JPRHC

Short Communication

EVALUATION OF EFFICACY AND TOXICITY OF DIFFERENT TREATMENT REGIMENS IN PLASMODIUM FALCIPARUM MALARIA

CHOGTU BHARTI, ADIGA SACHIDANAND, PRABHU MUKYAPRANA, K.L.BAIRY

For author affiliations, see end of text

This paper is available online at www.jprhc.com

ABSTRACT

The efficacy and toxicity of four commonly used antimalarials was evaluated. The combinations evaluated were Artesunate and Doxycycline, Quinine and Doxycycline, Artesunate and Quinine, Artesunate and Mefloquine. The four combinations did not show any statistically significant difference in terms of days of defervescence, parasite clearance and hospital stay. All the four combinations were well tolerated.

Keywords: Antimalarials, Artesunate, Doxycycline, Quinine, Mefloquine.

INTRODUCTION

Malaria is one of the most important infectious diseases causing hundreds of millions of illnesses and an estimated 1 million deaths each year[1]. Nearly all serious illnesses and deaths from malaria are caused by Plasmodium falciparum. There are almost 515 million episodes of clinical Plasmodium falciparum malaria infections[2].The incidence of malaria was 0.46 million in 2006 and there were about 890 deaths that year[3]. The treatment of malaria is highly effective if provided rapidly, used correctly and is not limited by drug resistance[4]. Antimalarials combination therapy is currently regarded as a major strategy to combat drug-resistant malaria. Combination therapy involves the simultaneous use of two or more blood schizonticides that have independent modes of action and different biochemical targets in the parasite[5]. The combination of artemisinin derivatives with other antimalarial drugs is widely advocated because it produces rapid clinical and parasitological response, may delay the development of resistance, and may reduce malaria transmission[5]. Different antimalarial regimens are being used for treatment of falciparum malaria in different centers. Each one of these combination has its own advantages and disadvantages. In this study we have compared the efficacy and toxicity of different regimens used in our tertiary care hospital.

MATERIALS AND METHODS

This was a retrospective study. The study was approved by institutional ethics committee and permission to access the data was given. Data was collected from medical records department of the in-patients diagnosed as Plasmodium falciparum malaria in the year 2006-2007. Efficacy was measured in terms of number of days for: parasite clearance, defervescence, hospital stay. Parasitological diagnosis was made by light microscopy and rapid diagnostic tests. Body temperature was recorded six hourly. Defervecence days gave the time in which patient became afebrile. The number of days patient stayed in hospital was also recorded .Toxicity was assessed by monitoring the adverse events in patients as per their clinical symptoms. Adverse events secondary to antimalarial drugs in the patient's record was noted.

RESULTS

A total of 100 prescriptions of in-patients were evaluated, of which 79 were of males and 21 of females. Prescriptions of patients diagnosed as P. falciparum malaria were included in the study. Prescriptions were analyzed as per the performa which included patient particulars, complete diagnosis, the drugs used along with their dosage, formulation and duration of use .The commonly used antimalarial combinations were Artesunate + Doxycycline (Art+Doxy), Quinine+Doxycycline (Quinine+Doxy), Artesunate + Quinine(Art+Quinine), Artesunate + Mefloquine (Art+Mef) and others. The percentage of patients prescribed these combinations is shown in Fig 1. The other combinations included drugs like clindamycin, chloroquine, sulphadoxine, pyrimethamine.

Dosage Schedule

Drug regimen	Dose	Duration (days)
Artesunate+ Doxycycline	60 mg BD*# 100mg BD.	7
Quinine + Doxycycline	600mgTDS 100mgBD	4-7
Artesunate + Quinine	600mg TDS 60mg BD	3-7
Artesunate + Mefloquine	60mgBD 700mg+500mg	4-5 12 hours apart

