Plasmodium falciparum: sensitivity to chloroquine *in vivo* in three ecological zones in Ghana

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Abstract

4690 children aged 6–15 years in 5 urban and 4 rural communities in 3 ecological zones in Ghana were screened from June 1988 to December 1990 to provide suitable candidates for the World Health Organization standard *in vivo* test for susceptibility of *Plasmodium falciparum* to chloroquine. 1880 (40·1%) had parasitaemia, mostly (83·7–98·6%) due to *P. falciparum* infection. Of the 626 *in vivo* tests performed, 570 (91·1%) showed sensitivity to chloroquine and 56 (8·9%) responses were classified as resistant to chloroquine at RI (5·1%) and RII (3·8%). The resistance responses were commonest (17·1–22·7%) in the coastal zone, followed by the savanna zone (8·6–10·0%), and lowest in the forest zone (3·1–6·3%). The RII responses occurred mainly in communities in the coastal zone. There was no RIII resistance in any zone. The pattern of RI (early) and RII responses of *P. falciparum* to chloroquine in this study suggested an increase in sensitivity, or a reduction in resistance, of *P. falciparum* to chloroquine from the coast to the forest and northern savanna zones, and from the urban to the rural communities in each zone in Ghana.

Introduction

Malaria is hyperendemic in Ghana and its distribution follows distinct ecological zones. More cases of malaria are reported from the forest zone, followed by the coastal zone and then the northern savanna in decreasing order. The major parasite species in Ghana is *Plasmodium falciparum* (AHMED, 1989).

Resistance of *P. falciparum* to chloroquine was first reported in Ghana in a semi-immune patient at the Korle-Bu Teaching Hospital by NEEQUAYE (1986). Subsequently, NEEQUAYE *et al.* (1988) and OFORI ADJEI *et al.* (1988) documented *P. falciparum* resistance *in vivo* at RI and RII levels in semi-immune in-patient children at the same hospital. There has been no community study to investigate the sensitivity of *P. falciparum* to chloroquine and other antimalarial drugs in Ghana.

The aim of the present study was to assess the sensitivity of *P. falciparum in vivo* to chloroquine in the 3 ecological zones of Ghana as part of a national programme to map areas of *P. falciparum* resistant to antimalarial drugs in use in Ghana.

Materials and Methods

Ghana is broadly divided into 3 ecological zones: coastal, forest and northern savanna. A multi-stage sampling method was used to select 3 primary schools (one urban, one periurban and one rural) from the coastal zone, 4 primary schools (2 urban and 2 rural) from the forest zone, and 2 primary schools (one urban and one rural) from the northern savanna zone for the survey. All children aged 6–15 years who were present on the day of the survey in the selected primary schools were screened for the study, which was conducted from June 1988 to December 1990.

Study in vivo

A slightly modified World Health Organization standard field test (7 d test) for the response of *P. falciparum* asexual parasites to chloroquine was used. The schoolchildren were examined for malaria parasitaemia using Giemsa-stained thick and thin blood films. The modified Haskins MM II test (MOUNT *et al.*, 1987) was used to test for the presence of chloroquine and its metabolites in urine on the day the blood films were prepared. Children with at least 1000 *P. falciparum* asexual parasites per 8000 white blood cells (one μl of blood) and with no chloroquine detected in their urine were included in the study; those with mixed infections were excluded.

Children were given (under supervision) 10 mg/kg body weight of chloroquine base (Ghana Industrial Holding Corporation, Pharmaceutical Division, Accra) orally on the following day, designated as day 0, and on day 1, and 5 mg/kg body weight of chloroquine base orally on day 2. Urine specimens were collected on days 0, 2, 4 and 7 and tested for the presence of chloroquine or its metabolites. Finger-prick capillary blood films were prepared on days 0, 2, 4, and 7 and stained with

Table. Sensitivity *in vivo* of *Plasmodium falciparum* asexual parasites to chloroquine in children in three ecological zones in Ghana, 1988–1990

