A CLINICAL STUDY OF FALCIPARUM MALARIA - 302 CASES

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ABSTRACT

Three hundred and two cases of falciparum malaria including 30 cases of severe falciparum malaria admitted between Jan 93 - Dec 93 were studied for their clinical features and response to treatment. Intermittent or remittent fever with chills and headache were the commonest presentation noted (99.3%). Cough (46.4%), hyperbilirubinemia (31.8%), and pyuria (52.9%) were the other notable features. Anaemia was uncommon (16.6%). Hypoglycaemia was detected in none of the cases. Quinine for 3 days along with tetracycline and sulfadoxine - pyrimethamine achieved a 100 per cent cure rate in uncomplicated chloroquine resistant falciparum malaria. Amodiaquine along with tetracycline and sulfadoxine - pyrimethamine was effective in 76.2 per cent of uncomplicated cases.

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KEYWORDS : Falciparum malaria.

Introduction

There has been an increase in Plasmodium falciparum infections in India over the last decade [1,2]. The clinical diagnosis of malaria may not be simple because of non specific nature of symptoms which may suggest some other illness, causing delay in institution of appropriate therapy [1]. This study was done in a service hospital in north west Bengal to highlight various clinical manifestations of falciparum malaria. The hospital is located in a known endemic area of chloroquine resistant falciparum malaria [3].

Quinine for 7 days with or without pyrimethamine - sulfadoxine or tetracycline is the recommended treatment for chloroquine resistant malaria [1,4,5]. In view of large number of cases and a relative shortage in supply of quinine, an alternative quinine regime was tried in this study [3].

Material and Methods

Three hundred and two patients with falciparum malaria admitted to our hospital from Jan 93 to Dec 93 were studied. The study included 20 cases of cerebral malaria. Diagnosis in all cases was confirmed by demonstration of asexual parasites in peripheral blood smear except in 8 cases of cerebral malaria in whom malaria parasite could not be detected. Diagnosis in the above said 8 cases of cerebral malaria was based on clinical findings (fever with persistent coma), cerebral fluid analysis and response to quinine. Parasitaemia was calculated by multiplying the number of asexual parasites per field by 750 [3]. Relevant history and clinical data were recorded. Initial laboratory investigation consisted of estimation of haemoglobin, total and differential leucocyte counts and urinalysis. Peripheral blood smear was checked daily for asexual parasites till discharge and thereafter weekly for next 4 weeks.

Blood sugar, blood urea, serum bilirubin and cerebrospinal fluid studies were done when clinically indicated. The following 2 treatment regimes were followed :

Regime I

1. Quinine 10 mg/kg 8 hourly x 3 days.
2. Tetracycline 250 mg 6 hourly x 7 days.
3. Sulfadoxine - Pyrimethamine (500 mg/25 mg) 3 stat.
4. Primaquine 45 mg stat.

Regime II

1. Amodiaquine (200 mg base) 3 stat; 2 OD x 2 days.
2. Tetracycline 250 mg 6 hourly x 7 days.
3. Sulfadoxine - Pyrimethamine (500 mg/25 mg) 3 stat.
4. Primaquine 45 mg stat.

For children the dosages were reduced proportionately and for those below 12 years, cotrimoxazole was substituted in place of tetracycline.

Regime I was administered to 254 cases including 15 cases which did not respond to Regime II. All cases of severe falciparum malaria (30 cases) and cases in whom fever lasted despite 9 doses of quinine (10 cases), extended quinine therapy (10 mg/kg 12 hourly or 5 mg/kg 8 hourly) was administered till patient was afebrile for 24-36 hours. Patients with cerebral malaria received loading dose of quinine.

Regime II was administered to 63 patients with uncomplicated malaria when quinine was in short supply.

