Exchange Transfusion Therapy in Severe Complicated Malaria

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Abstract

Two groups of sixteen cases of severe complicated falciparum malaria on two different regimens of treatment were retrospectively studied. The first group including 12 patients, were treated by anti malarial drugs alone. The second group including 4 patients, were treated by exchange transfusion. Multisystemic complications were observed in both groups. It was observed that in complicated Acute Respiratory Distress Syndrome (ARDS), renal and hyperparasitemia were >30 per cent. The result of the exchange transfusion group was superior to the non exchange group. Exchange transfusion is therefore recommended in the treatment of malarial patients who present with parasitemia >30 per cent and severe multisystemic complications paticularly those who have severe acute renal failure or have lung complications. The amount of blood used for each exchange transfusion should be at least 10-14 units for rapid removal of parasites and toxic metabolites from the circulation.

Malaria, one of the most common infectious diseases of the world is still a great health problem especially in tropical countries covering 50 per cent of the world population of nearly 4,700 million people. This large population is in risk infectious areas[1]. Results of a WHO sponsored malaria eradication program was initiated in 1956. Despite technical and socioeconomic difficulties there has been a decrease in the disease in many areas of Thailand[2,3]. At present, there are two major problems regarding the natural history of malaria in man. These are the resistance of organisms to drug therapy leading to hyperparasitemia and occurrence of systemic complications and the difficulty of treatment modality of severe multisystems complicated cases[4,5]. Prior to 1980, the mortality rate of patients with severe complicated malaria was 29 per cent - 40 per cent[5]. On the other hand, in cases accompanied by lung complications the mortality rate was increased to 60 per cent - 70 per cent[4,5]. After 1980, with early dialysis for renal failure and full respiratory sup-

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portive measures, the mortality rate of complicated malaria was reduced to 20 per cent, but was still higher at 40 per cent in cases with lung complications[4]. Exchange transfusion therapy in malaria was introduced in early 1974[6], with successful results in certain cases. This adjunct therapy has been widely used. Up until the present time, according to reports in the literature, exchange transfusion has been performed in more than 50 cases of complicated falciparum malaria[7,8].

We would like to present the result of exchange transfusion used as adjunct therapy in cases with complicated falciparam malaria performed at Petchabun Hospital from 1991 to 1995. The survival rate of these 4 exchange transfusion cases was compared to the other 12 matched non exchange, complicated malarial cases in the same period 1991-1995. The analysis attempts to answer the unsolved questions regarding the indication, time and amount of blood used for each exchange transfusion and the benefit of this therapy regarding the improvement of survival in cases with certain systemic complications.

MATERIAL AND METHOD

From April 1991 to December 1995, sixteen falciparum malarial cases with systemic complications including brain, renal, lung, liver, coagulopathy defects and disseminated intravascular coagulopathy (DIC) were retrospectively studied. All of these cases were treated by the same regimen. All cases were divided into two groups, the first 12 cases were treated by anti malarial therapy. The second 4 cases were treated by adjunct exchange transfusion. All sixteen severe falciparum cases were admitted to Petchabun Hospital, some cases were referred from community hospitals. On admission, routine laboratory regimens including thick and thin malarial film, malarial count per 5,000 red cells, CBC, chest X-ray, ECG, anti HIV, VDRL, HBsAg, liver function test (LFT), renal function test (RFT), pCO_2, were performed. Coagulation test including partial thromboplastin time (PTT), prothrombin time (PT), thromboplastin time (TT), also fibrinogen degradation product (FDP) Fibrin monomer (FM) Euglobulin clotlysis (ECL) in some cases, were repeated as necessary. In cases of comatose patients, routine care by insertion of nasogastric tube, retained urethral catheter and central venous pressure (CVP) were carried out as indicated. Symptoms and signs of laboratory findings showing severe complicated malarial cases were indicated by WHO criteria[9] : CNS stuporous, restless = + coma and convulsion = + + , impaired renal function test and oliguria = + + , pulmonary oedema = + , pulmonary oedema + hypoxia = + +, jaundice, bilirubin = 1-3 mg% = + , bilirubin > 3 mg% = + + , bleeding skin and mucosa = + , severe gastro- intestinal bleeding = + +.

