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Case Report

Internal Medicine Section

Exchange Transfusion in Severe Falciparum Malaria

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ABSTRACT

Malaria is endemic in India with the incidence of *P. falciparum* Malaria increasing gradually over the last decade. Severe malaria is an acute disease, caused by *P. falciparum*, but increasingly also by *P. vivax* with major signs of organ dysfunction and/or high levels of parasitaemia (>10%) in blood smear. Use of exchange transfusion with antimalarial drug therapy as an additional modality of treatment in severe Falciparum malaria is controversial and is unclear. We report a case of severe malaria complicated by multiorgan failure and ARDS. Patient responded well to manual exchange transfusion with standard artesunate-based chemotherapy.

Keywords: Exchange blood transfusion, Malaria, *Plasmodium falciparum*

CASE REPORT

A 21-year-old, male was admitted with high grade fever associated with chills, abdominal pain, vomiting (3 episodes/day) and yellowish discolouration of urine for 5 days. He became ill 2 days after week long trip to Mumbai. On admission, he was febrile (102^0 F), had bradycardia and hypoxia & blood pressure was 90/60 mm of Hg. He had icterus, fine bilateral respiratory crackles and right hypochondriac tenderness. Rest of physical examination was normal. With provisional diagnosis of tropical infection, symptomatic treatment was started and he was given rapid infusion of IV fluids and blood investigations were sent. The patient's initial laboratory reports revealed mild anaemia, normal leukocyte count and severe thrombocytopaenia [Table/Fig-1]. Renal function tests were normal while liver function tests revealed mildly elevated SGOT, SGPT and moderately increased Sr.Bilirubin. Peripheral smear was positive for *P. falciparum* malaria parasite with parasitic index of > 40%. USG abdomen and pelvis revealed hepatomegaly with gall bladder sludge and bilateral mild pleural effusion. The patient was started on parenteral Artemisinin based treatment for severe malaria.

On the 2nd day, patient became drowsy, tachypneic and oliguric and he had 3 episodes of hypoglycaemia for which he received 25% dextrose. He was shifted to the ICU. The 3rd day patient became severely hypoxic; Chest X-ray revealed ARDS and the patient was put on Non-invasive ventilation. The parasite index now was 70%. He was started on ionotropes for persistent hypotension and shock. On day 4 he was intubated and put on mechanical ventilation. His LFTs and RFTs gradually deteriorated [Table/Fig-1] and he landed in multiorgan failure.

On the 5th day, decision was taken to do an exchange transfusion. Under Ultrasonographic guidance the right femoral vein was cannulated with a central venous catheter. A manual exchange transfusion was done replacing 2000 ml of patient's blood with 4 bags of whole blood, 2 bags of packed cell volume and 4 bags of Fresh frozen plasma. During the procedure patient had one episode of bradycardia (45/min) which reverted with injection atropine (0.6 mg). The total duration of procedure was 4 hours. After exchange transfusion the laboratory reports showed decrease in serum Bilirubin and renal function tests [Table/Fig-1]. Urine output improved. On third day after exchange transfusion, patient was extubated. On ninth day after admission, patient was shifted outside the ICU and on eleventh day, patient was discharged.

DISCUSSION

Exchange transfusion removes infected red blood cells and thus decreases the parasite load. Exchange transfusion is used as an additional modality to reduce the mortality of severe Falciparum malaria. Blood viscosity is improved due to removal of infected red blood cells with reduced deformability which in turn reduces sludging in microcirculation. It also improves oxygen carrying capacity of blood [1]. Exchange transfusion not only decreases the parasite load but also removes products of inflammatory response and improves viscosity and flow characteristics of blood.

	Day1	Day2	Day3	Day4	Day5 ET done	Day6	Day7	Day8	Day9	Day10
Hb	9.4	9.2	8.7	9.4	9.2	11.2	10.6	10.9	9.8	10.1
TLC	6200	7400	13400	23000	20000	13100	8000	11400	10700	12300
Platelet count	15000	Adequate	20000	15000	30000	60000	90000	1,20000	100000	Adequate
Parasite	Ring of *P.Falciparum*		Ring of *P.Falciparum*			Not seen	Not seen	Not seen	Not seen	Not seen
PT	21.8	19.8		17.1	12.5	13.1	14.5			
INR	1.68	1.52		1.32	0.9	1.01	1.12			
BUN	38	48	54		52	109	103		53	33
Sr.Creatinine	0.83	2.15	1.02	1.2	0.8	0.7			0.47	0.40
Na+	135	139	133		138	142	145		135	144
K+	3.4	2.9	4		5	4.2	4.9		3.5	3.5
Cl-	109	110	109		106	107	111		105	111
SGOT		70		134		65	58		47	29
SGPT	73	75		68		63	80		58	48
Alkpo4		98		92		79	87		65	73
Sr.Billirubin—Total	7.98	8.13		14.15	22.37	6.97	4.7		3.64	4.23
D. bill	4.4	1.7		8.6	14	3.8	2.6		1.8	2.1

[Table/Fig-1]: Serial daily Investigation chart.

