

Treatment of Severe Falciparum Malaria With Artemisinin and Exchange Transfusion Case Report

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Abstract :

In this communication a young patient presented with severe Falciparum Malaria with multiple organ involvement. He did not respond to conventional anti-malarial treatment e.g. Chloroquine, Quinine in full courses, However he showed remarkable improvement and finally cured after treatment with exchange transfusion and Artemisinin,

Introduction:

Malaria associated with complications or fatal outcome is almost always caused by Plasmodium Falciparum. The mortality due to this disease parallels the degree of Parasitemia. Successful use of exchange transfusion as a therapeutic adjunct for this infection was first reported in 1974, although the efficacy of this procedure has not been established by randomized, controlled trials.

The rationale for this form of therapy is based on: rapid reduction in the parasite load by direct removal, decrease risk of severe intravascular haemolysis and its consequences (disseminated intravascular coagulation and renal dysfunction), improve rheology with transfused blood , reduce micro-circulatory sludging and improved oxygen-carrying capacity with transfused erythrocytes.

Artemisinin or Qinghaosu - Artemisia annua (Sweet wormwood) is found in many parts of the world. In the early 1970's Chinese scientist recognized its potential for treating malaria and isolated the active principle artemisinia or ginghaosu.⁽¹⁾ To combat increasing problems with drug resistance to Plasmodium Falciparum, Vietnam has turned increasingly to artemisinia derivatives. Oral and suppository formulations are produced from locally grown plants. These compounds have been rapidly effective in the treatment of malaria in a large number of studies.⁽²⁾

Case Report:

A previously healthy 39 years male Filipino was admitted to the hospital with a 4 days history of fever, chills, backache, vomiting and diarrhea. He had recently been to Najran area 10 days before admission. He was treated with Chloroquine full course before coming to our hospital.

On admission, the patient was ill, pale, temperature 39⁰C, pulse 116 per minute, blood pressure 110/80 mmHg, respiratory rate 30 per minute. He had jaundice. His heart, chest were normal. In the abdomen the spleen and liver were not palpable. He was alert, oriented and there were no neurologic deficits.

His initial investigations were as follows: HB 13.7g/dl (13.5-18), WBC 3100 (4-11), platelets 70,000 (150-400,000), Reticulocytes 0.9%, ESR 30mm in the first hour. Blood film showed normocytic normochromic red cells, studded with ring forms of plasmodium falciparum. (No parasite count was done) LDH 560 (31.3-618), blood sugar 6.1 mmol/L (3.6-6.8), creatinine 111 umol/L, (70-133) BUN 5.9 mmol/L, (2.5-7.5) Albumin 36 gram/L, (39-50) SGOT 102 U/L, (50-57) SGPT 71 U/L, (5-56) GGT 162 U/Lm, (8-78) total bilirubin 27 umol/L. His urine and stool analysis were normal. Blood, urine and stool cultures were all negative. He was treated with oral chloroquine sulphate in a dose of 600 mg initially, followed by 300mg single dose after 8 hours, then 300 mg daily for 2 days. He continued to have fever and positive blood films. Oral Quinine sulphate in a dose of 600mg TID with Doxycycline 100mg BID was started for 10 days.(I.V. Quinine was not available)

The patient continued to deteriorate inspite Quinine Sulphate, Doxycycline therapy which was later changed to intravenous Clindamycin 600 mg 8 hourly on day 7. He became more ill, continued to have high grade fever, 39-41oC, dyspnoea, his chest was full of crepitations and his chest x-ray showed features of pulmonary oedema, inspite adequate fluid balance and urine output. This was thought to be due to capillary leak syndrome. His haemoglobin and platelets started to drop (Table 1). LDH increased as well as unconjugated bilirubin.

His blood film showed fragmented red cells and polkiloanisocytosis and was full of parasites. He continued on Quinine and Clindamycin for 10 days. Twelve days after admission, exchange transfusions were started and he was given Artemisinin 3.2mg per kg body weight intramuscularly (I.M),

followed by 1.6mg per kg. (I.M) every 24 hours for 5 days.⁽⁸⁾ He was also treated with fluid restrictions and frusemide for his pulmonary oedema.

Four sessions of partial exchange transfusions was performed manually with saline replacement and 250 mls packed cells were transfused each session. Following the use of Artemisinin and exchange transfusion malaria parasites were cleared from the blood as checked by several blood films.

Two weeks after discharge from hospital, he was in good health, afebrile, his chest was clear. Hb was 14 grams, platelets normal and his blood film for malaria was negative.