Results

Fever was present in 298 cases (98.7%). It was predominantly high grade, intermittent or remittent (82.8%). One case showed the classical tertian pattern of fever (0.3%). Chills (92.7%), nausea (69.5%) and dry cough (46.4%) were the other major symptoms. Rigors were uncommon (7.3%). Four patients presented with low grade fever, malaise, anorexia, general debility, anaemia and splenomegaly of 1 to 2 months duration (1.3%). Two patients

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TABLE 1
Age distribution of malaria cases

Age (years)	Cases
0 - 5	18
6 - 12	26
13 - 18	54
> 18	204

TABLE 2
Various presentations

Presentations	Cases
Fever with chills	274
Altered sensorium with fever	14
Low grade fever, malaise and anorexia of insidious onset	4
Seizures with fever	3
Icterus with fever	2
Headache (no fever)	2
Asymptomatic	2
Acute abdomen	1

TABLE 3
Signs and symptoms

Symptoms	Cases	Signs	Cases
Fever			
Intermittent/remittent	255 85.6%	Pallor	42 13.9%
Continuous	42 14%	Icterus	86 28.5%
Tertian	1 0.4%	Blood Pressure	
Headache	300 99.3%	< 90/60 mmHg	60/242 24.8%
Chills	280 92.7%	Dehydration	54 17.9%
Nausea	210 69.4%	Hepatomegaly	54 17.9%
Cough	140 46.4%	Splenomegaly	52 17.2%
Vomiting	102 33.8%	Hepatosplenomegaly	32 10.6%
Rigors	22 7.3%	Altered sensorium, no lateralising signs	20 6.6%
Abdominal pain	20 6.6%		
Diarrhoea	4 1.3%	Acute renal failure	5 1.7%
		Subconjunctival haemorrhage	1 0.3%

TABLE 4
Complications

Complications	Cases
Black water fever	1
Sudden death	1
Transient organic psychosis	2
Hemiparesis	2

presented with anorexia, malaise and icterus of insidious onset initially suggesting a diagnosis of viral hepatitis (0.6%). Twenty patients presented with abdominal pains (6.6%) of which 1 had acute abdomen (0.3%). Among the unusual presentations, 2 had severe diffuse headache with no fever and 2 were asymptomatic at the time of diagnosis. In both asymptomatic cases, asexual parasites were detected in peripheral blood smear during routine blood analysis as part of medical examination.

TABLE 5
Cerebral malaria (Total cases 20)

Parameters	Cases
Clinical features	
Fever	20 100%
Seizures	10 50%
Papilloedema	Nil
Dysconjugate gaze palsy	Nil
Upper motor neuron signs	20 100%
Meningism	2 10%
Extensor posturing	4 20%
Laboratory	
Abnormal CSF findings	Nil
Asexual malarial parasite in PBS	12 60%
Hypoglycaemia	Nil
Complications	
Hemiparesis	2 10%
Psychosis	2 10%
Death	2 10%

PBS : Peripheral blood smear

Sixty out of 242 adult uncomplicated cases had blood pressure varying between 80-90/60-70 mmHg throughout the course of their illness (24.8%). In all these cases response to hydration and saline infusion was partial. Quinine infusion did not lower blood pressure any further.

Anaemia (Hb<10g/dL) and leucocytosis was present in 50 cases (16.6%) and 8 cases (2.6%) respectively. Pyuria (ranging from few pus cells to 10-12 cells/HPF) was detected in 160 cases (52.9%). Hyperbilirubinaemia was present in 96 cases (31.8%). Serum bilirubin levels varied between 1.5-8 mg/dL. Hyperbilirubinaemia was predominantly unconjugated in 54 cases (56.3%) and conjugated in 42 cases (43.7%). Biochemical evidence of hypoglycaemia was not detected in any of the 102 cases in whom it was clinically suspected, including patients of cerebral malaria who had extensor posturing.

Mean duration of fever was 3 days. Initial parasitaemia count ranged between 750/cumm to 100,000/cumm. Mean parasite clearance was 48 ± 24 hours with both regimes. Ten cases of uncomplicated malaria receiving regime I were successfully treated with extended quinine therapy as fever failed to subside within first 3 days of treatment. Fifteen cases receiving regime II did not respond and were finally treated with regime I. Fifty patients had features of cinchonism (16.6%). In one case quinine had to be withdrawn as the patient developed severe bronchospasm, hypotension and urticarial rash (0.3%). Out of the 302 cases treated, 8 were readmitted (3.3%) and 2 were readmitted twice (0.7%) for falciparum malaria. In all cases, re-admission was after 1 month of previous hospitalisation.

