Comparative efficacy and safety of an artemisinin-based combination therapy (ACT) and a non – ACT in the management of uncomplicated malaria in an area with high degree of drug resistance in Nigeria

Ademowo OG[1, 2] Dada-Adegbola HO[3], Falade CO[1,2].

[1]Postgraduate Institute for Medical Research & Training,, [2]Department of Pharmacology & Therapeutics, [3]Department of Medical Microbiology College of Medicine, University of Ibadan. Ibadan, Nigeria

Background and Objectives

- Artemisinin based combination therapy (ACT) is now gold standard for treatment of malaria in areas experiencing drug resistant infection
- However, ACT is often not affordable or available to those who need them most.
- *The Objectives of the study are*;
- To compare the efficacy of an ACT - Artemether-lumefantrine (AL) and a non ACT - Amodiaquine + Sulfadoxine-pyrimethamine (AMQ-SP) in children with acute uncomplicated malaria.
- To evaluate the comparative safety of AL and AMQ-SP in children

Patients and methods 1

Study design: Open randomized study at the University College Hospital, Ibadan Nigeria

Inclusion criteria

- Children aged 6 months to 10 years.
- Clinical features compatible with acute uncomplicated malaria
- Confirmed *P. falciparum* malaria with parasite density ≥ 1000/μL
- Written informed consent from a parent or legal guardian

Exclusion criteria

- Concomitant illness.
- History of allergy to AMQ, SP or Artemisinin.
- Severe malaria

Treatment

  - Group 1 received 6 doses of AL according to weight groups over 3 days.
  - Group 2 received Amodiaquine (AMQ) at 25mg/kg over three days and Sulfadoxine-Pyrimethamine (SP) at 25mg/kg sulfadoxine to the next quarter tablet as a single dose on Day 0. (AMQ-SP)

  - All drugs were admistered supervised

Patient Methods 2

- All patients were seen and examined daily from Day 0 - Day 3, then on Days 7,14, 21 and 28
- Thick and thin blood films prepared from finger prick on Day 0 and at each visit for identification and quantification of malaria parasites.
- Venous blood (2ml) was obtained for hematology (FBC) and blood chemistry (liver function test and electrolyte & urea) at baseline, Days 3 and 28.
- Blood spots taken on filter paper for PCR examination at baseline and Day 28 or recurrence of patent parasitaemia, whichever came first to distinguish re-infection from recrudescence
- Fever and parasite clearance times were evaluated in both groups.
- Adverse events were recorded for each patient.

Results 1

- 120 patients (60 in each group) were enrolled
- Baseline characteristics were comparable between the 2 groups
- Fever clearance time (FCT) was significantly shorter among the AL group than AMQ-SP group (1.19±0.44 and 1.52±0.78 days respectively), $P<0.05$.
- But by Day 4, all children treated with AL were afebrile while 2 children on AMQ-SP were still febrile
- Parasite clearance time (PCT) was also more rapid and sustained in those treated with AL compared to AMQ-SP (1.300± 0.497 and 2.220± 0.83 for AL and AMQ-SP respectively).
- By Day 2, none (0%) of the patients on AL has patent parasitaemia while 19 (31.7) on AMQ-SP still had parasitemia ($P=0.0001$)
- Days 7 and 14 cure rates was 100% in both groups.
- Day 28 parasitological failure rate was 3.3% for AL and 6.7% for AMQ-SP.

Results 2

- All cases of parasite recurrence were confirmed as re-infections by PCR.
- Gametocyte clearance time was significantly shorter in patients treated with AL compared with AMQ-SP. ($P<0.05$). By day 3 all gametocytes had cleared in the AL but still persisted till day 28 in the AMQ-SP group.
- Blood chemistry and liver function were not adversely affected by either treatment regimen.
- No patient developed any severe adverse event in both treatment groups

CAPACITY BUILDING ACTIVITIES

-Workshop on Clinical Trial and GCP are being organised by our Institute

-Postgraduate students and young scientists are participating in clinical trials carried out by us.

- We have a working cooperation with the State Ministry of Health on training of staff for malaria surveillance and control

Conclusion

- Although AL has shorter FCT and PCT relative to AMQ-SP, the cure rate for both drugs was 100% by days 7 and 14
- The parasitological failure rate by Day 28 was not significantly different.
- AMQ-SP is as effective and safe as AL in the treatment of acute uncomplicated malaria.
- AMQ-SP can therefore serve as a good alternative combination therapy especially in communities where ACT is not available or affordable.

Future Perspective

- It will be necessary to monitor periodically the efficacy and safety of the ACTs and non-ACT combinations among;
  -Different age groups
  -Pregnant women.
  -Rural and Urban areas

- It will be necessary to monitor disposition of the currently used antimalarials particularly the artemisinins among Africans

- Intensify effort at building capacity in clinical trials in African Institutions