Interscalene brachial plexus anaesthesia with 0.5%, 0.75% or 1% ropivacaine: a double-blind comparison with 2% mepivacaine

A. Casati*, G. Fanelli, G. Aldegheri, M. Berti, E. Colnaghi, V. Cedrati and G. Torri

Department of Anaesthesiology, University of Milan, IRCCS H. San Raffaele, Via Olgettina 60, 20132 Milan, Italy

*Corresponding author

We have compared interscalene brachial plexus block performed with ropivacaine or mepivacaine in 60 healthy patients undergoing elective shoulder surgery. Patients were allocated randomly to receive interscalene brachial plexus anaesthesia with 20 ml of 0.5% ropivacaine (n=15), 0.75% ropivacaine (n=15), 1% ropivacaine (n=15) or 2% mepivacaine (n=15). Readiness for surgery (loss of pinprick sensation from C4 to C7 and inability to elevate the limb from the bed) was achieved sooner with 1% ropivacaine (mean 10 (SD 5) min) than with 0.5% ropivacaine (22 (7) min) (P<0.001) or 2% mepivacaine (18 (9) min) (P<0.02). Postoperative analgesia was similar with the three ropivacaine concentrations (11.5 (5) h, 10.7 (2) h and 10 (2.4) h with 0.5%, 0.75% and 1% concentrations, respectively) and nearly two-fold longer compared with 2% mepivacaine (5.1 (2.7) h) (P<0.001).

Keywords: anaesthetic techniques, regional, brachial plexus; anaesthetics local, ropivacaine; anaesthetics local, mepivacaine

Accepted for publication: June 9, 1999

Ropivacaine is a new amide local anaesthetic with a higher toxic threshold than other long-acting local anaesthetics.1 Various controlled clinical studies have demonstrated that ropivacaine may be a suitable choice for peripheral nerve block, including axillary and subclavian perivascular brachial plexus anaesthesia2-5 and combined sciatic–femoral nerve block.6,7 Because of its favourable properties, ropivacaine may be useful for interscalene brachial plexus anaesthesia for shoulder surgery. However, to date, few data are available on the use of ropivacaine for interscalene brachial plexus anaesthesia.

In this prospective, randomized, double-blinded study, we have evaluated both intra- and postoperative clinical properties of interscalene brachial plexus block performed with 20 ml of 0.5%, 0.75%, 1% ropivacaine or 2% mepivacaine.

Patients and methods

After obtaining approval from the Local Ethics Committee and written informed consent, we studied 60 ASA I–II patients, aged 18–65 yr, undergoing interscalene brachial plexus anaesthesia for elective shoulder capsuloplastic or acromioplasty surgery. Patients with respiratory or cardiac disease, diabetes or peripheral neuropathy and those receiving chronic analgesic therapy were excluded.

To calculate the required study size, we considered the results of a previous study evaluating changes in pulmonary function after interscalene brachial plexus anaesthesia with 0.5% or 0.75% ropivacaine.8 We wished to detect a 5–10-min difference in the time required to achieve adequate surgical anaesthesia between 0.5% ropivacaine and the two* other commercially available ropivacaine concentrations, accepting a one-tailed α error of 5% and a β error of 20%.9 Based on these calculations, the required study size was 12–19 patients per group.

Without premedication, a 20-gauge i.v. cannula was inserted in the forearm and infusion of lactate Ringer’s solution 5 ml kg⁻¹ h⁻¹ was given i.v. Using sealed envelopes, patients were randomized to receive 20 ml of 0.5% ropivacaine (n=15, injected dose 100 mg), 0.75% ropivacaine (n=15, injected dose 150 mg), 1% ropivacaine (n=15, injected dose 200 mg) or 2% mepivacaine (n=15, injected dose 400 mg). Sterile syringes containing the solutions were prepared in a double-blind manner by one of the authors who took no further part in the management of patients. Standard monitoring was used throughout the study, including non-invasive arterial pressure, heart rate and pulse oximetry.