Criteria for diagnosis of DIC were based on these following findings : ischemia of end organs with concomitant findings of thrombocytopenia, increased FDP of more than 10 microgm/ml and one or more abnormalities of the coagulation test namely prolongation of PTT PT, TT, low fibrinogen and/or positive fibrin monomer (FM).

All 16 severe falciparum cases with or without adjunct exchange transfusion were admitted to the intensive care unit (ICU) during their acute illness. Every case was treated by quinine intravenous drip, loading dose in non previous treated cases. Subsequently, the drugs were changed to oral administration, as soon as the parasitemia became negative and the patient recovered completely from systemic complications. The period of treatment was 7 days or more. Doxycycline was additionally given in cases who were resistant to quinine therapy (parasitemia more than 5 per cent after receiving antimalarial treatment for more than 24 hours).

Every patient was taken care of by nasal or endotracheal tube. Positive end expiratory pressure (PEEP) was applied in cases with hypoxia. Early peritoneal dialysis was performed in cases with severe renal failure. Other supportive measures including adequate amount of intravenous fluid and antibiotics were given as indicated.

Decision for adjunct exchange transfusion included one of the two major criteria : hyperparasitemia of over 10 per cent accompanied by at least one severe systemic complication and/or sustained symptoms of severe systemic complication more than 24 hours after receiving effective antimalarial drugs and full supportive therapy. Exchange transfusion was performed manually.

Fresh whole blood (FWB) or Packed red cell (PRC) stored less than 5 days with fresh frozen plasma (FFP) were used. The amount of blood for each exchange was 10-14 units. Concentrated platelets 4-6 units were given at the end of exchange transfusion in every case, if signs of thrombocytopenia occurred. The exchange transfusion was

Table 1. Clinical manifestations of 4 severely complicated falciparum malaria patients treated by adjunct exchange transfusion.

Case No.	Age / sex	CNS	Renal	Lung	Jaundice	Bleeding	Sepsis	DIC	Parasite %	Outcome
1	22/M	+	++	+	++	+	+	-	10%	S
2	25/M	++	+	+	++	-	-	-	15%	S
3	39/F	++	-	-	++	-	-	-	40%	S
4	45/M	++	+	++	++	+	-	+	60%	D

S = survived; D = died (mortality rate = 25%)

repeated if parasitemia was over 10 per cent or the symptoms of severe systemic complications were sustained or became worse in the following 24 hours. Duration of each exchange transfusion was about 3-6 hours.

RESULTS

Multisystemic complications of severe falciparum cases are shown in Table 1. Brain, jaundice were the most common complications found, followed by renal and lung. Bleeding tendency was found in 2 cases, while DIC was found in only one case. One case died from hyperparasitemia, intractable shock and acute respiratory distress syndrome (ARDS). The mortality rate in this group was 25 per cent. Improvement of some complications after adjunct exchange transfusion was observed in 3 surviving cases as shown in Table 2 and Fig. 1.

Table 2. Complications and duration of inprovement in 3 surviving cases.

Type of complications	Duration of improvement
CNS	2-5 days
Renal	2-7 days
Lung	1-2 days
Jaundice	1-3 week
Parasitemia decreased	36-72 hours
Platelets increased	2-8 days