*after initial loading dose #shifting the drug from i.v to oral

TABLE 1. Showing the dosage schedule and duration of treatment

The dosage schedule of different combinations is shown in Table 1. The hospital stay days and the days required for smear conversion is shown in Fig.2.The mean of hospital stay days was from 7.0 to 9.0 days and there was statistically no difference between the four groups (P= 0.15). 5.6-7 days were required for smear conversion in the four groups (P= 0.15). The days for defervescence i.e the days patient took to become afebrile were 3.15 to 4.4 days and the difference between the four groups was insignificant (P=0.21) as shown in Fig.3.Six patients did

not respond to treatment. Two of these had other complications and died. Three patients had history of relapse and one left against medical advice. Two patients in quinine groups developed ototoxic manifestations secondary to quinine. One patient had tinnitus and the other patient had tinnitus in addition to difficulty in hearing. Both the patients developed these adverse effects after three days of quinine treatment and the symptoms abated after quinine was stopped. One patient on Mefloquine developed anemia and hemoglobin dropped from 11.6mg/dl to 5.3mg/dl.

Fig. 1. Antimalarial combinations prescribed with percentage of patients

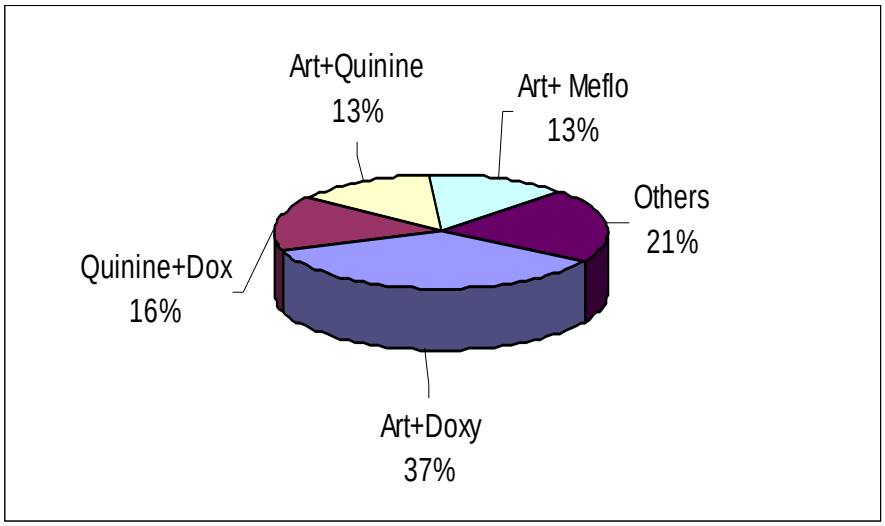


Fig 2:

Days for hospital stay and smear conversion

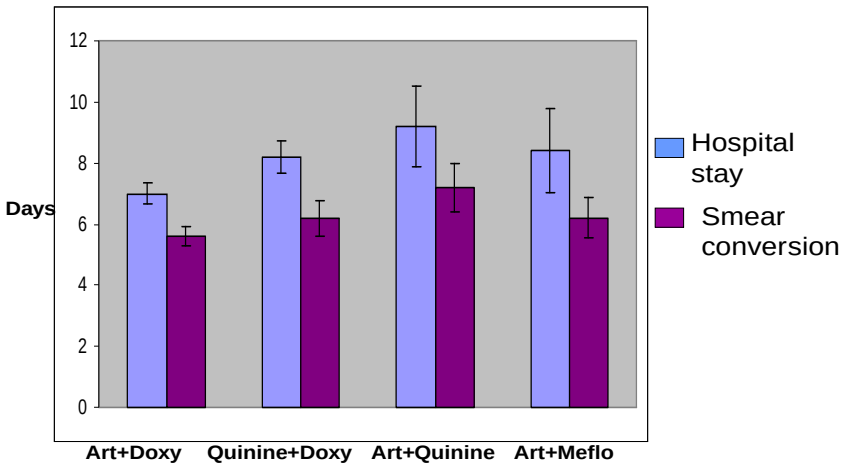
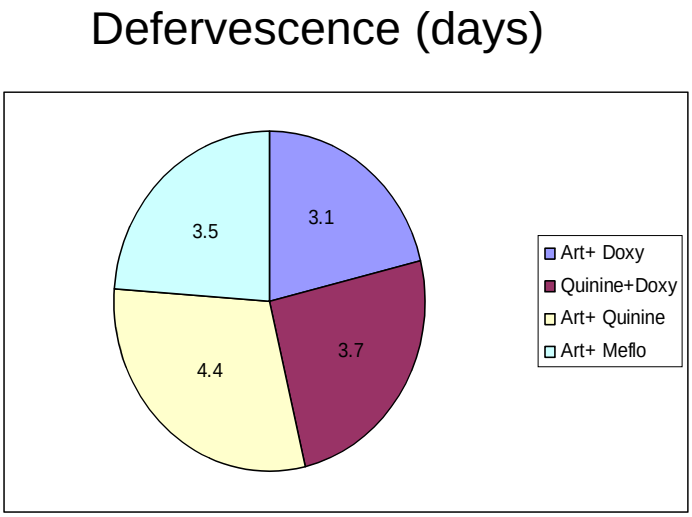


