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Antimalarial efficacy of chloroquine, amodiaquine, sulfadoxine-pyrimethamine, and the combinations of amodiaquine + artesunate and sulfadoxine-pyrimethamine + artesunate in Huambo and Bié provinces, central Angola

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Summary We studied three antimalarial treatments in Caala and Kuito, Angola, in 2002 and 2003. We tested chloroquine (CQ), amodiaquine (AQ) and sulfadoxine-pyrimethamine (SP) in Caala, and AQ, SP and the combinations AQ + artesunate (AQ + AS) and SP + artesunate (SP + AS) in Kuito. A total of 619 children (240 in Caala, 379 in Kuito) with uncomplicated *Plasmodium falciparum* malaria were followed-up for 28 days, with PCR genotyping to distinguish recrudescence from reinfection. PCR-corrected failure proportions at day 28 were very high in the CQ group (83.5%, 95% CI 74.1—90.5), high in the SP groups (Caala: 25.3%, 95% CI 16.7—35.8; Kuito: 38.8%, 95% CI 28.4—50.0), around 20% in the AQ groups (Caala: 17.3%, 95% CI 10.0—27.2; Kuito: 21.6%, 95% CI 14.3—30.6) and very low in the artemisinin-based combination groups

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(1.2%, 95% CI 0.0—6.4 for each combination AQ + AS and SP + AS). These results show that CQ and SP are no longer efficacious in Caala and Kuito and that the moderate efficacy of AQ is likely to be compromised in the short term if used as monotherapy. We recommend the use of AQ with AS, though this combination might not have a long useful therapeutic life because of AQ resistance.

1. Introduction

In Africa, *Plasmodium falciparum* resistance to common antimalarials represents a major obstacle for malaria control. In the Republic of Angola, which reports 1.5 million clinical cases of malaria each year (MINSA, 2001), the development of resistance to first-(chloroquine, CQ) and second-line (sulfadoxine-pyrimethamine, SP) treatments represents an important problem for the national health authorities. The first cases of resistance of *P. falciparum* to CQ and SP in Angola were reported almost 20 years ago (Martinez et al., 1985; Peña et al., 1988). Additional data were collected during the 1980s and 1990s (Kyronseppa et al., 1984; Laureillard et al., 1996; Lindberg et al., 1985; Suleimanov, 1994). However, these data were difficult to interpret and compare as different study designs had been used. Although observations from local clinicians suggested that CQ and SP were losing their efficacy, no recent data on antimalarial drug efficacy were available to the Angolan Malaria Control Program for the formulation of a sound national drug policy. In 2001, in order to fill this gap and explore potential alternatives to the current policy, the Ministry of Health carried out several in vivo studies in Luanda, Cabinda, Malange, Huambo, Bié, Benguela and Huila provinces. At three sites, the studies were carried out in collaboration with Medecins sans Frontiéres (MSF). In this paper, we report the results obtained from two of these sites (Caala, Huambo province; Kuito, Bié province) where, unlike the other sites, the follow-up was extended to 28 days and artemisinin-containing treatments (ACT) were evaluated. The protocols were discussed with a Scientific Committee of the Ministry of Health (MOH) in Luanda and eventually approved by the national and provincial health authorities. Specific changes introduced to our study protocols in Caala and Kuito (duration of 28 days, use of PCR for genomic analysis, use of ACT) were also approved by the MOH at national and provincial level.

2. Materials and methods

2.1. Study site and population

The studies were conducted in the towns of Caala and Kuito, located in central Angola. Both areas have been heavily affected by the civil war that divided the country for more than two decades. This explains the deterioration of roads and buildings, the lack of basic services (water, sanitation and electricity), the limited communications with the rest of the country, and the presence of a large internally displaced population (IDP), residing in camps, whose access to health care has been largely insufficient. Medecins sans Frontiéres has been present in Kuito since 1989 and in Caala since 1994, working in IDP camps and supporting the hospitals of the towns. Huambo and Bié provinces have been classified as mesoendemic, with malaria being stable and seasonal with a peak of transmission from September to April. Annual temperatures range from 21 to 26 °C and annual rainfall between 200 and 1000 mm (MINSA, 2001). In Caala, patients were recruited from Caala Health Centre where malaria represents an important cause for attendance: between January and April 2002, 5220 cases of malaria diagnosed on clinical bases were reported, representing 24% of the total consultations. In Kuito, patients were recruited from the Out Patient Department (OPD) of Bié Provincial Hospital. Four weeks after the start of the study and because of the low recruitment, patients were also recruited from three health posts and one Maternal and Child Centre, all located within a 10 km distance of the hospital.

2.2. Inclusion criteria and procedures

The studies were based on current WHO recommendations (WHO, 2002) and conducted in accordance with the ethical principles contained in the Declaration of Helsinki. In brief, children aged 6 to 59 months, living within 1 hour's walk of the clinic,