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REVIEW

Transfusion in Haemoglobinopathies

Review and recommendations for local blood banks and transfusion services in Oman

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نقل الدم في أمراض الدم الوراثية

مراجعة و توصيات لبنوك الدم المحلية وخدمات نقل الدم في عمان

أروى زكريا الريامي و شاهينا دار

ABSTRACT: Sickle cell disease and homozygous β-thalassaemia are common haemoglobinopathies in Oman, with many implications for local healthcare services. The transfusions of such patients take place in many hospitals throughout the country. Indications for blood transfusions require local recommendations and guidelines to ensure standardised levels of care. This article summarises existing transfusion guidelines for this group of patients and provides recommendations for blood banks and transfusion services in Oman. This information is especially pertinent to medical professionals and policy-makers developing required services for the standardised transfusion support of these patients.

Keywords: Hemoglobinopathies; Sickle Cell Disease; Thalassemia Major; Blood Transfusion; Blood Banks; Oman.

الملخص: يعتبر مرض الخلايا المنجلية والثلاسيميا النوع بيتا المتماثل من امراض الدم الوراثية الشائعة في عمان، والتي لها العديد من الآثار على خدمات الرعاية الصحية المحلية. تتم عمليات نقل الدم لهؤلاء المرضى في العديد من المستشفيات في جميع أنحاء البلاد. تتطلب محددات نقل الدم عمل توصيات وإرشادات محلية لضمان معايير موحدة من الرعاية. تلخص هذه المقالة المبادئ التوجيهية لنقل الدم الحالية لهذه المجموعة من المرضى وتقدم توصيات بشأن بنوك الدم وخدمات نقل الدم في عمان. وتعد هذه المعلومات ملائمة بشكل خاص للمهنيين الطبيين وصانعي سياسات تطوير الخدمات المطلوبة لدعم نقل الدم العياري الموحد لهؤلاء المرضى.

الكلمات المفتاحية: امراض الدم؛ مرض فقر الدم المنجلي؛ الثلاسيميا العظمى؛ نقل الدم؛ بنوك الدم؛ عمان.

Sickle cell disease (SCD) and transfusion-dependent thalassaemia, also known as thalassaemia major (TM), are complex haemoglobinopathies common in Oman, with estimated carrier prevalence rates of 5.8% and 2.2%, respectively.[1,2] The rate of SCD is 3.7 per 1,000 live births and, in a community-based survey of 6,342 children, the prevalence rates of SCD and homozygous β-thalassaemia were reported to be 0.2% and 0.07%, respectively, among children under five years of age.[2] This high prevalence can partly be explained by the previous endemic of *Plasmodium falciparum* malaria in the country and other parts of the Mediterranean region, the Middle East, Africa, India and Southwest Asia.[3,4] An additional factor is the high prevalence of consanguineous marriages in Oman.[5] A previous study on the genetic epidemiology of the sickle haemoglobin (HbS) mutation showed that the three major haplotypes—Benin (typical and atypical), Arab-Indian and Bantu—coexist in Oman, reflecting the influence of gene migration in the past from neighbouring countries.[6]

The management of SCD and TM has a strong economic impact on the available national health services and the quality of life of the local population, raising the need for immediate public health action.[7] A hospital-based study of ≤12-year-old Omani children with SCD reported a severe morbidity profile, defined as either six or more vaso-occlusive crises, hospitalisation for 11 days or longer, three or more blood transfusions or a life-threatening event, such as a haemoglobin (Hb) level of <5 g/dL, acute chest syndrome (ACS), acute splenic sequestration crises, septicaemia or stroke.[8] Another study of thalassaemic children aged 5–18 years old found that those with higher pre-transfusion haemoglobin levels (i.e. ≥9 g/dL) and those who received red blood cell (RBC) transfusions at intervals of over three weeks had better overall scores according to the Pediatric Quality of Life Inventory™.[9] Low scores in the school function domains were associated with pre-transfusion Hb levels of <9 g/dL and increased transfusion frequency (every ≤3 weeks).[9] The former has been attributed to fatigue, general weakness and decreased mental alertness. Transfusion is also

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associated with risks of alloimmunisation which has been reported among 31.6% of Omani patients with SCD.[10] Moreover, according to unpublished data, the rate of alloimmunisation is 9.3% among TM patients in Oman.

