

Pathophysiology and Perioperative Care of Sickle Cell Patients, towards a better outcome: A Literature Review

Dr. Nabeel shamsan¹, Dr. Elficki Yahya², Abdullah Alamry³, Tarnim Alghamdi³, Faisal Aljedani³, Ekram Tahir³

¹Chairman Internal Medicine Department, King Abdul Azziz Hospital, Jeddah, KSA

²FRCP-UK, Consultant Internal Medicine. King Abdul Aziz Hospital, Jeddah KSA

³Research Assistant and Coordinator, Internal Medicine. King Abdul Aziz Hospital Jeddah, KSA
profelficki@yahoo.com

Abstract: Sickle cell anemia (SCA) primarily affects people with African, Mediterranean, South American, Middle Eastern, and Indian ancestry. Sickle cell disease is an inherited hemoglobinopathy that develops from a genetic mutation and the production of a dysfunctional variant of hemoglobin. A number of physiological disturbances encountered during the perioperative period (blood loss, hypotension, acidosis, and hypoxia) may induce "sickling" of the biochemically altered hemoglobin, producing painful microvascular occlusion, hemolytic anemia, and impaired oxygen delivery. The only available curative therapy requires bone marrow transplantation. The purpose of this article is to review the pathophysiology of sickle cell disease and the pertinent preoperative, intraoperative, and postoperative care of patients with the disease. Persons with sickle cell anemia are more likely to undergo surgery than are the general population during their lifetime. As surgery exposes patients to many of the factors that are known to precipitate red blood cell sickling, persons with SCD undergoing surgery require specific clinical care to prevent peri-operative sickle cell related complications.

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1. Introduction

In the first part of this literature review, clinical features and complications found in patients with Sickle cell Disease are discussed. Secondly, the therapeutic approaches used with this population are reviewed and finally the diagnostic techniques and main precautions to be taken in the preoperative period are discussed. This review aims at providing information about the impact of surgery on sickle cell anemia patients and guidelines on the most important measures that should be taken to ensure such patients are well cared for in the peri-operative period in order to reduce the occurrence of complications.

Sickle cell disease (SCD), sickle cell anaemia (SCA) or drepanocytosis, is a type of chronic haemolytic anaemia, characterised by an abnormality in the oxygen-carrying haemoglobin molecule in red blood cells. This abnormality causes the cells to assume an abnormal, rigid, sickle-like shape, and is exaggerated under certain circumstances like dehydration, decreased oxygen tension, hypothermia, infections and others which shall be discussed further on. Sickling of red blood cells increases adherence of these cells to endothelium, therefore occluding the vessel and impeding the blood flow. (1,2)

Sickle cell anaemia primarily affects people with African, Mediterranean, South American, Middle Eastern, and Indian ancestry. Every year almost

300000 children are born with a form of sickle cell disease in these areas. (3,4)

This condition was first announced in in 1910 in the medical literature by James B. Herrick and in the middle of the 20th century by Nobel prize-winner Linus Pauling who made it the first disease where the exact genetic and molecular defect was uncovered. (4)

Persons with sickle cell anaemia are more likely to undergo surgery than are the general population during their lifetime. (4) For example, cholecystectomy as a consequence of gallstones is more frequent in persons with SCD, as is hip arthroplasty in younger people as a result of avascular necrosis of the femoral head. Because surgery exposes patients to many of the factors that are known to precipitate red blood cell sickling, persons with SCD undergoing surgery require specific clinical care to prevent perioperative sickle cell-related complications. Even with meticulous care, approximately 25% to 30% of patients will have a postoperative complication. (5) In the first part of this review, clinical features and complications found in patients with SCD shall be discussed. Secondly, the therapeutic approaches used with this population will be reminded and finally, the diagnostic techniques and main precautions to be taken in the preoperative period will be discussed. This article aims at

providing information about the role of surgery in SCA and the most important measures that should be taken to ensure such patients are well cared for in the peri-operative period in order to reduce the occurrence of complications.

2. Materials and Methods

The present review is based on information from published research studies from the electronic searches through Cochrane, Medline and PubMed, and textbooks and downloaded relevant evidence based articles using respecified search terms and key words to identify randomised clinical trials, nonrandomised intervention studies and observational studies since the year 1999 to present. Information from reviews of current work and consultations with experts and health providers in the speciality of sickle cell disease in Saudi Arabia where the prevalence is high was also extracted.

