MALARIA TREATMENT USING ORAL MEDKAFIN: CHANGES IN BIOCHEMICAL AND HAEMATOLOGICAL PARAMETERS IN NIGERIAN ADULTS WITH UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

BY

UDOSEN EO AND AKPAN EE

Department of Biochemistry, College of Medical Sciences, University of Calabar, Calabar, Nigeria

SUMMARY

Objective: To observe the changes in the biochemical and haematological parameters of patients with uncomplicated *Plasmodium falciparum* malaria after treatment with oral medkafin.

Method: The activities of aspartate aminotransferase (AST) E.C.2.6.1.1, alanine amino transferase (ALT) E.C.2.6.1.2, the levels of total and conjugated bilirubin, haemoglobin (Hb) and packed cell volume (PCV) in the serum of patients with uncomplicated malaria prior to (PT) and after treatment (AT) with oral medkafin, a new antimalarial drug, were assayed in consenting patients with plasmodium *falciparum malaria* treated at the University of Calabar Medical Centre in June 1997.

Result: The activity of ALT and the level of Hb decreased significantly ($p< 0.05$) after treatment in the serum of male and female patients compared with their pre-treatment values. The activity of AST, total and conjugated bilirubin increased significantly ($p < 0.05$) in the serum of male and female patients (except that of female total bilirubin) compared with the PT levels. The PCV of males decreased significantly AT ($p < 0.05$) compared to the PT levels.

Conclusion: This study showed that the levels of ALT, Hb and PCV decreased while those of AST, total and conjugated bilirubin increased in males after treatment with oral medkafin.

Key Words: *Medkafin, Malaria, Falciparum malaria, Treatment of Malaria*

INTRODUCTION

Malaria is primarily a disease of the developing countries, and it is estimated to cause 200-300 million new cases and 2 million deaths annually, the majority in sub-Saharan Africa[1]. Increasing multidrug resistance is challenging the efficacy of current antimalarial drugs not only in the management of severe malaria but also in the treatment of uncomplicated malaria[2]. Resistance of *plasmodium falciparum* to chloroquine has increased[3], stimulating the search for effective alternative drugs for treatment. Unfortunately, many apparently safe new drugs later proved to have serious side effects. For example amodiaquine and mefloquine, which are cheap and were initially very promising are now associated with bone marrow, liver and severe neuropsychiatric side effects[4,5].

One of these new drugs which are useful in treating chloroquine resistant malaria is medkafin[6]. At present there is not enough information on the possible side-effects of medkafin. We therefore decided to conduct this study of the biochemical and haematological parameters in adult Nigerians treated with medkafin to search for any possible side effects associated with this drug.

MATERIALS AND METHODS

This work was carried out in Calabar, a coastal town in the Eastern part of Nigeria. Calabar is endemic for malaria and *Plasmodium falciparum* is the dominant parasite.

The study was done in June 1997 during the rainy season. All the patients (20 men and 20 women) who attended the out patient clinic of the University of Calabar Medical Center with uncomplicated *Plasmodium falciparum* malaria and consented to inclusion in the study, participated. Pregnant women and individuals who had taken antimalarial drugs two weeks

Correspondence Author:
Esua O. Udosen, Department of Biochemistry
College of Medical Sciences, University of Calabar
PMB 1115, Calabar, Nigeria
Accepted for publication: 9th September 2000

before presentation and patients below 15 years of age and those above 50 years were excluded. The malaria patients were chosen on the basis of having a positive blood smear for *Plasmodium falciparaum* using the Giemsa-stained thick and thin blood films. The study protocol was approved by the ethics Committee of the Medical Center.

The forty patients were chosen randomly and given oral medkafin (MEDEL GMBH, PINNERBERG, GERMANY) at the normal dose of 22.5mg/kg body weight. The blood samples were taken prior to treatment (PT). After one week, the patients were reviewed and their blood samples were taken after treatment (AT). The activities of ALT E.C.2.6.1.2 and AST, E.C.2.6.1.1, were determined according to Annino and Giese[7], the total and conjugated bilirubin were determined as described by Routh[8], while haemoglobin (Hb) and packed cell volume were determined according to the method of Dacie and Lewis[9]. The results were expressed as means ± SEM. All statistical comparisons were made by means of the Student t-test and $p<0.05$ was regarded as significant.

RESULTS

In table 1 the ALT levels in both males and females are shown to be significantly reduced ($p<0.05$) in the serum of patients after treatment compared with their levels prior to treatment. For the AST, the levels are significantly increased ($p<0.05$) in the serum of AT patients compared with those of PT. patients. The total and conjugated bilirubin levels AT increased significantly ($p<0.05$) compared with the PT levels. However, the total and conjugated bilirubin levels for the females did not change significantly ($p>0.05$).