Clinical manifestations and optimal treatment modalities differ for patients with SCD and TM. Nevertheless, RBC transfusion is an important component in the management of both conditions. Patients with TM require life-long RBC transfusions for survival, while those with SCD require transfusions in specific clinical settings.[11] Moreover, transfusion-related complications, such as acute and delayed transfusion reactions, alloimmunisation and iron overload, can create additional challenges. For patients with SCD, the medication hydroxyurea is indicated in different settings, including recurrent moderate-to-severe pain crises, a history of severe and/or recurrent ACS and symptomatic chronic anaemia, among others.[12] This article summarises the existing literature and recommendations for transfusing patients with SCD and TM and discusses the potential impact of these recommendations on local blood banks and transfusion services in Oman. However, it is important to note that these recommendations serve only as a guide and should not replace clinical judgment in individual situations. Consultation with a haematologist with expertise in managing SCD and TM patients is advised.

Transfusion in Sickle Cell Disease

Transfusions in SCD patients can occur in either acute care settings or as part of long-term transfusion therapy. In some cases, transfusions are strongly recommended, while in others insufficient evidence exists to support use of this procedure. However, it is worth mentioning that few randomised clinical trials (RCTs) are available to direct clinicians as to when a transfusion should be considered.[13–16] For patients in whom the indications for transfusion have limited evidence, the decision as to whether to transfuse should be based on a clinical assessment of the individual patient by an experienced team.

ACUTE SETTINGS

Acute Stroke

Transfusions are often beneficial in the management of ischaemic stroke. Urgent transfusion is required in patients with acute neurological symptoms, with the aim of achieving an HbS proportion of <30%.[17,18] While this often requires an exchange transfusion, an initial top-up transfusion may be necessary, depending on the patient's Hb level.[17] It is important to avoid hypervolaemia during the procedure and to keep the patient's post-transfusion Hb level at 10 g/dL, as a high haematocrit (Hct) level may worsen the neurological insult.[17,18] No data are available at present to support transfusion in the acute management of haemorrhagic stroke or in preventing its recurrence.[18] However, transfusion is warranted and may be a life-saving procedure for other SCD complications, such as acute haemolytic anaemia, aplastic crises, ACS and splenic and hepatic sequestration crises.[18]

Acute Anaemia

Top-up transfusions may be necessary for SCD patients admitted with acute anaemia, especially symptomatic patients, those who show signs of imminent or established cardiovascular compromise or when accompanied by reticulocytopaenia suggestive of a parvovirus B19 infection.[17] The threshold level for transfusion will depend on the patient's baseline Hb level and clinical status, while the target Hb level should be the patient's own steady-state Hb level.[17] An exchange transfusion is also indicated for patients with exacerbated anaemia due to acute multiorgan failure and mesenteric syndrome.[18,19]

Acute Chest Syndrome

In cases of suspected ACS, it is advisable to ensure the availability of blood for an exchange transfusion ahead of time, as acute respiratory failure can develop rapidly and a blood transfusion can be life-saving.[18] Depending on the clinical severity of the case, either a simple or exchange transfusion may be warranted. In SCD patients with an Hb level of <9 g/dL, an early top-up transfusion may be all that is necessary. However, an exchange transfusion is recommended for patients who have an initial Hb level of >9 g/dL, those who do not respond to an initial simple transfusion or in cases of severe or rapid ACS progression as manifested by an oxygen saturation level of <90% despite supplemental oxygen, increasing respiratory distress, progressive pulmonary infiltrates and/or declining Hb levels despite having undergone a simple transfusion.[12,18,20] Although a target HbS proportion of 30–40% is often used, it is more important that the physician be guided by the patient's clinical response.[20]

Splenic and Hepatic Sequestration Crises

In SCD patients with splenic and hepatic sequestration crises, transfusions should be performed cautiously with small volumes following fluid resuscitation; this is so as to avoid hyperviscosity due to the return of the sequestered RBCs to the circulation system.[18] For this reason, it is recommended that Hb levels of 8 g/dL

are not exceeded. A splenectomy should be considered in patients with recurrent episodes of two or more splenic sequestration crises.[18]

Vaso-Occlusive Crises

Transfusion is not recommended for SCD patients with uncomplicated painful vaso-occlusive crises, if no other indications for transfusion are present.[12] However, it should be considered if the baseline Hb level has dropped substantially or there is haemodynamic compromise or concern of impending critical organ complications.[18] Hydroxyurea is recommended as a first-line treatment for repeated painful crises, although it may take some time before the effect is perceived; transfusions can therefore be useful in the interim.[18]

