Role of exchange transfusion in patients with severe *Falciparum* malaria: report of six cases

Plasmodium falciparum malaria is associated with substantial mortality that parallels the degree of parasitemia or the development of complications. In addition to medical management, exchange transfusion (ET) has been occasionally used in the treatment of the most severe cases. We review the cases of six patients with severe falciparum malaria successfully treated with ET.

Plasmodium falciparum malaria is the most dangerous form of malaria with a mortality exceeding 20% depending on the degree of parasitemia and the development of complications such as cerebral malaria, renal failure, adult respiratory distress syndrome (ARDS), and disseminated intravascular coagulation (DIC).[1,2] Survival depends upon the prompt institution of medical therapy. Besides this, exchange-transfusion (ET) allows a brisk reduction in the level of parasitemia and can be considered as an useful adjunctive measure in the management of the most severe cases of falciparum malaria.[2,4,5]

We present six patients with poor prognosis severe falciparum malaria successfully treated with ET in the Hematology Service of the University Hospital La Fe. At diagnosis, all patients were febrile and had acute renal failure (2 requiring hemodialysis), four had hepatic impairment, two had cerebral malaria, and one pulmonary edema requiring mechanical ventilation. The main characteristics of the patients are shown in Table 1. Drug therapy was started immediately after diagnosis, and ET was decided within 36 hours of the diagnosis due to the unfavorable evolution of the patients' disease. ET was performed using either a discontinuous (3 cases) or continuous-flow blood cell separator (3 cases). The median blood volume removed was 7,000 mL and was substituted by an equivalent amount of a mixture of packed red blood cells (RBC) and fresh frozen plasma (FFP). A decrease in the infected erythrocyte rate was observed in every case. Three patients developed ARDS after the ET, requiring mechanical ventilation, and in two patients the renal failure progressed, requiring hemodialysis. However, all patients survived without sequelae.

Plasmodium falciparum infects erythrocytes of any age with the potential for development of high-grade parasitemia.[6] Clinical complications observed in falciparum malaria are the result of microthrombi caused by the presence of mature parasites in the microcirculation of various organs such as brain, kidneys, spleen, liver, intestines and limbs.[7,8] Despite appropriate medical treatment, the mortality in patients with a greater than 10% parasitemia ranges from 20% to 40% when cerebral or renal function is impaired and up to 80% in the presence of ARDS.[2] In these cases, the use of ET is a valid approach to achieve a prompt reduction in parasitemia, and may improve prognosis. However, ET treatment is still considered a matter of debate because some authors consider that similar results to that achieved with ET could be obtained with chemotherapy alone.[9] In the only randomized, prospective study reported comparing antimalarial chemotherapy with or without ET, all four patients who received ET survived, whereas three out of four patients who did not receive ET died, supporting the benefit of ET in preventing malaria mortality.[10] Likewise, in the report of a collective experience in the United States of 16 patients managed with ET (10 with parasitemia >10%) and intravenous quinidine or quinine, 7 out of the 10 patients survived, suggesting a potential effective role of ET as adjunct treatment to chemotherapy.[2]

The main advantages of ET could be due to a rapid correction of the anemia, a rapid decrease in the level of parasitemia and the elimination of several cytokines and parasite toxins.[3] Other advantages associated with the ET are that it ensures an adequate fluid balance and hemodynamic status and absence of interference with drug therapy. The technical procedure of ET for the treatment of severe malaria is not definitively established. Although some authors have reported successful results with partial RBC exchange transfusions, we used RBC and FFP as replacement therapy in an attempt to correct coagulation abnormalities, to replenish unparasitized cells and to correct severe anemia simultaneously. Finally, according to our results a two-volume exchange procedure is generally associated with an important reduction in the level of parasitemia, and can help to control the disease by conventional measures. Patients with complicated malaria are extremely vulnerable to fluids shifts, and occasionally severe side effects have been reported after ET.[7] In our series, three patients developed ARDS needing mechanical ventilation. However, due to the severity of the infection in these patients it is difficult to know whether these complications were related to the procedure or secondary to the disease itself. All patients were discharged from the hospital in a good clinical status.

In conclusion, ET seems to be a valid adjuvant therapy for Plasmodium falciparum infection that should be considered for patients with high levels of parasitemia, or with an unfavorable evolution with conventional treatment. However, only prospective trials will resolve the exact role of ET in the management of severe malaria.

Table 1. Patient characteristics.

Case No.	Sex/Age(yrs)	Adverse features	Volume removed (mL)	Parasitemia (%) Pre-ET	Post-ET	Status
1	Female/44	Renal failure; DIC; ARDS; Cerebral malaria; Liver impairment*	7000	23	10	Alive
2	Female/40	Renal failure; Liver impairment	6000	43	13	Alive
3	Male/49	Renal failure; DIC; ARDS; Cerebral malaria	7250	58	18	Alive
4	Male/36	Renal failure; Liver impairment	7000	45	20	Alive
5	Male/47	Renal failure; ARDS	7000	80	20	Alive
6	Male/25	Renal failure; ARDS; Liver impairment	6000	40	15	Alive

*Abbreviations: ET: Exchange transfusion; DIC: Disseminated intravascular coagulation; ARDS: Adult respiratory distress syndrome. *Defined as jaundice (serum total bilirubin >2.5 mg/dL) and elevated aminotransferase levels (>3 times normal).*

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