Abstract

AIM:

To investigate the pharmacokinetics and clinical efficacy of intravenous (i.v.) and intramuscular (i.m.) lorazepam (LZP) in children with severe malaria and convulsions.

METHODS:

Twenty-six children with severe malaria and convulsions lasting > or =5 min were studied. Fifteen children were given a single dose (0.1 mg kg(-1)) of i.v. LZP and 11 received a similar i.m. dose. Blood samples were collected over 72 h for determination of plasma LZP concentrations. Plasma LZP concentration-time data were fitted using compartmental models.

RESULTS:

Median [95% confidence interval (CI)] LZP concentrations of 65.1 ng ml(-1) (50.2, 107.0) and 41.4 ng ml(-1) (22.0, 103.0) were attained within median (95% CI) times of 30 min (10, 40) and 25 min (20, 60) following i.v. and i.m. administration, respectively. Concentrations were maintained above the reported therapeutic concentration (30 ng ml(-1)) for at least 8 h after dosing via either route. The relative bioavailability of i.m. LZP was 89%. A single dose of LZP was effective for rapid termination of convulsions in all children and prevention of seizure recurrence for >72 h in 11 of 15 children (73%, i.v.) and 10 of 11 children (91%, i.m), without any clinically apparent respiratory depression or hypotension. Three children (12%) died.

CONCLUSION:

Administration of LZP (0.1 mg kg(-1)) resulted in rapid achievement of plasma LZP concentrations within the reported effective therapeutic range without significant cardiorespiratory effects. I.m administration of LZP may be more practical in rural healthcare facilities in Africa, where venous access may not be feasible.