determination of total and unbound ropivacaine plasma concentrations and α1-acid glycoprotein concentration. Samples were obtained before infiltration and 15, 30, 45, 60, 90, 120, and 240 min after administration. Postoperative pain was treated with IV PCA boluses of the μ receptor agonist piritramid (3.5-mg boluses, 6-min lock-out).

In the second portion of the study, patients were assigned randomly to one of three groups (n = 15 each): 1) isotonic saline, 2) 3.75 mg/mL ropivacaine, and 3) 7.5 mg/mL ropivacaine. Anesthetic management, administration of the local anesthetic or saline control, and supplemental PCA were performed as above. However, a central venous catheter was inserted only when clinically indicated. Both the orthopedic surgeon who administered the local anesthetic or saline control and the attending anesthesiologist were blinded to the drug assignment. All subjective measurements were obtained and recorded by another investigator who was also blinded to the study drug.

The day before surgery, patients were introduced to the 100-mm–long visual analog scale (VAS) and asked to score their preoperative shoulder pain. Motor function of the hand ipsilateral to the surgical site was assessed with a dynamometer (Aesculap, Tuttingen, Germany). The patient was asked three times to press
the dynamometer with maximal force. The mean value of these measurements was considered preoperative hand strength.

Perioperatively, we recorded heart rate, systolic, mean, and diastolic arterial blood pressures (Critikon, Tampa, FL), and oxygen saturation (pulse oximeter; Nellcor, Hayward, CA). Core temperature was recorded from the tympanic membrane (Mallinckrodt Anesthesiology Products, Inc., St. Louis, MO). Pain was scored by the patients using the visual analog scale.

Blood samples for local anesthetic analysis were taken from the central venous catheter (8 mL) of the first 18 patients and immediately centrifuged for 10 min at 3000 rpm. The resulting plasma samples were immediately refrigerated at −20°C. Ropivacaine plasma concentrations were evaluated by high-performance liquid chromatography with ultraviolet detection as described previously (15). The accuracy of this assay is nearly 95% and the confidence interval is ±1.25%.

Arousal state was assessed by patients’ responses to the verbal command “Open your eyes and lift your arms.” Absent or incomplete responses were graded as arousal state zero, prompt and appropriate responses were graded as arousal state one. An investigator blinded to group assignment made all measurements. In the first portion of the study, data were collected before and 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, and 240 min after administration of the respective local anesthetic. In the second portion, data were collected at those times, and additionally at 5, 6, 7, 8, 9, 10, and 24 h after administration of ropivacaine or saline.

Changes in the measured variables over time within each group were evaluated using repeated-measures analysis of variance (ANOVA) and Scheffé F tests. Differences among the groups were compared with unpaired, two-tailed t tests (two groups) or one-way ANOVA and Scheffé F tests (three groups). Descriptive (categorical) variables were analyzed using χ² tests. Data are expressed as mean ± SEM in the text and Tables and as mean ± SD in the Figures; P < 0.05 was considered statistically significant.

**Results**

**Part One**

The patients of the first portion of the study were aged 52 ± 16 yr, weighed 74 ± 16 kg, were 172 ± 9 cm in height, and were split evenly between the sexes. The duration of surgery was 79 ± 33 min and the time to a postoperative arousal score of one was 37 ± 14 min. Final intraoperative core temperatures were near 36°C and the time to arousal score one was 24 ± 9 min. Postoperative pain scores (mean values during the first 4 h postoperatively) were 17 ± 17 mm and the patients required 1 ± 2 mg piritramid during the first 4 h postoperatively. Heart rate and mean arterial blood pressure did not change over time (Table 1).

We failed to identify any neurologic or cardiac complications that could be attributed to ropivacaine administration. Ropivacaine concentrations peaked 15 min after administration. At that time, the total concentration was 1.4 ± 0.9 μg/mL and the maximum was 2.7 μg/mL; the unbound concentration was 0.08 ± 0.09 μg/mL and the maximum was 0.30 μg/mL. The α₁-acid glycoprotein concentrations were similar throughout the study (Table 2).

**Part Two**

Morphometric and demographic characteristics, duration of surgery, time to reach arousal score one, and core temperature were similar in the three study groups. Types of shoulder surgery were distributed comparably among the study groups. Final intraoperative core temperatures were near 36°C in each group. Arterial blood pressure and heart rate were lower during the initial 10 h postoperatively in patients given 7.5 mg/mL ropivacaine than in those given saline. Peripheral oxygen saturation was comparable among the groups. Postoperative ipsilateral hand strength was greater in the patients given 7.5 mg/mL ropivacaine than in those given saline or 3.75 mg/mL ropivacaine (Table 3).

