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Asymptomatic malaria parasitaemia in sickle-cell disease patients: how effective is chemoprophylaxis ?

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Abstract

Background & objectives: Sickle-cell trait confers protection against malaria while homozygote sickle-cell disease (SCD) patients are at greater risk of malaria infection, hence the use of malaria chemoprophylaxis in SCD patients. The use of malaria chemoprophylaxis and asymptomatic parasitaemia were studied in SCD and non-SCD patients.

Study design: A semi-structured questionnaire was administered to both patients and controls; a thick blood film was also examined in both the groups.

Results: Sixty-nine percent of patients use proguanil, 22% do not use any form of chemoprophylaxis, while 9% use pyrimethamine. There was no significant difference between level of parasitaemia in patients and controls ($p = 0.1$), a positive smear was found in equal numbers of patients on chemoprophylaxis and those not on chemoprophylaxis ($p = 0.3$). In the month preceding the study, 31% of patients vs 18% of controls had received treatment for malaria. There were no significant differences between patients and controls in frequency of malaria attacks ($p = 0.06$), last episode of malaria ($p = 0.2$). Ten percent of patients and 2% of controls use bednets.

Conclusion: This study did not find any advantage in the use of malaria chemoprophylaxis in SCD patients over controls or SCD patients not on chemoprophylaxis. Vector control should also be considered in the fight against malaria. There is a need to look into why both patients and controls fail to use bednets in a malaria endemic country.

Key words Chemoprophylaxis – malaria – sickle-cell disease (SCD)

Introduction

Malaria is endemic in tropical Africa and some individuals including pregnant women, children and sickle-cell disease (SCD) patients have an increased susceptibility to its infection[1–3]. In addition, it is a factor that has maintained the prevalence of SCD at a constant level in the tropics over the years with the sickle-cell trait acting as a genetic modifier against malaria infection.

Malaria is believed to be a major cause of morbidity in SCD patients, it is a precipitating factor for the frequent vasoocclusive crises experienced by these patients; and may thus be responsible for hospital admission. It is customary, therefore, to prescribe malaria chemoprophylaxis for almost every SCD patient who is in crisis regardless of whether they are symptomatic or not[4].

Autosplenectomy, which occurs because of frequent

spleenic infarction, is believed to be responsible for the frequent malaria infection; these patients are, therefore, placed on life-long malaria chemoprophylaxis[5]. The use of bednets either as insecticide-treated or untreated as well as the use of window and door screens are other intervention methods to reduce mosquito bites and in turn malaria infection but the role of these in the control of malaria infection in SCD patients is yet to be fully evaluated. Parasitaemia was, therefore, compared between asymptomatic SCD patients and asymptomatic non-SCD controls to ascertain if asymptomatic parasitaemia differs between the two groups and to consider the role of chemoprophylaxis. The use of other intervention methods was also compared between the two groups.

Material & Methods

The study was done in the southwestern Nigeria where the climate is equatorial and malaria is predominantly caused by *P. falciparum* and transmission hyperendemic[6]. The study was conducted during the rainy season and consisted of SCD patients who came for routine follow-up in the clinic and were in the steady state. The non-SCD subjects included volunteer medical students who live in the same city. A previous study has shown that the mean age of SCD patients in the same locality is 22 yr[7], hence students whose age range are similar to this and are more likely to know their genotype were chosen as controls. Verbal informed consent was obtained from both patients and controls.

A semi-structured questionnaire was administered to the participants; information obtained included demographic data, the frequency and last episode of malaria attack, drugs used for malaria treatment and chemoprophylaxis, the use of bednets and window/door-screens, etc. The haemoglobin genotype of the patients was obtained from their case files while the same information was obtained directly from the volunteer students.

Thick blood film stained with Giemsa for malaria parasite was read following standard, quality controlled procedure. The haematocrit value for each participant was determined at the same time by the microhaematocrit centrifugation method.

Data were analysed using SPSS statistical software programme. Chi-square analysis was used for categorical variables while students' t-test was used for continuous variables, and p-value of < 0.05 was considered significant.

