Blood Transfusion Therapy in Anaemias Benefits vs Complications

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INTRODUCTION

THE DEMAND for blood and its products has been ever increasing since the concept of blood banking and investigations in methods of preservation of blood were introduced (1). New techniques in medicine, surgery, oncology and now transplantation have given an important role for transfusion of blood and its products and have put some pressure on hospital blood banks. At Salmaniya Medical Centre, of the total blood transfusions, approximately 50 to 55% blood transfusions are required in the patients with indication of anaemia. In anaemias blood transfusion is not a definative therapy and its indications are limited.

Though ready availability of blood is a remarkable scientific and administrative achievement, it is at best supportive in anaemias. It is a form of short-lived tissue transplantation given to provide temporary support to a critically ill patient. It also is not without risk and may be expensive for the patient.

INDICATIONS FOR TRANSFUSION

The purpose of blood transfusion in anaemias is to improve the oxygen carrying capacity of the blood and to improve the stability of the circulatory system in situations where blood volume has been reduced considerably and imperils the patient. Generally, marrow failure, haemolysis and blood loss are three major causes of reduced blood volume and oxygen transport. The clinical variations of these indications are many (Table II). In anaemias, usually the compensatory mechanism involves increased release of oxygen to the tissues as a result of tissue acidosis caused by accumulating lactate and pyruvate and increased cardiac output. Therefore, mildly anaemic patients do not require blood transfusions. Blood transfusions are usually unnecessary in blood loss upto the volume of 1 to 1.5 litres if volume is replenished by colloids or other non-red cell fluids. Mendelson (2) has shown that a healthy young man can lose upto 50 percent of his red cell volume and yet not become oxygen deficient when colloids and other fluids were used to treat hypovolaemia.

Use of whole blood has very limited value in anaemic patients because of the dilution of red cells and the presence of sodium, potassium, citrate, ammonia, formed elements, plasma proteins, potential allergens and waste products. It is imperative therefore to use red cells concentrates when transfusing an anaemic patient. In situations where anaemia is associated with bleeding as in disseminated intravascular coagulation or leukaemias, it is probable that red cell concentrates are used supplemented by platelets and coagulation factor concentrate.

Every gram of haemoglobin in an adult carries 1.34 ml of oxygen at an oxygen tension (PO_2) of 100 mm of Hg. Thus, each 100 ml of arterial blood contains about 20 ml of oxygen. Usually a minimum of 250 ml of available oxygen is sufficient for normal basal metabolic needs of the body each minute. This means that a reduction of 50% is just enough to carry normal basal metabolic functions without leading to tissue hypoxia. Similarly, a reduction of Hb to 8g/l will allow basal metabolic function without tissue hypoxia or symptoms from anaemia under resting conditions.

Therefore, the general assessment of the patient and his Hb level is an essential preliminary step before serious consideration can be given to blood transfusion therapy. For patients presenting with symptoms of weakness, orthopnea and anginal attacks and in whom the Hb is very low (less than 6 - 8 gm/dl) transfusion therapy may be the treatment of choice where anaemia cannot be cured by administration of haematinics or other means of treatment are not available. In patients with Iron and B^{12}/Folic acid deficiency, transfusion is rarely required unless the subject is seriously ill or it is necessary to prepare the patient for surgery at an early date.

In thalassaemia major, where specific therapy is not available, chronic transfusions are unavoidable. Many reports (3 and 4) confirm that this is a logical approach which follows the pioneering work of Wolman (5). He suggested that children maintained at a high Hb level show better all-round growth and development and fewer complications of disease. Patients on low transfusion protocols require a disproportionately large amount of blood. This is because the blood volume is grossly expanded to perfuse the enormously expanded bone marrow which is attempting

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futilely, to compensate the anaemia. High transfusion protocols allow the expanded marrow to regress and the pathologically increased volume to fall. This will reduce the blood requirement and maintain a relatively high level of Hb. Recently, supertransfusion therapy along with transfusion of young red cells has been shown to be effective in decreasing the transfusion requirement and rate of iron accumulation (6). At Salmaniya Medical Centre, amongst anaemic patients, approximately 26% of transfusions are received by thalassaemic patients (Table I). This high percentage may probably be due to the fact that most of our patients are on low transfusion protocols. If supertransfusion protocols are adapted in these patients, the total blood requirement may be reduced. However, such a protocol needs adequate and reliable supply of blood, alliance between the blood bank, clinician and voluntary donation service.

