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Comparative study on the efficacy of artesunate plus amodiaquine combination (act) and amodiaquine plus sulfadoxine-pyrimethamine combination (non-act) in the treatment of acute uncomplicated malaria in Enugu State, Nigeria

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ABSTRACT

Nigeria has changed the recommended treatment for acute uncomplicated *P.falciparum* malaria to artemisinin-based combination therapy (ACT). However, non-ACT regimen of Amodiaquine and Sulfadoxine-pyrimethamine (AQ + SP) are reported to be effective, safe, readily available and affordable compared to ACT. In a randomized controlled trial involving 120 children aged 6 to 59 months (M:F, 1:1.32) with clinically characterized malaria; the efficacy of non-ACT combination, (AQ + SP) and ACT combination, Artesunate plus Amodiaquine (AT + AQ) was evaluated. Results revealed that mean Fever Clearance Time (FCT) of 28.3±2.3 hours in non-ACT was not significantly different (P>0.05) from 25.4±2.3 hours reported for ACT combination. Similarly, there was no statistically significant difference (P>0.05) in the mean Parasite Clearance Time (PCT) for both ACT and non-ACT combinations. Again, there was no statistically significant difference (P>0.05) in the haematocrit and axillary temperatures between pre and post-treatment in both non-ACT and ACT treatment groups. In conclusion, the AQ + SP combination (non-ACT) is strongly recommended as a cost effective and therapeutic alternative to ACT for the treatment of uncomplicated *P.falciparum* malaria especially in under five children in Enugu State, Nigeria.

Key words: ACT, efficacy, malaria, non-ACT.

INTRODUCTION

It has been shown that artemisinin-based combination therapy (ACT) could improve therapeutic effectiveness, reduce gametocyte carriage and delay the emergence and spread of drug resistant parasite[1]. It is noteworthy, that despite the recent change in national malaria drug policy in favour of artemisinin-based combination therapy (ACT) in Nigeria, the non-ACT regimens still remain the commonest antimalarial drugs widely prescribed as a result of low cost and availability[2]. There is, therefore, the need for continuous monitoring and evaluation of the efficacy of these combination therapies in the management of acute uncomplicated *P.falciparum* malaria. This study attempts to evaluate the current status in respect of clinical and therapeutic efficacy of non-ACT (AQ + SP) and ACT (AT + AQ) in the treatment of acute uncomplicated *P.falciparum* malaria among under five children in Enugu State, Nigeria.

METHODS

Patients

Patients (n = 120) enrolled in this study were selected by stratified random sampling from children with clinically characterized uncomplicated malaria aged 6 to 59 months (M:F = 1:1.32) who presented at Amafor primary healthcare facility, Ugbakwa; a rural farming population with high endemicity of malaria transmission, under the Asu Nkanu Local Health Authority of Enugu State. They presented with a history of fever in the preceding 24 to 48 hours or axillary temperature ≥ 37.5°C and parasitemia > 2000 asexual forms/mL of blood. Patients with concomitant illness, intense vomiting, recent history of convulsion, lethargic or unconscious state and sickle cell anaemia were excluded. Ethical clearance was obtained and informed consent of the parent or guardian for each child was sought. The patients were subsequently assigned randomly to any of the drug treatment groups: AQ + SP or AT + AQ. Thus, 60 patients were allotted to each treatment group. Drug dosages were computed using the weight of the patients. AQ was given at a dose of 10mg/kg daily for 3 days and SP at 25mg/kg as single dose on Day 0. AT was given at a dose of 2mg/kg twice daily on Day 0, and 1mg/kg twice daily for the next 4 days. Drugs were administered orally by direct observation and monitored by the clinician to ensure they were not vomited. Drugs were re-administered within 1 hour following initial vomiting but withdrawn from the study with another episode of vomiting. Patients were followed up for 2 weeks after treatment. Evaluation of response carried out on days 1,2,3,7 and 14 according to WHO criteria[1]. Data obtained were statistically analyzed using Student *t*-test and presented in tabular form.