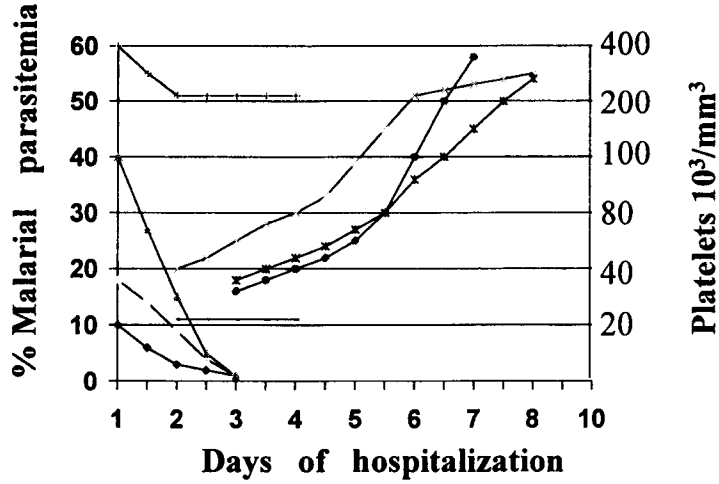

Fig. 1. Relation between malarial parasitemia and platelets count within 10 days of hospitalization.

Table 3. Clinical manifestations of 12 matched non exchange falciparum cases.

Case No.	CNS	Renal	Lung	Jaundice	Bleeding	Sepsis	DIC	Parasites %	Outcome
1	+	+	+	+	-	-	-	3%	S
2	+	+	-	+	-	-	-	2%	S
3	+	+	+	+	-	+	+	5%	D
4	+	+	-	+	-	-	-	10%	S
5	++	-	-	-	-	-	-	15%	S
6	+	-	+	++	+	-	+	40%	D
7	++	-	-	-	-	-	-	10%	S
8	+	-	+	-	-	-	+	8%	D
9	++	-	+	+	+	-	-	15%	D
10	+	-	-	-	-	-	-	3%	S
11	++	-	-	-	-	-	-	20%	S
12	++	-	-	-	-	-	-	3%	S

S = survived; D = died (mortality rate = 33.33%)

The clinical manifestations and survival of the 12 non exchanged cases are presented in Table 3. All these cases were admitted to Petchabun Hospital from 1991 to 1995. All of these cases were treated by the same regimens as used for 4 exchange transfusion cases. The total survival of this group was less than the adjunct exchange transfusion group approximately 67 per cent : 75 per cent. It was seen that the severely affected organs, lung, acute respiratory distress syndrome (ARDS), and the survival rate in the adjunct exchange group were greater than to the non exchange transfusion group.

DISCUSSION

Exchange transfusion in severely complicated malaria has been shown to be a useful adjunct therapy by many previous authors[10-16]. The problems of inadequate quinine therapy or multidrugs resistant falciparum strain may lead to multisystemic complications[17]. For these reasons the adjunct blood exchange became the alternative regimen in severe cases. The rationale of exchange transfusion therapy is based on three major factors. The first one is the direct rapid removal of parasites as well as various toxic substances from the blood. The other two include the improvement of the blood rheology by replacement with new red cells and finally to slow down the process of DIC and bleeding by removal of procoagulants and high FDP from the circulation[18]. Furthermore, the particular usefulness of exchange transfusion is seen in cases which resist quinine therapy[19], as observed in one case in our series in whom resistance of malarial parasite to quinine therapy was evident by means of exchange transfusion. The malarial parasites in this case rapidly declined to less than 5 per cent on the following day. Regarding the amount of blood used in each exchange, it was shown by our studies that the amount of blood, approximately 10-14 units, was sufficient to lower parasitemia to less than 5 per cent in 24 hours. However, in the presence of very high parasitemia (over 60%), the amount of blood should be increased to at least 15 units or twice the human blood volume for each exchange[8].

Our observation agrees with those reports by previous authors that this amount of blood (over 10 units) for each exchange could eradicate 80 per cent of the parasites in the blood[8-10]. From this study, survival of our patients was quite comparable to the previously reviewed nearly 54 patients who received exchange transfusion for the treatment of complicated malaria[6-9]. On the other hand, when survival was compared with our patients between exchange and non exchange groups who were admitted for a similar period of time and were treated by the same regimen (Table 1 and Table 3), there was no significant difference regarding survival of the total patients of the subgroups with brain and renal complications. However, comparing the extent of hyperparasitemia of these two groups, this important risk factor was less severe in the non exchange groups. Furthermore, when comparing the subgroups who had lung complications, with the non exchange group it was demonstrated

