The role of sequential administration of sulphadoxine/pyrimethamine following quinine in the treatment of severe falciparum malaria in children

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AbstractSulphadoxine/pyrimethamine (SP) is often administered with quinine in the treatment of severe falciparum malaria to shorten the course of quinine. The efficacy of SP alone in the treatment of non-severe malaria has been declining rapidly in East Africa, raising concerns of the usefulness of a shortened course of quinine followed SP. We audited the efficacy of quinine/SP in the treatment of severe malaria in Kenyan children. Children with severe falciparum malaria were treated with parenteral quinine followed by a single oral dose of SP. A clinical evaluation was performed 3 weeks later in which a blood sample was obtained for full haemogram, blood slide and analysis of the parasite dihydrofolate reductase (DHFR) and dihydropteroate synthase (DHPS) codons, mutations of which are associated with resistance to SP. A total of 452 children were enrolled, of whom 374 completed the study. Fifty-two (13.9%) children were parasitaemic by 3 weeks of whom 17 (4.5%) had fever as well. The treatment failure group had a significantly higher parasitaemia (129 061 vs. 43 339; $P<0.001$) and haemoglobin on admission, but only admission parasitaemia independently predicted treatment failure. Those with treatment failure had a significantly lower rise in haemoglobin at 3 weeks compared with treatment successes (9.0 vs. 10.0 g/dl). Of the 76 parasite isolates collected before treatment, 40 (53%) were triple mutant DHFR-double DHPS (Tp-Db), the genotype most associated with SP resistance. Three weeks after SP treatment, the proportion of Tp-Db increased to 72% (31/43). The high treatment failure rate and proportion of parasites with Tp-Db negate the use of SP to shorten the course of quinine treatment in East Africa