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Early pharmacokinetic of ropivacaine without epinephrine after injection into the psoas compartment

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Editor's key points

- This study investigated the early pharmacokinetics of ropivacaine without additional vasoconstrictor given as a psoas compartment block (PCB).
- Ropivacaine plasma concentrations were detected within 30 s after injections.
- Maximum measured plasma concentrations were measured within the first 10 min, but stayed below toxic threshold.
- As some fraction of ropivacaine is systemically absorbed rapidly, caution is required and the use of a vasoconstrictor could be considered.

Background. Large amounts of local anaesthetics (LA) are used during psoas compartment block (PCB), especially if combined with sciatic nerve block. Data regarding early pharmacokinetics of ropivacaine for PCB are lacking, notably when a vasoconstrictive agent has not been added.

Methods. PCB was established in 11 patients using 150 mg ropivacaine without epinephrine. Free and total arterial plasma concentrations of ropivacaine were measured at nine time points during the following 30 min. Also total protein, albumin, and α_1-acid glycoprotein concentrations were analysed.

Results. Ropivacaine plasma concentrations were found in all patients within 30 s after injections. Maximum measured plasma concentrations were measured in all but two patients within the first 10 min. One patient experienced partial intravascular injection. Plasma concentrations showed wide inter-individual variability. Ranges of maximum measured plasma concentrations of total and free ropivacaine were 422–3905 and 5–186 ng ml^{-1}, respectively. The Pearson correlation between total and free concentrations was 0.96. No obvious relationship between concentrations of different plasma proteins (total protein, albumin, α_1-acid glycoprotein) and ropivacaine concentrations was found. Maximal 5% of the measured ropivacaine was unbound. All blocks were successful and no signs of toxicity were observed.

Conclusions. Maximum measured plasma concentrations of ropivacaine after PCB must be expected within 10 min. Although plasma concentrations stayed below toxic thresholds, our study demonstrates the risk of this regional anaesthesia technique.

Clinical trial registration. The clinical study was not registered because enrolment of study patients occurred in 2006.

Keywords: anaesthetics local, ropivacaine; nerve block; pharmacokinetics, ropivacaine; toxicity, local anaesthetics

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Psoas compartment block (PCB) is used for surgery and pain relief in patients undergoing hip or knee surgery. The block does not provide anaesthesia of sciatic nerve and additional sciatic nerve block is necessary in the case of surgery. In consequence, large doses of local anaesthetics (LA) are administered with potential risk of LA intoxication. Factors influencing systemic concentrations of LA are the amount of LA injected, the site of injection, and the addition of vasoconstrictive agents.[1]

Only two studies investigated ropivacaine pharmacokinetics after PCB alone.[2 3] Both used epinephrine as vasoconstrictive and took venous samples for testing. Arterial plasma concentrations are known to be higher during the early phase of systemic absorption and therefore of more value regarding toxicity of LA.[4 5] Total knee replacement is a typical surgery in the elderly. Often, these patients present with cardiovascular comorbidity and epinephrine might have adverse effects.[1]

Only one study investigated ropivacaine pharmacokinetics after PCB without the use of epinephrine.[6] PCB was combined with sciatic block and blood sampling was started thereafter. This design represents clinical practice but is not useful when only psoas compartment kinetics are investigated.

Free plasma concentrations are responsible for LA toxicity,[1] but no study has investigated it so far in the setting of PCB. The aim of our study was to measure free and total plasma concentrations of ropivacaine after PCB. We were especially interested in the early phase of systemic absorption, analysed arterial samples, and omitted the use of vasoconstrictive additives.

Methods

The local Ethics Committee approved the study protocol (EK218122003) and written informed consent was obtained from all patients. The clinical study was not registered because enrolment of study patients occurred in 2006. Patients offered enrolment included adults (≥18 yr) undergoing total knee joint replacements in combined PCB and sciatic nerve block, BMI between 25 and 35 kg m^{-2}, and ASA physical status I–III. Exclusion criteria included allergy to study medications, diabetes mellitus, anaemia, arterial vessel disease, and renal or liver dysfunction.

Eleven patients participated in the study. One hour before intervention, midazolam 7.5 mg (Roche Pharma AB, Grenzach-Wyhlen, Germany) was administered orally to all patients. A peripheral vein and radial artery were cannulated. Subjects received a continuous infusion of 5 ml kg^{-1} h^{-1} of an isotonic electrolyte infusion (E153, Serumwerk Bernburg AG, Bernburg, Germany). Monitoring included invasive arterial pressure, pulse oximetry (Sp_{O_2}), and electrocardiography with ST-segment analysis. All patients received fentanyl 100 μg (JANSSEN-CILAG GmbH, Neuss, Germany) i.v. to increase comfort. Supplemental oxygen via a face mask was administered to maintain Sp_{O_2} >93%.

