Title : D-Tubocurarine: Pharmacodynamics and Kinetics in Children

Authors : C. O'Keeffe, G.A. Gregory, M.D., D.R. Stanski, M.D. and R.D. Miller, M.D.

Affiliation: Departments of Anesthesia, Pharmacology and the Cardiovascular Research Institute, University of California, San Francisco CA 94143

Introduction: Previous investigators have shown a variable response to d-Tubocurarine (dTC) in children.[1] Others have suggested that children have an increased sensitivity to dTC.[2] The pharmacokinetics and pharmacodynamics of dTC have not been examined in children. The present study was designed to evaluate the effects of dTC on both pharmacodynamics and pharmacokinetics and to answer the question whether pediatric patients are indeed more sensitive to dTC.

Methods: Nine healthy pediatric patients, ages one month to 15 years, scheduled for elective surgery that required muscle relaxation were studied. They had normal renal function. Parental, and where appropriate, patient consent were obtained. The study was approved by the Human Research Committee at the University of California at San Francisco. Anesthesia was induced with nitrous oxide, 70% and 0.58 MAC end-tidal halothane adjusted for age. Ventilation was adjusted to maintain normcarbia. Paralysis was assessed by quantitating the electromyographic twitch height in response to supramaximal stimulation of the ulnar nerve. dTC was infused over several minutes to depress twitch height 70-90%. Blood samples were withdrawn from a separate catheter for analysis of dTC concentration by immunoassay. The pharmacokinetic data were analyzed by the two-compartment model. The effect data were fitted to the pharmacodynamic model of Sheiner et al.[3] These results were compared to identical studies performed in adults.[4]

Results:

1. The computed Cpss50 (plasma level at steady state at which 50% depression of twitch height occurred) were not different between children and adults. We conclude that children are not more sensitive to dTC than are adults.

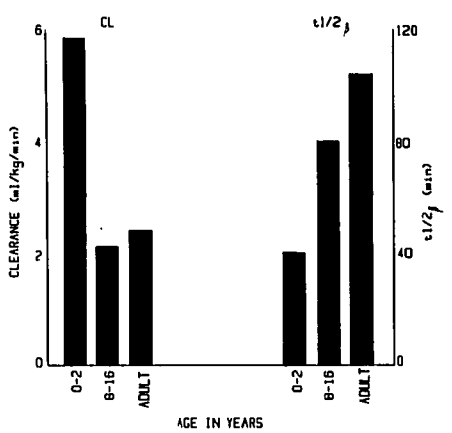
2. There were no differences in the central (V_1) and steady state volumes of distribution (Vd_{ss}) and distribution half lives (t 1/2) between children and adults.

3. The elimination half-life (t 1/2) (Fig 1) were shorter in children when compared to adults. The clearance (Cl) was correspondingly greater (Fig 1).

Discussion: During nitrous oxide-halothane anesthesia, the pharmacokinetics of dTC in children differed in only one respect from adults - a shorter elimination half-life, and therefore increased clearance. Given a sensitivity equivalent to adults, children may require repeated doses of dTC at a greater frequency than adults.

Figure 1

The Relationship of Age, t1/2 and Clearance for Curare



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