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Short Communication

Therapeutic Red Cell Exchange (RCE) and Its Clinical Utilisation

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ABSTRACT

There are many case reports and studies available in the medical literature that emphasise the importance of erythrocytapheresis usage in treatment of severe sickle cell anaemia and severe malarial infection. In the present study therapeutic red cell exchange was performed in two cases of homozygous sickle cell disease and one case of severe malarial infection. In case one and two the red cell exchange was performed to prevent the perioperative complications in sickle cell disease. In the third case the procedure was performed as an adjunct therapy to reduce the parasitic index of severe malarial infection. The study concludes that with one cycle of RCE patient's pathological RBCs such as HbS in sickle cell disease has come down drastically and the patient underwent successful hip transplantation procedure without complications. In the case of malarial infection therapeutic red cell exchange was helpful in rapid reduction of the parasitic load. However, the patient couldn't survive due to multiorgan failure.

KEYWORDS: Red cell exchange; Sickle cell disease; Multiorgan; Malarial infection.

INTRODUCTION

Red cell exchange is the replacement of a patient's RBC with homologous donor RBC and can be performed manually or automated. Red cell exchange has an advantage over simple transfusions i.e., patient RBCs are replaced without increasing haematocrit or exposing the patient to the risk of fluid overload or hyperviscosity [1]. Manual RBC exchange implies sequential phlebotomies and isovolumic replacement with crystalloid and donor RBC. On the other hand, automated exchanges were based on apheresis principle which separates RBCs from other blood components. Defective RBCs are selectively removed and replaced with donor RBCs and colloid or crystalloid solutions [2]. Automated apheresis machine has substantially facilitated the collection and replacement procedures. Based on clinical data, gender, age, height, weight, initial and final haematocrit, as well as average replacement fluid haematocrit and fluid balance instruments calculate exchange volumes [3].

However automated system allows determining the percentage of patients' remaining RBCs (fraction of remaining cells) which is of particular interest for the calculation of remaining pathological RBCs in patients with sickle cell disease and malaria and babesiosis. The introduction of an automated RBC exchange procedure substantially improves standardisation of the procedure and can be performed with similar results on recent apheresis devices. The main advantage of RBC exchange transfusion is rapid reduction of pathological RBCs without increasing haematocrit fluid overload reduced risk of iron accumulation particularly in patients requiring chronic transfusion therapy. The procedure is faster and associated with less hemodynamic stress for the patients. High cost, requirement for equipment's and trained apheresis staff are the main limitations of the procedure. Adequate vascular access is the other potential issue in the case of therapeutic exchange. In patients with long-term exchanges and children of young age, adequate vascular access might be an issue. Though peripheral venous access is used for majority of the procedures, some patients may also require permanent central venous catheter or arteriovenous fistula [4-6]. the anticoagulant of choice for RBC exchange transfusion is acid citrate dextrose. RBC exchange transfusions requires more PRBC transfusions so alloimmunisation, transfusion transmitted diseases and transfusion reactions are the common side effects associated with the procedure [7-9].

CASE 1

28-year-old patient Yemeni patient visited our hospital for hip replacement procedure for chronic avascular necrosis of hip joint. The patient was a known case of homozygous sickle cell disease. Hence the haematologist advised automated red cell exchange for this patient to avoid sickling related complications during the perioperative period.

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Immunohematology work-up

Blood grouping and antibody screening were performed on an semiautomated platform Biovue(ortho clinical diagnosis, USA) using column agglutination technique. Three cell panel (surgiscreen,OCD,USA) was used for antibody screening. The Patient's blood group was found to be O positive and anti-body screening was negative. The hemoglobin of the patient was 8.3 g/dl, so we transfused two units of O positive leukoreduced PRBCs on 2 consecutive days to raise the hemoglobin level to 10.3 g/dl before red cell exchange.

Red blood cell units

These RBC units were prepared from 450 ml whole blood collected in a TAB quadruple blood bag CPD/SAGM. All units were leukcodepleted by using the leukofilter (BioR max,Fresenius Kabi,Germany). All were of fresh units.

Automated red cell exchange

Very high HBS concentration of 89.5% alarmed the patient to undergo RBC exchange before surgical intervention. Automated RBC exchange was performed through double-lumen 13.5F catheter on apheresis machine, using standard TPE kit (Spectra Optia). Both the peripheral and femoral veins were used for the procedure with the inlet connected to the femoral vein and the outlet to the right median cubital vein. The machine has an inbuilt software programme version11 for performing RBC exchange. The patient details such as gender, height, weight, patient hematocrit and average hematocrit of donor RBC were entered into the system. Target hematocrit was kept at 27%. The fraction of sickled red cells to have remained in the patient circulation at the end of the procedure was kept as 25% as per the American society for apheresis guidelines. The machine calculated the patient's total blood volume as 4675 ml and red cell volume to be replaced as 3726 ml. Two third of the total red cell volume was replaced as nine O positive leukoreduced PRBC and one third as 500 ml saline. The ionised calcium levels were checked in between the procedure. The entire procedure duration was two hours, and it was uneventful.