Priapism

To date, no RCTs have been conducted to evaluate the efficacy of transfusion in acute priapism. For priapic episodes, transfusions are not recommended as an immediate treatment modality; early interventions should instead include analgaesia and oral or intravenous hydration. However, if the episode lasts for longer than four hours, SCD patients may require transfusion in preparation for a shunt or drainage procedure under general anaesthesia, if the latter is recommended by a urologist.[12] Long-term transfusion has been shown to reduce the incidence of priapism.[21] Patients may also benefit from an exchange transfusion to reduce the HbS proportion if there is no response to these procedures.[13,18]

Other Indications

There is insufficient evidence to support the benefit of blood transfusions in the management of SCD patients with leg ulcers, pulmonary hypertension, end-stage liver disease or progressive sickle cell retinopathy.[18] It is therefore important to consult an experienced haematologist for a full risk assessment and to create a plan for managing such patients. However, an exchange or simple transfusion may be useful in cases of severe sepsis.[18,22]

LONG-TERM SETTINGS

Stroke Prevention

Long-term RBC transfusion is the mainstay of primary and secondary ischaemic stroke prevention in SCD patients.[18] Multiple RCTs in paediatric SCD patients have assessed the benefit of transfusions in primary stroke prevention and in the secondary prevention of silent cerebral infarcts.[14,21,23] Annual transcranial Doppler (TCD) ultrasound assessments are recommended for children with SCD from the age of two years, based on the benefits of regular transfusions among children with raised cerebral blood flow velocities (≥200 cm/second).[14,17] In these chronic transfusion programmes, the aim is to maintain an HbS proportion of <30%.[17,18] These transfusions should be continued throughout child-hood as a significant number revert to high TCD velocities or develop overt stroke after the transfusions are discontinued.[18,23]

In children with SCD and high cerebral blood flow velocities without new magnetic resonance imaging-related changes, severe magnetic resonance angiography (MRA)-defined cerebral vasculopathy or prior transient ischaemic attacks, hydroxyurea should be considered after initiating a regular transfusion programme for primary stroke prevention for a minimum of one year. Data from the Transcranial Doppler with Transfusions Changing to Hydroxyurea (TWiTCH) trial indicated that hydroxyurea was efficacious and not inferior to blood transfusions for primary stroke prevention in children.[15] However, transfusions should be continued in patients with severe MRA-defined cerebral vasculopathy and are effective in reducing recurrence among SCD children with silent cerebral infarcts.[21] No studies have been conducted to assess the efficacy of regular transfusions for primary stroke prevention in adult SCD patients or in patients undergoing long-term transfusion programmes since childhood. Moreover, TCD has not been validated in adults; therefore, its utility in assessing stroke risk in this patient group is unknown.[18]

According to the results of the Stroke with Transfusions Changing to Hydroxyurea (SWiTCH) RCT, monthly transfusions and iron chelation were more effective than hydroxyurea in preventing ischaemic stroke recurrence among SCD children with a history of stroke, with seven stroke events occurring in the hydroxyurea group compared to no events in the transfusion group.[16] Long-term transfusions to maintain an HbS proportion of < 30% rather than hydroxyurea are therefore recommended for secondary stroke prevention. Transfusions may be needed indefinitely, although they do not completely abolish the risk of recurrence; as such, risk factors should be reviewed regularly with patients and/or their parents or guardians.[18] As with primary stroke prevention, there is no evidence of the benefit of transfusions for secondary stroke prevention among adult SCD patients. However, based on paediatric trials, long-term regular transfusions are recommended to maintain an HbS proportion of <30%.[18] Other indications for long-term transfusions include patients with contraindications for hydroxyurea and those with progressive organ failure, recurrent ACS or vaso-occlusive crises not prevented by hydroxyurea.[17,18] The specific management approach for these patients should be decided on an individual case-by-case basis.