In aplastic anaemia, acquired autoimmune haemolytic anaemias, sickle cell anaemia and refractory anaemias, blood transfusion has an important role to play, but its requirement will vary from patient to patient.

It is not necessary to maintain normal haemoglobin level if patient is able to undertake normal activity at a low Hb and is free of distress. Achievements in marrow transplantation have considerably reduced the chronic transfusion requirements in aplastic anaemias. However, in autoimmune haemolytic anaemias (AIHA), one must avoid transfusion if at all possible, since the autoantibodies will interfere with the compatibility testing and make it difficult to detect coexisting alloantibodies and increase the risk of acute haemolytic transfusion reaction. Autoantibodies will also result in a markedly shortened survival of donor red cells. However, if transfusion is required, washed red cells or leucocyte poor red cells are advantageous in avoiding antibodies developing against leucocytes and platelets. Patients with sickle cell anaemia usually adapt themselves to the chronic anaemic state and transfusion therapy is not often required in them unless patient has an aplastic or vaso-occlusive crisis. Lanzkowsky et. al. (7) have suggested that there are advantages of partial exchange transfusion during vaso-occlusive crisis and reduce the risk of iron overload. It should however be remembered that simple transfusion may equally be effective in alieviating in vivo sickling (8). 15% of blood transfusions are required for these patients in our hospital.

Asymptomatic patients with chronic illnesses like malignancy, uraemia, rheumatoid arthritis, liver diseases etc. may temporarily improve after transfusion but in these patients compensatory mechanisms become effective despite very low haemoglobin levels and patient remains asymptomatic (10). Transfusion should be used only as last resort, since transfused blood may suppress erythropoiesis and will increase the risk of hepatitis (9). It is unnecessary to fully correct the anaemia by transfusion prior to surgery. If present, symptoms in such patients are often due to underlying disease of which anaemia is merely a sign (10). Usually such patients have achieved an equilibrium between red cell production and destruction and blood transfusion only serves to alter this equilibrium temporarily. In our hospital, blood requirement in this group is approximately 30 - 35%.

Indications of transfusion are not clear in paroxysmal nocturnal haemoglobinurea (PNH), pure red cell aplasia, leukaemia and severe myelofibrosis (11). Patients with leukaemia, lymphomas and other malignancies may need packed cell transfusions specially while undergoing therapy.

SINGLE UNIT TRANSFUSIONS

It is not precisely known how many patients receive a single unit transfusion at the Salmaniya Medical Centre. The authors have observed quite a number of surgical and obstetric patients receive this treatment. Their haemoglobin levels are often relatively high. It is recognised that, since an adult donor can give approximately 450 to 500 ml of blood without significant effect, then it is inappropriate to transfuse patients with a single unit of blood. Graham-Stewart (12) considered that single unit transfusion should not constitute more than 5% of blood used in an adult general hospital and has suggested the criterias for adequate and conservative use of red cells (Table III). Myhre (13) when reviewing the occurance of single unit transfusions in U.K. showed concern at the number of surgical and obstetric patients treated in this way. In obstetric patients the transfusions may lead to alloantibody formation and stimulation, and perhaps endanger future pregnancies.

