

# TREATMENT OF FALCIPARUM MALARIA

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## SUMMARY

**Falciparum malaria is a potentially fatal disease. Early and appropriate chemotherapy is the corner stone in its management. Uncomplicated cases can be treated with chloroquine, Fansidar or Halfan. Complicated falciparum malaria would require parenteral quinine preferably under supervision of a clinician. All newer antimalarial drugs should be reserved for the treatment of falciparum malaria only.**

## INTRODUCTION

"If we take as our standard of importance the greatest harm to the greatest number, then there is no question that malaria is most important of all infectious diseases."

"Sir Macfarlane Burnett"<sup>1</sup>

Malaria is a parasitic disease caused by a protozoan of the genus *Plasmodium* (P). Four species of *Plasmodium*, namely *P.falciparum*, *P.vivax*, *P.ovale* and *P.malaria*, are generally pathogenic to man. *P.falciparum* is the most virulent species and is held responsible for the estimated one million malaria-related-deaths each year.<sup>2</sup>

Drug resistance is one of the reasons for the high mortality associated with falciparum malaria. Chloroquine resistance was first noted in 1959 in Latin America and in 1962 in Thailand.<sup>3</sup> Resistance to both chloroquine and Fansidar is now widespread in Thailand, Burma, Cambodia and the Amazon basin area of South America.<sup>4</sup> Such multi-drug resistant strains have also been reported from East Africa.<sup>5</sup> The resistance can be garded into three levels i.e, R-I, R-II, R-III according to World Health Organisation.

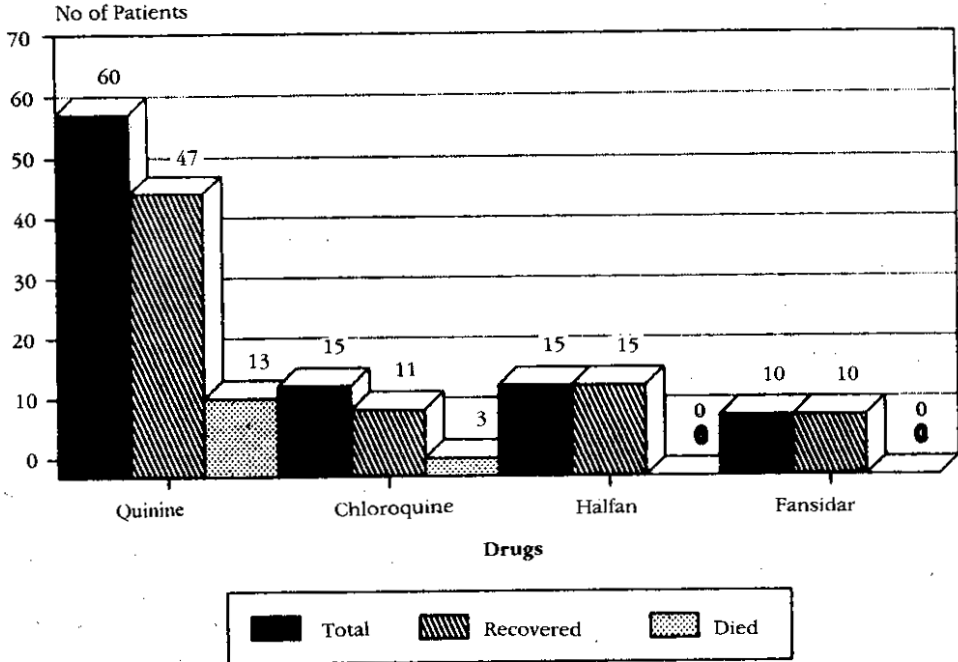
At R-I level chloroquine produces a clinical cure and clearance of asexual parasitaemia for at least two consecutive days, followed by recrudescence upto 28 days after therapy. R-II resistance is defined as reduction of the parasitaemia during the first 48 hours of treatment to 25 percent or less of the pretest level. At R-III level of resistance, the parasite density decreases less than 25 percent or actually increases during the first 48 hours.<sup>6</sup>

Chloroquine resistance was first reported in Pakistan in 1984.<sup>7</sup> Many subsequent reports have confirmed the existence of resistant strains in the Punjab.<sup>8</sup> The situation in North West Frontier Province (NWFP) is less clear. Some workers have reported high grade resistance to chloroquine,<sup>9</sup> while others have mentioned the phenomenon casually.<sup>10</sup> This study was conducted to assess the response of the local strains of *P.falciparum* to the available antimalarial compounds.