Preoperative Indications

There is currently no consensus as to which SCD patients require preoperative transfusions.[17] The Transfusion Alternatives Preoperatively in Sickle Cell Disease trial provides the most compelling evidence to support the use of preoperative transfusions.[13] In this trial, patients undergoing low- or medium-risk surgeries were randomised to receive either a preoperative transfusion—a simple transfusion if Hb levels were <9 g/dL or an exchange transfusion if Hb levels were ≥9 g/dL—or no transfusion at all. Patients in the non-transfused group had significantly higher rates of complications and serious adverse events, particularly ACS, as compared to the transfused patients.[13] While the optimal method of transfusion is debatable, currently available evidence indicates that simple transfusions are not inferior to exchange transfusions.[13,24]

Vichinsky *et al*. reported that conservative transfusions aiming to raise Hb levels to 10 g/dL were as effective in preventing postoperative complications as aggressive exchange transfusions intending to reduce HbS proportions to <30%.[24] Both simple (in patients with Hb levels of <9 g/dL) and exchange (in patients with Hb levels of ≥9 g/dL) transfusions for an Hb target level of 10 g/dL are recommended for SCD patients undergoing low- (e.g. adenectomies and dental procedures) or medium-risk (e.g. tonsillectomies and abdominal or orthopaedic surgeries) procedures. However, exchange transfusions are recommended for patients undergoing high-risk surgeries such as cardiovascular operations.[18] For patients requiring emergency surgeries, as long as they are not unduly delayed, simple transfusions can be given preoperatively with the aim of achieving an Hb level of 10 g/dL.[18]

Pregnancy

Prophylactic transfusions should be considered in pregnant patients with previous or current medical, obstetric or fetal SCD-related complications, patients who were previously taking hydroxyurea for severe SCD and those with multiple-gestation pregnancies.[18] However, routine prophylactic transfusions are not recommended during pregnancy as there is insufficient evidence to substantiate their role.[25,26] Women receiving long-term transfusions for other indications should continue regular transfusions throughout their pregnancy.[27]

Transfusions in Homozygous β-Thalassaemia

Homozygous β-thalassaemia is a genetic disorder that affects the synthesis of β-globin chains, leading to chronic anaemia and ineffective erythropoiesis due to imbalanced globin synthesis. It can be broadly categorised clinically as either TM or thalassemia *intermedia* (TI). In TM, Hb production is markedly reduced and regular transfusions from infancy are critical to keep the patient alive.[28] In TI, patients can survive without lifelong regular transfusions; however, certain indications may necessitate transfusion.[29] Transfusion therapy in β-thalassaemia is effective in supplying normal erythrocytes and suppressing ineffective erythropoiesis to a large extent.[30]

THALASSAEMIA MAJOR

Regular blood transfusions every 3–4 weeks are the standard therapy for TM.[11] Once an infant is diagnosed with homozygous β-thalassaemia, close monitoring from the age of three months is required to detect clinical signs indicative of the need to initiate regular transfusions, with Hb levels checked on at least a monthly basis. The current guidelines of the Thalassemia International Federation for initiating regular transfusions include severe anaemia (<7 g/dL on two occasions one to two weeks apart) or Hb levels of >7 g/dL accompanied by inappropriate fatigue, poor feeding, developmental delay or regression or symptoms of heart failure, after excluding contributing causes such as infections.[11] Other reasons to initiate transfusion regardless of Hb levels include a failure to thrive, progressive splenomegaly, fractures, clinically-significant extramedullary haematopoiesis and/or the appearance of thalassaemic *facies*.[11,31]

It is important to reassess infants after the initial transfusion; if Hb levels fall again, it is reasonable to assume long-term dependency necessitating a regular transfusion programme.[31,32] The decision to begin regular transfusions usually occurs within the first two years of life.[11] Where possible, this decision should not be delayed beyond three years as the risk of alloimmunisation increases with age, as does the difficulty of finding suitable RBC units.[31] Regular transfusion programmes in children should aim for trough pre-transfusion Hb levels of 9–10.5 g/dL.[31,33] Occasionally, TM patients with cardiac disease, extramedullary haematopoiesis and/or inadequate bone marrow suppression benefit from higher transfusion Hb thresholds of 11–12 g/dL, although there is limited evidence to support this approach.[31]

Once initiated, transfusions are usually given every 2–4 weeks.[31] With older patients, a transfusion every two weeks may be necessary to maintain a trough Hb level of 9–10.5 g/dL.[31,34] A splenectomy is sometimes indicated for patients with hypersplenism and for those with high transfusion requirements.[35] A transfusion record should be maintained and

include the volume or weight of administered units, the Hb/Hct level of the units, the patient's weight, the occurrence of any transfusion reactions and if any RBC antibodies have formed.[11,36] Transfusion requirements are likely to increase in pregnant patients.[27] In patients undergoing elective surgery, a preoperative assessment should include the transfusion history and pre- and perioperative transfusions should be planned to ensure an Hb level of 10–12 g/dL. Post-transfusion Hb levels should not be higher than 14–15 g/dL to avoid the risk of hyperviscosity and stroke.[11]

