Date

Title : THE PHARMACOKINETICS OF NORCURON IN PATIENTS WITH NORMAL AND IMPAIRED RENAL FUNCTION

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Introduction. Norcuron is a monoquaternary analogue of pancuronium which is 1.5 times more potent but has one third the duration of action of pancuronium. Although the pharmacokinetics of norcuron have not been determined, Durant et al.[1] found that absence of renal function does not significantly prolong the duration of neuromuscular blockade produced by norcuron in cats. Therefore we proposed to study the pharmacokinetics of norcuron in patients with normal and impaired renal function.

Methods. Four adult surgical patients with normal renal function and three adult surgical patients with chronic renal failure scheduled to receive cadaver renal transplants were selected. This study was approved by the Committee on Human Experimentation and informed consent was obtained in all cases. Patients were premedicated with diazepam and anesthetized with thiopental, halothane, and nitrous oxide. Body temperature and $PaCO_2$ were maintained within normal limits. Norcuron, 0.14 to 0.28 mg/kg, was administered as a two minute controlled infusion. Blood sampled intermittently for four hours was assayed for norcuron using a high pressure liquid chromatography technique. Data were analyzed by nonlinear least squares regression analysis and fitted to a two compartment open pharmacokinetic model.

Results and Conclusions. The pharmacokinetic variables computed from the norcuron serum concentrations are summarized in Table 1. The elimination half-life of norcuron in patients with normal renal function (72 ± 6.1 min, mean ± SD) is approximately one-half that estimated for pancuronium (132 ± 25 min).[2] This may offer a pharmacokinetic explanation for the shorter duration of neuromuscular blockade for norcuron as compared to pancuronium.

Patients with chronic renal failure showed a 12% reduction in clearance of norcuron. This compares favorably to the 55% reduction in pancuronium clearance found by Somogyi.[2] Furthermore, the duration of neuromuscular blockade was 137 minutes in renal failure patients following norcuron administration. This represents only a 32% prolongation of blockade compared to patients with normal renal function receiving the same dose of norcuron.

Thus, norcuron offers the clinical advantage of rapid elimination from plasma and lesser dependence on renal mechanisms for clearance.

References.

1. Durant N, Houwertjes M, Agoston S: Renal elimination of Org-NC45 and pancuronium. Anesthesiology 51:266, 1979

2. Somogyi A, Shanks C, Triggs E: The effect of renal failure on the disposition and neuromuscular blocking action of pancuronium bromide. Europ J Clin Pharmacol 12:23-29, 1977

Table 1.

	Central Volume ℓ/kg	Steady State Volume ℓ/kg	Elimination Half-life min	Clearance ml/min/kg
Normal Renal Function	.12 (±.055)	.35 (±.086)	72 (±6.1)	5.8 (±.69)
Renal Failure	.18 (±.036)	.52 (±.10)	100 (±20)	5.1 (±.99)

Values are mean ± SD

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