## MATERIAL AND METHODS

The study was conducted in Medical "A" unit of Lady Reading Hospital, Peshawar during the period 1990 - 1991. The hospital is a tertiary

Fig-1. Efficacy of Antimalarial drugs



referral centre with a very wide catchment area. Febrile patients presenting to the hospital were screened for malaria and those having trophozoites of *P.falciparum* in their peripheral blood were included in the study.

Patients having cerebral malaria, renal failure, pulmonary oedema, gross anaemia, liver dysfunction or other complication were classified as 'severe falciparum malaria' and were treated with quinine. The drug was administered by intravenous infusions of 600 mg of quinine salt given over 4 hours. Such infusions were repeated every 8 hours until the patients were able to swallow the drug. Oral therapy was then continued at a dose of 600 mg salt 8 hourly for 7 days.

Those having uncomplicated falciparum malaria received either chloroquine (25 mg base/Kg body weight) over 3 days or halofantrin (Halfan) administered as 3 doses of 2

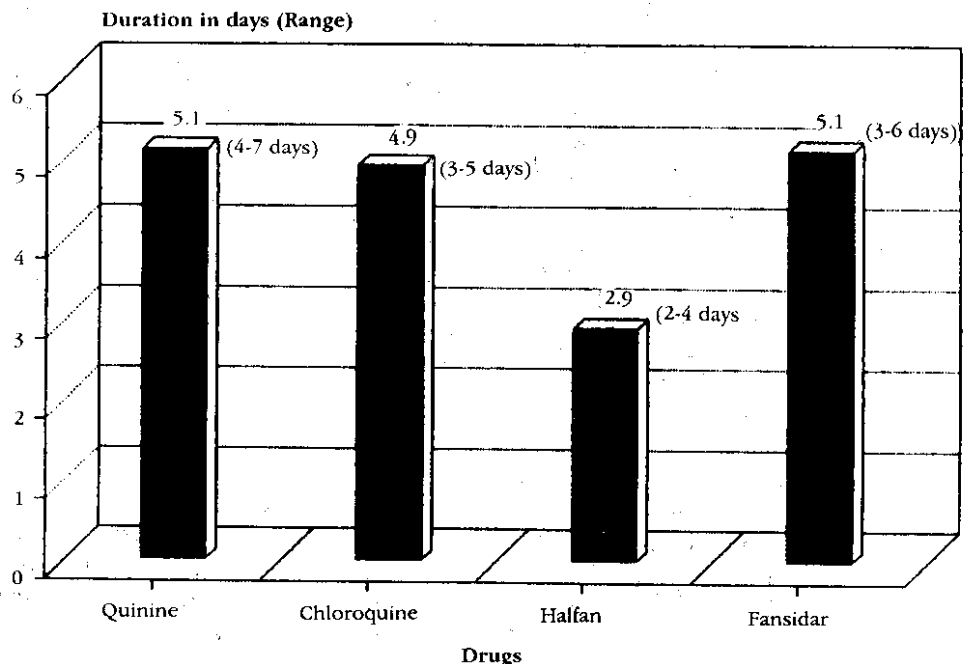
tablets (250 mg each) 6 hours apart. A single dose of 3 tablets of sulfadoxine-pyrimethamine (Fansidar) was also used in some of the stable patients.

Clinical assessment was made daily while parasitaemia was evaluated at the beginning and at the end of therapy. Asymptomatic patients were declared cured and were allowed home if they had no parasitaemia. The importance of immediate consultation in case of relapse was emphasized to the patients and their attendants.

## RESULTS

One hundred patients were found to have asexual form of *P.falciparum* during the study period and were included in the study. Sixty patients were treated with quinine, 15 each with chloroquine and Halfan and 10 with Fansidar.