PCB blocks

All blocks were performed in a holding area by one experienced anaesthetist (M.H.). Patients were placed in the lateral decubitus with the operative knee up. PCBs were performed according to Chayen's approach with the insertion point 3 cm below Tuffier's line (transverse line between the upper borders of iliac crests) and 5 cm laterally to the spinous process line.[7] After sterile preparation and draping, an LA skin wheal was raised using lidocaine 20 mg (AstraZeneca GmbH, Wedel, Germany).

A 15 cm long insulated needle (Plexolong, Pajunk, Geisingen, Germany) was inserted perpendicularly to all cutaneous planes. The needle was connected to a nerve stimulator (Stimuplex® HSN 11, Braun, Melsungen, Germany) initially set at 1 mA, 1.0 ms, and 2 Hz. Needle position was judged as correct when quadriceps contractions and patellar motion were elicited with a stimulating current below 0.5 mA at 0.1 ms pulse width. After gentle aspiration to exclude vessel penetration, 30 ml of ropivacaine 0.5% (AstraZeneca, Wedel, Germany) was administered within 45 s. Subsequently, an indwelling 20 G end-hole catheter (Plexolong, Pajunk, Geisingen, Germany) with a metal guide wire was threaded 5 cm beyond the needle tip. The onset of sensory block of PCB was assessed bilaterally every 5 min at the medial, anterior, and lateral regions of the thigh until 30 min after ropivacaine administration. Motor block of femoral and obturator nerve was tested by inability of extension in the knee joint and adduction and flexion of the thigh in the hip joint. Haemodynamic data were collected during the whole study period. Complications such as vascular puncture, intoxication signs, and bilateral block were registered.

Plasma ropivacaine sampling

Baseline blood samples were obtained for measurements of α_1-acid glycoprotein and albumin concentrations. After drawing and discarding 5 ml of blood, an additional 5 ml of arterial blood was collected for determination of drug concentrations at the following time points: 0 (end of injection), 0.5, 1, 2, 3, 5, 10, 20, and 30 min after injection of ropivacaine. Blood samples were stored at 4°C and centrifuged. Plasma was frozen at −18°C and stored until analysis. Plasma concentrations of ropivacaine were determined by means of liquid chromatography-tandem mass spectrometric method. A detailed description of the exact methodology has been described elsewhere.[8] Protein precipitation was used to determine total plasma concentration of ropivacaine. Plasma concentrations of unbound ropivacaine were determined after ultrafiltration of the samples without prior protein precipitation.[9]

Statistics

Values are given as means with 25/75 percentiles and diagrammed in boxplots. The area under the plasma concentration–time curve (AUC) was calculated using the trapezoidal rule. The Pearson correlations were calculated to assess dependencies between protein concentrations and concentrations of total and unbound ropivacaine.

Results

Patient characteristic data of the patients are shown in Table 1. Measurements of the different plasma proteins yielded decreased total protein values in four patients and decreased albumin value in one patient. Total and unbound plasma concentrations of ropivacaine are given in Table 2. In Patient 11, maximum measured plasma concentration was measured at time point 0, suggesting that intravascular injection of ropivacaine occurred. The plasma concentrations in this patient declined with every further measurement and were 1686 ng ml^{-1} (total concentration) and 42 ng ml^{-1} (unbound concentration) at time point 30. The data of this patient were not included into the graphs but are part of the discussion.

In nine of the remaining 10 patients, we measured the plasma concentration of ropivacaine at time point 0. The first drawn plasma probes yielded a mean total ropivacaine concentration of 165 (range 0–763) ng ml^{-1}. Thirty seconds later, all plasma samples contained measurable concentrations of ropivacaine. In most patients, maximum free and total plasma concentrations were measured 10 min after ropivacaine injections (Table 2). The time course of the plasma concentrations are depicted in Figures 1 and 2. The maximum measured plasma concentrations showed wide inter-individual range. Unbound fractions of ropivacaine were between 1% and 5%. The Pearson correlation between plasma concentrations of total and unbound ropivacaine was 0.96. All other correlations were very weak or negative.

No signs of LA toxicity or other complications were observed, also in the patient with the presumed partial intravascular injection. Cardiovascular parameters remained unchanged.