THALASSAEMIA *INTERMEDIA*

Patients with TI have mild or moderate haemolytic anaemia and can maintain an Hb level of >7 g/dL without regular transfusion support.[32] These patients may have worsening anaemia, particularly upon exposure to physiological stress or other triggers. The decision to transfuse in TI cases depends on several factors beyond Hb level.[37] Children should be monitored carefully for evidence of thalassaemic features resulting from ineffective erythropoiesis, bone marrow expansion, a reduction in growth or progressive splenomegaly. If there is evidence of any of the above, the child should receive regular transfusions until they have reached their full adult height and the bones are fused.[31] Older children, adolescents and adults should continue to be monitored regularly for any indications that may arise. Some adolescents require transfusions because of poor growth, delayed/absent puberty or complications due to bone expansion.[38]

During adulthood, periodic transfusions may be indicated during acute episodes of anaemia, especially for pregnant patients, those suffering from infections or prior to surgery.[38–40] Transfusions should be considered in the management of certain conditions, for primary prevention in high-risk populations and for secondary prevention in some settings. Indications include the development of thrombotic or cerebrovascular disease, pulmonary hypertension with or without secondary heart failure, extramedullary haematopoietic pseudotumours and leg ulcers.[38] Although transfusions have been shown to protect against these complications, increased risks due to iron overload, endocrinopathies and alloimmunisation should be taken into account when deciding the optimal time to transfuse such patients.[41] During pregnancy, transfusions should be considered in mothers with TI and worsening anaemia or if there is evidence of fetal growth retardation; the aim should be to maintain a pre-transfusion Hb level of >10 g/dL.[42] Once the transfusion programme is initiated, patients should be closely monitored and therapy should be individually tailored to meet their needs.[38] Some patients with TI may need to continue regular transfusions. Such a decision should be made in consultation with a specialist with experience in managing TI patients.[31,43]

Alloimmunisation

A major complication of transfusion in patients with SCD and homozygous β-thalassaemia is the risk of alloimmunisation. Risk factors for alloimmunisation are complex and involve at least three contributing elements: (1) RBC antigenic differences between the blood donor and the recipient, (2) the recipient's immune status and (3) the immune-modulatory effects of the transfused RBCs on the recipient.[44] Increased systemic inflammation and dysregulation of the immune system may also be responsible for alloimmunisation in SCD patients.[45,46] Several studies have shown a rising risk of alloimmunisation among SCD patients corresponding with an increase in the number of transfusions received.[47–49]

Red cell alloimmunisation presents a challenge to blood banks, especially when trying to find compatible blood for affected patients. Following alloimmunisation, serious complications may occur such as life-threatening delayed haemolytic transfusion reactions and transfusion delays due to difficulties in finding compatible units. Alloimmunisation further triggers autoantibody formation in transfused SCD and thalassaemic patients, with a cumulative incidence of 6–10%.[44,50–52] Although the development of these autoantibodies is less frequent compared to the development of alloantibodies, they can cause clinically significant haemolysis and difficulty in obtaining compatible RBC units.[53] The most common antibodies observed in patients with SCD and homozygous β-thalassaemia are those against the rhesus (Rh), particularly the C and E antigens, and the Kell (K) systems.[54] Other antibodies that tend to develop are against the Kidd, Duffy, Lewis and MNS systems.[54]

Reported alloimmunisation rates in SCD vary. In patients with SCD receiving only ABO- and D-matched RBCs, the rate of alloimmunisation ranges from 18% to as high as 76%.[47,48,52,55–59] The exact rate is dependent on many factors, including the extent of RBC antigen matching, the degree of homogeneity between the recipients' and donors' ethnic backgrounds and the frequency of transfusion. The Rh and anti-K antibodies comprise over two-thirds of the RBC antibodies encountered.[60] The risk of alloimmunisation has been shown to be reduced to 5–11% with additional limited antigen phenotype matching for C, E and K antigens and to 0–7% with extended phenotype-matched RBCs.[45,59,61,62] Therefore, compatible RBCs which have

been fully cross-matched for all Rh and K antigens is the minimum recommended standard of transfusion care for patients with SCD.[17,18,60,63] Extended RBC phenotypes should ideally be performed in the first year of life, before the start of a regular transfusion programme.[31,36] If the patient has been recently transfused, DNA-based methods can be used to determine the predicted phenotype.[64]

