Sensitivity of *Plasmodium falciparum* to chloroquine and sulfadoxine/pyrimethamine in Nigerian children

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The in vivo *sensitivity of* Plasmodium falciparum *to chloroquine and sulfadoxine/pyrimethamine was evaluated in children under 5 years of age in two areas of southern Nigeria in 1987. A modification of the WHO Standard Field and Extended Tests* (in vivo) *was used, with follow-up on days, 2, 3, 7, and 14 after treatment with 25 mg chloroquine per kg body weight given over 3 days, or with standard doses of sulfadoxine/pyrimethamine. Clinical and parasitological evaluations were performed.*

At Igbo Ora, in Oyo State, where by day 7 chloroquine was clinically successful in 94.4% of 36 children and sulfadoxine/pyrimethamine in 91.7% of 36 children, there were no parasitological failures in either treatment group. Fever regressed significantly more rapidly with chloroquine than with sulfadoxine/pyrimethamine. At Oban, in Cross River State, initial parasite densities decreased markedly with the chloroquine regimen but 63.6% of 44 children were parasitological failures on day 3, 7, or 14; and all of the 26 children who failed parasitologically and completed follow-up were successfully treated with sulfadoxine/pyrimethamine. By day 7, clinical success was demonstrated for 77.3% of the children treated with chloroquine. The in vitro *sensitivity to chloroquine, quinine, and mefloquine at Igbo Ora indicated that isolates of* P. falciparum *were sensitive to chloroquine and quinine, but had reduced sensitivity to mefloquine.*

Because of its continued clinical efficacy, chloroquine remains the recommended treatment for children with uncomplicated malaria in Nigeria. Health providers are, however, encouraged to maintain supplies of sulfadoxine/pyrimethamine as an alternative and to refer patients promptly if necessary.

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Introduction

In Nigeria, malaria is the most common cause of outpatient visits to health facilities and is consistently reported as one of the five leading causes of death at government health institutions (*1*). Transmission occurs throughout urban and rural areas and is perennial in the tropical rain forest areas. Within primary health care, malaria control activities focus on the provision and use of appropriate antimalarial therapy. Nationally, the recommended malaria treatment consists of chloroquine at a dose of 25 mg per kg body weight, administered in a 3-day regimen (10 mg/kg, 10 mg/kg, and 5 mg/kg, respectively). Control activities against the vectors of the disease have been concentrated in urban areas.

The efficacy of chloroquine has been compromised by the occurrence of chloroquine-resistant *Plasmodium falciparum* (CRPF) throughout East, Central, and West Africa. Since 1978, when CRPF was documented in an American tourist returning from the United Republic of Tanzania (*2*), chloroquine resistance has been reported from more than 15 African countries (*3*). CRPF occurred in

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Nigeria's eastern neighbour, Cameroon, in 1985 (*4*) and western neighbour, Benin, in 1986 (*5*).

P. falciparum infection accounts for more than 90% of all cases of malaria in Nigeria (population, about 108.6 million in 1987). Although reports of *in vivo* CRPF in Nigeria have appeared since 1974 (*6–11*), the first case was confirmed only in 1987 (*12, 13*). These prior studies focused on parasitological response to treatment and *in vitro* testing, but did not assess clinical response, an important consideration for developing a treatment policy.

Nigeria is currently participating in the Africa Child Survival Initiative–Combatting Childhood Communicable Diseases (ACSI–CCCD) Project, which focuses on vaccine-preventable diseases, diarrhoea, and malaria in children under 5 years of age. The strategy for reducing mortality from malaria relies primarily on the prompt use of effective drugs for the treatment of suspected cases (*14*). The confirmation of CRPF in Nigeria prompted a reassessment of national practices for malaria therapy and plans were formulated to establish a national malaria surveillance network. To determine whether chloroquine was still effective as a first-line drug for children and to gather drug-sensitivity data, which could be useful for selecting alternative drugs, we carried out field studies in 1987 and report our results here.

