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Plasmodium vivax trophozoites insensitive to chloroquine

(2008) *Malaria Journal*, 7, art. no. 94, . Cited 33 times.

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Abstract
Background. Plasmodium vivax is a major cause of malaria and is still primarily treated with chloroquine. Chloroquine inhibits the polymerization of haem to inert haemozoin. Free haem monomers are thought to catalyze oxidative damage to the Plasmodium spp. trophozoite, the stage when haemoglobin catabolism is maximal. However preliminary in vitro observations on P. vivax clinical isolates suggest that only ring stages (early trophozoites) are sensitive to chloroquine. In this study, the stage specific action of chloroquine was investigated in synchronous cryopreserved isolates of P. vivax. Methods. The in vitro chloroquine sensitivity of paired ring and trophozoite stages from 11 cryopreserved P. vivax clinical isolates from Thailand and two Plasmodium falciparum clones (chloroquine resistant K1 and chloroquine sensitive FC27) was measured using a modified WHO microtest method and fluorometric SYBR Green I Assay. The time each stage was exposed to chloroquine treatment was controlled by washing the chloroquine off at 20 hours after the beginning of treatment. Results. Plasmodium vivax isolates added to the assay at ring stage had significantly lower median IC50sto chloroquine than the same isolates added at trophozoite stage (median IC5012 nM vs 415 nM p < 0.01). Although only 36% (4/11) of the SYBR Green I assays for P. vivax were successful, both microscopy and SYBR Green I assays indicated that only P. vivax trophozoites were able to develop to schizonts at chloroquine concentrations above 100 nM. Conclusion. Data from this study confirms the diminished sensitivity of P. vivax trophozoites to chloroquine, the stage thought to be the target of this drug. These results raise important questions about the pharmacodynamic action of chloroquine, and highlight a fundamental difference in the activity of chloroquine between P. vivax and P. falciparum. © 2008 Sharrock et al; licensee BioMed Central Ltd.

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Document Type: Article
Source: Scopus