ABSTRACT

A study, to observe and compare in-vitro sensitivity of P. falciparum isolates from two provinces in Thailand to pyrimethamine, sulfadoxine and combination of the two, and to measure plasma PABA in malaria patients and normal Thai people in Bangkok.

Blood samples from 47 falciparum malaria patients from Phetchabun Province (July 21 to August 6, 1982) and 36 falciparum malaria patients from Chantaburi Province (October 12 to 26, 1982) were cultured by microtechnique (Rieckmann et al., 1978; Yisunsri and Rieckmann, 1980), using Waymouth MB 752/1 medium.

Eighty five percent of blood specimens from Phetchabun Province and 86% of blood specimens from Chantaburi Province were successfully cultured. Minimal inhibitory concentrations (MIC_s) of pyrimethamine (Pyr), sulfadoxine (Sulf) and combination of the two (Pyr:Sulf; 1:200) were determined. Two values of MIC_s (MIC_1 and MIC_2) were recorded in this study. MIC_1 was the first concentration which no normal schizont was observed, where as MIC_2 was the first concentration which complete inhibition (no schizont) was detected.

Mean values of MIC_1 of pyrimethamine of P.falciparum isolated from Phetchabun and Chantaburi Provinces were 1.57×10^{-6} M (range 1.2×10^{-7}M to 5×10^{-6}M) and 4.97×10^{-6}M (range 10^{-6}M to 2×10^{-5}M) respectively.

Mean values of MIC_2 of pyrimethamine of P.falciparum isolated from Phetchabun and Chantaburi Provinces were 1.9×10^{-5} (range 2×10^{-7} M to 1.2×10^{-4}M) and 4.80×10^{-5}M (range 10^{-5}M to 1.2×10^{-4}M).

These findings indicated that P.falciparum isolated from Phetchabun and Chantaburi Provinces were pyrimethamine resistant.

Mean values of MIC_1 of sulfadoxine of P.falciparum isolated from Phetchabun and Chantaburi Provinces were 1.56×10^{-3}M (range 1.6×10^{-4}M to 4.8×10^{-3}M) and 2.09×10^{-3} (range 4×10^{-4}M to 6×10^{-3}M) respectively.

Mean values of MIC_2 of sulfadoxine of P.falciparum isolated from Phetchabun and Chantaburi Provinces were 2.42×10^{-3}M (4×10^{-4}M to 6×10^{-3}M) and 3.0×10^{-3}M (8×10^{-4}M to 7.2×10^{-3}M).

Mean values of MIC_1 of the combination of pyrimethamine and sulfadoxine of P.falciparum isolated from Phetchabun Province and Chantaburi Province were $6.66 \times 10^{-7}/1.49 \times 10^{-4}$M (range $8 \times 10^{-8}/1.6 \times 10^{-5}$ to $2 \times 10^{-6}/4 \times 10^{-4}$M) and $1.79 \times 10^{-6}/3.48 \times 10^{-4}$M (range $10^{-6}/2 \times 10^{-4}$ to $4 \times 10^{-6}/8 \times 10^{-4}$M) respectively.

Mean values of MIC_2 of the combination of pyrimethamine and sulfadoxine of P.falciparum isolated from Phetchabun Province and Chantaburi Province were $4.63 \times 10^{-6}/9.29 \times 10^{-4}$M (range $8 \times 10^{-7}/1.6 \times 10^{-4}$ to $1.2 \times 10^{-5}/2.4 \times 10^{-3}$M) and $6.68 \times 10^{-6}/1.33 \times 10^{-3}$M (range $4 \times 10^{-6}/8 \times 10^{-4}$ to $2 \times 10^{-5}/4 \times 10^{-3}$M) respectively.

Plasma PABA concentrations in blood-medium and drugs mixture of the 34 falciparum malaria patients (with negative plasma sulfadoxine concentration) ranged from 4.50 to 36.92 ng per ml, these values were more or less in a good range which may not interfere parasite growth (Brockelman and Tan-Ariya, 1982).

In conclusion, results from these in-vitro studies indicated that P.falciparum isolates from Phetchabun and Chantaburi Provinces are pyrimethamine resistant and pyrimethamine susceptibility of P.falciparum is responsible for the sensitivity of P.falciparum to pyrimethamine-sulfadoxine combinations, in-vitro the MIC_s of pyrimethamine and pyrimethamine-sulfadoxine combinations of P.falciparum isolated from Phetchabun Province were significantly lower than the MIC_s of pyrimethamine and pyrimethamine-sulfadoxine combinations of P.falciparum isolated from Chantaburi Province. These results were in consistant with the results of the in-vivo responses previously reported. Plasma concentrations of PABA in falciparum malaria sufferers were more or less similar to the concentrations in normal persons.