Materials and methods

Study sites

The studies were conducted at Igbo Ora, Oyo State, and Oban, Cross River State, both of which are located in the tropical rain forest belt of southern Nigeria. Igbo Ora, which lies approximately 60 km east of the border with Benin, has an estimated population of 60 000 that is served by three health centres. Oban, approximately 65 km west of the border with Cameroon, has an estimated 5000 inhabitants who are served by a primary health care centre. Malaria is endemic and perennial at both sites, and the peak transmission period is from June to November, during the rainy season. The principal vectors at both sites are *Anopheles gambiae, A. arabiensis*, and *A. funestus*.

In vivo *tests*

The investigations were part of a training exercise for personnel who had been selected to form the national network for testing malaria drug sensitivity. Studies were conducted at both sites in July–August 1987, the peak transmission period. All children less than 5 years of age who were brought to health centres at each site were screened for parasitaemia, and those who satisfied the following criteria were enrolled in the study: age 6–59 months; pure *P. falciparum* parasitaemia of ≥ 1000 asexual parasites per mm^3 whole blood; no history of taking antimalarial drugs in the 7 days prior to the screening visit; no history of intolerance to chloroquine, e.g., pruritus; absence of other causes of illness; able to take oral medication; negative Haskins urine test (*15*) for 4-aminoquinolines; and the informed consent of their guardians to participate in the study.

The *in vivo* procedure used in the study was a 14-day modification of the WHO 7-day test for chloroquine, whereby children were enrolled on day 0 (D0) and followed-up on days 1, 2, 7, and 14. Children were also examined on D3 if their parasitaemia on D2 was $\geq 25\%$ of that on D0 (*16, 17*). An observation period of 14 days rather than 7 days was used to identify parasitaemia caused by strains of *P. falciparum* that were sensitive to chloroquine on D7 but which underwent recrudescences between D7 and D14 (*18*). Such recrudescences are unlikely to have been caused by reinfection in view of the long half-life of chloroquine in humans (5–14 days) (*19*).

The children were examined by experienced clinicians who recorded their clinical status and determined whether they had vomited or experienced diarrhoea or pruritus during the previous 48 hours. Each child was weighed and the axillary temperature measured using an electronic digital thermometer.[a]

Parasitological therapy was considered to have been successful if the parasite density on D2 was $< 25\%$ of that on D0, or if the density on D2 was $\geq 25\%$ of that on D0 but that on D3 was $< 25\%$ of that on D0, and with no parasites detected on D7 and D14. The therapy was considered to have failed if the parasite densities on D2 and D3 were $\geq 25\%$ of the density on D0 or if parasites were present on either D7 or D14.

A history of febrile illness or of an axillary temperature of $\geq 37.5\,^{\circ}C$ was given a clinical score of unity. If the guardian stated that the child had been ill during the previous 48 hours (or since the last visit to the study site) or if the clinician assessed the child to be ill, an additional score of unity was given. Children who scored ≥ 1 on D0 and zero on D7 and D14 were considered to be clinical successes, while those who scored ≥ 1 on D0 and on D7 or D14 were classified as failures.

Therapy regimens

Two antimalarial regimens were used: 25 mg chloroquine per kg body weight (10 mg/kg on D0

[a] Model MC-7. Omron Tateisi Electronics Co., Japan.

and D1, and 5 mg/kg on D2); and a single dose of sulfadoxine/pyrimethamine (half a tablet for children aged 6–47 months and a whole tablet for those aged 48–59 months). Chloroquine was administered in tablet form (chloroquine phosphate, 150 mg chloroquine base per tablet),[b] as syrup (10 mg chloroquine base per ml),[c] or as a combination of both tablet and syrup. The chloroquine content of the tablets and syrup was determined prior to the study at the Centers for Disease Control (CDC), Atlanta, GA, USA. Sulfadoxine/pyrimethamine was given in tablet form (500 mg sulfadoxine + 25 mg pyrimethamine per tablet).[d] Children were observed for a minimum of 30 minutes after receiving the drug, and if they vomited or spat were re-administered the estimated amount that was thus lost.

