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Tolerance and haematological findings with antimalarials (chloroquine and Fansidar [pyrimethamine plus sulfadoxine]) in adults and children during field trials in Nigeria

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Introduction

This paper reports on the clinical and haematological tolerance of Fansidar compared with chloroquine during field trials in Nigeria among adults and children, natives and expatriates.

Materials and methods

Nigerian natives

Clinical and haematological tolerance were assessed in 1103 Nigerian children (age 6–11 years) receiving SP (Fansidar) or chloroquine for the treatment or suppression of malaria in randomised prospective studies.

548 children were on Fansidar. 201 children had single dose treatment of 25 mg S + 1.25 mg P per kg body weight. 66 were on weekly suppressive treatment (½ of the curative doses) for 8 weeks, and 281 children were on monthly curative doses for 1 year. The chloroquine group consisted of 555 children, 198 were given single curative doses of 10 mg/kg, 58 on weekly suppressive doses of 5 mg/kg and 299 on monthly curative doses.

Clinical enquiry and examination were undertaken during the period of drug administration to record any side effects. Also the haemoglobin levels of children on monthly suppressive treatment with antimalarials were measured every 2 months using American Optical Hb meter. The acceptability of the tablets of Fansidar and chloroquine was assessed as 'good' when the drug was willingly taken, 'moderate' when taken with signs of disapproval and 'poor' when persuasion or compulsion was necessary. The tablets were usually chewed before swallowing with water.

Expatriates in Nigeria

A retrospective study of the clinical and haematological tolerance of SP compared with chloroquine for a homogenous group of expatriates resident in Nigeria was undertaken between December 1979 and February 1980. The subjects of the study were those taking prophylactic Fansidar or chloroquine regularly for at least 6 months and were in general good health without any underlying diagnosed chronic disease.

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98 expatriates were included in the study. 4 were taking SP weekly for 6–12 months, 29 for 12–24 months and 15 for over 24 months. Among those on weekly chloroquine, 8 had been on the drug prophylaxis for 6–12 months, 21 for 12–24 months and 21 for over 24 months. Children aged 5–15 years took ½ tablet of SP (each tablet contains 25 mg P and 500 mg S) or 150 mg base chloroquine. Adults received 1 tablet of SP or 300–600 mg base chloroquine. The side effects noticed by each individual as being attributable to the antimalarial taken were recorded. Clinical and haematological examinations were made. The white cell and red cell counts were measured with electronic counters (Digicell 3100) and the haemoglobin values were assessed by an automatic analyser (Haemocele 400). The differential white cell counts as well as counts of neutrophil segmentation were made.

Results

The acceptability of Fansidar by the Nigerian children was generally good, while it was generally moderate for chloroquine.

All the 548 Nigerian children on Fansidar, whether on single curative doses, weekly or monthly suppressive treatment, showed *no adverse effects.* Out of 555 Nigerian children on chloroquine 65 showed transient blurring of vision lasting from 1 to 3 hours. Nausea was recorded in 79 children and one child vomited consistently after chloroquine consumption even after meals.

Among the expatriates episodes of itching after drug intake were reported by 4 on Fansidar and 6 on chloroquine. One taking Fansidar reported unilateral transient paraesthesia on the right foot and one taking chloroquine on the left hand, respectively. Only those on chloroquine reported brown skin pigmentation (n = 3), diarrhoea (n = 3) and transient blurring of vision (n = 1).

Anaemia was frequent in all Nigerian children and haemoglobin levels as low as 6.0 g/100 ml prior to therapy; at the end of the treatment the lowest value was 10.0 g/100 ml. The comparative result was as shown in Table 1.

Table 1. Haemoglobin values before and at the end of 1 year suppressive treatment with 300 mg chloroquine base or 1 tablet Fansidar monthly

Age (years)	No. of children treated with		Extreme haemoglobin values (in g/100 ml)	
	Fansidar	chloroquine	before treatment	at the end of treatment
6–7	62	–	6.0–12.5	10.0–14.5
	–	69	7.0–12.0	10.5–14.5
7–8	44	–	8.0–13.0	11.0–13.0
	–	48	8.5–13.5	10.5–13.5
8–9	43	–	6.5–14.0	11.0–14.0
	–	47	8.5–14.0	11.0–14.0
9–10	61	–	10.5–14.0	11.5–14.0
	–	57	9.0–13.5	12.0–14.5
10–11	71	–	11.0–14.5	11.0–15.0
	–	78	11.0–14.5	12.0–14.5

Table 2. Haemoglobin values g/100 ml. For Europeans resident in Nigeria taking regular prophylaxis (Fansidar or chloroquine) for average periods of 1½ years

