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Research on New Antimalarial Drugs in the Bangkok Hospital for Tropical Diseases

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With the emergence of multidrug resistant falciparum malaria in Thailand, new drugs and drugs in combination are urgently needed. New antimalarial drugs have been investigated at the Hospital for Tropical Diseases in the recent years. Atovaquone, a hydroxynaphthoquinone, was evaluated and found that Atovaquone alone proved safe and effective. All patients treated had clinical cure, however, one third of the patients had late recrudescence (RI). When it was combined with proguanil, the cure rate increased to 100%. Artemisinine derivatives such as artesunate, artemether, arteether, dihydroartemisinin are also tested at the Bangkok Hospital for Tropical Diseases. Artesunate and artemether alone with a total dose of 600 to 750 mg produced cure rates of 80 to 95%. Artesunate suppositories have been proved successfully for the treatment of severe malaria. The artemisinin derivatives when used in combinations with mefloquine, cure rates improved to 95-100%. Dihydroartemisinin alone with a total dose of 480 mg given over 5 days gave a cure rate of 90%. Arteether, a WHO/TDR supported drug, are being evaluated in phase III clinical trial for severe falciparum malaria in the hospital. Other combinations (artemisinin derivatives combined with doxycycline, mefloquine combined with tetracycline or doxycycline) have also been evaluated with the improvement in cure rates. At present, studies with the combination of artemisinin derivatives plus mefloquine in various doses and duration of treatment, are being investigated. Until proven otherwise, the drug combinations are still recommended for all adult patients suffering from acute uncomplicated falciparum malaria contracted in multidrug resistant areas. Other antimalaria drugs such as pyronaridine and new 8 aminoquinolone (WR238605) are being evaluated.

In severe malaria the choice of antimalarial chemotherapy depends on the clinical severity, the drug sensitivity of the parasites and the availability and preparation of the drug. Chloroquine is still the drug of choice for chloroquine-sensitive parasites occurring in some areas in Africa. Quinine and quinidine are the only widely available drugs which are effective against chloroquine-resistant strains. Two new synthetic antimalarial drugs, mefloquine and halofantrine are also effective against chloroquine resistant strains, but they have no parenteral formulation and cases of resistance to these drugs have already been reported. Qinghaosu (artemisinin: and ancient Chinese herbal medicine) and its derivatives have been used successfully in treating both uncomplicated and severe falciparum malaria. Their effectiveness in eliminating the parasites have been extensively documented, however, the recrudescent rate is rather high (10-30%). In Thailand, drugs for the treatment of uncomplicated malaria are mefloquine in a dose of 25 mg/kg given in 2 divided doses 6 hours apart or quinine 10 mg/kg 8 hourly plus tetracycline 250 mg 6 hourly for 7 days, in patients aged 8 years and over. In treating severe malaria, early diagnosis and early treatment are vital and the aim is to save patient's life. Prompt administration of an adequate and effective antimalarial drug is needed once the diagnosis is made. The antimalarial drugs of choice are quinine, quinidine, chloroquine (for chloroquine-sensitive strains) and artemisinin derivatives. Other symptomatic and supportive treatment include careful monitoring of fluid input and urine output, frequent observations for complications with appropriate treatment and good nursing care. In spite of these efforts, the mortality of severe malaria is still high.

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