If alloantibodies are identified, the RBCs used for the transfusion should be negative for the corresponding antigen. Extended RBC phenotype-matching for Duffy, Kidd and MNS antigens has also been recommended to reduce the risk of alloimmunisation against these antigens.[65] However, this can be problematic, as such additional testing increases costs and is dependent upon the availability of the necessary inventory, laboratory personnel and resources. That being said, establishing a limited inventory of O group RBCs negative for the C, c, E, e and K antigens in blood banks may be cost-effective, as well as decreasing the need to process blood on an urgent basis and shortening the time to transfusion.[66] Molecular methods are particularly useful in patients with recent transfusions and no baseline phenotype as well as patients with autoantibodies and complex alloimmunisation.[67] Comparative studies show that alloimmunisation and delayed haemolytic transfusion reactions are less frequent in automated RBC exchange transfusions compared to chronic simple transfusions, despite increased blood exposure.[68–70] However, this finding may be due to the fact that some patients receive RBCs with a higher degree of phenotype-matching during automated exchange transfusions.[71] These types of transfusions also have the advantage of limiting iron overload in these patients, a variable which has been associated with increased morbidity.[72]

According to various reports, the rate of alloimmunisation among TM patients ranges from 5.2–37%, although it appears to be lower among more homogeneous populations.[44,60,73–78] This variation has been linked to the extent of the homogeneity between the donor-recipient populations, divergent testing methods and differences in the patient population of each study.[75,79] Other factors include the use of non-leukoreduced RBC units and differences in providing antigen-matched blood.[67] The lower rates of alloimmunisation in TM compared to SCD are probably due to the fact that transfusions for thalassaemic patients begin at a relatively younger age and are continued on a regular basis. No consensus exists on the provision of extended antigen-matching in TM patients due to limited data on the impact of RBC-matching policies on alloimmunisation rates in such patients. Research has been published regarding the impact on the rate of alloimmunisation of providing limited C, E and K antigen-matched RBCs in comparison to ABO and D antigen phenotype-matched RBCs.[44,80] Nevertheless, this approach has been questioned considering the low rate of alloimmunisation in this population.[79] However, clinical standards recommend antigen-matching for all Rh and K antigens in order to minimise the risk of alloimmunisation in patients with homozygous β-thalassaemia.[11,31,34,36]

Alloimmunisation is more common in TI than in TM.[80,81] Risk factors for alloimmunisation in TI patients include a history of splenectomy, pregnancy and patients who have never been transfused or have been only minimally transfused before.[31,39,43,82] Previous research has demonstrated the value of providing extended RBC antigen-matching for the Rh (C, c, E and e), K (K, Kp^a and Kp^b), Kidd (Jk^a and Jk^b), Duffy (Fy^a and Fy^b), S and s antigens in reducing alloimmunisation rates among patients with TI.[82] As RBC alloimmunisation is common in TI, phenotype-matched units are recommended.[31,39,43,82]

The association between leukoreduction and RBC alloimmunisation has not been well established.[75] It has been hypothesised that leukoreduction lowers the frequency of RBC alloimmunisation.[83] Hussein *et al*. reported a higher rate of RBC alloimmunisation among patients receiving non-leukoreduced RBCs compared to those always receiving leukoreduced RBCs.[84] Due to its benefit in reducing the risk of febrile reactions and cytomegalovirus transmission, leukoreduction has become an increasingly common procedure and standard of care in many centres caring for patients with SCD and thalassaemia.[67,85]

Other Transfusion Requirements

For both SCD and TM patients, the RBC units to be transfused should be fresh (between <7–14 days old) and, in the case of SCD patients, negative for sickle cells.[17,31] If possible, a hepatitis B immunisation course should be completed prior to the first transfusion. Serological testing for hepatitis A, B and C and HIV should also be performed to obtain baseline values. It is recommended that all patients who lack serological immunity to the hepatitis B virus begin a vaccination programme and show evidence of immunity before the start of the transfusion.[17,34,36] Following the start of the transfusion programme, patients should be regularly screened for hepatitis and HIV.

