Date

Title : PHARMACOKINETICS OF EDROPHONIUM IN PATIENTS WITHOUT RENAL FUNCTION

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Introduction. Impaired renal function decreases plasma clearance and increases the duration of action of d-tubocurarine and pancuronium in anesthetized patients.[1,2] Prolonged neuromuscular blockade may result if clearance of the antagonist (neostigmine, pyridostigmine or edrophonium) is not decreased by renal failure. Edrophonium (0.5 to 1.0 mg/kg) recently has been shown to provide reliable and sustained antagonism of non-depolarizing neuromuscular blockade.[3,4] We have shown that neostigmine and pyridostigmine have prolonged elimination half-lives and decreased clearances in renal failure, however no information exists for edrophonium.[5,6] Using a pharmacokinetic analysis, this study determined the influence of renal failure on the elimination of edrophonium in anesthetized patients.

Methods. After informed consent approved by our Committee on Human Research, patients with normal renal function (n=6) were compared to those undergoing renal transplant nephrectomy (n=3). Patients premedicated with diazepam were anesthetized with thiopental, nitrous oxide, and halothane. d-Tubocurarine was administered as an intermittent intravenous bolus to maintain a 90% blockade of muscle twitch tension. Edrophonium (0.5 or 1.0 mg/kg) combined with atropine (1.0 mg) was administered by a two minute intravenous infusion and venous blood was then sampled intermittently for four hours. Serum concentrations of edrophonium were determined by high pressure liquid chromatography. Data were analyzed using a model independent pharmacokinetic analysis. The terminal half-life was estimated using linear regression of log plasma concentrations with time. Total body clearance was estimated as dose/area under the concentration curve (linear trapezoid method). Volume of distribution at steady state was estimated by the method of Benet.[7]

Results. The volume of distribution of edrophonium at steady state did not differ significantly between patients with normal renal function (.87 ± .2 ℓ/kg mean ± SD) and anephric patients (.64 ± .2 ℓ/kg. The elimination half-life was significantly prolonged in anephric patients (206 ± 21 min) compared to those with normal renal function (114 ± 47). Total serum clearance was significantly decreased from 8.2 ± 2.7 ml/kg/min in patients with normal renal function to 2.2 ± .5 ml/kg/min in anephric patients.

Conclusions. We conclude that renal excretion accounts for 70% of the clearance of edrophonium and in renal failure its elimination half-life is prolonged similar to that of pancuronium and d-tubocurarine.[1,2] If pharmacologic effects are proportionately prolonged, recurarization may be unlikely in renal failure patients even when edrophonium is used as the antagonist. Also the pharmacokinetic variables for edrophonium are comparable to those for neostigmine and pyridostigmine in renal failure.[5,6]

References

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