Fig 3



DISCUSSION

All the efficacy parameters did not show any statistically significant difference among the four groups. But from the graphs of smear conversion and hospital stay days artemisinin combinations appear superior to quinine combinations. The superiority of Artemisinin is due to its rapid action against all the erythrocytic stages of the parasite and a limited resistance[6].

As per the WHO guidelines Artesunate and mefloquine is one of the first line combination used in Plasmodium falciparum malaria[7].Though Artemisinin and Doxycycline is the second line combination as per the WHO guidelines[7] but the physicians are justified in using it as first line as it is equally efficacious and well tolerated as compared to Artesunate and mefloquine in this study. Artemisinin and Doxycycline combination has the advantage of simplicity and coformulation which improves adherence[7]. Quinine and doxycycline is not well tolerated and adherence is poor if the treatment is not observed[7].In patients with malaria, anemia results from accelerated RBC removal by the spleen, obligatory RBC destruction at parasite schizogony, and ineffective erythropoiesis. In severe malaria, both infected and uninfected RBCs show reduced

deformability, which correlates with prognosis and development of anemia. Two patients in Art + mefloquine developed anemia three days after the drug administration.

It cannot be solely attributed to drug as disease progression can also lead to anemia. One patient with quinine developed tinnitus and other complained of tinnitus with difficulty in hearing. Quinine causes functional impairment of eighth nerve leading to tinnitus and decreased auditory acuity[8]. The four regimens used to treat Plasmodium falciparum malaria did not differ significantly with regard to days of defervescence, hospital stay and smear conversion. Most of the patients tolerated all the four regimens well.

REFERENCES:

1. Greenwood BM, Bojang K, Whitty CJ, Targett GA. Malaria. Lancet 2005;365: 1487-1498.

2. Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of Plasmodium falciparum malaria. Nature.2005;434: 214-217.

3. www.malariasite.com/malaria/MalariaInIndia.htm-73k-13 Jan 2009

4. Baird JK. Effectiveness of antimalarial drugs. N Engl J Med 2005;352:1565-1577

5. Bukirwa H, Orton L. Artesunate plus mefloquine versus mefloquine for treating uncomplicated malaria. Cochrane Database of Systematic Reviews 2005, Issue 4.

6. Philip J Rosenthal. Artesunate for the treatment of severe falciparum malaria. N Engl J Med 2008; 358:1829-36.

7. Guidelines for the treatment of malaria. Geneva: World Health Organisation, 2006. (Accessed March 28, 2009, athttp://www.who.int/malaria/docs/ Treatment Guidelines 2006.pdf.)

8. Shapiro TA. and Goldberg DE. Chemotherapy of protozoal infections Malaria. In Goodman's Gilman's The Pharmacological basis of therapeutic 11th ed.(Bruton LL, Lazo JS, Parker KL eds) Mc graw Hill Publications USA,2006,pg1029-47.

ADDRESS FOR CORRESPONDENCE

Dr.K.L.Bairy, MD, PhD, Professor of Pharmacology

Kasturba Medical College, Manipal-576104

Email: klbairy@gmail.com

Fax: 0820 2571999

Phone: 0919449208478