SEASONAL MALARIA CHEMOPREVENTION WITH SULPHADOXINE-PYRIMETHAMINE AND AMODIAQUINE SELECTS DHFR-DHPS QUINTUPLE MUTANT GENOTYPE IN MALI

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Background Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine (SP)+amodiaquine (AQ) is being scaled up in countries of the Sahel in West Africa. However, the potential development of Plasmodium falciparum resistance to the respective component drugs is a major concern.

Methods Two cross-sectional surveys were conducted before (August 2012) and after (June 2014) a pilot implementation of SMC in Koutiala, Mali. Children aged 3–59 months received 7 rounds of curative doses of SP+AQ over two malaria seasons. Genotypes of P. falciparum dhfr codons 51, 59 and 108; dhps codons 437 and 540, pfcrt codon 76 and pfmdr1 codon 86 were analysed by PCR on DNA from samples collected before and after SMC, and in non-SMC controls.

Results In the SMC population 191/662 (28.9%) and 85/670 (13.7%) of children were P. falciparum-positive by microscopy and were included in the molecular analysis before (2012) and after SMC implementation (2014), respectively. In the control population 220/310 (71%) were successfully PCR analysed. In the SMC children the prevalence of all molecular markers of SP resistance increased significantly after SMC including the dhfr-dhps quintuple mutant genotype, which was 1.6% before but 7.1% after SMC (p=0.02). The prevalence of Pfmdr1–86Y significantly decreased from 26.7% to 15.3% (p=0.04) while no significant change was seen for pfcrt K76T. In 2014, prevalence of all molecular markers of SP resistance were significantly higher among SMC children compared to the non-SMC control population (p<0.01). No dhfr – 164 mutation was found neither at baseline nor post SMC.

Conclusions SMC increased the prevalence of molecular markers of P. falciparum resistance to SP in the treated children. However, there was no significant flow of these resistance genes into the general parasite population after 2 years and 7 rounds of SMC.