In Igbo Ora, chloroquine therapy was received by one group of children and sulfadoxine/pyrimethamine by another, while in Oban, one group of children received chloroquine. Children treated with chloroquine and who were parasitological therapy failures were given a single dose of sulfadoxine/pyrimethamine on the day that failure was detected and were followed for an additional 14 days.

Follow-up procedure

The guardians of the subjects were given appointments to bring children back to the clinic on D1, D2, D7 and D14, but, if necessary home visits were made to complete the follow-up. During follow-up visits, parents were asked whether their child had been ill or had experienced fever, vomiting, diarrhoea, or pruritus since the previous interview. The axillary temperature of the children was measured and urine was tested for chloroquine on D2, and thin and thick blood films were taken.

Parasitological testing

Blood films were stained with Giemsa and examined by oil-immersion light microscopy. Parasite densities were estimated by counting the number of asexual forms per 1000 leukocytes or by counting 500 asexual parasites whichever was attained first. The mean leukocyte count was assumed to be 6000 per mm^3 of whole blood.

Sample size

A sequential sampling scheme was used for the analysis (*20–21*). In order to detect a treatment success rate of at least 99% (confidence level, 95%) and a failure rate of at least 10% (confidence level, 90%), a minimum of 31 enrolled children are required. If 31 consecutive children were treatment successes, the true failure rate would be $< 1\%$, while if two or more failures occurred in the first 31 enrolled children, the true failure rate would be $> 10\%$. However, if only one failure occurred in the first 31 enrolled children, 24 additional children would have to be enrolled to obtain an estimate of the success rate with the desired precision (*17*).

Data analysis

Results were analysed separately for each treatment group at each study site. Differences in proportions, were tested using the χ^2 test and Fisher's exact test (one-tailed), while differences in means were analysed using Student's *t*-test.

Levels of chloroquine in blood

Samples of finger-prick blood (100 μl) from a subsample of children were absorbed on filter-paper to determine the concentration of chloroquine in order to confirm whether the drug had been absorbed by those who did not clear their parasitaemia. The determinations were carried out at CDC using high-performance liquid chromatography with fluorescence detection (*22*).

In vitro tests

In vitro tests were performed on D0 for children at Igbo Ora who had a pure *P. falciparum* parasite density of 1000–90 000 per mm^3 of blood. A 24-hour parasite culture technique based on methods described by Rieckmann et al. and Wernsdorfer (*23, 24*) was used; the end-point was defined as parasite maturation to schizonts. Cultivations were performed at 37 °C in WHO predosed plates containing chloroquine, quinine, or mefloquine. After 24 hours' culture, samples were taken to make thick blood films, which were stained with 1% Giemsa for 45 minutes. Slides were examined by oil-immersion light microscopy ($\times 600$). Schizonts were counted per 200 asexual parasites and isolates that exhibited $< 10\%$ schizogony in the control well of the plate were discarded. For successful cultures, the *in vitro* schizontocidal activity of the drug was determined by calculating the percentage inhibition of schizogony at various drug concentrations, assuming that the growth in the control well was 100% schizogony. The minimum inhibitory concentration (MIC) was defined as the lowest drug concentration at which there was complete inhibition of maturation to schizonts. The IC_{50} and IC_{99} for each drug were determined from a probit plot of the

[b] Federal Pharmaceutical Manufacturing Laboratory, Yaba, Nigeria.

[c] Rivoquine®. Rivopharm Laboratories, Manno, Switzerland.

[d] Fansidar®. Hoffmann-La Roche, Basle, Switzerland.

percentage inhibition of schizont maturation against the molar concentrations of the antimalarial drugs (*24*). International standards were used to define cut-off values for resistance to chloroquine (*24*) and quinine,* while the cut-off value for resistance to mefloquine is currently being assessed by comparing the results of the *in vivo* and *in vitro* tests.

Results

In vivo *tests*

Igbo Ora. Table 1 summarizes the findings for the two treatment groups. There were no parasitological therapy failures. Although the proportion of febrile children and the mean axillary temperatures of children in both groups were similar on D0, fever cleared more rapidly in children who were treated with chloroquine than in those who received sulfadoxine/pyrimethamine (Table 2). By D7, both groups had similar proportions of febrile children.

