

Two mutations in dihydrofolate reductase combined with one in the dihydropteroate synthase gene predict sulphadoxine–pyrimethamine parasitological failure in Ugandan children with uncomplicated falciparum malaria.

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Abstract

The point mutations in the *Plasmodium falciparum* dihydrofolate reductase (*dhfr*) and the dihydropteroate synthase (*dhps*) genes that are linked to sulphadoxine–pyrimethamine (SP) resistance in vitro have been well characterised. To determine whether a few of these mutations could predict SP treatment failure in vivo, two mutations (Asn-108 and Arg-59) in the *dhfr* gene and one (Glu-540) in the *dhps* gene were analysed according to the risk of SP parasitological failure (RI–RIII) at day 28 in pre-treatment isolates in 79 Ugandan children aged 6–59 (mean = 18.4, S.D. = 8.8) months with uncomplicated falciparum malaria. Neither the *dhfr*-108 ($P=0.3$) nor the *dhps*-540 ($P=0.6$) or *dhfr*-108 + *dhps*-540 ($P=0.08$) mutations were significantly associated with SP parasitological failure. However, the *dhfr*-108 + *dhfr*-59 ($P = 0.04$), the *dhfr*-59 + *dhps*-540 ($P = 0.04$) and the *dhfr*-108 + *dhfr*-59 + *dhps*-540 ($P = 0.02$) mutations significantly increased the risk for SP parasitological failure. Our findings confirm an earlier report that the *dhfr*-59 and the *dhps*-540 mutations could be useful genetic markers for rapid screening of populations at high risk of SP resistance.