Recrudescence in artesunate-treated patients with falciparum malaria is dependent on parasite burden not on parasite factors

Ittarat W.\textsuperscript{a}, Pickard A.L.\textsuperscript{b}, Rattanasinganchan P.\textsuperscript{a}, Wilairatana P.\textsuperscript{c}, Looareesuwan S.\textsuperscript{c}, Emery K.\textsuperscript{d}, Low J.\textsuperscript{e}, Udomsangpetch R.\textsuperscript{f}, Meshnick S.R.\textsuperscript{g}

\textsuperscript{a} Department of Clinical Microscopy, Faculty of Medical Technology, Mahidol University, Bangkok 10700, Thailand
\textsuperscript{b} Department of Epidemiology, Univ. of NC School of Public Health, Chapel Hill, NC 27599, United States
\textsuperscript{c} Dept. of Clinical Tropical Medicine, Bangkok Hosp. for Tropical Diseases, Mahidol University, Bangkok 10700, Thailand
\textsuperscript{d} c/o Foxman Research Group, Univ. of Michigan Sch. of Pub. Hlth., 109 S. Observatory, Ann Arbor, MI 48109, United States
\textsuperscript{e} Box 0944, Dock 5, 6431 CCGC, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, United States
\textsuperscript{f} Dept. of Experimental Pathobiology, Faculty of Science, Mahidol University, Bangkok 10700, Thailand
\textsuperscript{g} Department of Epidemiology, Univ. of NC School of Public Health, Chapel Hill, NC 27599-7435, United States

\textbf{Abstract}

Artemisinin derivatives are first-line antimalarial drugs in Thailand. No firm evidence of clinically relevant artemisinin resistance exists. When used as monotherapy, artesunate has been associated with a high treatment failure (recrudescence) rate, which could be due to low-level artemisinin resistance. To understand the causes of recrudescence, we retrospectively studied a cohort of 104 malaria patients treated with artesunate monotherapy, 32 of whom recrudesced. There was no difference in in vitro artesunate sensitivities between 6 nonrecrudescent isolates and 16 paired admission and recrudescent isolates. Paired admission and recrudescent isolates from 10 patients were genotyped; only 3 had pfmdr1 mutations. Patients with admission parasitemias $>10,000$ per $\mu l$ had a 9-fold higher likelihood of recrudescence (adjusted odds ratio) compared with patients with lower parasitemias. This study suggests (1) recrudescence after treatment with artesunate is not the result of inherent parasite resistance, and (2) admission parasitemia may be useful in choosing therapeutic options.

American Journal of Tropical Medicine and Hygiene. 2003; 68(2) : 147-152