

Efficacy and safety of artemether-lumefantrine dispersible tablets compared with crushed commercial tablets in African infants and children with uncomplicated malaria: a randomised, single-blind, multicentre trial

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Summary

Background Combination treatments, preferably containing an artemisinin derivative, are recommended to improve efficacy and prevent *Plasmodium falciparum* drug resistance. Our aim was to show non-inferiority of a new dispersible formulation of artemether-lumefantrine to the conventional crushed tablet in the treatment of young children with uncomplicated malaria.

Methods We did a randomised non-inferiority study on children weighing 5–35 kg with uncomplicated *P falciparum* malaria in Benin, Kenya, Mali, Mozambique, and Tanzania. The primary outcome measure was PCR-corrected 28-day parasitological cure rate. We aimed to show non-inferiority (with a margin of –5%) of dispersible versus crushed tablet. We constructed an asymptotic one-sided 97.5% CI on the difference in cure rates. A computer-generated randomisation list was kept centrally and investigators were unaware of the study medication administered. We used a modified intention-to-treat analysis. This trial is registered with ClinicalTrials.gov, number NCT00386763.

Findings 899 children aged 12 years or younger were randomly assigned to either dispersible (n=447) or crushed tablets (n=452). More than 85% of patients in each treatment group completed the study. 812 children qualified for the modified intention-to-treat analysis (n=403 vs n=409). The PCR-corrected day-28 cure rate was 97.8% (95% CI 96.3–99.2) in the group on dispersible formulation and 98.5% (97.4–99.7) in the group on crushed formulation. The lower bound of the one-sided 97.5% CI was –2.7%. The most common drug-related adverse event was vomiting (n=33 [7%] and n=42 [9%], respectively). No signs of ototoxicity or relevant cardiotoxicity were seen.

Interpretation A six-dose regimen of artemether-lumefantrine with the new dispersible formulation is as efficacious as the currently used crushed tablet in infants and children, and has a similar safety profile.

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