

Azithromycin plus artesunate versus artemether-lumefantrine for treatment of uncomplicated malaria in Tanzanian children: a randomized, controlled trial.

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BACKGROUND: Acute febrile illness is the most common cause of outpatient attendance and mortality for children in Africa. Malaria and bacterial disease are difficult to differentiate with limited diagnostic facilities. Combinations of antibiotics and antimalarials are potentially attractive for treatment of the syndrome. Azithromycin plus artesunate (AZ+AS) is an effective antimalarial combination for adults in Asia.

METHODS: We performed an individually randomized, open-label trial of AZ+AS versus artemether-lumefantrine (AL) involving children (age, 6-59 months) with uncomplicated malaria in Muheza, Tanzania. The primary outcome was parasitological failure by day 28. Parasitological failure by day 42 and failure corrected for reinfection were major secondary outcomes.

RESULTS: Of 2497 children screened, 261 were eligible; 129 were randomized to the AZ+AS arm, and 132 were randomized to the AL arm; 92% and 91%, respectively, underwent follow-up to 28 days. Planned interim analysis was performed after 200 patients reached day 28 follow-up and led the Data and Safety Monitoring Board to halt further recruitment. All children had a complete initial response to treatment, but 69 (58%) of 119 children in the AZ+AS arm and 24 (20%) of 120 in the AL arm had asexual parasites at or by day 28 (adjusted odds ratio for failure with AZ+AS treatment, 6.1; 95% confidence interval, 3.3-11.4; $P < .001$). When analysis was restricted to children with recrudescence, the parasitological failure rate was 32% in the AZ+AS arm and 9% in the AL arm. This difference was maintained at day 42.

CONCLUSIONS: This trial does not support the use of AZ+AS as treatment for malaria or acute febrile illness in children in areas of Africa with high levels of existing antimalarial drug resistance.

CLINICAL TRIALS REGISTRATION: ClinicalTrials.gov NCT00694694.

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