Of the 36 children who completed the chloroquine regimen, 34 (94.4%) had clinical scores ≥ 1 on D0 (mean score, 1.7); of these 34, seven (20.6%) had scores ≥ 1 on D2 and only two (5.9%) had scores ≥ 1 on both D7 and D14. Of the 36 children who completed the sulfadoxine/pyrimethamine regimen, 33 (91.7%) had clinical scores ≥ 1 on D0 (mean score, 1.6); of these 33, 12 (36.4%) had scores ≥ 1 on D2; three (9.1%) had scores ≥ 1 on D7; and one (3.0%) had a score ≥ 1 on D14. Although the children who received the sulfadoxine/pyrimethamine regimen returned to clinical normality more slowly than those who received chloroquine, the differences were not statistically significant.

Oban. Table 3 summarizes the results for the children in Oban. Of the 44 children who completed initial therapy with chloroquine and were followed through until D14, 28 (63.6%) were parasitological therapy failures on D3, D7, or D14. These children received alternative therapy with sulfadoxine/pyrimethamine. Absorption of chloroquine was adequate for children who were parasitological therapy failures, as indicated by the level of the drug in samples of finger-prick blood. One child in this group who was febrile at the start of the alternative therapy became afebrile on D1 and remained so throughout the 14-day follow-up period. None of the children treated with sulfadoxine/pyrimethamine were parasitological therapy failures on D3, D7, or D14.

Table 1: ***In vivo* responses to chloroquine or sulfadoxine/pyrimethamine, of the two study groups of children aged less than 5 years, Igbo Ora, Nigeria**

	Treatment group	
	Chloroquine	Sulfadoxine/pyrimethamine
No. of enrolled children	66	60
Mean age ±S.D. (months)	33.3±14.8	25.3±15.2
Mean weight ±S.D. (kg)	11.9±3.1	10.0±2.9
No. who completed follow-up	36 (54.5)[a]	36 (60.0)
No. febrile on day 0	25 (69.4)	23 (63.9)
GMPD on day 0 (per mm³)[b]	17 677	14 765
Range	1177–103 200	1129–130 222
No. with parasites on day 2	14 (38.9)	18 (50.0)
GMPD on day 2 (per mm³)	48	23
Range	6–2899	6–2845
No. with parasite density on day 2 and day 3 ≥25% of that on day 0	0	0
No. with parasites on day 7	0	0
No. with parasites on day 14	0	0

[a] Figures in parentheses are percentages.
[b] GMPD = geometric mean parasite density.

Of the 44 children who received the chloroquine regimen, 18 (40.9%) had clinical scores ≥ 1 on D0 (mean score, 1.0). Of these, 15 (83.3%) had scores ≥ 1 on D2; six (33.3%) had scores ≥ 1 on D7; and two (11.1%) had a score ≥ 1 on D14. All 11 children who were initially febrile on D0 became afebrile on D2. Of the 26 children who completed follow-up with sulfadoxine/pyrimethamine, 10 (38.5%) had clinical scores ≥ 1 on D0 (mean, 0.5), and of the latter children two (20.0%) had scores ≥ 1 on D2 and one (10.0%) had a score ≥ 1 on D7 and D14.

In vitro *tests*

In vitro tests were successfully carried out on 29 children from Igbo Ora. The MIC for chloroquine was 1.14 pmol/μl blood, while for quinine it was 3.2 pmol/μl blood medium mixture, and for mefloquine, 2.56 pmol/μl blood. The slope of the probit linear regression lines for percentage inhibition of schizogony against molar drug concentration was steep for chloroquine, intermediate for quinine, and more gradual for mefloquine (Fig. 1). The IC_{50} values were 0.27 pmol/μl, 0.33 pmol/μl, and 0.47 pmol/μl for chloroquine, quinine, and mefloquine, respectively, and the corresponding IC_{99} values were 0.90 pmol/μl, 1.65 pmol/μl, and 7.20 pmol/μl.

* In vitro *micro-test (mark II) for the assessment of the response of* Plasmodium falciparum *to chloroquine, mefloquine, quinine, sulfadoxine/pyrimethamine and amodiaquine.* WHO unpublished document MAP/87.2.