Nerve block was performed with the aid of a nerve stimulator using a short-bevelled, Teflon-coated stimulating needle (Locoplex, Vygon, France) (3.5-cm long, 25-gauge). The needle was introduced at or caudal to a line through the cricoid cartilage according to the method of Winnie.10

© British Journal of Anaesthesia
Paraesthesia was never intentionally sought, and a multiple injection technique was used eliciting specific muscular twitches on nerve stimulation to confirm the needle location. The stimulating needle was, in sequence, inserted and redirected eliciting each of the following muscular twitches: shoulder abduction (contraction of the suprascapularis muscle), flexion of the arm (contraction of the biceps muscle) and extension of the arm (contraction of the triceps muscle). Stimulation frequency was set at 2 Hz while the intensity of the stimulating current was initially set to deliver 1 mA and then gradually decreased to less than 0.5 mA. The total volume of local anaesthetic solution was divided among the three elicited twitches as follows: abduction of the shoulder 8 ml, flexion of the arm 6 ml and extension of the arm 6 ml.

Haemodynamic variables and pulse oximetry were recorded before block placement (baseline) and then at 5, 10, 20 and 30 min after completion of injection. Further measurements were performed at 10-min intervals until adequate surgical anaesthesia had been achieved. The start time for clinical assessments was completion of injection of local anaesthetic. Motor function was tested by asking the patient to lift the arm at the shoulder and also to flex the elbow against gravity. Sensory block was assessed using the pinprick test (22-gauge hypodermic needle). Onset of surgical anaesthesia (readiness for surgery) was defined as loss of pinprick sensation at the skin dermatomes involved in the surgical field (from C4 to C7) with inability to elevate the operated limb from the bed. Data collection was always performed by an independent observer blinded to the anaesthetic solution injected (A. C. or V. C.).

The adequacy of block was judged according to the need for supplementary i.v. analgesics and sedation: adequate nerve block = no analgesics required to complete surgery; inadequate nerve block = need for additional i.v. analgesic (fentanyl 0.1 mg) to complete surgery; failed nerve block = general anaesthesia required to complete surgery.

Postoperative analgesia consisted of ketoprofen 100 mg i.v. if required. Postoperative pain relief was defined as the time lasting from block placement to first requirement for postoperative pain medication. The degree of pain at this time was measured on a 100-mm visual analogue scale (VAS). Patients were also questioned regarding neurological complications (pain, dysaesthesiae or both) at discharge from the orthopaedic ward and 1 week after hospital discharge (at the first routine postoperative orthopaedic examination).

Statistical analysis was performed using the program Systat 7.0 (SPSS Inc, Chicago, IL, USA). After normal distribution of collected data had been checked, analysis of variance was used to compare patient data, onset of block and duration of postoperative analgesia between the four groups. Tukey and Scheffe tests were used for post hoc comparisons. Analysis of variance for repeated measures was used to analyse changes over time. Ordinal data were analysed using the contingency table analysis with Fisher's exact test. A value of P<0.05 was considered significant. Continuous variables are presented as mean (SD) while ordinal data are presented as number (%).

Results

The four groups of patients were similar in age, weight, height and male/female ratio (Table 1). No failed blocks were reported; two patients in the 0.5% ropivacaine group, two in the 1% ropivacaine group and three in the 2% mepivacaine showed inadequate nerve block requiring intraoperative analgesic administration (fentanyl 0.1 mg i.v.) to complete surgery (ns).

The injected doses of local anaesthetic solution were 1.5 (0.3) mg kg\(^{-1}\) in the 0.5% ropivacaine group, 2 (0.3) mg kg\(^{-1}\) in the 0.75% ropivacaine group, 2.9 (0.5) mg kg\(^{-1}\) in the 1% ropivacaine group and 5.7 (1.1) mg kg\(^{-1}\) in the mepivacaine group. There were no changes in arterial pressure, heart rate or haemoglobin oxygen saturation throughout the study (data are shown) and no signs of central nervous system (CNS) or cardiovascular toxicity. There were no other adverse events reported in any patient.

