

MEFLOQUINE EFFICACY AND *PFMDR1* POLYMORPHISMS ON THE THAI-MYANMAR BORDER

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Polymorphisms in the *Plasmodium falciparum* gene *pfmdr1* have been shown to correlate with mefloquine resistance *in vitro*. In this study, we test whether polymorphisms in *pfmdr1* will be useful predictors of *in vivo* drug failure. Patients presenting with uncomplicated *falciparum* malaria in Sangkhlaburi, Kanchanaburi province, Thailand, were enrolled and seen at least once a week for a six-weeks. Patient isolates were cultured, assessed for *In vitro* drug sensitivity, and genotyped. 36 patients were enrolled and completed follow-up. The average age was 28.3 years. This study population of migrants from Myanmar are generally known to be semi-immune although at the initial visit only 30 (83.3%) of them reported no other episode of malaria in the previous 12 months. Four patients were treated with artesunate-mefloquine and none recrudesced. 15 of 32 patients receiving mefloquine (750 mg single dose) and primaquine therapy recrudesced, yielding a mefloquine efficacy of 53.1%. There was no difference in parasitemia between recrudescing and non-recrudescing patients. Mean time to malaria recrudescence was 31.9 days (± 2.45). One patient recrudesced at 8 days of follow-up, six more patients recrudesced between 21 and 29 days, and eight patients between 35 and 42 days. *Pfmdr1* genotyping was completed for isolates cultured from 17 patients. Five isolates were wildtype, nine isolates had the Phe184 mutation and one mixed. There were 5 cases of mefloquine failure and 10 of success in this group. There were also one patient with Tyr86 mutations and one with Phe184 plus Asp1042 mutations. Both were successfully treated with mefloquine. Thus, *pfmdr1* mutations alone do not appear to be useful predictors of treatment outcomes in this semi-immune population. Because of the poor mefloquine efficacy on this part of the western border of Thailand, the need to predict and prevent treatment failure is immediate. Most of these treatment failures would not have been detected without the extended, 42-day follow-up. Possible links between the *in-vitro* utility of *pfmdr1* mutations with treatment failure should be further explored.

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