

# Chloramphenicol pharmacokinetics in African children with severe malaria

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## **Abstract:**

The objective of this study was to determine if the current dosage regimen for chloramphenicol CAP administered to children with severe malaria SM for presumptive treatment of concomitant bacterial meningitis achieves steady state plasma CAP concentrations within the reported therapeutic range of 10-25 mg/l. Fifteen children (11 male, 4 female) with a median age of 45 months (range: 10-108 months) and having SM, were administered multiple intravenous doses (25 mg/kg, 6 hourly for 72 h) of chloramphenicol sodium succinate CAPS for presumptive treatment of concomitant bacterial meningitis. Blood samples were collected over 72 h, and plasma CAPS, CAP and CSF CAP concentrations determined by high performance liquid chromatography. Average steady state CAP concentrations were approximately 17 mg/l, while mean fraction unbound (0.49) and CSF/plasma concentration ratio (0.65) were comparable to previously reported values in Caucasian children. Clearance was variable (mean = 4.3 l/h), and trough plasma concentrations during the first dosing interval were approximately 6 mg/l. Simulations indicated that an initial loading dose of 40 mg/kg CAPS, followed by a maintenance dose of 25 mg/kg every 6 h would result in trough CAP concentrations of approximately 10 mg/l and peak concentrations <25 mg/l throughout the treatment period. The current dosage regimen for CAP needs to include a loading dose of 40 mg/kg CAPS to rapidly achieve plasma CAP concentrations within the reported therapeutic range.