**Zeitschrift:** Acta Tropica
**Herausgeber:** Schweizerisches Tropeninstitut (Basel)
**Band:** 38 (1981)
**Heft:** 1

**Artikel:** Single dose therapy with a combination of chloroquine and pyrimethamine (darachlor) in the treatment of malaria : short communication

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**DOI:** https://doi.org/10.5169/seals-312809

Acta Tropica *38*, 91–93 (1981)

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# Single dose therapy with a combination of chloroquine and pyrimethamine (darachlor) in the treatment of malaria

**Short communication**

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A mixture of chloroquine (600 mg base) and pyrimethamine base (50 mg) has been widely used for presumptive treatment in malaria eradication programmes (WHO Technical Report Series No. 375, 1967). This report further states that the combination appeared to be effective in Haiti when given once every three weeks but no final conclusion was reached; while this dosage was found to be ineffective when used in West Africa, the failure was rather due to operational and administrative difficulties than reduced susceptibility to the drug. Reports regarding the use of darachlor are few. Thompson and Carter (1961) found the drug to be highly effective in the prevention of malaria in semi-immune adults of the Ghana Army stationed in Accra when given in fortnightly doses over a period of two months. Two dosage schedules were followed, viz, one tablet, and two tablets fortnightly, respectively, both of which were equally effective. Thompson (1961), a year later, conducted a prophylactic trial among adult members of the Ghana army and their children and found that darachlor had become less efficient in the suppression of malaria than was the case a year earlier. Bruce-Chwatt and Horn (1958) deduced that pyrimethamine and chloroquine were the most favoured drugs for malaria prophylaxis in Nigeria after proguanil from questionnaires circulated to nearly 18,000 of the expatriate population. One must of course take into consideration the fact that resistance of *P. falciparum* to the standard dose of chloroquine never existed in Africa at the time of the study.

However, with increasing evidence that chloroquine resistance is widely distributed throughout Southeast Asia as reported in several scientific journals too numerous to be recorded here, malariologists would be curious to know whether a combination of chloroquine and pyrimethamine would be more effective in suppressing parasitaemia than chloroquine alone. The development of pyrimethamine resistant strains appears to be a potential hazard of using the

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drug alone, and that the addition of suitable amounts of chloroquine will either delay or prevent the development of resistant strains (Bruce-Chwatt and Horn, 1958).

### Materials and methods

The randomised trial was conducted between June 1976 and August 1979 among aborigine patients admitted to Gombak Hospital, Selangor. Many of the aboriginal settlements are situated in the jungle areas of Peninsular Malaysia close to the main range of mountains dividing the country longitudinally in two. *A. maculatus* is the predominant vector in most parts while *A. balabacensis balabacensis* is confirmed mostly to the northern parts bordering with Thailand.

Forty-eight patients were admitted to the study of whom 32 were children and 16 adults. The average age of the children was 4.7 years while that of the adults was 24.21 years. Each tablet contained 150 mg chloroquine base and 15 mg pyrimethamine. The dose was administered according to body weight, viz, the dose of chloroquine was 10 mg/kg body weight while that of pyrimethamine 1 mg/kg body weight. If dosage required division of the tablet into smaller parts this was done to the nearest quarter of a tablet so as to be approximate. The drug was administered with adequate sweetened drinks and a biscuit in order to reduce the incidence of nausea and vomiting. Blood films were examined daily for malaria parasites for seven consecutive days followed by examination at weekly intervals thereafter for a further three weeks, making a total of 28 days as the recommended follow-up period. Single dose therapy was claimed to be effective if there was no reappearance of parasites by the 28th day. If parasites re-appeared alternative treatment was prescribed.

## Results

The asexual parasite count varied from 40/mm$^3$ to 100,000/mm$^3$ with an average density count of 6042/mm$^3$. Six patients were followed up for periods longer than 28 days, the longest period of follow-up being 39 days. Of the 48 patients two were suffering from vivax malaria while the rest were infected with *P. falciparum*. Ten patients were negative for malaria parasites on day 28 and all these were cases of falciparum malaria with an average parasite density of 2690/mm$^3$, the lowest being 40/mm$^3$ and the highest 18,600/mm$^3$. Among the remaining 38 cases, four patients showed no clearance of parasites during the first week and were given alternate drugs; nine showed recrudescence of parasites from day 4 to day 7; in the remaining patients recrudescence occurred at varying intervals up to day 28.

As regards fever, fifteen of the cases showed a variable degree of pyrexia from 99° F–102° F at the onset of therapy; the remaining cases were afebrile. Fever cleared 24–48 hours after commencement of treatment.

## Discussion

Single dose therapy with darachlor has been used extensively in Malaysia as presumptive treatment in the malaria control programme (1978). This form of treatment was probably effective before the widespread emergence of strains of *P. falciparum* resistant to chloroquine were recognised. With resistance fairly

widespread, presently, throughout Malaysia, as determined by recent surveys carried out at the Institute for Medical Research, single dose treatment would hardly be effective. In fact presumptive treatment on a large scale could be positively dangerous by increasing the rate of emergence of strains of *P. falciparum* resistant to chloroquine. Further, it may suppress clinical symptoms without eradicating the infection. Field workers in malaria eradication programmes are instructed to give presumptive treatment if individuals are suffering from fever and chills. As shown only fifteen of the forty-six patients with falciparum parasitaemia had fever. This is so with many of the rural populations living in malarious areas who have varying degrees of immunity to the disease according to age.

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