Post red cell exchange therapy the Fraction of Red Cell (FCR) levels had come down to 24% and the patient underwent successful hip replacement within one week.

Patient follow-up

The patient underwent successful sequential hip replacements within one week after the procedure. The clinical course of the patient was uneventful.

CASE 2

Another 30-year-old Saudi national visited our hospital for hip replacement procedure for the chronic avascular necrosis of the hip joint. It is a known case of homozygous sickle cell disease and his HbS level was 85%. Since the HbS level was too high that the patient could not undergo general anaesthesia for the hip surgery, the patient was advised with red cell exchange therapy.

Immunohemataogical work

Blood grouping and antibody screening were performed on a semiautomated platform Biovue(Orth clinical diagnosis, USA) Using the column agglutination technique. Three cell panel (surgiscreen, OCD,USA) was used for antibody screening. The patient's blood group was found to be B positive and anti-body screening was negative.

Red blood cell units

These RBC units were prepared from 450 ml whole blood collected in the TAB quadruple blood bag CPD/SAGM. All units were leukodepleted by using the leukofilter (BioR max,Fresenius Kabi,Germany) All were of fresh units.

Automated red cell exchange

Therapeutic red cell exchange was done using the Spectra Optia apheresis machine. Both the peripheral and femoral veins were used for the procedure with the inlet connected to the femoral catheter 13.5F and the outlet to the right median cubital vein. The patient details such as gender, height, weight, patient haematocrit and average haematocrit of donor RBC were entered into the system. Target haematocrit was kept at 27%. The fraction of sickled red cells to have remained in the patient circulation at the end of the procedure was kept as 25%. The machine calculated the patient's total blood volume as 5570 ml and red cell volume to be replaced as 4064 ml. Two third of the total red cell volume was replaced as ten B positive leukoreduced PRBC and one third as 500 ml saline.

Post red cell exchange therapy the FCR levels had come down to 21% from 85% and underwent successful hip replacement procedure.

Patient follow-up

The patient underwent successful sequential hip replacements within one week after the procedure. The clinical course of the patient was uneventful.

CASE 3

Therapeutic red cell exchange was performed as adjunctive therapy in this case of post liver transplant patient with severe life threatening plasmodium falciparum infection.

Immunohemataogical work

Blood grouping and antibody screening were performed on a semiautomated platform Biovue (Orth clinical diagnosis, USA) Using column agglutination technique. Three cell panel (surgiscreen, OCD, USA) was used for antibody screening. The patient's blood group was found to be A positive and anti-body screening was negative.

Red blood cell units

These RBC units were prepared from 450 ml whole blood collected in the TAB quadruple blood bag CPD/SAGM. All units were leukodepleted by using the leukofilter (BioR max,Fresenius Kabi,Germany) All were of fresh units.

Automated red cell exchange

Therapeutic red cell exchange was carried out in a mechanically ventilated patient at liver transplantation ICU. Both the peripheral and femoral veins were used for the procedure with the inlet connected to the femoral vein and the outlet connected to the right median cubital vein. The patient details such as gender, height, weight, patient haematocrit and average haematocrit of donor RBCs were entered into the system. Target haematocrit of the patient was kept at 31%. The fraction of red cells to have remained in the patient circulation at the end of the procedure

was kept as 25%. The machine calculated the patient's total blood volume as 5062 ml and red cell volume to be replaced as 3293 ml. Two third of the total red cell volume was replaced as 12 units of A positive leukoreduced PRBC and one third as 200 ml saline. The ionised calcium levels were checked in between the procedure. The complete blood count of the patient was checked during the procedure, since the platelet count was low platelet transfusion was given through the central line. The patient's haemoglobin level was checked after the procedure and was found to be 8.3 g/dl. The parasite index of the patient came down to 2-4% from 16% immediately post procedure. Unfortunately, patient succumbed to severe falciparum malarial infection with multi organ dysfunction syndrome.