Patients required significantly less IV piritramid when 7.5 mg/mL ropivacaine was administered into the shoulder when compared with saline. Less opioid was also required in patients given 3.75 mg/mL ropivacaine during the first 3 h postoperatively.
the first 10 h after shoulder surgery, patients required 35 ± 6 mg piritramide after wound infiltration with saline, but required 21 ± 3 mg piritramide after 3.75 mg/mL ropivacaine wound infiltration, and only 12 ± 4 mg piritramide after 7.5 mg/mL ropivacaine wound infiltration (P < 0.05, one-way ANOVA and Scheffé F tests; Figure 1). The time period to the first required bolus of piritramide was longer in the patients given ropivacaine 7.5 mg/mL (123 ± 141 min) and ropivacaine 3.75 mg/mL (126 ± 92 min) than in those given saline (30 ± 14 min).

Preoperative pain scores were comparable in the three treatment groups. Pain scores during the initial 10 h postoperatively were significantly lower with each ropivacaine concentration than with saline. Additionally, pain scores were significantly lower during the initial 4 h postoperatively in patients given ropivacaine 7.5 mg/mL than in those given 3.75 mg/mL ropivacaine (Fig. 2).

**Discussion**

In the first portion of the study we used the highest commonly administered concentrations of ropivacaine for wound infiltration of the shoulder. Nonetheless, unbound ropivacaine plasma concentrations were well within a safe range. This is consistent with studies showing that local wound infiltration is associated with slow absorption of ropivacaine into the systemic circulation (16). Ropivacaine combines a rapid clearance and a short terminal half-life of 1.7 hours (17) to produce relatively low plasma concentrations (8). Our data thus suggest that a relatively large concentration of ropivacaine for infiltration and wound lavage after major shoulder surgery is effective and can be administered with minimal risk of systemic toxicity.

Previous studies indicate that local administration of ropivacaine is effective after minor procedures including herniotomy and cholecystectomy (18). Our data extend these results by indicating that wound infiltration and lavage with 30 mL of 7.5 mg/mL ropivacaine safely and effectively reduced postoperative pain scores after major shoulder surgery from 10 millimeters to 10 millimeters during the first 10 h postoperatively (P < 0.01, compared with saline). Our data further indicate that ropivacaine 3.75 mg/mL reduced pain scores only to 20 millimeters to 20 millimeters in the first 24 hours postoperatively than those given saline (17 ± 13 vs 36 ± 20 millimeters).

### Table 2. Plasma Concentrations of Ropivacaine and α1-Acid Glycoprotein in the First Portion of the Study (n = 18; μg/mL)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Total</th>
<th>Unbound</th>
<th>α1-Acid Glycoprotein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>—</td>
<td>—</td>
<td>0.65 ± 0.2 (0.97)</td>
</tr>
<tr>
<td>15 min</td>
<td>1.42 ± 0.9 (2.67)</td>
<td>0.079 ± 0.09 (0.30)</td>
<td>0.68 ± 0.15 (0.98)</td>
</tr>
<tr>
<td>30 min</td>
<td>1.28 ± 0.8 (2.38)</td>
<td>0.067 ± 0.07 (0.24)</td>
<td>0.66 ± 0.16 (0.98)</td>
</tr>
<tr>
<td>45 min</td>
<td>1.17 ± 0.6 (1.97)</td>
<td>0.057 ± 0.05 (0.17)</td>
<td>0.63 ± 0.23 (0.95)</td>
</tr>
<tr>
<td>60 min</td>
<td>1.11 ± 0.6 (1.98)</td>
<td>0.048 ± 0.03 (0.10)</td>
<td>0.64 ± 0.22 (0.91)</td>
</tr>
<tr>
<td>90 min</td>
<td>0.94 ± 0.5 (1.56)</td>
<td>0.043 ± 0.04 (0.13)</td>
<td>0.66 ± 0.17 (0.99)</td>
</tr>
<tr>
<td>120 min</td>
<td>0.94 ± 0.5 (1.52)</td>
<td>0.033 ± 0.02 (0.09)</td>
<td>0.60 ± 0.23 (0.98)</td>
</tr>
<tr>
<td>240 min</td>
<td>0.73 ± 0.5 (1.54)</td>
<td>0.018 ± 0.01 (0.04)</td>
<td>0.63 ± 0.15 (0.90)</td>
</tr>
</tbody>
</table>

The unbound toxic threshold is 0.6 μg/mL for ropivacaine (14). Data are expressed as mean ± sd; maximum values in parentheses.