For the haematological parameters, the Hb and PCV in both male and female patients decreased significantly ($p<0.05$) after treatment compared with the PT levels except for the female PCV level which were not significantly altered ($p>0.05$).

DISCUSSION

This study shows that ALT and AST activities are high in both PT and AT sera relative to the expected normal levels. For ALT, the activity decreased after treatment unlike for AST. The increased activity of AST indicates a probable hepatotoxicity of medkafin, a common feature of some antimalarials[3].

Total and conjugated bilirubin were high in both the PT and AT sera compared with the normal values. This could be due to the combined effect of the malaria infection and the oral medkafin. Similar results were observed with other antimalarials[2].

Table 1: Biochemical and Haematological Parameters Prior to and After Treatment of *Plasmodium falciparum* malaria with Oral Medkafin

Parameter	Males		Females		Normal levels	
	PT	AT	PT	AT	Males	Females
ALT (IU/L)	57.1±9.7	39.9±6.0	22.6±8.3	17.8±4.7	6-21	4-17
AST (IU/L)	69.8±5.0	79.0±8.0	26.3±4.3	29.5±6.6	7-21	6-18
Total Bilirubin (umol/L)	14.3±2.7	16.8±2.7	8.4±1.9	8.6±1.0 (ns)	3.4-17.1	
Conjugated Bilirubin (umol/L)	9.7±1.2	16.9±1.8	4.6±0.6	8.4±1.8	0-5.13	
Haemoglobin (g/dL)	16.6±2.0	14.0±0.6	14.0±0.6	10.5±1.0	14-18	12-16
Packed Cell Volume (%)	46.4±3.3	41.9±2.0	30.3±4.7	31.8±5.8 (ns)	40-52	37-47

ALT Serum Alanine Aminotransferase
AST Serum Aspartate Aminotransferase
Ns Not Statistically Significant $p> 0.05$

The haemoglobin is reduced. Haemoglobin is a major energy source for intra-erythrocytic *Plasmodium falciparum* hence the medkafin by interfering with Hb catabolism makes it toxic to the parasite[10]. This reduction in Hb after treatment indicates that medkafin can give rise to agranulocytosis as amodiaquine[3]. The PCV also decreased in the AT sera of males, while in the female the levels were unchanged. Malaria causes a decrease in the PCV of both the males and females, but the reduction is more pronounced in the females.

CONCLUSION

The results showed that treatment of patients with uncomplicated *Plasmodium falciparum* malaria with medkafin reduces ALT, Hb and PCV, while AST, total and conjugated bilirubin levels are increased. The reductions in haematological parameters are pronounced especially in the females and may give rise to anaemia[11]. This drug should thus not be given to pregnant women in developing countries who are prone to anaemia. The probable effects of medkafin are hepatotoxicity and haemolysis.

REFERENCES

1. Crutcher JM, Jones TR and Hoffman SL. Immunology, pathophysiology and treatment of malaria. Current Opinion in Infectious Diseases. 1994; 7: 529-535.
2. Alin MH, Kihamia CM, Bjorkman A et al. Efficacy of oral and intravenous artesunate in male Tanzanian adults with *Plasmodium falciparum* and in vitro susceptibility to artemisin, chloroquine, and mefloquine. Am J Trop Med Hyg 1995; 53: 581-585.
3. Gill G. Malaria prophylaxis: Problems with Mefloquine. Afr. Health 1997; 19: 27-31.
4. Gill G. Malaria -- New drugs, New problems. Afr. Health 1996; 18: 31
5. Croft AMJ and World MJ. Neuropsychiatric reactions with mefloquine chemoprophylaxis. Lancet 1996; 347: 326
6. MEDREL-GmbH Data on file. MEDREL-GmbH Manual 1996.
7. Annino JS and Giese RW. Clinical Chemistry Principles and Procedures. Little Brown and Company, London 1976: 240-267.
8. Routh JI. In Tietz NW (ed): Fundamental of Clinical Chemistry. WB Saunders London 1982: 1026-1062.
9. Dacie JV, Lewis SM. Practical Haematology. JA Churchill Ltd, 1968: 34-54
10. Gluzman IY, Francis SE, Oksman A et al. Order and Specificity of *Plasmodium falciparum*. Haemoglobin Degradation pathway. J. Clin. Invest. 1994; 93: 1602-1608
11. Topley E. Anaemia in Rural Africa. FSH Medimedia, Cambridge 1998: 2-4.