The rate and amount of blood transfused is guided by the clinical status of the patient. Usually a relatively slow transfusion is preferred in anaemic patients, unless patient is shocked due to massive blood loss. During the first 10 to 30 minutes of transfusion, a slow drip (5ml/min) should be used. Such a rate allows the transfusion to be stopped immediately at the first symptoms or signs of a transfusion reaction. Thereafter, the rate is increased. The subject who is

TABLE I

Blood Transfusions in various Anaemias at Salmaniya Medical Centre (1982 - 83)

Anaemias	*Percentage*
1. Thalassaemia	26.2
2. Chronic disorders, nutritional deficien-cies, anaemias of uncertain aetiology	27.0
3. Sickle cell anaemias	15.0
4. Anaemia with pregnancy (other than thalassaemia and sickle cell anaemia)	8.9
5. Patients on haemodylasis	5.0
6. Patients undergoing surgery	4.9
7. Haemolytic anaemias (other than thalassaemias and sickele cell anaemia)	4.8
8. Malignancies	3.4
9. Leukaemias	3.7

Based on blood bank records

TABLE II

Indications of Transfusion Therapy in Anaemias

Invariably

Thalassaemia Major

Severe haemolytic disease of the newborn.
(exchange transfusions)

Commonly

Aplastic anaemia

Refractory normoblastic anaemia

Leukaemia

Paroxysmal nocturnal haemoglobinuria (in crisis)

Acquired autoimmune haemolytic anaemia.

Occasionally

Agnogenic myeloid metaplasia

Pure red cell aplasia
(when unresponsive to other therapy)

Sickle cell anaemia (in aplastic or vaso-occlusive crisis)

Hereditary haemolytic anaemias due to enzyme deficiency.

Rarely

Anaemia secondary to chronic disease

Deficiency anaemias (in severely ill)

TABLE III

Criteria for Adequate and Conservative Use of Red Cells
(Graham – Stewart, 1960)

1. Single unit transfusion should not be given to adults.
2. Anaemia not due to acute blood loss should not be treated with transfusions unless it is drug resistant.
3. Patients dyeing of incurable diseases should be transfused only if the anaemia is symptomatic and if its correction will be followed by a period of enjoyable existence.
4. Preoperative transfusion is indicated by the emergency and not the expediency of the operation.
5. Massive acute blood loss requires rapid and adequate replacement of red cells and plasma.
6. Moderate acute blood loss does not require transfusion of red cells unless it is causing or is likely to cause significant symptomatic anaemia.
7. Post-operative transfusion is indicated more by the extent of the residual pathology than by the presence of anaemia.

severely anaemic, in cardiac failure should receive no more than 7ml/Kilo/hour (28). The use of concentrated (packed) red cells in severely anaemic patient is the management of choice because it enables the desired increase of haemoglobin to be achieved by transfusing small volume and meets the immediate needs. Monitoring of central venous pressure may be necessary in these patients.

Complications of Transfusion Therapy

Due to meticulous care taken in blood banks, complications occur in a small percentage of patients who receive blood products. They are sometimes serious and occasionally cause death. Therefore, no transfusion should be administered unless the benefits to be gained outweigh the risks involved, and not until simpler and safer therapy has proved ineffective or impossible under the circumstances. The most common complication of transfusion therapy is transmission of infection.

A. HEPATITIS

Viral hepatitis is still the most serious post-transfusion complication. Even now exact criteria for the diagnosis of post-transfusion hepatitis have not been established. Generally, the definition for diagnosis of acute anicteric post-transfusion hepatitis is made with the observation, between 14 and 180 days after transfusion, of two consecutive elevations (at least 5 days apart) of the recipient's serum alanine amino-transferase level in the absence of another possible causative factor such as congestive heart failure, alcohol and certain drugs that can mimic or simulate viral hepatitis. Both transaminase elevations must be at least two standard deviations above the geometric mean value for healthy persons. Icteric hepatitis may be diagnosed if the recipient's total serum bilirubin level exceeds 2.0 mg/dl (14). However, recent studies have failed to support this definition (15).

