Pharmacokinetic Modeling of Ropivacaine Following Single Shot Erector Spinae Plane Block in Anesthetized Children

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Protocol

This pilot study was a prospective, observational investigation approved by the Baylor College of Medicine IRB (H-4638). In compliance with the EQUATOR network, all reporting was conducted under the STROBE guidelines. Written informed consent (with assent where applicable) was obtained by the parent(s) or legal guardian(s) for all enrolled participants. Eligibility criteria included patients aged 6 months to 18 years weighing more than 4kg, scheduled to undergo minimally invasive video-assisted thoracoscopic surgery at Texas Children's Hospital. Exclusion criteria included allergy to local anesthetics, liver or renal dysfunction, pre-existing hypoalbuminemia, tumor or infection/abscess at the injection site, and a BMI > 95th percentile.

Patients received an inhalational or intravenous induction with a general endotracheal tube anesthesia at the discretion of the attending anesthesiologist. After the airway was secured, patients were placed in the lateral decubitus position and a single-shot unilateral ultrasound-guided ESP block, as all the procedures were unilateral incisions, was performed as previously described 1-2 dermatomal levels above the surgical incision site.[7] All patients received Ropivacaine 0.5% at 0.3ml/kg (1.5mg/kg) in the fascial plane deep to the erector spinae muscle. Since there are no standardized dosing guidelines for ESP blocks in children, we chose a slightly higher dose from the previously published Ropivacaine dosing for TAP blocks of 0.25-0.75mg/kg but remaining within the consensus maximum dosing of 1.5mg/kg for peripheral nerve blocks.[2,8] Post-anesthesia care unit (PACU) dermatomal assessments to ice were performed to validate ESP block accuracy. Intraoperative morphine equivalents (mg/kg) were additionally collected. Total and free serum Ropivacaine concentrations were obtained at baseline and the following time point after block

injection: 30, 60, and 90-minutes and 2, 4, and 6-hours. These time-points reflect those previously noted in the literature, recognizing that serum capture of Ropivacaine is likely undetectable beyond 6-hours.[8-10] A baseline alpha-1 acid glycoprotein (AAG) was also collected.

Samples were centrifuged for 15-minutes at 1100G within 2-hours of collection and the plasma was frozen at -80°C for processing at Lab ExperTox Inc. We applied the same laboratory analysis as previously described, demonstrating the reproducibility of total and free Ropivacaine levels with liquid chromatography/mass spectroscopy (LC-MS/MS).[8-12] The LC-MS/MS analysis was performed with the Agilent Technologies 6460 mass spectrometer connected with the Agilent 1200 series HPLC system via electrospray ionization mode. The samples were analyzed in positive ionization mode with the voltage set at 3000V. Data acquisition and data analysis were performed with the Agilent Mass Hunter software (Version B.07.00). The total Ropivacaine concentrations were measured after protein precipitation in methanol. The free Ropivacaine concentrations were measured with the same technique after ultracentrifugation of the samples with Vivaspin 2, 10 KDa molecular weight cut-off Concentrators (GE Healthcare, UK). The assay was validated by spiking negative serum with known concentrations of Ropivacaine. The assay method was linear over the concentration range 5 -3000 ng/mL, with a limit of detection of 1 ng/mL and a limit of quantification of 5 ng/ml.

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