3. Pre-Operative Typical Features and Symptoms

Several typical features and symptoms are specific to SCD and have to be diagnosed as early as possible and notably in the pre-operative stage. Sickle cell disease usually manifests early in childhood. For the first 6 months of life, infants are protected largely by elevated levels of foetal haemoglobin (Hb F), later on foetal haemoglobin is replaced by homozygous sickle haemoglobin (Hb S) which makes the condition evident, two major problems ensue, chronic haemolytic anaemia and tissue infarction.(6)

3.1. Vaso-occlusive Crisis

The most common clinical manifestation of SCD is vaso-occlusive crisis which occurs when the sickled red blood cells reduce microcirculation causing ischemic injury to the organ supplied and resulting in severe pain, there for pain crisis represent the most distinguishing clinical feature of sickle cell disease and constitutes the main cause of emergency department visits and hospitalizations for affected patients. (5,6,7)

Pain crisis is characterised by a sudden onset of severe pain and may last several hours to several days and ends as suddenly as it began. The frequency of these crisis is extremely variable from patient to patient.(6)

The pain can affect any body part and it often involves the abdomen, bones, joints, and soft tissue but can affect any parts of the body as well. It may present as dactylitis, priapism, acute joint necrosis or avascular necrosis, or acute abdomen. With repeated episodes of infarctions in the spleen, this organ becomes fibrosed resulting in gradual autosplenectomy predisposing the patient to life-threatening infections. The liver may also infarct and gradually progress to failure as well. Papillary

necrosis is a common renal manifestation of vaso-occlusion, leading to isosthenuria.(8)

Bone pain is often due to bone marrow infarction. During the first 18 months of life, pain involves the metatarsals and metacarpals later on pain often involves the long bones of the extremities, sites that engulf marrow activity during childhood. Proximity to the joints and occasional sympathetic effusions lead to the belief that the pain comes from the joint itself. With the decrease of marrow activity during adolescence, pain usually involve the vertebral bodies, especially in the lumbar region.(8)

These are the most common presentations found even though any area with blood supply and sensory nerves can be affected.

3.1.1. Triggers of Vaso-occlusive Crisis

Because deoxygenated haemoglobin S becomes semisolid, the most important physiologic trigger of vaso-occlusive crises is hypoxemia. This may be due to the presence of the patient in a high altitude area where oxygen is less concentrated in the air, acute chest syndrome or accompany respiratory complications.(4,6)

Dehydration can also trigger pain because haemoconcentration represents a common mechanism and acidosis results in a shift of the oxygen dissociation curve causing sickled haemoglobin to desaturate.(4,6)

Another common trigger is changes in body temperature, like hyperthermia due to fever after infection or hypothermia due to exposure low temperatures. Hypothermia represents an important precipitating factor as it causes peripheral vasoconstriction and resultant pain crisis.(4,6)

3.2. Acute Haemolytic Crisis

Anaemia, chronic or haemolytic in nature, is usually very well tolerated by SCA patients who present with an Hb level of 7-8 g/dL and are able to participate in daily activities although their tolerance and endurance for exercise is reduced. This Hb level is acceptable for SCD patients because Hb S has a low affinity to oxygen making oxygen extraction easier.(4,6) Few manifestations of anaemia are seen in these patients because they readily adjust by increasing heart rate and stroke volume. Acute haemolytic crisis is diagnosed when patients present with generalised jaundice, decreased haematocrit level and normocytic normochromic anaemia associated with reticulocytosis. Gall stones may also be seen in this case. When this crisis is concomitant with Glucose 6 Phosphate Dehydrogenase deficiency, this defines a hyper-haemolytic crisis.(6)

3.3. Aplastic Crisis

A serious complication of SCA is the aplastic crisis which is caused by infection with Parvovirus B-19. This virus causes fifth disease, a normally benign

childhood disorder associated with fever, malaise, and a mild rash.(9) This virus infects the bone marrow of the infected person resulting in impaired cell division for a few days. In people with SCD, the RBC lifespan is shortened to 10-20 days causing a very rapid drop in haemoglobin. In this case bone marrow recovers within 7-10 days causing brisk reticulocytosis.(6)