Hepatitis A virus is now recognised as insignificant in post-transfusion hepatitis. Hepatitis B surface antigen (HBsAg), a marker of the presence of hepatitis B virus, until recently was the major cause of post-transfusion hepatitis (16). In patients receiving repeated blood transfusions such as children with thalassaemia, the incidence of HBsAg has been shown as high as 10.6% (17) and HBsAb 94% (18). Recently, Al-Adnani et.al. (19) suggested that jaundice in thalassaemic children may not always be due to haemolysis. In the United States 60 - 90% of cases now involve Non-A and Non-B or type C virus as the cause of post-transfusion hepatitis (15)

Despite routine screening of HBsAg by radioimmunoassay in an attempt to reduce the incidence of Hepatitis-B associated disease, it has been shown that HBsAg negative blood can still transmit disease when positive for antibody to hepatitis B core antigen (HBcAg) or incompletely characterized cytomegalovirus and Epstein-Barr virus (20).

Major risk factors responsible for post-transfusion hepatitis include the number of units transfused and the use of blood from high risk paid donors. However, Alter et.al. (21) showed a marked reduction in the prevalence of type B post-transfusion hepatitis and reduction in the mortality as a result of antigen screening of donor blood in the United States. This group also demonstrated a progressive fall in the prevalence of type B disease by a shift from commercially to voluntarily donated blood.

Serologic requirements for the etiologic diagnosis of type B hepatitis include the appearance of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (Anti-HBs), or hepatitis B core antibody (anti-HBc) or any combination of these, not explained by passive transfer via transfusion. The absence of serologic markers indicative of active hepatitis A and B infection and the presence of liver enzyme abnormalities as defined above are taken as presumptive evidence of 'non/A, non-B' virus hepatitis, a classification of hepatitis that remains at present a diagnosis of exclusion.

High risk blood componants such as pooled plasma carry the risk of hepatitis. There have been conflicting reports of whether freezing or washing of red cells eliminate post-transfusion hepatitis or substantially decrease post-transfusion hepatitis. Bryant (22) found no case of hepatitis after transfusion of more than 3000 units of frozen erythrocytes. On the other hand, Haugen (23) reported that during a 52 months study period in which 31,125 units of whole blood componants were transfused, 56 patients developed post-transfusion hepatitis (non-A and non-B in 95%). In 37 of these patients, frozen or washed red cells were used. The other infections transmitted by transfusion include syphilis, malaria, toxoplasmosis, brucellosis, cytomegalovirus E.B. virus and Chaga's disease.

B. IRON OVERLOAD

The second complication of transfusion therapy related to anaemias is iron overload in patients with chronic anaemia who require repeated transfusions. It is possible to maintain a child with

transfusion dependant thalassaemia in excellent health throughout childhood by the use of supertransfusion regime. However, by the age of 18 years, the patient will have accumulated a minimum of 60 gm of iron intravenously and probably more through intestinal absorption. These patients sometimes die in second or third decade of life due to cardiac failure secondary to iron deposition in the heart. There is much of evidence which favour the use of desferrioxamine B by continuous I/V or sub-cutaneous infusions in patients of iron overload (24, 25, 26).

C. HAEMOLYTIC REACTIONS

Haemolytic reactions due to blood group incompatibility may be immediate or delayed. A major reaction will often begin with when the first few millilitres are transfused. The patient complains of back pain, tightness in the chest, breathlessness and headache. Fever, flushing and a fall of blood pressure may be associated signs. Later on, jaundice, oliguria and anuria may develop. There are about 400 different red cell antigens which have been identified but in practice only two immunologic systems are important — ABO and Rh. Procedural error in grouping, crossmatching and incorrect labelling of patient blood samples at bed side and identification of correct patient as recipient may result in immunologic transfusion reactions. Meticulous care and painstaking attention should be given to avoid these problems. Sensitization against one or more blood group antigens is another complication in patients receiving multiple blood transfusions. After the Rh antigen D, the red-cell antigens most likely to sensitise the multi-transfused patient are C, c, E, Kell, FyA, Lu^a and Lu^b. Such antigens complicate the cross-matching procedure and therefore accurate genotyping should be carried out before the transfusion is started.

