IN VIVO SENSITIVITY OF P. falciparum TO CHLOROQUINE IN ACCRA, GHANA.


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Summary

The in vivo sensitivity of P. falciparum to chloroquine was studied in an urban paediatric hospital in Ghana in 1984 and 1987. 36 children were studied in 1984 and 100% parasite clearance was obtained in 74.25 ± 25.5 hours (48 to 120 hours), mean ± SD (range), after treatment with chloroquine 25mg base/kg body weight total dose. 41 out of 44 children studied in 1987 similarly had parasite clearance in 68.5 ± 27.7 hours (24 to 120 hours). Resistance at the R1 and RII levels were noted in one and two of the children respectively. The proportion of children parasitaemic at 72 hours was age related and suggests the role of immunity in the sensitivity of P. falciparum to chloroquine. In 1984 estimation of whole blood chloroquine levels before treatment in hospital indicated prior administration of the drug before attending hospital.

Key words: P. falciparum; Chloroquine, in vivo sensitivity

Introduction

Since the first reports of chloroquine-resistant falciparum malaria in East Africa there has been a gradual spread westwards. It is important for each country to have information on the sensitivity of P. falciparum to chloroquine.

The aim of the present study was to determine in vivo, the susceptibility of P. falciparum to chloroquine in an urban paediatric population and compare it with results of a similar study performed three years earlier.

Materials and Methods

Between March 1984 and September 1987 children with malaria seen by one Unit in the Child Health Department of the Korle-Bu Teaching Hospital, Accra, were admitted into the study. Parental consent was obtained. The children were admitted for seven days and then followed up weekly for a month. Thick and thin blood films were done daily during admission and at each of the weekly visits after discharge. Quantitative counts of trophozoites were performed on the thick film. Asexual forms were counted per 300 white blood cells and the results expressed as number of trophozoites per microlitre of blood. During the 1984 study, samples for whole blood chloroquine levels were taken before treatment. In some of the children whole blood chloroquine levels were estimated on the 7th and 28th days after admission. Chloroquine levels were determined by high pressure liquid chromatography. Malaria was treated with chloroquine 5mg/kg body weight intramuscularly 12 hourly for 5 doses, because most of the children could not tolerate oral medication.

Results are expressed as mean ± standard deviation (range).

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Results

36 children: 14 males and 22 females aged between 4 months and 11 years, mean age, 4.4 ± 3.1 years, were studied in 1984 and 44 children: 26 males and 18 females aged between 6 months and 14 years, with a mean age 4.0 ± 3.4 years were studied in 1987. Three of these showed evidence of resistance to chloroquine.

They are not included in the parasite clearance estimation. Table 1 summarises the results obtained in 1984 and 1987. In 1987 three children aged 7 months, 4 years and 11 years were not free from parasitaemia after treatment with the curative dose of 25mg/kg body weight of chloroquine base.

Case 1.

A 7-month old female child weighing 7kg had no parasitaemia by the fourth day, having received a total of 486mg of chloroquine orally. Asexual parasitaemia appeared again on the sixth day and persisted on the seventh and eighth days although the child remained well. Parasitaemia was cleared with a further total dose of 187.5mg of chloroquine base.

Case 2.

A 4-year old female child weighing 12.5kg was admitted very ill, having received chloroquine earlier at a private clinic. Her parasitaemia, qualitatively described as 3+ on admission, fell to 1+ by the third day. The child remained unwell and parasitaemia persisted up to the ninth day before clearing, on a total dose of 810mg chloroquine base over 7 days. The child was also treated for staphylococcus epidermidis septicaemia with cloxacillin and streptomycin.

Case 3.

An 11-year old male child was admitted with malaria. His parasitaemia on admission of 25 400/µl fell to 1 240/µl on the third day on a total dose of chloroquine of 25 mg/kg body weight. His parasite count rose to 19 040/µl on the fourth day and continued to rise to 82 480/µl on the 7th day despite further treatment with chloroquine. He was given sulfadoxine/pyrimethamine combination tablets and he became aparasi-taemic on the 9th day. He was still free of asexual parasites when seen four days later.

