ion, and efficacy of ceftriaxone versus cefazolin in open heart surgery.

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Abstract:

The effects of cardiopulmonary bypass (CPB) with hypothermia and systemic heparinization on ceftriaxone disposition were evaluated in seven male patients. A bolus dose of drug (14 mg/kg of body weight) was given, and blood and urine specimens were collected before, during, and after CPB for 96 h. Creatinine, albumin, and total and free ceftriaxone concentrations in plasma were measured. The ceftriaxone free fraction (ff) in vitro was estimated by equilibrium dialysis, and the in vivo ff was obtained by the ratio of renal clearance due to filtration to creatinine clearance. Pharmacokinetic parameters were based on concentrations of total drug and free drug. Albumin decreased from 3.10 +/- 0.29 g/dl presurgery to 1.42 +/- 0.17 g/dl and recovered to 2.46 +/- 0.26 g/dl on postoperative day 4. CPB markedly increased the in vitro ff, which was reversed by protamine post-CPB (ff pre-CPB, 0.15 +/- 0.01; during CPB, 0.53 +/- 0.20; post-CPB, 0.16 +/- 0.02). The in vitro ff exceeded the in vivo ff (0.53 +/- 0.20 versus 0.24 +/- 0.07), probably due to continued free fatty acid release caused by heparin during dialysis. Clearances based on free drug decreased, and the renal clearance due to filtration increased (7.6 +/- 2.8 versus 15.0 +/- 4.5 ml/min) while the creatinine clearance decreased (114 +/- 29 versus 72 +/- 28 ml/min) during CPB. Diminished binding owing to low albumin and free fatty acids explain this behavior. Lower binding also increased the volume of distribution (154 +/- 41 ml/kg) and extended the half-life (15 +/- 6 h). In summary, ceftriaxone disposition was significantly altered by CPB, resulting in marked increases in free drug concentrations, half-life, and volume of distribution and in decreased intrinsic clearance.