D. FEBRILE REACTIONS

Other complication is febrile, non-haemolytic reactions caused by the in-vivo destruction of transfused leucocytes. Though mild and short-lived, these often occur in patients with multiple transfusions. Leucocyte poor red cell preparations are usually indicated in such patients who need further transfusions. Polesky (26) has used an automated batch-wash procedure (IBM 2991 Blood Cell Processor) and reported a consistently high yield of red cells when removing an average of 92% leucocytes in each unit of blood stored for upto 12 days before washing. Revill and Gregory (27) have been able to remove 86% of leucocytes from blood stored 14 to 21 days.

SUMMARY

Indications for transfusion therapy in anaemias are very limited and it is necessary in each case to determine whether the likely benefit outweighs the risks. Transfusion therapy is a supportive measure but is potentially hazardous. It should not be regarded as an innocuous procedure. The diagnosis should be established wherever possible unless the patient is critically ill. Sagacious consultations may be necessary between clinicians and blood bank in avoiding the risks of blood transfusions.

ACKNOWLEDGEMENT

We are thankful to Dr. T. Agnew, Chairman, Department of Medicine and Dr. K.V. Nadkarni for their valuable comments on the article. We are also thankful to Miss Fakhriya for technical assistance and Mrs. R. Nair for typing the manuscript.

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INTERNATIONAL SYMPOSIUM ON ISCHAEMIC HEART DISEASE RECREATION CENTRE AUDITORIUM ARMED FORCES HOSPITAL, RIYADH KINGDOM OF SAUDI ARABIA

PROGRAMME

19th Rabii Al Thani **22nd January 1984**

09.10 FIRST SESSION
Chairman : Dr. David A. Price Evans, M.D., D.SC., Ph.D., F.R.C.P.

09.10 "What Causes Ischaemic Heart Disease"
Professor W.A. Littler, M.D., F.R.C.P.

09.50 QUESTIONS

10.00 BREAK

10.15 "Primary and Secondary Prevention"
Dr. D.A. Chamberlain, M.A., M.D. (Cantab)., F.R.C.P.

10.55 QUESTIONS

11.05 "The Significance of Hypertension"
Dr. J.C. Petrie, M.B.Ch., F.R.C.P., M.R.C.P. (Ed).

11.45 QUESTIONS

11.55 PANEL DISCUSSION

12.15 BREAK

13.30 SECOND SESSION
Chairman : Dr. Muayed Al Zaibag, M.B., Ch.B., M.R.C.P.

13.30 "Management of Acute Myocardial Infarction"
Dr. E. Mercer, M.D., F.R.C.P.(c), F.A.C.C.

14.10 QUESTIONS

14.20 "Coronary Artery Spasm in Ischaemic Heart Disease"
Dr. E.G. Davies, M.A., M.B. (Camb)., M.R.C.P.

14.50 QUESTIONS

15.00 BREAK

15.20 "New Trends in the Management of Ischaemic Heart Disease"
Dr. W. Willis, M.D., F.A.C.C.

16.00 QUESTIONS

16.10 PANEL DISCUSSION

20th Rabii Al Thani **23rd January 1984**

08.15 THIRD SESSION
Chairman : Dr. M. Al Fagih, M.B., Ch.B., F.R.C.S.

08.15 "The Role of Coronary Arteriography in Ischaemic Heart Disease"
Dr. Muayed Al Zaibag, M.B., Ch.B. M.R.C.P.

08.50 QUESTIONS

09.00 "The Role of Myocardial Revascularisation in Ischaemic Heart Disease"
Dr. C.N. Oakley, M.D., F.R.C.P., M.R.C.S., F.A.C.C., L.R.C.P.

09.40 QUESTIONS

09.50 BREAK

10.10 "Myocardial Revascularisation : Surgical Review"
Dr. M. Al Fagih, M.B., Ch.B., F.R.C.S.

10.50 QUESTIONS

11.00 PANEL DISCUSSION

11.30 CLOSING ADDRESS :
Dr. Rashid Al Kuhaymi, M.B., Ch.B., F.R.C.S.