### Table 3. Morphometric and Demographic Characteristics, Duration of Surgery, Arousal Time, Core Temperature, Hemodynamic Variables, and Hand Strength in the Second Portion of the Study

<table>
<thead>
<tr>
<th></th>
<th>Saline</th>
<th>Ropivacaine 3.75 mg/mL</th>
<th>Ropivacaine 7.5 mg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>56 ± 18</td>
<td>48 ± 15</td>
<td>55 ± 12</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>7/8</td>
<td>9/6</td>
<td>8/7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 ± 13</td>
<td>82 ± 20</td>
<td>79 ± 17</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173 ± 10</td>
<td>169 ± 9</td>
<td>171 ± 10</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>76 ± 36</td>
<td>77 ± 39</td>
<td>78 ± 27</td>
</tr>
<tr>
<td>Time to arousal score one (min)</td>
<td>21 ± 16</td>
<td>29 ± 17</td>
<td>30 ± 13</td>
</tr>
<tr>
<td>Heart rate (1–10 h, bpm)</td>
<td>79 ± 8</td>
<td>77 ± 11</td>
<td>72 ± 7</td>
</tr>
<tr>
<td>Mean arterial blood pressure (1–10 h, mm Hg)</td>
<td>105 ± 10</td>
<td>102 ± 15</td>
<td>96 ± 11</td>
</tr>
<tr>
<td>P O2 (1–10 h, %)</td>
<td>98 ± 1</td>
<td>97 ± 2</td>
<td>98 ± 2</td>
</tr>
<tr>
<td>Hand strength (1–10 h, k Pascals)</td>
<td>6.2 ± 3.5</td>
<td>6.4 ± 3.5</td>
<td>13.2 ± 8.5*†</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± sd. *P < 0.05 versus saline; †P < 0.05 versus 3.75 mg/mL ropivacaine.
milligrams of piritramid). Patients given ropivacaine also had better hand strength. It is apparent from these data that effective pain treatment was the most important determinant of strength.

Beyond injuries of nerves by the surgical procedure itself (19), interscalene nerve blocks are associated with specific risks. This technique therefore has limitations and relative contraindications for postoperative pain treatment after shoulder surgery. For example, interscalene block causes transient (20) or persistent (21) phrenic nerve paralysis which decreases diaphragmatic motion and mechanical chest wall motion (22). Phrenic nerve paresis decreases respiratory reserve because abdominal organs are compressed when the diaphragm is in the supine position. The technique should thus be avoided in patients who depend on intact diaphragmatic function or are unlikely to tolerate a 25% reduction in pulmonary function (22). In routine anesthetic practice, however, it may be difficult to predict whether such a reduction in pulmonary function will produce serious side effects such as hypoxia and ventilatory arrest (4).

The overall impact of these unpredictable and potentially serious side effects of interscalene plexus block makes wound infiltration a safe alternative for pain treatment after shoulder surgery. Furthermore, systemic toxicity after wound infiltration with ropivacaine is unlikely because even injecting the entire standard dose IV would not produce life-threatening plasma concentrations (14).

A limitation of our study is that we measured central venous rather than arterial plasma ropivacaine concentrations. Our use of venous samples may somewhat underestimate anesthetic toxicity because arterial concentrations of ropivacaine, at least after epidural administration, may exceed venous concentrations by as much as 50% (23). Nonetheless, the concentrations we observed, even after administration of 7.5 mg/mL ropivacaine, were well below the established toxic thresholds. Under the circumstances of this study, it is thus unlikely that arterial concentrations would have reached concerning levels. Because ropivacaine is eliminated predominantly by hepatic metabolism (only 1% is excreted unchanged in the urine), ropivacaine should be administered cautiously in patients with a reduced liver function (24).

Anesthesia in our patients was induced and maintained with propofol and alfentanil. Because alfentanil is a short-acting opioid, relatively little opioid effect persisted throughout the recovery period. Effective pain relief in the patients given infiltration anesthesia can thus be attributed to the local anesthetic per se.

Longer-acting opioids would obviously provide better postoperative pain relief. However, they would also be associated with routine opioid toxicity including respiratory depression and nausea. Our data demonstrate that wound infiltration of local anesthetics accompanied by drain lavage is an effective treatment for postoperative pain after shoulder surgery. However, even the patients given 7.5 mg/mL ropivacaine were not completely pain free. It seems likely, however, that nonopioid analgesic techniques could be substituted for the small doses of patient-controlled opioid that proved necessary. Possible treatment strategies include coadministration of nonsteroidal antiinflammatory drugs or transcutaneous electric nerve stimulation (25).
In summary, wound infiltration with 30 milliliters of 7.5 mg/mL ropivacaine after major shoulder surgery produced plasma concentrations well within safe limits. Patients given ropivacaine 7.5 or 3.75 mg/mL had lower pain scores during the recovery period and required less supplemental piritramide than those given saline. Pain scores were significantly lower after 7.5 mg/mL than 3.75 mg/mL ropivacaine, as were supplemental opioid doses. Our data thus indicate that wound infiltration and lavage with 30 milliliters of 7.5 mg/mL ropivacaine is an effective treatment for postoperative pain in patients recovering from major shoulder surgery.

References