A randomized comparison of sulphadoxine-pyrimethamine and combination of sulphadoxine pyrimethamine with chloroquine in the treatment of uncomplicated falciparum malaria in Eastern Sudan

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Early diagnosis and effective treatment with appropriate drug is the main component of the World Health Organization (WHO) strategy to reduce malaria-related mortality.[1] For many years the treatment of malaria in Africa has relied on chloroquine, sulphadoxine-pyrimethamine (SP), and quinine, with the latter being used mainly to treat severe cases. Chloroquine and SP are failing and leading to an increase in mortality from malaria especially in East Africa.[2]

The increasing resistance of *Plasmodium falciparum (P. falciparum)* in Sudan to chloroquine created urgent needs for evaluation of alternative antimalarial drugs.[3] These should be effective, safe, readily available and affordable. Several African countries have adopted SP as the first line treatment for malaria after chloroquine failure. Sudanese health authority has now adopted SP as the first line treatment for uncomplicated falciparum malaria. High level of resistance to SP across Eastern and Southern parts of Africa has been reported and Eastern Sudan is not an exception.[4] Combination of SP with chloroquine could slow down the development of resistance to these drugs. Chloroquine is safe, cheap and has antipyretic effect and it was recently reported to be synergistic to SP in other African countries.[5] No data exist in Sudan about combination of SP with chloroquine, hence, this has been the objective of this work. The study was conducted in Elsawagi Alganoubi, Kassala, Eastern Sudan during the period September - November 2003. Patients with documented axillary temperature ≥37.5^{o}C and with confirmed uncomplicated *P. falciparum* infection were included in the study after obtaining informed consent. Patients were excluded if they have concurrent infection, allergy to sulfonamide, or treatment within the last 2 weeks with sulfonamide, quinine, mefloquine or chloroquine. All enrolled patients underwent a thorough history and physical examination by the medical officer and received either SP alone (sulphadoxine 25 mg/kg, Amipharma laboratory, Sudan), or SP as per mentioned dose plus chloroquine (Amipharma laboratory, Sudan) 25 mg/kg, 10 mg at day 0, 10 mg at day1 and 5 mg at day 2. The patients were given the medication orally under supervision and monitored for 30 minutes. A second full dose was administered if the patient vomited within 30 minutes. Patients who vomited the drug for the second time were excluded from the study and were given parenteral quinine. Thick and thin blood films were prepared from capillary blood, stained with Giemsa (pH 7, diluted in phosphate buffered saline) and 100 oil immersion fields were examined. The parasite density was examined by counting the parasites and leucocytes, assuming 6000 leucocytes per µl. All the slides were double-checked blindly. The blood films were repeated on days 1, 2, 3, 7, 14, 21 and 28 or at any time if symptoms reoccur. Patients were asked to attend for follow up on days 1, 2, 3, 7, 14, 21 and 28 or if they developed febrile symptoms or if they feel unwell. Patients were asked about the presence of fever, vomiting and diarrhea. At each visit, brief physical examination, including axillary temperature was performed and the blood was taken for thick films. The efficacy of the 2 regimens SP and SP plus chloroquine was assessed by (28 days) a modified WHO protocol for uncomplicated falciparum malaria for areas of moderate or low malaria transmission. Patients were classified as early treatment failure, if they developed dangerous signs of severe malaria on day 3, the parasite density on day 2 exceeded that on day 0 or the parasite density on day 3 ≥ 25% of that on day 0. Late treatment failure (LTF) means development of symptoms or signs of severe malaria, or development of any parasitemia with or

Table 1 - Different admission variables of patients treated with sulphadoxine pyrimethamine alone or sulphadoxine pyrimethamine plus chloroquine.*

Variable	Sulphadoxine pyrimethamine (N = 40) mean ± SD	Sulphadoxine pyrimethamine plus chloroquine (N = 40) mean ± SD
Age, years	15.5 ± 15.2	17.8 ± 12.1
Weight, kg	37.04 ± 23.1	38.5 ± 17.6
Temperature, ^{O}C	38.06 ± 0.96	38.2 ± 0.66
Parasite count, rings/µ	17450.8 ± 20601.2	15097.92 ± 14896.406

* There were no significant differences between the 2 groups.

without fever after day 3. All others were regarded as adequate clinical and parasitological response (ACPR). Those with treatment failure were given quinine 10 mg/kg for 7 days. Data was entered into the microcomputer using statistical package for social sciences / personal computer batching for data analysis. Simple frequency, percentage, means and standard deviation were calculated. The data of the 2 groups of patients were compared with students' t-test, X^2 and Fisher's exact test when applicable; $p \leq 0.05$ was regarded significant. Eighty out (forty in each group) of ninety-eight patients completed the follow up. The rest were excluded since they changed their addresses (12 patients), developed concomitant infections (4 patients) or they withdrew their consent (2 patients). The baseline demographic, clinical and laboratory data were compared for the 2 treatment regimens (**Table 1**). There were no significant differences between SP alone and SP plus chloroquine with respect to the distribution of baseline attributes. There were no deaths and none of the patients developed manifestations of severe falciparum malaria. On day 3, although not statistically significant, more patients were febrile (temperature > 37.5ºC) in SP alone than in SP plus chloroquine; 19/40, 47.5% (95% CI, 0.71-1.71) vs.17/40, 42.5 (95% CI, 0.57-1.4), p=0.6. There were 6/40, 15.0% (95% CI, 0.36-0.80) patients in SP group who showed treatment failures all were LTF seen on days 7, 14 (2 patients), 21 and 28 vs. 1/40, 2.5% (95% CI, 0.60-23.2) patient in the SP plus chloroquine who developed LTF on day 14. The difference was statistically significant, p=0.04.

Combination of chloroquine with SP resulted in adequate synergistic action and antipyretic effect; such regimen can be adopted at the national level in the light of high resistance to monotherapy in Sudan, especially to chloroquine.

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Analysis of documents used in referral system in Wad Medani, Sudan

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Referral system has many benefits, however, in Sudan and in many parts of the world, this system is of poor quality. The referral system is a means of communication between physicians at all levels in the health system and it is one of the indicators for health care services.

This analytical, explanatory and exploratory study was carried out in Wad Medani Teaching Hospital in Sudan during the period January 2003 to June 2003. In the study, randomly selected referral documents for 206 patients were collected in 7 hospitals in Wad Medani city. These hospitals were: Wad Medani Teaching Hospital, Wad Medani Pediatric Hospital, Wad Medani Dermatology Hospital, Wad Medani Ophthalmology Hospital, Wad Medani Obstetric and Gynecology Teaching hospital, Wad Medani Dentistry Hospital and Wad Medani Oncology Hospital. The documents were compared with a list, which included the components that should be integrated in the ideal referral document. This includes 10 items. The quality of referral documents was estimated by granting one score to the presence of each item with a total range of 0-10. For more accuracy and preciseness, each item was subdivided into its integral components and each component was