Minimum effective local anaesthetic dose of isobaric levobupivacaine and ropivacaine administered via a spinal catheter for hip replacement surgery

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Background. Continuous spinal anaesthesia with spinal catheters allows incremental dosing of local anaesthetic and, consequently, less haemodynamic changes. However, little is known about the required doses. Therefore, we designed a study to assess the minimum effective local anaesthetic dose (MLAD) of levobupivacaine and ropivacaine in this context.

Methods. Forty-one patients undergoing hip replacement surgery were randomly allocated to one of the two local anaesthetic groups in a double-blind manner. The initial dose of local anaesthetic was determined by the response of the previous patient: the effective dose resulted in a 1 mg decrease in the dose of levobupivacaine or ropivacaine, and an ineffective dose resulted in a 1 mg increase. The MLAD was calculated by the Dixon up-and-down method.

Results. The MLAD of levobupivacaine was 11.7 mg (95% CI, 11.1–12.4) and that of ropivacaine 12.8 mg (95% CI, 12.2–13.4).

Conclusions. These doses are significantly smaller than doses reported before for single-shot spinal anaesthesia. Continuous spinal anaesthesia allows the use of relatively small doses of local anaesthetic.

Keywords: anaesthetic techniques, spinal; pharmacology, levobupivacaine; pharmacology, ropivacaine; surgery, orthopaedic

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Continuous spinal anaesthesia (CSA) with spinal catheters allows incremental dosing of the local anaesthetic. CSA provides greater haemodynamic stability, control of the duration of anaesthesia and motor block, the possibility of increasing the extent of anaesthesia, and good postoperative analgesia. The concept of minimum local anaesthetic concentration has been established to determine the median effective concentration of local anaesthetics and their relative potencies for spinal and epidural anaesthesia. More recently, the median effective dose (ED50) has been developed to assess the minimum analgesic doses for epidural opioids. There is, however, little data on the minimum dose requirements of local anaesthetics administered intraspinaly for surgery. The use of the spinal catheter technique and incremental dosing allows the determination of the minimum effective local anaesthetic dose (MLAD) without the risk of failure of the block in normal clinical practice. We designed this study to assess the MLAD of levobupivacaine and ropivacaine in hip replacement surgery.

Patients and methods

After local ethical committee approval and written informed consent, 41 ASA physical status I–III patients (age 37–79 yr) scheduled for hip replacement surgery under CSA were included in this prospective, randomized, double-blinded study. Exclusion criteria included pregnancy, morbid obesity (body mass index >35 kg m−2), diabetic and other neuropathies, skin infection at the site of injection and other common contraindications for spinal anaesthesia, and allergy to the study drugs. The patients were randomly allocated to two groups: group L received levobupivacaine (Chirocaine®; Abbott Laboratories S.P.A., Latina, Italy;
2.5 mg/ml, with a density of 0.9999 mg ml\(^{-1}\) at 37°C) and group R received ropivacaine (Naropin\(^{\text{R}}\); AstraZeneca AB, Södertälje, Sweden; 2 mg ml\(^{-1}\), with a density of 0.9996 mg ml\(^{-1}\) at 37°C) for CSA. These solutions can be considered isobaric with the cerebrospinal fluid.\(^7\)

A spinal catheter with a tip hole and an additional side hole 7 mm from the tip (Spinocath\(^{\text{R}}\); B. Braun, Melsungen, Germany) was introduced 2–2.5 cm into the subarachnoid space at the L3–4 interspace in the midline with the patient in the lateral position and the side to be operated up. The study drug (3.2–8.5 ml) was administered manually via the intraspinal catheter at an injection speed of 2 ml in 30 s. The dose of the study drug was determined by the up-and-down method of Dixon.\(^8\) Based on our previous clinical experience, the intraspinal levobupivacaine dose for the first patient allocated to receive levobupivacaine was 12 mg. Similarly, the ropivacaine dose was 14 mg for the first patient. Twenty minutes after administration of the study drug, the following criteria were assessed: (i) response to pinprick at T12 dermatome level on the side of surgery; (ii) response to transcutaneous tetanic electric stimulation (50 Hz at 60 mA) for 5 s at T12 level on the side of surgery; and (iii) motor function on the side of surgery assessed with the modified Bromage scale (0=no motor block, 1=inability to raise extended legs, 2=inability to flex knees, 3=inability to flex ankle joints).\(^9\) Anaesthesia was considered successful when there was loss of sensation to pinprick and to tetanic electric stimulation, and complete motor block. If successful anaesthesia according to the above criteria was achieved within 20 min from study drug injection, the dose of the study drug for the next patient was decreased by 1 mg in that group (levobupivacaine or ropivacaine). Conversely, if successful anaesthesia was not observed, the dose of the study drug for the next patient was increased by 1 mg in that group. The study ended at the time when clinical anaesthesia was assessed. However, if successful clinical anaesthesia was not achieved within 20 min, additional doses of 2–6 mg of the study drug were administered for surgical anaesthesia. Patient monitoring included ECG, non-invasive measurement of blood pressure at 3-min intervals and recording of peripheral oxygen saturation. In addition, all drugs administered throughout surgery were recorded. Ephedrine was used for hypotension at the discretion of the attending anaesthetist.

