

Pharmacokinetics of high-dose methotrexate in infants treated for acute lymphoblastic leukemia

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Background. Interfant-99 was an international collaborative treatment protocol for infants with acute lymphoblastic leukemia (ALL). **Procedure.** We collected data on 103 infants at the time of their first treatment with high-dose methotrexate (HD MTX), 5 g/m². Children <6 months of age received two-third of the calculated dose based on body surface area (BSA), children 6-12 months three-fourth of the calculated dose, and children >12 months full dose. **Results.** The median steady-state MTX concentration at the end of the 24-hr infusion was 57.8 mM (range 9.5-313). The median systemic clearance was 6.22 L/hr/m² BSA, and tended to increase with age (P = 0.099). Boys had higher clearance than girls, 6.77 and 5.28 L/hr/ m² (P = 0.030), and tended to have lower median MTX concentration at 24 hr. Eight infants had MTX levels below 20 mM, a level judged to be sufficient in B-lineage ALL in children >1 year of age. All infants tolerated the dose well enough to receive a second dose of HD MTX with