ance before and after its withdrawal in Kenya

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Abstract:

Background The spread of resistance to chloroquine (CQ) led to its withdrawal from use in most countries in sub-Saharan Africa in the 1990s. In Malawi, this withdrawal was followed by a rapid reduction in the frequency of resistance to the point where the drug is now considered to be effective once again, just nine years after its withdrawal. In this report, the polymorphisms of markers associated with CQ-resistance against Plasmodium falciparum isolates from coastal Kenya (Kilifi) were investigated, from 1993, prior to the withdrawal of CQ, to 2006, seven years after its withdrawal. Changes to those that occurred in the dihydrofolate reductase gene (dhfr) that confers resistance to the replacement drug, pyrimethamine/sulphadoxine were also compared. Method :Mutations associated with CQ resistance, at codons 76 of pfcrt, at 86 of pfmdr1, and at codons 51, 59 and 164 of dhfr were analysed using PCR-restriction enzyme methods. In total, 406, 240 and 323 isolates were genotyped for pfcrt-76, pfmdr1-86 and dhfr, respectively. Results :From 1993 to 2006, the frequency of the pfcrt-76 mutant significantly decreased from around 95% to 60%, while the frequency of pfmdr1-86 did not decline, remaining around 75%. Though the frequency of dhfr mutants was already high (around 80%) at the start of the study, this frequency increased to above 95% during the study period. Mutation at codon 164 of dhfr was analysed in 2006 samples, and none of them had this mutation. Conclusion: In accord with the study in Malawi, a reduction in resistance to CQ following official withdrawal in 1999 was found, but unlike Malawi, the decline of resistance to CQ in Kilifi was much slower. It is estimated that, at current rates of decline, it will take 13 more years for the clinical efficacy of CQ to be restored in Kilifi. In addition, CQ resistance was declining before the drug's official withdrawal, suggesting that, prior to the official ban, the use of CQ had decreased, probably due to its poor clinical effectiveness