Comments:

This case illustrates the beneficial effects of exchange transfusion as prompt reduction in parasitemia is required to halt the progression of pathophysiologic changes occurring in the microcirculation.⁽³⁾ Exchange transfusion was first reported by Gyr et.al.⁽⁴⁾ in 1974. Several reports since then were noted.⁽⁷⁾ Data from these reports although obtained in uncontrolled trials, provide compelling evidence in the efficacy of this treatment modality for severe malaria. The use of exchange transfusion should be considered for the treatment of severe falciparum malaria in any of the following situations: parasitemia in >10% of circulating erythrocytes; cerebral malaria; disseminated intravascular coagulation and acute renal failure.⁽³⁾

In this patient Parasite count was not done before and after treatment with exchange transfusion and Artemisinin. ARTEMISININ or qinghaosu is the active principle of the Chinese medicine herb *Artemisia annua* & mdash; composite (sweet wormwood), which has been used as a treatment for fevers in China for more than 1000 years. Antimalarial activity resides in the endoperoxide structure. It destroys young trophozoites as well as other blood stages of *P. Falciparum* including chloroquine-resistant strains, and clears parasitaemia more rapidly than any other antimalarial drug.⁽⁵⁾ Dihydroartemisinin, the active metabolite, is cleared rapidly. In China, clinical trials with intravenous artesunate (a water-soluble hemisuccinate), intramuscular artemether (the methyl ether suspended in peanut oil), and oral suppository preparations of artemisinin produced very encouraging results in the treatment of multiresistant *P. Falciparum* infections, suggesting perhaps a halving of mortality in cerebral malaria compared to quinine.⁽⁵⁾ More recently, studies in Southeast Asia, Africa and South

America in cerebral and other severe forms of falciparum malaria have provided evidence of a rapid effect judged by fever and parasite clearance, suggestion of a reduction of mortality, and negligible toxicity.^(9,10) The high recrudescence rates reported in earlier trials were attributed to inadequate dosage. In animal toxicity studies, there has been evidence of neurotoxicity, brainstem neuronal damage, and QT prolongation but these effects have not been seen in human patients.⁽⁶⁾

In conclusion, our patient with severe Falciparum Malaria resistant to multiple drugs responded very well to Artemisinin and exchange transfusion.

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TABLE (I)
Flowsheet of Patient Paratmeters During Stay in Hospital

	Hb g/dL	WBC x10 ⁹ /L	Plat x10 ⁹ /L	Urea mmol/L	Crea Umol/L	Na mmol/L	K mmol/L	Alb g/L	Bil Umol/L	LDH u/L	Treatment
06-01-1998	13.7	3.1	70	5.9	111	134	4.1	36	27	3752	Quinine + Doxycycline
10-01-1998	9.8	7.2	38					23	138	3582	
11-01-1998	9.9	7.5	35	14.4	183	128	3.7	23	119		
12-01-1998	10	9.9	37	6.5	170	130	3.5	21	96	3597	
14-01-1998	8.2	10.0	61	7.0	101	130	3.6	19	50	2995	
15-01-1998	10.2	4.2	78	3.4	89	122	3.3	20	42	2857	
16-01-1998	13.5	4.1	252	2.7	90	128	2.7	24	35		
17-01-1998	10.3	3.8	72	3.1	78	130	3.0	24	33		
18-01-1998	11.9	4.4	85	3.5	79	133	3.8	28	35		
19-01-1998	11.6	5.0	84	20.6	128	127	5.2	32	83		
20-01-1998	10.9	2.8	90	5.7	73	134	4.5	26	32		
21-01-1998	10.7	2.4	90	5.2	76	135	4.4	28	32		
22-01-1998	11.1	4.0	115	3.6	87	132	4.6	31	35		
23-01-1998	10.4	4.0	125	2.9	77	130	4.3	30	33	2029	
24-01-1998	9.7	3.2	128	3.0	70	133	4.4	31	32	1998	
25-01-1998	10.2	4.5	158	3.3	73	133	4.3	31	29	1700	

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مستشفيات المانع العامة
ص.ب ٢٣٦٦ الدمام ٣١٤٥١
المملكة العربية السعودية

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فيما يتصل بهذا الموضوع فإن مريض شاب كان قد حضر يعاني من ملاريا فالسيبارم حادة مع تأثيرها على أعضاء مختلفة لم يستجب للعلاج بمضادات الملاريا التقليدية مثل الكلوركوين والكوينين و على كل في النهاية كان قد تم شفاؤه تماماً بعد العلاج بواسطة تغيير الدم وعقار الأرتشمسينين.