Results

The mean age of the SCD patients was higher than that of the control because this study included patients with sickle-cell haemoglobin C disease who live longer than HbS patients since they run a milder course of the disease, while the age of the control was determined based on a study that included only HbS patients[7]. The distribution of the haemoglobin genotype in the control group was similar to what was observed in the locality of the study[8]. Seventy-three individuals (36 patients and 37 controls) were studied. The mean age of the SCD patients was 25 yr while for the control subjects it was 23 yr ($p = 0.1$). Ninety percent of the patients have sickle-cell anaemia (HbS) and 10% have sickle-cell haemoglobin C disease (HbS + C). Among the control subjects; 71% have HbA while 28% have the sickle-cell trait (HbA+S), nine of the controls were unsure of their haemoglobin genotype. Sixty-nine percent of the SCD patients used proguanil (200 mg daily) for chemoprophylaxis, 22% did not use any form of chemoprophylaxis. Only 5% of the controls used chemoprophylaxis. Chloroquine and artemisinin are the most widely used drugs for the treatment of acute malaria; this is followed closely by sulphadoxine-pyrimethamine (Table 1).

In the month preceding the study, 31% of the SCD patients had been treated for malaria in contrast to 18% of the controls. Similarly, 43% of controls and 22% of the patients have not had malaria in the last one

Table 1. Drugs used in the treatment of malaria by patients and controls

Drug	Frequency	Percentage
Chloroquine	23	31.9
Sulphadoxine	16	22.2
Artemisinin	24	33.3
Aminoquinolines	6	8.3
Others	3	4.2
Total	72	100

Table 2. Results of blood smear examination for malaria in patients and controls

	Negative	Positive	Total
Cases	27	9	36
Controls	21	16	37
Total	48	25	73

p = 0.1.

year and 24% of the patients and 43% of the controls had a positive blood smear for malaria parasite (p = 0.1), (Table 2), while 25% each of patients on chemoprophylaxis and those not on chemoprophylaxis had positive smear for malaria parasite (p = 0.3). There were no significant differences between the patients and controls in the frequency of malaria attacks (p = 0.06), last episode of malaria (p = 0.2), the use of window/door-screens (p = 0.7). Only 10% of the patients and 2% of the controls used bednets, while 90% of patients and controls had window/door-screen. The mean haematocrit for the patients was 25% and 40% for the controls.

Discussion

Twenty-four percent of the patients in contrast to 43% of the controls had asymptomatic parasitaemia, which is similar to 30% vs 34% found in sickle-cell anaemic patients and controls in a study done on paediatric patients in Nigeria[9], indicating lack of significant difference in the level of asymptomatic parasitaemia in SCD patients on chemoprophylaxis compared to controls not on chemoprophylaxis. Similarly, the level of parasitaemia did not differ between SCD patients on chemoprophylaxis and those not on chemoprophylaxis. The presence of asymptomatic parasitaemia is, therefore, a feature not exclusive to adult patients but also described in paediatric patients[9]. Asymptomatic parasitaemia had also been described in pregnant women in the same locality at the time of booking (44.2% vs 33.6% in primigravidae and multigravidae, respectively), there was also no significant difference in parasitaemia between those who had malaria chemoprophylaxis before booking and those who did not[10].

A previous study showed that malaria infection is over treated in SCD patients, with treatment given for malaria regardless of blood smear results[4]. It was also observed in this present study that in the month preceding the study, 31% of SCD patients in contrast to 18% of controls had treatment for malaria and 60% of SCD patients have had to stop chemoprophylaxis at various times for economic reasons and/or non-availability of the drug[11]. The question, therefore, is what is the role of malaria chemoprophylaxis in the management of SCD patients? Can the reduced level of parasitaemia in SCD patients, compared to controls be attributed to chemoprophylaxis or to the frequent treatment for malaria?

Autosplenectomy is a reason given for the frequent malaria attacks in SCD patients, but parasite density has been found to be lower in sickle-cell patients without a spleen than those who retain their spleen[9], though a previous study on patients in the same locality did not show proof of anatomical autosplenectomy[12]. On the contrary, patients who had surgical removal of their spleen are twice likely to have *Plasmodium* parasitaemia than controls[13]. In SCD, it may, therefore, be functional asplenia rather than anatomical autosplenectomy. It is, therefore necessary to confirm that SCD patients are more prone to malaria

attacks than individuals with HbA and to decide on an appropriate drug which will be cheap and readily available for prophylaxis. Vector control is an intervention method that may also be used to limit the spread of malaria in a community and should, therefore, be considered as an adjunct to chemoprophylaxis.

Insecticide-treated nets are currently advocated for the control of malaria infection but often are not utilised; the reason for this has been attributed to socioeconomic reasons or non-availability[14]. We observed that 90% of both SCD patients and controls have both window and door screens with only 10% using bednets, it may, therefore, be more cost-effective to treat the materials used as window/door screens with insecticides than bednets. Many intervention methods have also been advocated for malaria control; these include impregnated bed sheets, larviciding, habitat manipulation, house spraying and even zoo prophylaxis. It may, therefore, mean that a combination of two or more of the intervention methods may be required for effective malaria control.

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