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Therapeutic Efficacy of Artesunate–Amodiaquine Combinations and the Plasma and Saliva Concentrations of Desethylamodiaquine in Children With Acute Uncomplicated *Plasmodium falciparum* Malaria

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The treatment efficacy of artesunate–amodiaquine (AQ) coformulated or copackaged, and the plasma and saliva concentrations of desethylamodiaquine (DEAQ), the active metabolite of AQ, were evaluated in 120 and 7 children, respectively, with uncomplicated *Plasmodium falciparum* malaria treated with oral daily doses of the 2 formulations for 3 days. All children recovered clinically. Fever clearance (1.1 ± 0.2 vs 1.0 ± 0 days) and parasite clearance times (21.1 ± 10.2 vs 19.0 ± 7.0 hours) in artesunate–AQ coformulated and artesunate–AQ copackaged treated children, respectively, were similar. All children remained aparasitemic for at least 28 days. Blood and saliva samples were collected over 35 days and DEAQ in plasma and saliva was determined by high-performance liquid chromatography. DEAQ was detectable in plasma and saliva within 40 minutes of oral administration of artesunate–AQ. DEAQ concentrations 7 days after the start of therapy were 247.8 and 125.1 ng/mL in plasma and saliva, respectively. The concentration–time curves of plasma and saliva in declining phases were approximately parallel giving a similar half-life of 169.1 ± 16.4 and 142.8 ± 6.5 hours in plasma and saliva, respectively. Clearance from plasma and saliva was also similar (335.6 and 443.4 $mL \cdot h^{-1} \cdot kg^{-1}$, respectively). Area under concentration–time curves (AUC_{0-35d}) for plasma and saliva were 94,744.9 and 74,004.2 $ng \cdot mL^{-1} \cdot h$, respectively. In general, Saliva–plasma concentration ratio was 0.25–0.4. DEAQ concentrations in saliva may be useful for monitoring therapy and for the evaluation of the disposition of AQ in children with falciparum malaria treated with AQ-based combination.

Keywords: artesunate–amodiaquine, desethylamodiaquine, plasma, saliva, malaria, children

INTRODUCTION

Of the recommended artemisinin-based combination therapies in Africa, artesunate–amodiaquine (AQ) is one of the most readily available and widely used.[1,2] In many endemic countries, artesunate–AQ combination drugs are available as copackaged drugs and, until recently, fixed dose combination. Despite ready availability of these 2 formulations, very few recent studies have compared the efficacy of these formulations.[3,4] In

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