DISCUSSION

Sickle cell disease is an autosomal recessive disease caused by nucleotide substitution of thymine for adenine in the sixth codon of the gene of beta globin chain leading to replacement of glutamic acid by valine at this site. This mutation leads to alteration in the surface charge of haemoglobin molecule (HbS), thus promoting the formation of lengthy polymers (gelation), when in deoxygenated state. At the cellular level this leads to the conversion of normal biconcave disc shaped RBCs to sickle shapes. For the most part, the process of HbS gelation and RBC sickling is a reversible process, but after repeated episodes of sickling and unsickling red cells become irreversibly sickled RBCs. These sickled RBCs have been shown to have abnormal interactions with the vascular endothelial cells, plasma proteins, coagulation factors, neutrophils and platelets leading to inflammation, oxidant damage, hence leading to excessive stimulation of coagulation system. These sickled RBCs' abnormal adherence to vascular endothelium causes increased transit time in micro circulation and enhances likelihood of Vaso-occlusion. Nitric oxide, an important vasodilator synthesised by vascular endothelium [10], is reduced in sickle cell disease due to its scavenging by free haemoglobin released from the destroyed RBCs. These also contribute to vaso-occlusive crisis in sickle cell disease.

Transfusion therapy and hydroxyurea are the current pillars of sickle cell disease management [11-13]. The main objectives of transfusion therapy are:

A) Correction of anemia.

B) Reduction of diseased sickle haemoglobin.

C) Suppression of defective RBC production and HbS synthesis.

D) Reduction of hemolysis.

The decision of simple versus exchange transfusion depends on current haemoglobin, steady state of haemoglobin level of the patient's pre-existing anaemia, percentage of HbS as well as general clinical condition [14]. In patients with pre transfusion anaemia below their individual haemoglobin baseline values , simple transfusion might be the best and cheapest option targeting post transfusion haemoglobin not exceeding 10 g/dl. While RBC exchange transfusion are indicated in patients with an increased HbS without severe anaemia compared to the baseline haemoglobin level. RBC exchange transfusion is the standard treatment in sickle cell patients with history of acute stroke and is clinical options for other acute complications of sickle cell disease.

Surgical interventions to treat problems associated with persistent or acute organ dysfunctions are relatively common in sickle cell disease [15]. Surgery and anesthesia are associated with increased risk of sickle cell disease complications in the perioperative period. TAPS (Transfusion alternative preop in sickle cell disease) study clearly demonstrates preop transfusions are associated with four-fold decrease in perioperative complications such as acute coronary syndrome [16]. Various regimens have been used in clinical practice that includes partial/full exchange transfusion or simple transfusion either immediately prior to surgery or two weeks prior to surgery to maximise oxygen carrying capacity of transfused blood.

It was observed in the study that one episode of exchange transfusion led to a dramatic reduction of HbS percentage, i.e., from 89.5 to 17.7% in the first case and 85 to 25% in the second case. RCE was performed prior to the hip replacement surgery and procedure underwent successfully. None of these patients showed presence of any allo or auto antibodies during the anti-body type and screen procedure.

Malaria remains significant and is associated with considerable mortality despite adequate treatment. While a majority of the patients with acute malaria have relatively low parasitic infestation approximately 10% of patients are classified as severe cases with high infectious load [17,18]. In these cases, the therapeutic aim is to rapidly reduce the parasitic load. Red cell exchange is used as an adjunct therapy in severe malarial infection and it has at least three beneficial effects:

1. Rapid reduction of parasitemia.
2. Improvement of rheological properties of the blood and oxygen delivery.
3. Reduction of intra vascular haemolysis and cytokines.

RBC exchange in malarial patients has been introduced more than 40 years ago for patients with severe parasitemia (more than 10%) mostly with plasmodium falciparum. Its efficacy as a primary therapeutic choice remains controversial since high quality evidence from randomised control trials is missing. Final judgement on the risk to benefit ratio of this adjunct therapy for severe malaria infection is not possible to date. In our study, we observed a reduction in the parasitic index from 16% to 2-4% with one episode of red cell exchange.

CONCLUSION

Erythrocytapheresis and RBC exchange transfusions are efficient treatment modalities in a patient with pathologically altered RBCs without significant side effects. Red cell exchange is an effective alternate treatment modality in sickle cell disease with complications such as stroke, acute coronary syndrome and acute pain crisis. Preoperative exchange transfusions in patients with sickle cell disease prevent complications associated with surgery and anaesthesia.

In severe malarial infection, RBC exchange reduces the parasite load to a certain extent and reconstituting reduced oxygen transport capacity without serious side effects.

The majority of the indications of red cell exchange transfusions are based on few studies in the literature. But decisions must be made depending upon the individual patient situations, availability of equipment and trained personal.

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