### Average duration of Parasitaemia



Forty seven patients in the quinine group made recovery while 13 succumbed to the disease. Vomiting and tinnitus were the commonest side effects of quinine noted in this study. Two patients became hypoglycemic after receiving rapid infusions of quinine in isotonic saline. One patient developed encephalopathy which improved after the drug was withdrawn.

Cure was achieved in 11 out of the 15 patients who received chloroquine. Of the remaining 4 patients, 3 died while one patient had evidence of R-11 resistance. Another four patients had received chloroquine before coming to the hospital but had a relapse within 28 days. These patients might have had R-I or R-II resistance but not even a single case of R-III resistance was recorded. Nausea and vomiting commonly occurred when the drug was administered orally.

Both Halfan as well as Fansidar

had 100 percent efficacy rate (Fig-I). Three patients had relapsed after having taken Halfan within the preceding fortnight and another 2 had a recrudescence after they were included in the study. All these 5 patients got cured when the same therapy was repeated. Side effects due to Halfan were limited to minor gastrointestinal symptoms. No serious adverse effects were noted in Fansidar-treated group.

Halfan was found to be the most rapidly acting drug as it cleared parasitaemia in an average period of 2.9 days (range 2-4 days). Mean duration of parasitaemia was 4.1 days (range 3-5 days) with Chloroquine, 4.9 days (range 3-6 days) with Fansidar and 5.1 days (range 4-7 days) with uinine (Figure-II).

### DISCUSSION

Falciparum malaria is a potentially fatal condition. An initially

mundane clinical picture can rapidly deteriorate into a syndrome of multi-organ failure.<sup>11</sup> Early and appropriate chemotherapy is of paramount importance.<sup>12</sup> Until recently the selection of drug was straightforward and chloroquine was the choice. The emergence of drug resistant strains has complicated the chemotherapy of falciparum malaria. Quinine is presently recommended for the treatment of 'severe falciparum malaria'.<sup>13</sup> Although quinine does not have any intrinsic superiority over chloroquine in the treatment of sensitive strains,<sup>14</sup> some workers suggest the use of the former drug in almost all cases of falciparum malaria.<sup>15</sup>

Higher mortality was noted in the quinine-treated group in the present study, presumably because: (i) more patients (60 percent) were treated with the drug, and (ii) all of them had presented with one or more complications of falciparum malaria. The overall mortality rate (16 percent) in the present series was, however, comparable with earlier reports.<sup>16,17,18,19</sup>

The efficacy of chloroquine, halofantrin and Fansidar, recorded in the present study is gratifying. Many workers have reported chloroquine-resistant strains of *P.falciparum* from different regions of Pakistan,<sup>7,8,9</sup> but a recent report from Malaria Control Programme of Pakistan has failed to detect high grade resistance in the local strains of the parasite.<sup>20</sup> This means that chloroquine retains clinical efficacy, albeit partial, in the face of emerging resistance. The present situation may not prevail for ever because chloroquine resistance is said to be initially patchy but spreads after a lag period of variable duration.<sup>13</sup>

The wide-spread empirical use of antimalarial drugs is believed to encourage the emergence of resistant strains of *P.falciparum*. Prescribing chloroquine loosely to patients with fever

is a common practice, especially in our rural areas. The drug is frequently administered in inadequate doses. Newer antimalarial drugs (eg. Halfan and Fansimef) may have a similar fate because the suave representatives of pharmaceutical industry promote them for the treatment of all forms of malaria. The three parasite species other than *P.falciparum* have remained sensitive to chloroquine. All the newer drugs are to be reserved for the treatment of chloroquine resistant strains of *P.falciparum*. Their indiscriminate use may lead to the emergence of disastrous multi-drug resistant strains of *P.falciparum*. Unrestricted sale of drugs over the counter is endemic in Pakistan. Thousands of patients indulge in selfmedication with one or two tablets of different brands of antimalarials for any febrile illness. Such indiscriminate use of antibiotics has rendered many of them impotent. The castration effect of life-saving antimalarials may not be far away unless our Federal Health Ministry formulates - and implements - rigid control over the sale of drugs.

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