Exchange transfusion was first introduced in 1974 [2]. Fluid overload, non cardiogenic pulmonary oedema, hypotension, cerebral haemorrhage, febrile and allergic reactions, metabolic disturbances, rapid exfusion and transmissible infections are the health hazards associated with exchange transfusion [3].

Automated erythrocytapheresis and manual exchange transfusion are two types of exchange transfusion. Approximately half of the blood volume is exchanged in 5 hours [3] in manual exchange transfusion with the goal of reducing parasite load by 40%. In automated exchange transfusion entire blood volume can be changed in 1.5 hours [4].

No standardized treatment protocol is available in terms of indications and volume to be exchanged and which method to be used. Exchange transfusion is usually indicated in patients with parasite load > 30% or parasite index >10% with presence of other severe complications, multiorgan failure or organ involvement with hyperparasitaemia [5].

Advantages of automated erythrocytapheresis are better haemodynamic stability, preservation of plasma and cellular components, efficient and rapidity but it is only available in specialised centres. Manual exchange transfusion does not require any special equipment so it can be implemented immediately in all centres in patients with severe Falciparum malaria [3].

Exchanging blood only removes circulating parasite antigen, RBC's sequestered in microvasculature of vital organs are not exchanged. But manual exchange transfusion removes burden of toxins and products of host immune response [5]. Rapid clearance is not only due to exchange transfusion but also due to anti-malarial drugs in particular artesunate [5]. But this case focused on parasite clearance alone, no conclusion can be drawn on the proposed beneficial mechanisms of exchange transfusion in removing parasite toxins and improvement in haemorrheology [5] and correction of anaemia.

As Randomised control trials have not been conducted the role of exchange transfusion is still unclear. A meta-analysis conducted by Riddle MS et al., in which they compared patients with severe malaria who received exchange transfusion with those who received only antimalarial chemotherapy [6]. They did not find any difference in survival rates. Although patients receiving exchange transfusion were more critically ill and had significantly higher parasitaemia levels.

Most of the studies [5-8] could not find a benefit of exchange transfusion in retrospective evaluations. The result's significance is limited by the small sample size in addition to lack of a standardized transfusion protocol and observer bias contaminating the result. There are few situations in clinical practice when treatment decisions have to be made without sufficient data from prospective clinical trials. We suggest that the theoretical advantages of exchange transfusion justify its use in extremely ill patients with falciparum malaria. Previously Centre for Disease Control [9], Atlanta, recommended that exchange transfusion be considered safe for certain severely ill patients. In 2013 CDC conducted analysis of cases of severe *Plasmodium falciparum* malaria treated with exchange transfusion and they did not find any survival benefits. So CDC does not recommend the use of exchange transfusion as an adjunct procedure for treatment of severe malaria.

A meta-analysis [10] showed that exchange transfusion does not improve the survival rate. Due to lack of standardized assessment system in treatment groups, it was difficult to compare various studies. Also, there is no evidence based guideline on the use of exchange transfusion in patients with severe malaria.

Suggested advantages are due to removal of toxins and inflammatory mediators. Some investigators have suggested that plasma exchange, plasmapheresis or haemodialysis are possible alternatives to exchange transfusion [6].

Electrolyte imbalance and haemodynamic complications associated with manual exchange transfusion can be avoided with use of automated exchange transfusion. Extremes of age groups like younger children and geriatric population are benefitted more because only a small amount of blood that is required in children can be easily obtained from parents and relatives and geriatric patients are more sick initially and more likely to have bad outcome [11]. A greater benefit from adjunct exchange transfusion is seen in patients in Asia due to differences and the processes and structure of health care systems, differences in the virulence and anti malarial sensitivities of *P. falciparum* strains in different geological regions or differences in host's abilities to deal with disease as a result of shared genetic factors.

CONCLUSION

Most meta-analysis suggest there is no survival benefit from adjunct use of exchange transfusion in severe malaria but there are lot of single case reports which suggest its advantage in prognosis. Until a correctly designed randomised control clinical trial is conducted adjunct exchange transfusion can be considered in all subjects who are critically ill with caution.

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