3.4. Acute Splenic Sequestration Crisis

As a life-threatening complication of homozygous SCA, it is rare in adolescents and adults due to progressive splenic fibrosis caused by repeated infarctions. This complication occurs mainly in infants and young children aged between 2 and 6 years old when the obstruction of the splenic venous outflow by sickled RBCs causes extensive pooling of blood in the spleen resulting in a sudden and massive enlargement of this organ, hypovolemia and even shock.(10) The spleen is then felt by palpation of the left hypochondrium, and associated with a rapid fall in haemoglobin and haematocrit. Major crisis is defined in literature by a fall in haemoglobin level to less than 6 g/dL requiring emergent whole blood transfusion whereas haemoglobin level of more than 6 g/dL indicates a minor episode that is self limited.(10)

The spleen is often affected with repeated acute sequestration crises or infection of an infarcted area with abscess formation.

Splenectomy is indicated for patients with repeated episodes of acute splenic sequestration crisis, large splenic abscess, a persistent massive splenomegaly after whole blood transfusion, or pancytopenia (thrombocytopenia, neutropenia and anaemia).(9)

3.5. Infections

Patients with SCD are more vulnerable to systemic bacterial infections due to hyposplenism and an inevitable auto-splenectomy due to repeated fibrosis which occurs in most patients.(10) They are also at greater risk of developing splenic abscess occurring secondary to infection of splenic infarcts. This association with SCA was first reported by Beet in 1949. A blood culture may be negative as patients may be on a course of wide spectrum antibiotics. Organisms that pose the greatest danger include encapsulated respiratory bacteria, particularly *streptococcus pneumoniae* associated with a high mortality rate.(11) Osteomyelitis should be considered when dealing with a combination of persistent bone pain and fever because a bone that is involved with infarct-related vaso-occlusive pain is prone to infection. *Staphylococcus* and *Salmonella* are the two most likely organisms causing osteomyelitis.(9,10)

Some radiological studies such as ultrasonography and computerised tomography scanning are indispensable in the diagnosis of some

conditions and can be used for guided percutaneous drainage.(10)

Susceptible patients should receive polyvalent pneumococcal and haemophilus influenzae vaccines as a prophylaxis or as early as possible, two weeks pre-operatively and at the beginning of the post-operative period of patients who underwent emergent splenectomy. Long-term penicillin prophylaxis should be administered as well for 2 years after splenectomy to reduce the incidence of post-splenectomy sepsis.(12)

3.6. Avascular Necrosis

Infarctions cause vascular occlusion of the femoral and humeral head resulting in avascular necrosis (AVN). AVN of the femoral head presents a greater problem because of weight bearing. In patients aged 12 years or younger, management with analgesics, NSAIDs, and protected weight bearing usually results in healing and remodelling of the involved capital epiphysis due to the immaturity of their skeleton. This aims at the preservation of the joint despite the persistence of deformity, such as coma magna and cox plana. Painful secondary degenerative arthritis is caused by the flattening and collapse of the weight bearing femoral head.(5,13)

3.7. Acute Chest Syndrome

Acute chest syndrome is a major complication of SCD and consists of chest pain, fever, cough, dyspnea and leukocytosis. New pulmonary infiltrates are seen in the upper lobes on a chest radiography whereas adults present with multi-lobe and lower lobe infiltrations. In children, acute chest syndrome is usually due to infection such as pneumonia. Other aetiologies include rib infarction and fat embolism.(14)

Acute chest syndrome is a medical emergency and must be treated immediately in order to avoid developing acute respiratory distress syndrome. Affected patients should immediately receive oxygen with bronchodilators and broad spectrum antibiotics. Effective analgesia should be given to alleviate pain and whole blood transfusion may be considered in case of hypoxemia or severe anaemia. In case of respiratory failure the patient with require mechanical ventilation and intensive care unit admission for proper management.(10,14)

3.8. Hand-foot Syndrome

Young children with SCD may develop hand-foot syndrome, a dactylitis presenting as pain and soft tissue swelling of the dorsum of the hands and/or feet. The syndrome occurs suddenly between the age of 6 months and 3 years and lasts for 10-14 days. It is not seen after the age 5 years because haematopoiesis stops in the small bones of the hands and feet.(11,12)