Table 2: **Percentage distribution of febrile children (axillary temperature ≥37.5 °C), by day of study and treatment group, Igbo Ora, Nigeria**

	Day 0	Day 1	Day 2	Day 7	Day 14
Chloroquine group (n=36)	69.4	5.6	5.6	5.6	5.6
Sulfadoxine/pyrimethamine group (n=36)	63.9	30.6	20.0 (n=35)	5.6	0
P value	0.80[a]	0.014[b]	0.019[b]	0.68[b]	0.50[b]

[a] χ^2 test.
[b] Fisher's exact test.

Table 3: ***In vivo* responses to chloroquine or chloroquine + sulfadoxine/pyrimethamine, of children aged less than 5 years, Oban, Nigeria**

	Treatment group	
	Chloroquine	Chloroquine + SP[a]
No. of enrolled children	49	28
Mean age ± S.D. (months)	32.9 ± 14.2	31.9 ± 12.6
Mean weight ± S.D. (kg)	11.6 ± 3.8	11.8 ± 3.2
No. who completed follow-up	44 (89.8)[b]	26 (92.9)
No. febrile on day 0	11 (25.0)	1 (3.8)
GMPD on day 0 (per mm³)[c]	6488	313
Range	1385–253 600	12–11 704
No. with parasites on day 2	41 (93.2)	2 (7.1)
GMPD on day 2 (per mm³)	155	8
Range	6–68 182	6–12
No. with parasite density on day 2 and day 3 ≥25% that on day 0	3 (6.8)	0
No. with parasites on day 7	20 (45.5)	0
GMPD on day 7 (per mm³)	150	0
Range	23–1563	
No. with parasites on day 14	6 (13.6)	0
GMPD on day 14 (per mm³)	1545	0
Range	72–11 704	

[a] SP = sulfadoxine/pyrimethamine; chloroquine + SP = chloroquine failures who were treated subsequently with sulfadoxine/pyrimethamine.
[b] Figures in parentheses are percentages.
[c] GMPD = geometric mean parasite density.

Adverse effects

The occurrence of pruritus was taken as an indicator of adverse effects caused by chloroquine. In Igbo Ora, no child in the chloroquine group had pruritus on D0 or D1, while two children exhibited this condition on D2 and one child on D7 and D14. In Oban, an area well-known for filariasis, 18.2% of children had a history of pruritus on D0, before beginning chloroquine therapy, and 29.5% reported pruritus on D2. On D7 and on D14, 11.4% of children complained of pruritus.

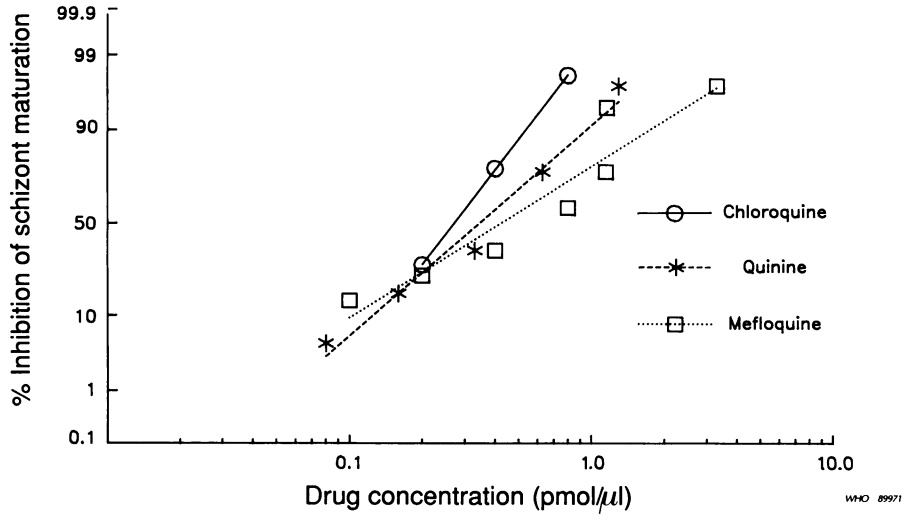
In Igbo Ora, vomiting and spitting was reported on D0 for 18.2% of the children in the chloroquine group but only for three children on D2, and none on D7 or D14. In Oban, vomiting was reported for 8.8% of children, none on D2, one child on D7, and none on D14. Less than three children in either Igbo Ora or Oban were affected by diarrhoea on any day.

