The Lancet | *Volume 365, ISSUE 9469, P1474-1480, April 23, 2005*

Amodiaquine alone, amodiaquine+sulfadoxine-pyrimethamine, amodiaquine+artesunate, and artemether-lumefantrine for outpatient treatment of malaria in Tanzanian children: a four-arm randomised effectiveness trial

Theonest K Mutabingwa, MD , Devota Anthony, RN , Archie Heller, MD , Rachel Hallett, PhD , Jalal Ahmed, MSc , Chris Drakeley, PhD

Published:April 23, 2005 DOI:https://doi.org/10.1016/S0140-6736(05)66417-3

Summary

Background

Many countries in Africa are considering a change to combination treatment for falciparum malaria because of the increase in drug resistance. However, there are few effectiveness data for these combinations. Our aim was to study the effectiveness of three drug combinations that have proven efficacious in east Africa compared with amodiaquine monotherapy.

Methods

We undertook a randomised trial of antimalarial drug combinations for children (aged 4–59 months) with uncomplicated malaria in Muheza, Tanzania, an area with a high prevalence of resistance to sulfadoxine-pyrimethamine and chloroquine. Children were randomly allocated 3 days of amodiaquine (n=270), amodiaquine +sulfadoxine-pyrimethamine (n=507), or amodiaquine+artesunate (n=515), or a 3-day six-dose regimen of artemether-lumefantrine (n=519). Drugs were taken orally, at home, unobserved by medical staff. The primary endpoint was parasitological failure by day 14 assessed blind to treatment allocation. Secondary endpoints included day 28 follow-up and gametocyte carriage. Analysis was by intention to treat.

Findings

Of 3158 children screened, 1811 were randomly assigned treatment and 1717 (95%) reached the 14-day follow-up. The amodiaquine group was stopped early by the data and safety

monitoring board. By day 14, the parasitological failure rates were 103 of 248 (42%) for amodiaquine, 97 of 476 (20%) for amodiaquine+sulfadoxine-pyrimethamine, 54 of 491 (11%) for amodiaquine+artesunate, and seven of 502 (1%) for artemether-lumefantrine. By day 28, the parasitological failure rates were 182 of 239 (76%), 282 of 476 (61%), 193 of 472 (40%), and 103 of 485 (21%), respectively. The difference between individual treatment groups and the next best treatment combination was significant ($p<0{\cdot}001$) in every case. Recrudescence rates by day 28, after correction by genotyping, were 48·4%, 34·5%, 11·2%, and 2·8%, respectively.

Interpretation

The study shows how few the options are for treating malaria where there is already a high level of resistance to sulfadoxine-pyrimethamine and amodiaquine. The WHO-packaged six-dose regimen of artemether-lumefantrine is effective taken unsupervised, although cost is a major limitation.