RESULTS

Table 1, clearly depicted the therapeutic response of patients in both AQ + SP and AT + AQ combinations. In the AQ + SP treatment group, mean Fever Clearance Time (FCT) of 28.3±2.3

Table 1: Therapeutic response of patients in the various treatment groups

	AQ + SP (Mean+SEM)	AT + AQ (Mean±SEM)	*P*-Value
Fever Clearance Time (Hours)	28.3±2.3	25.4±2.3	>0.05
Parasite Clearance Time (Days)	3.7±0.15	3.5±0.15	>0.05
Radical Cure Rate (%)	100±0.0	100±0.0	>0.05

Table 2: Pre and post- treatment haematocrit and axillary temperature of patients in the AQ + SP (non-act) treatment group

	Pre-Treatment, DO	Post-Treatment, D14	*P*-Value
Haematocrit (%)	28.9±2.5	30.1±2.5	>0.05
Axillary Temperature (°C)	39.1±1.6	37.0±1.5	>0.05

Table 3: Pre and post-treatment haematocrit and axillary temperature of patients in the AT + AQ (ACT) treatment group

	Pre-Treatment, DO	Post-Treatment, D14	*P*-Value
Haematocrit (%)	29.0±2.5	30.8±2.5	>0.05
Axillary Temperature (°C)	38.6±1.6	37.2±1.5	>0.05

hours was not significantly different (P>0.05) from 25.4±2.3 hours reported for AT + AQ combination therapy. Similarly mean Parasite Clearance Time (PCT) of 3.5±0.15 days in ACT (AT + AQ) did not differ significantly from 3.7±0.15 days reported in non–ACT (AQ + SP). Interestingly, there was no reported treatment failure in both combinations, with a radical cure rate of 100% reported for both ACT and non-ACT. It was also noted as shown in tables 2 and 3, that there was no statistically significant difference (P>0.05) in the haematocrit and axillary temperature of patients both at initial presentation, Day 0 and post-treatment, Day 14 in both AQ + SP and AT + AQ combination therapies.

DISCUSSION

The non-ACT regimen AQ + SP in this study has been demonstrated to be quite effective in the treatment of uncomplicated *P.falciparum* malaria with a radical cure rate recorded as 100%. This study also revealed as shown in table 1, that there was no statistically significant difference (P>0.05) in the various criteria used to assess therapeutic response between AQ + SP and AT + AQ combinations. Amodiaquine, a 4-aminoquinoline and effective blood schizonticide, is useful in areas where there is low-grade chloroquine resistance but recrudescence is not uncommon[3]. The AQ + SP combination was shown to be more effective than ACT for the treatment of uncomplicated malaria in Burkina Faso[4]. Although SP is still relatively effective in most areas in Africa, resistance is increasing and could potentially develop as it has in Asia, to render the drug useless in the near future[5]. The use of AQ + SP combination could also slow down development of parasite resistance to the individual drugs, increasing the life-span of each of them as an effective anti-malarial drug[6]. In the AT + AQ combination (ACT), a cure rate of 100% was also recorded in this study. Artesunate (AT) is a water soluble analog of artemisinin, a sesquiterpene lactone endpoperoxide. It is a very rapidly acting blood schizonticide. Its antimalarial activity results from the production of free radicals following the iron-catalyzed cleavage of the endoperoxide bridge in the parasite. The enhanced, cumulative blood schizonticidal effect of AT + AQ combination, therefore, is very beneficial in ensuring rapid fever clearance and relief of symptoms. Notwithstanding, the effectiveness and good therapeutic response of AT + AQ combination reported in this study, as evidenced by exceptionally high cure rate and no treatment failures; high cost and non-availability have seriously limited the effective use of ACT[7]. The change in treatment policy in Nigeria to ACT without adequate sensitization and education of medical personnel may pose some difficulties that could lead to high morbidity and mortality[8]. A resultant increase in resistance of *P. falciparum* to these new combinations may also arise since transition into an alternative compound may take some years before they are accepted and put into proper use[9]. Current World Health Organisation (WHO) recommendations have focused on the use of combination antimalarial therapy, particularly artemisinin-based combination therapy (ACT)[10,11]. However, several control programmes in Africa have switched to non-ACT, for example AQ + SP[12]. In conclusion, the AQ + SP combination (non-ACT) is strongly recommended as a cost effective and therapeutic alternative to ACT, for the treatment of acute uncomplicated *P.falciparum* malaria especially in under five children in Enugu State, Nigeria.

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