There were 3 deaths (0.9%). One died of sudden cardiovascular collapse. Two died of cerebral malaria within 24 hours of initiating quinine therapy.

Discussion

Tertian pattern of fever with rigors as a presentation of falciparum malaria has been found to be uncommon (0.3%). This is in agreement with various other studies [1,4,6,7]. Intermittent or remittent fever with chills and headache was the commonest presentation noted.

Falciparum malaria presenting as acute abdomen has been reported to be relatively frequent [8,9]. In this study only 1 case presented as acute abdomen (0.3%) and it did not cause any diagnostic problem because of high index of suspicion for malaria in a known endemic area. Similar findings have been reported by Panickar [6]. Upper respiratory tract infection and viral fever were the commonest differential diagnoses entertained followed by enteric fever, viral hepatitis and urinary tract infection. This re-emphasizes the need for repeated peripheral blood smear examination for malaria parasites in all cases of fever in an endemic area. Uppal et al in their study of 59 patients reported an incidence of hepatomegaly, splenomegaly and hepatosplenomegaly as 49.15, 42.46 and 32.20 per cent respectively [10]. We found low incidence of hepatomegaly (17.9%), splenomegaly (17.2%) and hepatosplenomegaly (10.6%) in our study, which corroborates the findings of other authors [6,11].

Anaemia is common in malaria [1,4,7]. In our study 50 per cent of the patients had haemoglobin less than 10 g/dL (16.6%). Low incidence of anaemia has also been reported by Panickar [6] and Uppal et al [10]. All the above studies were conducted in service hospitals. A predominantly non-immune population of soldiers and their families, staying in the endemic area for a short period of 1 to 3 years, may account for low incidence of anaemia in our study. Hyperbilirubinaemia was found in 96 cases (31.8%) as against 2.2 per cent reported by Panickar [6] and 10.17 per cent by Uppal [10]. Patients of malaria with jaundice may be diagnosed as having malaria hepatitis [4]. However, serum hyperbilirubinaemia as a marker of hepatic involvement in malaria is imprecise and coagulation abnormalities, hypoalbuminaemia with reduced metabolic clearance of alanine and lactate are more appropriate markers of hepatic impairment [4].

Presence of pus cells in an otherwise normal urine examination was found in 52.9 per cent of cases. Findings of pyuria in a patient with fever and chills accounted for urinary tract infection as a differential diagnosis in many cases. Absence of painful and increased frequency of micturition has been found to be reliable in excluding a primary urinary tract infection. Hypoglycaemia is common in malaria [1,4,5,7,11]. In none of our cases, hypoglycaemia could be established. Kawo et al [12], in their study of 97 Tanzanian children found hypoglycaemia in none of the cases on admission and after quinine infusion. The said study was faulted by White [13], for its design and patient study group (no case of severe falciparum malaria)

which were refuted by the author. Based on the WHO criteria [4] for severe falciparum malaria, there were 30 such cases in our study. Hypoglycaemia was detected in none of those 30 cases.

Various authors have advocated 7-14 days of quinine therapy [1,4,5,7,11,14]. Krishnan et al reported cure rates of 100 per cent with Q14T7, and 95 per cent with Q7T7 [15]. One of the alternative regime advocated by WHO recommends 3 days of quinine with 7 days of tetracycline [3]. This regime was preferred in this study because of large number of cases prevalent in the area and short supply of quinine. There were 224 cases of uncomplicated malaria who received regime I. All cases recovered, 10 cases received extended quinine therapy (1 to 2 days) due to persistence of fever after 72 hours. Thus a minimum of 72 hours of quinine in uncomplicated falciparum malaria achieved a 100 per cent cure rate in this area. Of the 30 cases of severe malaria, 3 died (mortality 10%). Regime II (amodiaquine, tetracycline, sulfadoxine-pyrimethamine) in this study achieved a cure rate of 76.2 per cent and thus is a viable alternative in uncomplicated cases, in absence of quinine.

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