Readiness for surgery was achieved sooner in the 1% ropivacaine group compared with the 0.5% ropivacaine and mepivacaine groups (P<0.0005 and P<0.02, respectively) (Fig. 1).

There were no differences in the degree of pain measured at the first requirement for postoperative analgesic between the four groups (62 (21) mm, 72 (19) mm, 53 (18) mm and 74 (20) mm after 0.5%, 0.75% and 1% ropivacaine, and 2% mepivacaine, respectively). Patients receiving ropivacaine (0.5%, 0.75% or 1%) showed a nearly two-fold longer

---

**Table 1** Patient data (mean (SD) or range) or number

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr) (min–max)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Sex (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ropivacaine 0.5% (n=15)</td>
<td>53 (23–65)</td>
<td>68 (12)</td>
<td>169 (8)</td>
<td>13/2</td>
</tr>
<tr>
<td>Ropivacaine 0.75% (n=15)</td>
<td>56 (27–65)</td>
<td>72 (10)</td>
<td>167 (8)</td>
<td>8/7</td>
</tr>
<tr>
<td>Ropivacaine 1% (n=15)</td>
<td>50 (20–65)</td>
<td>67 (13)</td>
<td>166 (8)</td>
<td>8/7</td>
</tr>
<tr>
<td>Mepivacaine (n=15)</td>
<td>49 (20–65)</td>
<td>71 (16)</td>
<td>169 (8)</td>
<td>8/7</td>
</tr>
</tbody>
</table>

---

*P<0.05, ***P<0.001 vs 0.5% ropivacaine; †P<0.05 vs 2% mepivacaine.*
duration in postoperative pain relief than those receiving 2% mepivacaine (Fig. 2). No differences in the duration of postoperative analgesia were observed between the three ropivacaine concentrations.

There was complete resolution of nerve block in all patients, and no neurological dysfunction was reported 1 week after surgery.

Discussion

The most interesting finding of our study was that 1% ropivacaine 20 ml was a useful agent for interscalene brachial plexus anaesthesia with an onset time faster than that of a widely used short onset–intermediate duration local anaesthetic such as mepivacaine, with the advantage of prolonged postoperative pain relief. Practitioners should always balance the advantage of long postoperative pain relief against the unavoidable delay in the resolution of motor block. However, if a delay in the mobilization of the operated limb after shoulder surgery is not a problem for either the surgeon or patient, 1% ropivacaine has a shorter onset time of interscalene brachial plexus anaesthesia and prolonged postoperative analgesia.

Because the focus of our investigation was evaluation of a long-acting local anaesthetic, bupivacaine might appear more appropriate as a control agent than mepivacaine. However, the wide and unpredictable latency of nerve block with bupivacaine has made it less popular, especially when small volumes of anaesthetic solution are injected. In our department, we currently use mepivacaine for peripheral nerve block because of its short onset–intermediate duration characteristics and this was the reason for choosing mepivacaine.

We have confirmed that increasing concentration of ropivacaine from 0.5% to 1% reduced the onset time of peripheral nerve block. Given the greater mass of drug injected, this may be regarded as predictable. However, recent reports by Klein and colleagues failed to demonstrate improved onset time of interscalene brachial plexus block after administration of 30 ml of either 0.5% or 0.75% ropivacaine with epinephrine 1:400 000. This difference could be explained by the lower volumes and doses given in our study. Previous investigations reported that the total injected volume of local anaesthetic solution is a crucial factor in successful peripheral nerve block. Furthermore, it has been reported that the speed with which neural block begins is also proportional to the concentration of the local anaesthetic solution. In our study, both the total dose and concentration of local anaesthetic solution around the nerves were two-fold greater in the 1% ropivacaine group than in the 0.5% ropivacaine group, possibly explaining our findings as more local anaesthetic molecules were available to penetrate the peripheral nerves per unit time.

A dose–response relationship would also be expected with ropivacaine for postoperative pain relief, but this was not the case. Even if similar findings have been reported by others, it should be remembered that when estimating study size, we considered only onset time of surgical block and we cannot exclude a type II error in the evaluation of duration of postoperative analgesia.

