Pyronaridine was effective and well tolerated in African patients with acute, uncomplicated falciparum malaria

Ringwald P, Bickii J, Basco L. ***Randomised trial of pyronaridine versus chloroquine for acute uncomplicated falciparum malaria in Africa.*** *Lancet. 1996 Jan 6;347:24-8.*

Objective
To compare the effectiveness of oral pyronaridine with chloroquine for acute, uncomplicated falciparum malaria in African adults.

Design
Randomised controlled trial with 14-day follow-up.

Setting
Urban outpatient clinic in Yaoundé, Cameroon, an area with a high rate of resistant malaria and of hypoendemic chloroquine-resistant falciparum malaria.

Patients
96 adult African patients (age range 15 to 64 y, 56% women) who had acute falciparum malaria, defined as > 5000 asexual parasites per μL, and fever within the past 24 hours or a temperature > 37.5 °C at the time of consultation. Exclusion criteria were signs and symptoms of severe and complicated malaria, recent self-medication, pregnancy, or mixed malaria infections. 81 patients (84%) were included in the on-active-treatment analysis.

Intervention
41 patients were allocated to 25 mg/kg of chloroquine, and 40 patients were allocated to 32 mg/kg of pyronaridine; both treatments were given orally in divided doses for 3 days. Patients were followed for 14 days on an outpatient basis.

Main outcome measures
Treatment success at day 14 (defined as absence of clinical relapse), parasite response (3 grades), fever clearance time, parasite clearance time, and adverse effects.

Main results
40 patients (100%) in the pyronaridine group were considered a treatment success at day 14 compared with 24 patients (59%) in the chloroquine group ($P < 0.001$). {This absolute risk improvement (ARI) of 41% means that 2 patients would need to be treated (NNT) with pyronaridine (rather than chloroquine) to have 1 additional treatment success, 95% CI 2 to 4; the relative risk improvement (RRI) was 71% CI 36% to 128%.}* Pyronaridine led to 100% parasite clearance by day 14 compared with 44% clearance in the chloroquine group ($P < 0.001$) {ARI 56%; NNT 2, CI 1 to 2; RRI 128% CI 69% to 231%}*. No significant differences occurred in the fever- or parasite-clearance times between patients with favourable responses in the pyronaridine group and those with favourable responses in the chloroquine group. Mild gastrointestinal symptoms were common with pyronaridine, but no serious adverse effects were noted.

Conclusion
Pyronaridine was effective and well tolerated in African patients with acute, uncomplicated falciparum malaria.

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For article reprint: Dr. L. Basco, Centre de Génétique Moléculaire, Centre National de la Recherche Scientifique, 91198 Gif-sur-Yvette, France. FAX 33-1-69-82-43-86.

*Numbers calculated from data in article.

Commentary

Malarial illness is common in areas where infection with *Plasmodium falciparum* malaria is widespread. Symptoms range from mild and non-specific to acute life-threatening episodes. Health care workers in endemic malarious areas often give antimalarial drugs for any fever-related symptoms. This policy appeared effective when the parasite responded to chloroquine, a cheap and safe antimalarial agent. However, with the spread of chloroquine-resistant parasites, many countries have changed to sulphadoxine-pyrimethamine, but parasite resistance to this combination already exists. Alternative treatments have limitations (1). This study by Ringwald and colleagues shows the effectiveness of pyronaridine compared with chloroquine in an African country. This study is important for those concerned with evaluating new antimalarial drugs for the treatment of disease in the face of existing and potential resistance to current drugs.

Pyronaridine was synthesized at the Chinese Academy of Preventive Medicine in 1971, tested in China between 1971 and 1974, and has been widely available there since 1980 (2, 3). Elsewhere it is only used in experimental studies (4). More data on the comparative effectiveness of pyronaridine in areas with a different pattern of antimalarial drug resistance are required, and toxicity will need to be carefully researched and monitored. Some of these studies, as well as work on bioavailability, are currently being done (5), but a lot more work is required if pyronaridine is to be considered for international registration. At U.S. $3 per dose, the cost of manufacturing pyronaridine will have to be reduced for it ever to be an option in many African countries (1).

Paul Garner, MD
Liverpool School of Tropical Medicine
Liverpool, United Kingdom

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