3.9. Central Nervous System Involvement

Central nervous system involvement is most commonly seen in childhood and adolescence such as strokes causing different degrees of neurological deficit which is usually ischemic in children and hemorrhagic in adults. Hemorrhagic stroke is often caused by rupture of aneurysms that might be a result of vascular injury and tend to occur later in life. Hemorrhagic stroke is associated with a mortality rate of more than 29%.(4,5,10)

Rapid and excessive blood transfusion to a haemoglobin level of greater than 12 g/dL increases blood viscosity and can lead to stroke.(15) Depending on the location of the infarct different deficits are found such as hemiparesis most commonly or hemiplegia.(6,4)

3.10. Cardiac Involvement

Chronic anaemia and micro-infarcts affect the heart. Both ventricles and the left atrium are dilated, according to Nicholson et al, the prevalence of coronary artery ectasia in patients with SCD was 17.7%, compared with 2.3% for the unaffected population.(4,9,10) On examination, a systolic murmur radiating over the precordium is usually present.

3.11. Hepato-biliary Involvement

Hepato-biliary complications represent a major share of the complication encountered by patients with SCD due to repeated blood transfusions, sickling, cholelithiasis, choledocholithiasis and acute hepatic failure.

3.11.1. Hepatic Involvement

Haemolysis contribute to the elevation of direct and indirect bilirubin. Serum alkaline phosphatase is elevated in adults but rises further with crises. The abnormalities in liver function tests are exaggerated in vaso-occlusive crisis. Hepatic damage in SCD may be due to a variety of causes such as obstruction of sinusoids by sickled cells with subsequent hepatic infarction during vaso-occlusive episodes, cholelithiasis and cardiac failure. But by far the most common causes are those related to repeated blood transfusion such as haemosiderosis and viral hepatitis which lead to chronic liver disease.(10)

3.11.2. Hepatic crisis

Studies show that hepatic crisis affects 10% of patients with SCD admitted to hospital.⁵ Hepatic crisis is differentiated from viral hepatitis by transaminases levels that are higher than 1000.(10)

3.11.3. Acute Hepatic Failure.

Acute hepatic failure may be due to viral infection precipitating severe hepatic occlusive crisis which may result in coma or even death. Patients usually present with severe abdominal pain, generalised jaundice and tender hepatomegaly. Prothrombin time is very prolonged. Their treatment

consists of intravenous dextrose, oral neomycin, lactulose, vitamin K and packed cell transfusion.(10)

3.11.4. Cholelithiasis

Cholelithiasis is common with SCD, as chronic hemolysis with hyperbilirubinemia is associated with the formation of gall stones which may be asymptomatic or may present with repeated attacks of biliary colic or with acute cholecystitis. Common bile duct obstruction can occur. (10)

3.11.5. Choledocholithiasis

Choledocholithiasis occurs in 14% of patients with gall stones and 18% of patients undergoing cholecystectomy according to a study done by Schubert.⁵ Choledocholithiasis should be excluded by performing endoscopic retrograde cholangio-pancreatography in any patient with dilated biliary tree on ultrasonography. Endoscopic sphincterotomy that is performed to clear the common bile duct and laparoscopic cholecystectomy are minimally invasive surgeries that offer advantages over the conventional open method such as a short hospital stay and a decrease in wound-related complications including wound pain and infection. There for, the use of minimally invasive surgery is encouraged in any patient with SCD requiring surgical intervention in any centre with laparoscopic facilities.¹⁰

3.12. Gastrointestinal manifestations

3.12.1. Peptic ulceration.

Peptic ulcers are caused by a decreased mucosal resistance due repeated ischaemic infarcts secondary to sickling crisis. With a certain degree of vascular impairment, healing of the ulcer is often impaired. The rate of complications such as stenosis and haemorrhage is high.⁵ The diagnosis has to be confirmed early by gastroscopy which should be repeated after 6-8 weeks of intensive medical treatment to monitor the size of the ulcer and the response to medical therapy. A surgical option should be offered early for ulcers showing poor healing as mortality associated with complications such as bleeding and perforation is high.(10)

