Revista da Sociedade Brasileira de Medicina Tropical
32(1):67-68, jan-fev, 1999.

Plasmodium vivax resistance to chloroquine (R2) and mefloquine (R3) in Brazilian Amazon region

Resistência do *Plasmodium vivax* pela cloroquina (R2) e mefloquina (R3) na amazônia Brasileira

Maria das Graças C. Alecrim, Wilson Alecrim and Vanize Macêdo

Abstract *We report for the first time a patient with malaria due to* Plasmodium vivax *who showed R2 resistance to chloroquine and R3 resistance to mefloquine in the Brazilian Amazon region based on WHO clinical criteria for diagnosis of malaria resistance. Failure was observed with unsupervised oral chloroquine, chloroquine under rigorous supervision and mefloquine in the same scheme. Finally, the patient was cured with oral artesunate.*

Key-words: Plasmodium vivax*. Drug resistance. Chloroquine resistance. Mefloquine resistance.*

Resumo *Estamos relatando pela primeira vez um paciente com malária por* Plasmodium vivax *que mostrou resistência R2 à cloroquina e resistência R3 à mefloquina na Amazônia brasileira, de acordo com os critérios clínicos da OMS para resistência da malária. A falha foi observada com cloroquina oral, não supervisionada, cloroquina oral administrada sob rigorosa supervisão e com mefloquina no mesmo esquema. A paciente curou com o artesunato oral.*

Palavras-chaves: Plasmodium vivax*. Resistência a drogas. Resistência à cloroquina. Resistência à mefloquina.*

We report for the first time R2 resistance to chloroquine and R3 resistance to mefloquine by *P. vivax* in the Brazilian Amazon region.

FSS, a 12 year-old female patient from Autazes Municipality in the State of Amazonas, Brazil, was diagnosed as having *P. vivax* malaria on July 14th 1997 (day 0) at the *Instituto de Medicina Tropical do Amazonas*, Manaus, Brazil. Day 0 parasitemia was 250 parasites/µl. The patient was treated with 10 mg/kg body weight oral chloroquine on the first day and 7.5mg/kg on the second and third days. On day 4 parasitemia was 500/µl. On day 7 blood was negative. On day 9 parasitemia was 1,000/µl when we treated her with 20mg/kg mefloquine. On day 19 parasitemia was 3,000/µl. She was treated again with the same chloroquine dosage in a directly observed schedule. On day 3 of the last scheme parasitemia was 3,100/µl.

On day 5 parasitemia decreased to 500/µl and increased to 800/µl on day 7, showing the R2 pattern of *P. vivax* chloroquine resistance.

The patient remained stable despite the level of parasitemia that increased to 1,720 on day 10. She was then treated with a supervised dose of 20mg/kg mefloquine. Parasitemia decreased to 258/µl on day 3 and increased to 4,472/µl on day 7, showing the R3 pattern of *P. vivax* resistance

Instituto de Medicina Tropical do Amazonas. Universidade do Amazonas, Manaus, AM. Núcleo de Medicina Tropical e Nutrição/Universidade de Brasília, Brasília, DF.
Endereço para correspondência: Drª Maria das Graças C. Alerim. Avenida Pedro Teixeira s/nº. Dom Pedro I. 69040-000 Manaus, AM.
Tel: 55 92 238-2801; Fax: 55 92 238-7220.
Recebido para publicação em 2/10/98.

to mefloquine. Because of therapeutic failure with chloroquine and mefloquine the patient was treated with oral 100mg/day artesunate, 50mg b.i.d. for five days. Parasitemia was negative on day 2. Primaquine treatment was started on day 3. The patient was followed up weekly until day 45 when she returned to Autazes Municipality.

P. vivax resistance to chloroquine was reported for the first time in 1989 by Schuurkamp et al in New Guinea[9]. Since then other authors confirmed it in the literature[1 2 3 6]. In 1996, Phillips et al[8] described for the first time *P. vivax* resistance in South America in a strain from Guyana.

In 1992 Garavelli and Corti[4] reported a patient with *P. vivax* malaria resistant to chloroquine in Brazil. However, Loyola and Rodriguez analyzed this case and concluded that it was a relapse after primaquine treatment[5].

We did not have any possibility to measure drug levels, but treatment was supervised and the patient did not have any gastrointestinal alteration which could impair drug absorption.

We conclude that the resistance patterns observed are compatible with a strain with R2 resistance to chloroquine and R3 resistance to mefloquine using the WHO classification of clinical resistance in malaria[7].

REFERENCES

1. Baird JK, Basri H, Purnomo, Bangs MJ, Subianto B, Patchen LC, Hoffman LS. Resistance to chloroquine by *Plasmodium vivax* in Irian, Jaya, Indonesia. American Journal of Tropical Medicine and Hygiene 44:547-552, 1991.
2. Baird JK, Canete-Miguel E, Masbar S, Bustos DG, Abrenica JA, Layawen AVO, Calulut JM, Leksana B, Wignall FS. Survey of resistance to chloroquine by *falciparum* and *vivax* malaria in Palawan, The Philippines. Transactions of the Royal Society of Tropical Medicine and Hygiene 90:413-414, 1996.
3. Dua VK, Kar PK, Sharma VP. Chloroquine resistant *Plasmodium vivax* malaria. India. Tropical Medicine Health 61:816-819, 1996.
4. Garavelli PL, Corti E. Chloroquine resistance in *Plasmodium vivax*: The first case in Brazil. Transactions of the Royal Society Tropical Medicine and Hygiene 86:128, 1992.
5. Loyola EG, Rodriguez MH. Chloroquine resistant *P. vivax* in Brazil? Transactions of the Royal Society of Tropical Medicine and Hygiene 86:570-571, 1992.
6. Marlan-Than, Myat-Phone-Kyaw, Aye-Yu-Soe, Khaing-Khaing-Gyi, Ma-Sabai, Myint-Oo. Development of resistance to chloroquine by *P. vivax* Myanmar. Transactions of the Society of Tropical Medicine and Hygiene 89:307-308, 1995.
7. Organização Mundial de Saúde. Quimioterapia del paludismo y resistencia a los medicamentos antipalúdicos. Organización Mundial de la Salud. Serie de Reportaje Tecnico nº 529, 1973.
8. Philips EJ, Keystone JS, Kain KC. Failure of combined chloroquine and high-dose primaquine therapy for *P. vivax* malaria acquired in Guyana, South America. Clinical Infectious Diseases 23:1171-1173, 1996.
9. Schuurkamp GJ, Spicer PE, Kereu RK, Bulungol PK. A mixed infection of *vivax* and *falciparum* malaria apparently resistant to 4-aminoquinoline: a case report. Transactions Royal of the Society Tropical Medicine and Hygiene 83:607-608, 1989.