All subjects had *P. falciparum* trophozoites in their thin films. All children who had completed the study were clinically well at each follow-up attendance.

In the 1984 study, by the 3rd day, 41.7% of children 2 years of age and under and 33.3% aged between 2 and 5 years were parasitaemic as compared to only 8.3% of children older than 5 years. A similar trend was noted in 1987 when children older than 5 years had parasite clearance quicker than younger children. Comparable figures on the third day were 16.7%, 27.3% and 0% respectively. These differences were however not statistically significant.

Mean whole blood chloroquine concentration before treatment in 1984 was 279.9 ± 524.5ng/ml (14.3ng/ml to 2285.7ng/ml). Mean whole blood chloroquine level on day 7 was 390.1 ± 305.3ng/ml. (83.2 to 1151.8ng/ml) and 163.4 ± 297.0ng/ml (18.0 to 1254.5ng/ml on day 28. Three children had parasite counts of 120/µl on day 21. The child with 26 100 parasites/µl had the lowest whole blood chloroquine concentration of 8.33ng/ml on day 7. His parasitaemia had cleared by day 21 and his chloroquine level of 77.1ng/ml, on day 28, indicates further treatment with the drug. In 1987, no parasitaemia was noted after discharge from hospital.

Discussion

Clinical resistance of *P. falciparum* to
The high proportion of children 5 years of age and below with parasitaemia on day 3 as compared to children older than 5 years reflects the role of immunity in the measure of sensitivity of \( P. falciparum \) strains to chloroquine. This trend has been observed elsewhere and it has also been noted that children, particularly those under 10 years of age in urban Ghana have low titres of malaria antibodies. In this study however, age does not appear to significantly influence the length of time it takes to clear parasites from the peripheral blood film. The children received the standard 25mg/kg total dose of chloroquine within the recommended schedule of 10mg/kg body weight on days 1 and 2 and 5mg/kg on day 3, intramuscularly. The use of intramuscular chloroquine in children with severe malaria has been questioned. However, children seen at this teaching hospital with malaria are usually very ill and have been referred from other primary health care facilities. These children have always been treated with chloroquine intramuscularly until able to tolerate chloroquine orally.

Quinine is not readily available in Ghana. It has been recommended for use in severe malaria. The emergence of resistant strains of \( P. falciparum \) at the RI and RII levels in 1987 indicates the presence of the resistance gene in the population studied.

The practice of chloroquine self-medication is common in Accra. The pretreatment and day 28 levels as compared to the 7th day levels suggests this in some patients. This practice may contribute to the selection of resistant strains.

Our results indicate the presence of \( P. falciparum \) resistant to chloroquine in the study population. The extent of the presence of the resistant gene must be

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<tr>
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<th>1984</th>
<th>1987</th>
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<tr>
<td>Number of patients</td>
<td>36</td>
<td>41</td>
</tr>
<tr>
<td>Age: mean ± SD</td>
<td>4.4 ± 3.1</td>
<td>4.0 ± 3.4</td>
</tr>
<tr>
<td>sex M:F</td>
<td>14:22</td>
<td>25:16</td>
</tr>
<tr>
<td>Parasite count before treatment/μl of blood</td>
<td>262,854 ± 285,256</td>
<td>40,490 ± 112968</td>
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<tr>
<td>Treatment/μl of blood</td>
<td>(1,400 - 960,000)</td>
<td>(208 - 480,000)</td>
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<tr>
<td>Time to 100% parasite clearance (hours)</td>
<td>74.25 ± 25.4</td>
<td>68.5 ± 27.7</td>
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<td>Parasite reduction rate in first 24 hours</td>
<td>73.1 ± 28.9%</td>
<td>81.2 ± 23.6%</td>
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<td>(2.8 - 99%)</td>
<td>(0 - 100%)</td>
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studied in the community. Without any effective vector control measures, chloroquine resistant *P. falciparum* may rapidly spread in the country.

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References