A Comparative Study of Dihydroartemisinin Compounds in Treatment of Uncomplicated Falciparum Malaria in Kampong of Cambodia

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ABSTRACT  Objective: To compare the safety and efficacy of two compounds of dihydroartemisinin (DHA) — Artekin and Artekin (T) in the treatment of uncomplicated falciparum malaria. Methods: The regimen of 8-tablet for 2 days of Artekin and Artekin (T) were applied to 100 patients with uncomplicated falciparum malaria, who were randomly divided into two groups. Each group contained 50 cases. The cure rate, the mean parasites clearance time, the mean fever clearance and side-effects were observed to assess the safety and efficacy of the compounds used. Results: The mean parasites clearance time was 31.7±9.0 hours in the Artekin group and 32.8±8.8 hours in Artekin (T) group respectively; the mean fever clearance time was 12.7±7.2 hours in Artekin group and 16.5±7.9 hours in Artekin (T) group; there were no recrudescence case in both groups within the 28 days of follow-up, the cure rates in Artekin group and Artekin (T) groups were 100%. It indicated that the tolerability of both compounds were very good, the side-effects such as nausea, abdominal pain were mild and self-limited. Conclusion: The study preliminarily indicated that the DHA and PQ compounds were of high efficacy, rapid acting and low toxicity. Artekin is very promising as a cheap, simple, effective treatment for multi-resistance malaria in Cambodia.

KEY WORDS  uncomplicated falciparum malaria, dihydroartemisinin compound, Artekin, Artekin (T), efficacy, tolerability

Both Artekin and Artekin (T) were compounds of dihydroartemisinin (DHA) and piperaquine (PQ), Artekin (T) was composed of DHA, PQ and Trimethoprim (TMP), which has been registered in China and Vietnam and was commercially available. Artekin was composed of DHA and PQ.

The clinical study was conducted by Guangzhou University of TCM and National Malaria Center of Cambodia in the Oral Health Center of Kampong, Cambodia, from June to September in 2001. The Oral District is located in the forest area at the western border between Cambodia and Thailand, which has been seriously stricken by multi-resistance malaria. The use of chloroquine, sulfadoxine combined pyrimethamine and mefloquine had been stopped in the area considering their side-effects and emergence of resistance, according to the research by WHO and National Malaria Center of Cambodia in recent years¹.² The purpose of this study, which has been conducted in Cambodia, is to demonstrate clinically if there is any difference between Artekin and Artekin (T), and to assess the role of TMP as a component in Artekin.

METHODS

Criteria for Enrollment

Enrollment: (1) Patients with fever and ages between 7—65 years old; (2) Plasmodium falciparum asexual form count 1000—100000/μl. No antimalarial or drugs with antimalaria effect, such as sulfonamide or dapsone or tetracyclines, has been used since the present onset.

Exclusion: (1) Ages less than 7 years or more than 65 years; (2) Accompanied with severe vomiting or diarrhea; (3) Pregnancy; (4) Other severe complications or diseases.

Therapeutic regimen: A total of 100 patients with uncomplicated falciparum malaria were randomly divided into Artekin and

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Artekin (T) groups, with 50 patients in each group according to the Random Numerical Table and the order of hospitalization. The administration method for the two groups is the same.

Fifty patients with uncomplicated falciparum malaria were recruited into Artekin group, of whom 28 patients were male, and 22 female. The ages were from 7 to 56 years, 32 were adults, 18 patients were children (9 cases between 11–15 years, and 9 cases between 7–10 years), and gametocytes were found in 4 cases. Another 50 patients were recruited into Artekin (T) group, of whom 28 cases were male, and 22 female. The ages were from 6 to 49 years, 31 cases were adults, 19 were children (8 cases were between 11–15 years, 11 cases between 6–10 years), and gametocytes were found in 4 cases. The duration of fever at admission was 6.6 ± 3.5 days in Artekin group, 6.5 ± 3.6 days in Artekin (T) group; the mean body temperature was 38.4 ±1.0°C in Artekin group, 38.0 ±0.7°C in Artekin (T); the mean parasite count was 34111 ± 11525/μl in Artekin group, and 14578 ± 43372/μl in Artekin (T) group. The basic conditions of the patients in Artekin group were similar to that in the Artekin (T) group, there was no remarkable difference between the two groups and therefore they were comparable.

Medication
Artekin and Artekin (T) were provided by Guangzhou Kincare Medicine Institute (Batch Number 010620 and 010626). Each tablet of Artekin contains 40 mg DHA and 320 mg piperaquine phosphate, with 32 mg of DHA, 320 mg of piperaquine phosphate and 90 mg of TMP in Artekin (T). The appearance of Artekin tablet is the same as that of Artekin (T) tablet, and neither the doctors nor the patients knew the difference of components between Artekin and Artekin (T). All the patients were treated in the same way: Each time 1 tablet for those between 7–10 years old; 1.5 tablets for those between 11–15 years old; 2 tablets for those ≥16 year old, taken at the 0, 8th, 24th, 32nd hour after hospitalization, with a total of 8 tablets taken in 2 days which was taken as one treatment course for adults.

Observation Methods
All the patients were hospitalized and observed for 7 days. Temperature was taken at 6 hours' interval until it maintained afebrile for 24 hours, and thereafter taken every afternoon until discharge. Medication in each patient was supervised by investigators. Inquiry was taken 2 hours after medication in order to find out nausea or vomiting or other side-effects in time.

Laboratory Findings
Parasitology investigation: Malaria patients’ plasmodium asexual form count was done twice daily at 7 am and 5 pm. Within the first 48 hours after the loading dosage, the number of the asexual form in 200 WBC in each thick film should be counted. It is regarded as negative when no parasite asexual form is found in 200 fields of thick films for 3 consecutive blood films, then once more on day 7. Follow-up for parasite examination was done on day 14, 21 and 28.

Hematology examination: Hematocrit and white blood cell and differential count was done on day 1 and day 7

Statistical Analysis
The t-test and Chi-square test (χ²) was used to analyze the mean parasite clearance, fever clearance time, the cure rate and the incidence rate of side-effects.

RESULTS
Efficacy Evaluation
It was done referring to the 4-week observation method of clinical sensitivity of chloroquine (S, R I, R II, R III) recommended by WHO(3). Efficacy was evaluated by parasite clearance time, fever clearance time, recrudescence and cure rate as well as side effects.