

Title: PHARMACOKINETICS, PLACENTAL TRANSFER, AND NEONATAL EFFECTS OF VECURONIUM (ORG NC45) ADMINISTERED PRIOR TO DELIVERY

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**Introduction.** Paralysis is frequently required in the lightly anesthetized patient undergoing cesarean section. Although pancuronium, d-tubocurarine, and succinylcholine are used currently, each has disadvantages. Vecuronium (ORG NC45) is a short-acting, non-depolarizing muscle relaxant that does not have the vagolytic effect of pancuronium; the potential for arrhythmias, hyperkalemia, irreversibility of block, or muscle fasciculations of succinylcholine; or the ganglionic blockade or liberation of histamine of d-tubocurarine. We evaluated the pharmacokinetics of vecuronium in the mother, the placental transfer of the drug, and its subsequent effects on the fetus and neonate.

**Methods.** We obtained approval from the local committees on human research, and informed consent from 9 healthy women at term who were scheduled for cesarean section. Patients were premedicated with 30 ml magnesium and aluminum hydroxide PO, 3 mg d-tubocurarine and 0.2 mg of glycopyrrolate IV, and were preoxygenated. General anesthesia was induced with thiopental (4 mg/kg) and succinylcholine (1.5 mg/kg) in rapid sequence with cricoid pressure. After endotracheal intubation, patients received 0.04 mg/kg of vecuronium IV. Prior to delivery, anesthesia was maintained with 50% N<sub>2</sub>O in O<sub>2</sub>; after delivery, 2 to 5 mg of butorphenol<sup>2</sup> were added to deepen anesthesia. Venous blood was sampled immediately before induction, and 2, 4, 6, 8, 10, 15, 20, 25, 30, 45, 60, 90, 120, 150, 180, 210, and 240 min after vecuronium. Blood samples were also obtained at delivery from the maternal vein and from an umbilical artery and vein in a doubly clamped segment of cord. Samples were centrifuged and frozen until analyzed.

We determined serum concentrations of vecuronium using direct inlet chemical ionization mass spectrometry, a method involving an ion-pair extraction and deuterated vecuronium as an internal standard. The sensitivity of this method was 1 ng/ml of serum. The pharmacokinetics of vecuronium were determined in 5 patients. A two-

compartment open pharmacokinetic model was fitted to resulting data.

We evaluated the condition of the infant using Apgar scores at 1 and 5 min, time-to-sustained respirations (TSR), and a neurobehavioral exam at 15 min, 2 hr, and 24 hours after birth in all nine patients.

**Results.** The mean interval between induction of anesthesia and delivery was  $8.6 \pm 1.7$  (mean  $\pm$  SD) min; and between administration of vecuronium and delivery,  $6.7 \pm 1.6$  min. Administration of vecuronium prior to delivery did not adversely affect Apgar or neurobehavioral scores, TSR, or acid-base status of umbilical cord blood.

At delivery, the concentration of vecuronium in the maternal vein was  $162 \pm 29$  ng/ml; and in the umbilical vein,  $17.9 \pm 5.5$  ng/ml. The ratio of the concentration in the umbilical vein to that in the maternal vein was  $0.11 \pm 0.04$ . The maternal distribution half-life was  $5.1 \pm 2.1$  min; the elimination half-life,  $36 \pm 4$  min; the volume of distribution at steady state,  $25 \pm 16$  ml/kg; and total clearance,  $6.4 \pm 1.6$  ml/kg/min.

**Discussion.** Administration of vecuronium prior to delivery had no adverse effect on the fetus or neonate. The elimination half-life of vecuronium was much shorter (36 min) in pregnant women than in those not pregnant (79 min).<sup>2</sup> The ratio of umbilical vein to maternal vein concentrations for vecuronium (0.11) was approximately half that previously reported for pancuronium (0.23).<sup>5</sup>

#### References.

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