**Statistics**

The sample size was based on previous literature, which has demonstrated that at least six independent pairs of patients with sufficient anaesthesia/insufficient anaesthesia (response/no response pairs) should provide reliable estimates of MLAD using the up-and-down method of Dixon.\(^5\)\(^10\) Dixon’s method was used to calculate the MLAD with 95% confidence intervals.\(^8\) The data are presented as mean (SD) unless mentioned otherwise.

**Results**

The patients’ characteristics are presented in Table 1. No major adverse events occurred in any of the patients. Two patients (one in each group) had postdural puncture headache of mild severity, which was treated successfully with fluids and NSAIDs.

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Group L</th>
<th>Group R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>66.2 (40–79)</td>
<td>61.6 (37–76)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165 (8)</td>
<td>171 (8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.2 (11.1)</td>
<td>80.6 (11.7)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>6/15</td>
<td>10/10</td>
</tr>
</tbody>
</table>

The sequences of patients with sufficient and insufficient anaesthesia are shown in Figure 1. The MLAD for levobupivacaine was 11.7 mg (95% CI 11.1–12.4) and that of ropivacaine 12.8 mg (12.2–13.4).

Anaesthesia was successful by the predetermined criteria in 12 patients in each group; out of these patients, the number needing additional local anaesthetic to complete surgery was three in group L and one in group R. The mean (SD) total dose of levobupivacaine required to complete surgery was 15.2 (4.0) mg in the 21 patients in group L and 15.5 mg (3.1) of ropivacaine in the 20 patients in group R. Nine patients in group L and 11 patients in group R required ephedrine for correction of hypotension during surgery.

**Discussion**

The MLAD defines that local anaesthetic dose which is effective in 50% of the patients. A similar concept has been applied to assess the dose requirements of analgesics and neuraxial anaesthetics.\(^5\) An intraspinal catheter can be used to administer local anaesthesia even after the initial dosing and thus increase the degree and extent of the block. We could therefore use small initial doses of local anaesthetic close to the minimum range anticipated to be required for hip surgery and determine the MLAD for levobupivacaine and ropivacaine in patients undergoing hip replacement surgery without compromising patient convenience. In this study, the MLAD for levobupivacaine was 11.7 mg and that of ropivacaine 12.8 mg. However, the small numerical difference (1.1 mg) in the MLADs does not allow us to make the interpretation that levobupivacaine would be more potent than ropivacaine, as the 95% confidence intervals overlap.

An index that would be more relevant clinically than the MLAD would be the local anaesthetic dose that provides sufficient anaesthesia for 95% of the patients. As we used Dixon’s up-and-down method to determine the MLAD, our data concentrate on the MLAD range. Thus, our study design does not allow us to evaluate the end of the dose–response curve.\(^10\)
There was a difference in the mean MLAD volumes of levobupivacaine (4.68 ml) and ropivacaine (6.4 ml), because of both the dose requirement in milligrams and also the slightly different concentrations of the available commercial formulations. However, previous studies indicate that the total dose of local anaesthetic in milligrams rather than the volume seems to be the more important in determining the extent of spinal anaesthesia.\textsuperscript{11,12} The total dose also determines the duration of the block.\textsuperscript{13} Thus, the difference in the volume of the study drugs in the present study probably has little or no effect on the extent of the block and the MLADs.

We defined sufficient anaesthesia for hip replacement surgery as loss of pinprick at the T12 dermatome. This definition, though often used clinically, might have been too low as one in six of the patients in whom anaesthesia was initially sufficient required additional local anaesthetic to complete surgery. Nevertheless, supplementary dosing with local anaesthetic was feasible using the intraspinal catheter. The previously reported dose of isobaric levobupivacaine for single-shot spinal anaesthesia for hip replacement surgery is 17.5 mg,\textsuperscript{14} and for isobaric ropivacaine doses of 17.5–25 mg have been used.\textsuperscript{15,16} The mean total doses of local anaesthetic required to complete surgery in our study are somewhat lower, though in the range of those reported earlier and higher than the calculated MLAD. Unfortunately, the clinical time frame did not allow us to assess the local anaesthetic requirements after the first 20 min post drug injection more closely (i.e. in small supplementary local anaesthetic increments). Another factor that may have influenced our result is the direction which the catheter tip takes upon insertion. It has been shown that in patients with cranially running catheters or catheters with the tip at the level of the puncture site, the onset of analgesia was faster and the required doses of local anaesthetics were smaller than in patients with caudally running catheters.\textsuperscript{17} Unfortunately, we were not able to assess whether the catheter tip slid cranially or caudally. As the catheter was inserted for 2.0–2.5 cm into the intrathecal space, this might potentially result in a difference of 5 cm (i.e. approximately one interspace) in the catheter tip position from one patient to another. Further studies assessing the effect of catheter tip position on the local anaesthetic dose requirements are warranted.

Potential neurotoxicity related to the use of intrathecal catheters has recently become a concern because of reports of cauda equina syndrome. Most published cases have been associated with the use of 5% lidocaine in hyperbaric (7.5%) dextrose.\textsuperscript{18} Unfortunately, only a few prospective studies have formally investigated the real incidence of neurological complications.\textsuperscript{19} At present we do not have sufficient proof that levobupivacaine or ropivacaine would be safer than lidocaine in this respect. Thus, neurological symptoms have to be surveyed carefully in all patients in whom the CSA technique is used until further evidence is available.

In conclusion, continuous spinal anaesthesia using an intraspinal catheter allowed the use of small doses of local anaesthetic without compromising patient comfort.

**References**

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