Interestingly, although the total dose of ropivacaine injected into the brachial plexus sheath increased progressively from 1.5 (0.3) mg kg⁻¹ with 0.5% ropivacaine to 2.9 (0.5) mg kg⁻¹ with 1% ropivacaine, no patient showed signs of CNS toxicity with the higher ropivacaine regimen. Ropivacaine has been reported to be a suitable local anaesthetic for brachial plexus block at doses of 2.5–2.6 mg kg⁻¹ without evidence of CNS or cardiovascular toxicity.

We did not determine plasma concentrations of ropivacaine in our patients but studies of systemic disposition of ropivacaine after brachial plexus injection have demonstrated that plasma concentrations increase slowly and up to 250 mg have been injected for peripheral nerve block without concern. A case of convulsion has been reported after unintentional intravascular injection of ropivacaine 2.3 mg kg⁻¹ during interscalene brachial plexus block. However, Geiger and colleagues reported a maximum plasma concentration of ropivacaine of 5.8 (1.4) mg litre⁻¹ after peripheral injection of 1% ropivacaine 500 mg. The maximum unbound ropivacaine concentration was 0.18 (1.1) mg litre⁻¹ while the unbound plasma concentration of ropivacaine tolerated in a human volunteer study before CNS toxicity developed was as high as 0.6 mg litre⁻¹.

The use of highly concentrated solutions of local anaesthetic for regional anaesthesia has given rise to concerns because of the theoretical risk of local neurotoxicity. Previous in vitro and in vivo studies with ropivacaine failed to produce evidence of direct neurotoxicity and our results demonstrated that 1% ropivacaine 200 mg did not affect recovery of neurological function after interscalene brachial plexus anaesthesia.

As we compared the clinical properties of interscalene brachial plexus block performed with 20 ml of 0.5%, 0.75% or 1% ropivacaine with those of 2% mepivacaine, the results of this investigation are relevant in comparison with mepivacaine only. However, we can conclude that because rapid onset of block and prolonged postoperative analgesia are important goals in regional anaesthesia, 0.75–1% con-
centrations of ropivacaine may be suitable for interscalene brachial plexus anaesthesia, allowing practitioners to produce a short onset time and long duration of peripheral nerve block.

Acknowledgements

We thank the staff of anaesthesia nurses (University Department of Anaesthesiology, IRCCS San Raffaele Hospital) without whose help and co-operation this study would not have been possible.

References

3 Hickey R, Hoffman J, Ramamurthy S. A comparison of ropivacaine 0.5% and bupivacaine 0.5% for brachial plexus block. Anesthesiology 1991; 74: 639–42
8 Casati A, Fanelli G, Cedrati V, Berti M, Aldegheri G, Torri G. Pulmonary function changes after interscalene brachial plexus anesthesia with 0.5% and 0.75% ropivacaine: a double-blind comparison with 2% mepivacaine. Anesth Analg 1999; 88: 587–92
14 Klein SM, Greengrass RA, Steele SM, et al. A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block. Anesth Analg 1998; 87: 1316–19
19 Wildsmith JAW. Peripheral nerve block and ropivacaine. Am J Anaesth 1997; 24 (Suppl. 5): 14–17
21 Geiger P, Oldenburger K, Ventour W, Mehrkens HH. Ropivacaine 0.5% vs 0.75% vs 1% for 3-in-1 block combined with sciatic nerve block in orthopedic knee surgery. 17th Annual ESRA Congress. Geneva, 1998; 47
22 Lambert LA, Lambert DH, Strichartz GR. Irreversible conduction block in isolated nerve by high concentrations of local anesthetic. Anesthesiology 1994; 80: 1092–3
25 Van Kleef JW, Veering BT, Burm AGL. Spinal anesthesia with 0.5% and 0.75% solutions in patients undergoing minor lower limb surgery. Anesth Analg 1994; 78: 1125–30