that the survival of the exchange group was superior to that of the non exchange group. This result indicates the benefit of exchange transfusion therapy in patients who have complicated malaria, particularly in those who already have or tend to have lung complications. From the author's, the mortality rate of the patients who have severe multisystemic complications together with hyperparasitemia over 30 per cent is rather high. Some authors recommended that exchange transfusion should be seriously considered in patients who have hyperparasitemia over 30 per cent together with severe systemic complications particularly those who present with severe acute renal failure[20,21]. The particular recommendation in the patients with severe acute renal failure is based on the observation that in this type of patient, the tendency to develop lung complications is very high. From this study, none of the patients who had parasitemia less than 10 per cent together with sustained cerebral malaria died. Whether this result indicates the benefit of exchange transfusion by removing the toxic cytokines from the blood of these patients cannot be proved definitely. However, the problems of a large amount of blood used in each transfusion exchange especially in rural areas where these is lack of blood. To avoid using large amounts of blood, partial exchange transfusion was reported beneficial and valuable in some cases of severe complicated falciparum malaria[7].

SUMMARY

Malaria is one of serious infectious diseases in the tropics, subtropic zones and is widespread all over the world. Nowadays, the regimens of treatment of falciparum malaria with severe multisystemic complications are now far advanced, despite, the problem of quinine resistance. Exchange transfusion in severe complicated falciparum malaria is the alternative procedure to be kept in mind. The benefit of exchange transfusion was discussed. The disadvantage of exchange transfusion in some rural areas, due to inadequate amounts of blood and blood donors. Partial exchange transfusion in falciparum with severe multisystemic complications was reported valuable. The benefit of partial exchange transfusion was a valuable alternative in hospitals which lack the machinery and large amounts of blood needed. However, these adjunct exchange transfusions must be carried out under sterile technic to prevent secondary infections e.g. Hepatitis A, B, C, sepsis or HIV, etc. The best procedure to avoid suffering from malaria is preventive care especially in endemic areas.

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การถ่ายเปลี่ยนเลือดในการรักษามาลาเรีย *P. falciparum* ที่มีโรคแทรกซ้อนอย่างรุนแรง

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ได้ทำการศึกษาผู้ป่วยมาลาเรียชนิด *P. Falciparum* ที่มีโรคแทรกในหลายระบบของร่างกายตั้งแต่ปี พ.ศ.2534-2538 จำนวนทั้งหมด 16 ราย โดยแบ่งการรักษาเป็นออกเป็นสองกลุ่ม กลุ่มแรก 12 ราย รักษาโดยการใช้ยารักษามาลาเรีย ส่วนอีก 4 ราย รักษาโดยการให้ยาในระยะแรกร่วมกับการถ่ายเปลี่ยนเลือด ในกลุ่มแรก 12 ราย ผลการรักษาตาย 4 ราย รอด 8 ราย ในกลุ่ม 4 ราย ที่รักษาโดยวิธีการให้ยาและการถ่ายเปลี่ยนเลือดร่วมด้วย มีตาย 1 ราย รอด 3 ราย พบว่ามีโรคแทรกอย่างรุนแรงที่มีต่อระบบสมอง ตับ ไต ปอด และความผิดปกติทางโลหิตทั้งสองกลุ่ม จากการศึกษาเปรียบเทียบผลการรักษาทั้งสองกลุ่มพบว่าในกลุ่มที่มีโรคแทรกอย่างรุนแรงในหลายระบบของร่างกายโดยเฉพาะโรคแทรกซ้อนต่อระบบไต, ปอด และจำนวนเชื้อในกระแสโลหิตที่มากกว่า 30% นั้นการรักษาโดยการให้ยาและการถ่ายเปลี่ยนเลือดจะได้ผลดีกว่า แม้ว่าจะต้องใช้เลือดประมาณ 10-14 ขวด ก็สามารถทำให้เชื้อในกระแสเลือดลดลงเร็วกว่าอาการในทุกระบบมีการฟื้นตัวเร็วกว่า

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