Table 1: Recommendations for blood banks and transfusion services in Oman

Category	Recommendation
Phenotyping and antigen-matching	• Extended RBC phenotyping for Rh (C, c, E and e), K (K, Kp^a and Kp^b), Kidd (Jk^a and Jk^b), Duffy (Fy^a and Fy^b), S and s antigens should be performed before the start of a regular transfusion programme, ideally within the first year of life. If this is not available, then extended RBC phenotyping can be performed on a pre-transfusion sample after a minimum of three months following an RBC transfusion. • If the patient has been recently transfused, DNA-based methods can be used to determine the predicted phenotype. • RBC antigen matching for Rh and K antigens is recommended as a standard of care in non-allo-immunised SCD cases due to the increased risk of alloimmunisation to these antigens. • RBC antigen matching for Rh and K antigens is recommended in TM patients to minimise the risk of alloimmunisation. • Extended RBC antigen matching is recommended in TI patients since they have an increased risk of alloimmunisation compared to TM patients. • If alloantibodies are identified in SCD or TM patients, extended RBC phenotype matching is recommended. The selected units should be serologically cross-match compatible with the patient's serum and tested to ensure negativity to the corresponding antigens. • If extended phenotype matching is unavailable, transfused RBCs in alloimmunised patients should be at the very least serologically cross-matched and tested to ensure negativity to the corresponding antigen.
Screening	• Antibody screening should be performed before each transfusion.
Serology and immunity	• Serological testing for hepatitis A, B and C and HIV should be performed at baseline and every six months thereafter. • All patients who do not have serological immunity to the hepatitis B virus should start a vaccination programme and show evidence of immunity before the start of the transfusion, if possible.
Monitoring	• Due to the risk of iron overload and related cardiac, hepatic and endocrinological complications, patients should be closely monitored and chelation therapy should be initiated when indicated.
Blood bank records	• Every patient should have a complete and up-to-date blood bank record of antigen typing, antibodies and transfusion reactions. This information should be used to assess the blood type and phenotype needed prior to each transfusion.
Other	• RBC units for both SCD and TM patients should be fresh (<7–14 days old). • RBCs for SCD patients should be sickle cell-negative. • Pre-storage leukoreduced RBC components should be used as much as possible for patients with SCD and homozygous β-thalassaemia. • An automated RBC exchange transfusion facility is recommended in centres that care for larger numbers of SCD patients as this transfusion method is a more efficient way to perform exchange transfusions and reduces the degree of iron overload.

RBC = red blood cell; Rh = rhesus; K = Kell; SCD = sickle cell disease, TM = thalassaemia major; TI = thalassaemia intermedia.

Recommendations in Oman

In Oman, patients with haemoglobinopathies are managed and treated at various regional hospitals throughout the country. Implementation of the aforementioned recommendations will necessitate that all blood banks have the required testing facilities for extended RBC phenotyping, antibody screening and identification. In addition, healthcare institutions will need to have access to pre-storage leukoreduced RBC units, maintain an accurate and comprehensive patient record database and develop facilities for automated RBC exchange transfusions. Accordingly, the development of an interconnected blood bank system throughout Oman is recommended, from which information on blood groups, baseline extended phenotypes and existing allo- and autoantibodies can be shared between different blood banks. Until these measures are implemented, patients should be provided with an up-to-date transfusion card detailing their blood group, baseline extended phenotype, existing antibodies and date of antibody formation, if any, as well as baseline Hb levels for patients with SCD. Such a measure would aid in ensuring that these patients receive adequate management and standard levels of care when presenting to different hospitals in Oman.

Moreover, an active donor recruitment programme is required to ensure the availability of blood for Omani patients with SCD or thalassaemia. A limited antigen-negative RBC inventory should be established in major hospitals treating patients with these haemoglobinopathies. A centralised database of phenotyped blood donors accessible to all blood banks is also needed to allow the identification of suitable RBC units for transfusing potentially problematic alloimmunised patients. In addition, a frozen blood facility of rare RBC phenotypes for use in difficult situations should be established, along with molecular testing methods in major centres to facilitate the immediate management of complex alloimmunised cases. Table 1 summarises recommendations for blood banks and transfusion services in Oman.

Conclusion

Major haemoglobinopathies such as SCD and TM have specialised transfusion requirements. This article provides various recommendations to enhance existing blood banks and transfusion services in Oman, based on a review of the current literature regarding the transfusion practices for such patients. The provision of such services will require additional funding, administrative support, expertise, training and human resources, as well as the development of an active donor recruitment programme and interconnected blood bank system within the country.

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