Discussion

Malaria was a more severe childhood illness in Igbo Ora than in Oban, as indicated by the children's axillary temperatures, clinical scores, and initial mean parasitaemia. Athough 63.6% of the children in Oban who were treated with chloroquine and followed up until D14 exhibited parasitological therapy failure, from D0 to D7 there was a 97.7% reduction in the geometric mean parasite density, and all children who were initially febrile became afebrile by D2. Because of its continued clinical efficacy, low cost and low toxicity, and wide availability, a regimen of 25 mg/kg chloroquine is the recommended initial treatment for uncomplicated malaria in children in south-east Nigeria and in other areas of the country. The high degree of *in vivo* and *in vitro* sensitivity of *P. falciparum* to chloroquine in Igbo Ora indicates that this regimen is still effective for treating malaria in children. Also, the MIC of 1.14 pmol/μl blood supports the clinical findings that isolates of *P. falciparum* were sensitive to chloroquine.

P. falciparum was very susceptible to sulfadoxine/pyrimethamine in both study areas, and this is an effective alternative treatment for children with suspected CRPF. However, in Igbo Ora a more rapid reduction of fever and clinical improvement was

Fig. 1. **Probit linear regression plots showing the *in vitro* susceptibility of *Plasmodium falciparum* ($n=29$) to various concentrations of chloroquine, quinine, or mefloquine, Igbo Ora, Oyo State, Nigeria, 1987.**



effected by chloroquine. Our results indicate that there is no advantage to using sulfadoxine/pyrimethamine in areas where *P. falciparum* is sensitive to chloroquine. Recent studies in Central Africa have demonstrated that chloroquine may have excellent clinical efficacy in areas with CRPF (*18, 25*). Health care providers in areas with reduced sensitivity to chloroquine should therefore be suspicious of cases that do not respond to chloroquine, but should have sulfadoxine/pyrimethamine available for chloroquine therapy failures and those children who cannot tolerate the drug.

The results of the *in vitro* tests for mefloquine indicate that 21% of the *P. falciparum* isolates in Igbo Ora grew in mefloquine concentrations greater than 1.14 pmol/μl blood. Although the correlation between *in vivo* and *in vitro* sensitivity for mefloquine has not yet been determined, the presence of such a high proportion of isolates with reduced sensitivity in Igbo Ora is surprising, since mefloquine has not been widely used in this area of Nigeria. Similar reduced *in vitro* sensitivity to mefloquine has been reported in Ibadan (*13, 26*) and other areas of West Africa (*27*). The clinical significance of these findings is not known and further evaluations are required.

The results of the *in vitro* tests with quinine are consistent with earlier *in vitro* findings in Ibadan (*28*) and support the use in south-west Nigeria of quinine as an alternative therapy for children with severe illness caused by *P. falciparum*. However, further *in vivo* studies are necessary to fully evaluate this potential.

Our findings have assisted the Nigeria Federal Ministry of Health in formulating national malaria therapy recommendations. The identification in a large country of *P. falciparum* that exhibits *in vivo* and *in vitro* sensitivity to chloroquine in one area and *in vivo* resistance to chloroquine in another supports the need for continued surveillance activities to monitor the distribution of CRPF. Emphasis will be maintained on testing alternative drugs so that recommendations for effective second-line therapy can be promoted. In addition, sentinel reporting of age-specific rates of malaria morbidity and mortality is being initiated to identify areas where the clinical efficacy of malaria therapy is changing. The results of these efforts should provide a continuing source of information that can be used to develop strategies to reduce the impact of malaria on the health of Nigerian children.