	Haemoglobin values		
	Minimum	Maximum	Mean
Fansidar group			
Adults ♂ (N = 19)	14.2	17.7	16.00
Adults ♀ (N = 19)	11.2	16.3	13.80
Children (N = 10)	13.3	17.7	14.90
Chloroquine group			
Adults ♂ (N = 25)	13.6	17.7	15.70
Adults ♀ (N = 13)	11.9	16.3	13.90
Children (N = 12)	11.3	15.5	13.60

Table 3. White blood cells (WBC) and neutrophil (NC) counts. For Europeans resident in Nigeria taking regular prophylaxis (Fansidar or chloroquine) for average periods of 1½ years

		Minimum	Maximum	Mean
Fansidar group				
Adults ♂ (N = 19)	WBC	3.350	8.000	5.050
	NC	2.020	5.760	3.140
Adults ♀ (N = 19)	WBC	3.500	5.600	4.520
	NC	1.440	4.830	2.840
Children (N = 10)	WBC	3.600	5.300	4.340
	NC	1.640	3.260	2.410
Chloroquine group				
Adults ♂ (N = 25)	WBC	3.350	6.700	4.960
	NC	1.520	4.360	3.130
Adults ♀ (N = 13)	WBC	2.920	7.640	4.960
	NC	1.780	3.960	2.830
Children (N = 12)	WBC	3.950	8.100	5.310
	NC	1.600	5.410	3.060

Haemoglobin values of the expatriates in the different drug groups were all practically normal. Isolated low values were found in females and also in children of the groups receiving chloroquine. The mean values correspond to normal values. Table 2 refers. The red cell counts were within normal limits in expatriates, adult males, adult females and children on either Fansidar or chloroquine.

The white cell counts in both the Fansidar and chloroquine groups were practically identical. Only one subject had less than 3000 leucocytes/ml. This was in the chloroquine group. Also the neutrophil counts in subjects taking

Fansidar was practically identical to those taking chloroquine. The white cell and neutrophil counts are summarized in Table 3.

The neutrophils showed no morphological abnormalities or any hypersegmentation in both, the Fansidar and the chloroquine groups.

Comments and conclusion

Our studies confirmed those of others including Lucas et al. (1969), Lewis and Ponnampalam (1975) that severe toxic side effects are rare in individuals treated or taking normal suppressive doses against malaria infection.

Surprisingly drug induced pruritus was uncommon in the study area. However, the incidence of chloroquine induced pruritus in Nigeria has been reported as 8% to 14% (Ekpechi and Okoro, 1964; Olatunde, 1969).

In our studies the haemoglobin values of the Nigerian children on monthly SP or chloroquine for one year increased considerably in spite of the relatively high incidence of G_6PD deficiency of about 19.1% (Gilles and Taylor, 1961) among ethnic populations in the study areas. There were no morphological changes in the neutrophils indicating early folate deficiency in any of the expatriates taking either Fansidar or chloroquine. No hypersegmentation of the neutrophils were found.

In conclusion we maintain that chloroquine remains the drug of choice for the suppressive treatment of malaria in Nigeria where chloroquine resistant *P. falciparum* is absent.

We have studied the acceptability and tolerance with emphasis on the haematological tolerance of an antifolate combination (sulfadoxine + pyrimethamine).

This drug combination, Fansidar, appears to be well accepted and tolerated among adults and children both natives and expatriates over a period of one year and more.

Anaemia or leucopenia did not occur whereas anaemia prior to therapy in Nigerian school children on Fansidar as well as chloroquine often disappeared after 6 months therapy.

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Ekpechi O. L., Okoro A. N.: A pattern of pruritus due to chloroquine. Arch. Derm. *89*, 631–632 (1964).

Gilles H. M., Taylor B. G.: The existence of the glucose-b-phosphate dehydrogenase deficiency trait in Nigeria and its clinical implications. Ann. trop. Med. Parasit. *55*, 64–69 (1961).

Lewis A. N., Ponnampalam J. T.: Suppression of Malaria with monthly administration of combined sulfadoxine and pyrimethamine. Ann. trop. Med. Parasit. *69*, 1–12 (1975).

Lucas A. O., Hendrickse R. G., Okubadejo O. A., Richards W. H. G., Neal R. A., Kofie B. A. K.: The suppression of malaria parasitaemia by pyrimethamine in combination with clapsone or sulphamethoxine. Trans. roy. Soc. trop. Med. Hyg. *63*, 216–229 (1969).

Olatunde I. A.: Chloroquine induced pruritus in Lagos, Nigeria. Nig. med. J. *2*, 23 (1969).