Ecological zones and communities	No. of patients examined	No. with malaria infection[a]	No. with *P. falciparum* infection	No. qualified for study	No. who completed study	Grading of sensitivity[a,b] S/RI (delayed)	RI (early)	RII	Total no. resistant
Coastal									
Nima (urban)	506	91 (18·0)	85	48	44	34 (77·3)	1 (2·3)	9 (20·5)	10 (22·7)
Madina (peri-urban)	275	128 (46·5)	126	59	59	48 (81·4)	3 (5·1)	8 (13·6)	11 (18·6)
Gomoa Fetteh (rural)	218	132 (60·6)	123	49	41	34 (82·9)	1 (2·4)	6 (14·6)	7 (17·1)
Forest									
Sunyani (urban)	715	152 (21·3)	137	62	57	55 (96·5)	2 (3·5)	0	2 (3·5)
Chiraa (rural)	966	529 (54·8)	443	153	131	127 (96·9)	4 (3·1)	0	4 (3·1)
Ho (urban)	451	135 (29·9)	130	65	64	60 (93·8)	4 (6·3)	0	4 (6·3)
Sokode Ando and Bagble (rural)	325	147 (45·2)	145	70	69	66 (95·7)	3 (4·3)	0	3 (4·3)
Northern savanna									
Bolgatanga (urban)	706	280 (39·7)	276	90	81	74 (91·4)	6 (7·4)	1 (1·2)	7 (8·6)
Kongo/Zaare (rural)	528	286 (54·2)	285	84	80	,72 (90·0)	8 (10)	0	8 (10·0)
Total	4690	1880 (40·1)	1750	680	626	570 (91·1)	32 (5·1)	24 (3·8)	56 (9·0)

[a]Numbers in parentheses are percentages.
[b] No RIII resistance was detected.

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Giemsa's stain. *P. falciparum* was considered sensitive or resistant depending on the persistence of asexual parasites during the follow-up period of 7 d after chloroquine administration (BRUCE-CHWATT, 1986).

Results

Screening for malaria infection

A total of 4690 school children, 999 from the coastal zone, 2457 from the forest zone, and 1234 from the northern savanna zone, were screened for malaria infection; 351 (35·1%) children in the coastal zone, 963 (39·2%) in the forest zone and 566 (45·9%) in the northern savanna zone had patent malaria infections (Table).

Chloroquine sensitivity

The Table shows that 91·1% of the tests showed sensitive or RI (delayed) responses, 5·1% showed RI (early) responses, and 3·8% showed RII responses. There was no RIII response in any ecological zone. The proportion of sensitive/RI (delayed) responses was lowest in the coastal zone, followed by northern savanna and then the forest zone. RII responses were found mainly in the coastal zone. There was no RII response in the forest zone. The RII responses in the coastal zone were higher in the urban community of Nima than in the peri-urban and rural communities. The total number of resistant responses (RI early and RII) was highest in the coastal zone and lowest in the forest zone.

Discussion

P. falciparum resistance *in vivo* to chloroquine at RI and RII levels in patients at the Korle Bu Teaching Hospital in Accra have been reported by NEEQUAYE *et al.* (1988) and OFORI-ADJEI *et al.* (1988). The present community survey has confirmed the presence of chloroquine-resistant *P. falciparum* malaria parasites in Ghana.

The pattern of RI (early) and RII responses of *P. falciparum* to chloroquine found in this study suggested an increase in the sensitivity, or a reduction in the resistance, of *P. falciparum* to chloroquine from the coast to the forest and northern savannah zones, and from the urban to the rural communities in each zone in Ghana. These findings have demonstrated the differences in *P. falciparum* responses to chloroquine in the different ecological zones in Ghana. Indications are that the emergence and spread of chloroquine resistance appear to have been precipitated by drug pressure in the coastal zone and urban areas of Ghana, where most medical facilities are concentrated and where there is greater accessibility and more frequent use of chloroquine and other antimalarial drugs. It is also possible that the population in the forest zone may have high immunity as a result of intense transmission, and that therefore chloroquine was more effective there.

The levels of sensitive/RI (delayed) responses were generally high; the prevalence of RI (early) resistance was also low in all the ecological zones, whilst RII resistance was recorded mainly in the coastal zone. There was no RII response in the forest zone, where the incidence of malaria is highest (AHMED, 1989). The development and the progression of RII/RIII resistance, which has implications in malaria treatment, has been slower than that experienced in East Africa among semi-immune populations (DRAPER *et al.*, 1988; WARSAME *et al.*, 1991).

Our findings also indicate that chloroquine at a dose of 25 mg/kg body weight should continue to be the first choice treatment of malaria in Ghana. However, sentinel sites for monitoring *P. falciparum* sensitivity to chloroquine and other antimalarial drugs should be established to provide the necessary data for regular assessment of malaria treatment policies in Ghana.

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Continued from p. 226

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