Selected Summaries

Azithromycin—A Potential Anti-malarial Drug

[Sadiq ST, Glasgow KW, Darkeley CJ, et al. Effects of azithromycin on malariometric indices in the Gambia. Lancet 1995, 346: 881-882.]

In the course of a randomized trial of trachoma control, azithromycin (AM) was used to evaluate its role in reducing ocular re-infection with *Chlamydia trachomatis* in endemic population and also to assess the effect of its use on malariometric indices during the high transmission rainy season. The study included children between 5-14 years from 8 villages in the Farafenni study area in the Gambia, West Africa. The entire population of four treatment villages received three doses of AM 20 mg/kg weekly (days 1,8,15) and four control villages received tetracycline (TC) eye ointment topically (days 1-42). Among 226 children studied before treatment and at day 28, AM reduced the proportion with *P. falciparum* parasites (rate ratio 0.56, 95% confidence Interval 0.44-0.71; p <0.0001), palpable spleens (RR 0.50, 95% CI 0.36-0.70; p <0.0001), febrile parasitemia (RR 0.45; 95% CI 0.27-0.75, p <0.01) and with *P. malariae* infection (p <0.001). This effect was related more to resolution of parasitemia than to prevention of new parasitemia. Authors conclude that AM reduced all the 3 malarial indices by about 50% compared to topical TC but did not significantly prevent new malarial infection.

Comments

The search for new therapeutic and prophylactic agents against drug resistant malaria is continuing. In view of the prohibitive cost of developing and licensing new antimalarial formulations, it is quite encouraging to identify antimalarial activity in a drug already in use in children. AM, an azalide antibiotic, seems to be a potential antimalarial drug. AM is closely related to erythromycin but has greater bioavailability, better tissue penetration and a much longer elimination half life with drug detectable in urine 14 days after a single dose. Antimalarial effect of AM has been reported *in vitro* (1) as well as in animal models(2). Kuschener *et al*.(3) have suggested a protective effect against *P. falciparum* malaria in volunteers by its action on ex-erythrocytic stage of the parasite. In the present report, a significant reduction was documented in the malariometric indices in comparison to control group receiving only topical tetracyclines (TC). Even though TC has some antimalarial effect, the amount absorbed systemically after topical application is expected to have only a negligible effect on these indices. Therefore the authors believe that AM cleared pre-existing parasitemia. The role of AM in the treatment of resistant malaria appear to be quite encouraging. Since this study only provides indirect evidence of its antimalarial activity, more randomized controlled clinical trials along with other known antimalarial drugs need to be

undertaken to evaluate its clinical efficacy and to establish a place for AM as an alternative drug for resistant malaria.

The authors also observed that weekly AM failed to prevent emergence of parasitemia in more than l/3rd of children without parasitemia at baseline and hence they concludes that AM did not prevent new malarial infection. The role of AM for malaria prophylaxis was not properly evaluated in this study for obvious reasons (results being an offshoot of a study primarily aimed to evaluate the role of AM in trachoma control) and for logistic reasons blood samples were collected in the beginning and on day 28 (14 days after the last dose). The drug continues to be excreted for several weeks after multiple doses but it is not very clear as to when the peak prophylactic effect of AM regimen occurs. One does not know what would be the results if repeat blood sample were taken on day 7 after the last dose of the drug. It is even possible that the results may suggest that a weekly dose may not be sufficient for prophylaxis. Moreover, failure of AM to prevent new parasitemia needs to be differentiated from recrudescence based on strain typing which has not been done in this study. Future studies will have to evaluate all these aspects as well as the optimum dose of the drug necessary for prophylaxis.

REFERENCES

1. Gingras BA, Jensen JB. Antimalarial activity of azithromycin (CP-62, 993) and erythromycin against chloroquin sensitive and chloroquin resistant strains of *Plasmodium falciparum in vitro.* Am J Trop Med Hyg 1992, 47: 378-382.
2. Andersen SL, Ager A, McGreevy P, *et al.* Activity of azithromycin as a blood schizonticide against rodent and human plasmodia *in vivo.* Am J Trop Med Hyg 1995,52:591-612.
3. Kuschner RA, Heppner DG, Andersen SL, *et al.* Azithromycin prophylaxis against a chloroquin resistant strain of *Plasmodium falciparum.* Lancet 1994, 343:1396-1397.

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