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Résumé

Sensibilité de *Plasmodium falciparum* à la chloroquine et à la sulfadoxine/pyriméthamine chez des enfants nigérians

Dans le cadre d'un réexamen des politiques nationales de traitement du paludisme, on a déterminé, en juillet–août 1987, la sensibilité *in vivo* de *Plasmodium falciparum* à la chloroquine et à la sulfadoxine/pyriméthamine dans deux régions frontalières du sud du Nigéria, proches de pays où a été signalée la présence de *P. falciparum* chloroquino-résistant. En même temps, on a étudié la sensibilité *in vitro* de *P. falciparum* à la chloroquine, la quinine et la méfloquine dans le sud-ouest du Nigéria, au moyen d'une modification en épreuves de 14 jours des épreuves types *in vivo* de l'OMS (épreuve pratique et épreuve prolongée) et d'une épreuve sur 24 heures de culture des parasites *in vitro*. On a procédé aux évaluations cliniques et parasitologiques après administration sous surveillance d'une dose totale de 25 mg de chloroquine par kg de poids corporel sur trois jours ou de doses standard de sulfadoxine/pyriméthamine.

Les enfants jugés aptes à participer à l'étude remplissaient les conditions suivantes: âge 6 à 59 mois; parasitémie simple à *P. falciparum* supérieure ou égale à 1000 parasites asexués par mm^3 de sang; absence d'antécédents d'intolérance à la chloroquine; absence d'autres causes de maladie; aptitude à prendre des médicaments par voie orale; épreuve urinaire de Haskins négative pour les amino-4 quinoléines.

Pendant la période de suivi de 14 jours, aucun échec thérapeutique n'a été démontré par l'examen parasitologique chez 35 enfants appartenant à deux groupes traités soit avec la chloroquine soit avec la sulfadoxine/pyriméthamine à Igbo Ora dans le sud-ouest du Nigéria. Bien que 69,4% des enfants traités par la chloroquine aient présenté de la fièvre le jour de leur admission dans l'étude (jour 0), seuls 5,6% d'entre eux étaient encore fébriles les jours 2, 7 et 14. Parmi les enfants traités par la sulfadoxine/pyriméthamine, 63,9% avaient de la fièvre le jour 0, 30,6% le jour 1, 5,6% le jour 7 et aucun le jour 14. La température axillaire des enfants des deux groupes était du même ordre le jour 0, mais les enfants traités par la chloroquine ont vu leur fièvre baisser plus rapidement que ceux traités par la sulfadoxine/pyriméthamine ($P<0,01$ les jours 1 et 2). A Oban, dans le sud du Nigéria, 63,6% des 44 enfants traités par la chloroquine et suivis jusqu'au jour 14 ont été classés comme échecs parasitologiques précoces (jour 3 ou 7) ou tardifs (jour 14) et ont été ensuite traités par la sulfadoxine/pyriméthamine. Aucun des 26 enfants traités par l'association n'a présenté d'échec parasitologique les jours 3, 7 ou 14.

Les épreuves *in vitro* ont pu être pratiquées sur 29 enfants d'Igbo Ora. Les résultats montrent que *P. falciparum* était pleinement sensible à la chloroquine et à la quinine mais présentait peut-être une baisse de sensibilité à la méfloquine. Même si on a observé à Oban une sensibilité amoindrie de *P. falciparum* à la chloroquine, la grande efficacité clinique de ce médicament, la modicité de son coût, sa faible toxicité et sa facilité d'approvisionnement dans les deux localités étudiées plaident en faveur de son utilisation comme traitement de première intention pour le paludisme non compliqué chez l'enfant, dans tout le sud du Nigéria.

Nos résultats montrent une variation de la pharmacosensibilité de *P. falciparum* dans un vaste pays d'Afrique et, dans le cadre de cette étude, un réseau d'équipes a été créé afin de poursuivre la surveillance de l'efficacité des antipaludéens. Un système sentinelle de notification des taux de morbidité et de mortalité palustres corrigés de l'âge est actuellement mis en place afin de compléter les données d'efficacité, ce qui permettra d'aider le Ministère fédéral de la Santé à élaborer des stratégies efficaces en vue de réduire les répercussions du paludisme sur la santé des enfants nigérians.

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