3.12.2. Ischaemic colitis.

Ischaemic colitis should be considered in any patient presenting with sickle cell crisis who develops severe abdominal pain, rectal bleeding and signs of peritonitis. The presence of thumb-printing on an abdominal radiograph or barium enema suggest ischaemic colitis. Initial management includes nasogastric decompression, broad-spectrum antibiotic therapy and haemodynamic support. Once high fever, marked leucocytosis and generalized peritoneal signs suggesting bowel infarction are seen emergent treatment is needed.(10)

3.13. Leg Ulcers

Leg ulcers are a usual complication in SCD with no malignant changes noted. The ulcers occur spontaneously or as a result of local trauma with subsequent infection and skin necrosis. Other precipitating factors include tissue hypoxia vessel occlusion by sickled cells, and increased venous pressure. The majority of ulcers are located at the lower third of the leg above the ankle, medially or laterally.(13)The ulcer causes painful limitation of joint movement with oedema due to venous and lymphatic impairments. To treat this complication the ulcer should be kept clean by regular daily dressings with a mild antiseptic, topical antibiotics or steroids and occasional debridement under local anaesthesia. studies show that the rate of healing can be increased by prolonged administration of zinc sulphate tablets for a period of 9 months. Surgical procedures such as skin grafts are alternatives.(10,13)

3.14. Renal Involvement

Isosthenuria results in a large loss of water, precipitating dehydration in SCD patients. Renal failure may ensue, usually preceded by proteinuria usually precedes renal failure which may happen in some cases as well as. nephrotic syndrome.(6,10)

3.15. Ocular Involvement

Ptosis results from para-orbital infarctions. Retinal vascular changes and proliferative retinitis also occur.(6,9)

3.16. Priapism

Priapism, a sustained and painful erection is a common complication and may lead to impotence mainly due to fibrosis.(6)

Priapism can be classified as prolonged if it lasts for more than 3 hours or as stuttering if it lasts for more than a few minutes but less than 3 hours and resolves spontaneously.(10)

Prolonged priapism remains a medical emergency.

3.17. Pulmonary Hypertension

Infarctions and micro thrombi affect the pulmonary blood flow causing a resultant deoxygenation of blood and therefore a relatively increased sickling process in affected patients and later on pulmonary hypertension may develop.

This is increasingly recognised as a serious complication of sickle cell disease, with an incidence as high as 31.8%.(5) Contributing factors to pulmonary hypertension are haemolysis, chronic hypoxia due to SCD, and pulmonary diseases such as asthma and acute chest syndrome.

Pulmonary hypertension is diagnosed by a regurgitant pulmonary jet velocity of more than 2.5 m/s by echocardiography.(16)

4. Therapeutic Approach

The therapeutic approach resumes the main pharmacological and non-pharmacological treatments generally used in the management of SCD patients.

4.1. Pharmacotherapy

Main lines of treatment of SCD include the following:

- Antimetabolites mainly Hydroxyurea which increases the level of haemoglobin F is given at a daily dose of 500 to 750mg reduces the frequency of painful crisis. (6,17)
- Opioid analgesics such as oxycodone, methadone, pethidine, morphine, fentanyl, nalbuphine, and codeine.(12)
- Non steroidal analgesics such as ketorolac, ASA, APAP, and ibuprofen.(12)
- Antibiotics depending on the organisms to be covered include, cefuroxime, amoxicillin, clavulanate, penicillin, ceftriaxone, azithromycin, or cefaclor (4)
- Vaccines against encapsulated organisms such as streptococcal, meningococcal and influenza. As well as all recommended scheduled childhood and adult vaccinations. (12)
- Iron chelating agents such as Desferrioxamine to overcome iron overload due to repeated blood transfusions. (6,9)
- Vitamins supplementation such as folic acid taken as 5mg daily to support the greatly increased RBC production. (4)

4.2. Nonpharmacologic therapy

Other approaches to managing SCD include the following:

- Stem cell transplantation can be curative. (18)
- Blood Transfusions are indicated for sudden, severe anaemia or when Hb falls 2g/dL or more compared to the patient's usual Hb level. Indications also include acute splenic sequestration crisis, aplastic crisis, haemolytic and hyper-haemolytic crisis and parvovirus B19 infection. (4,9)
- Partial exchange transfusions are indicated in cases of acute chest syndrome, priapism and CVA.(6)
- Physical therapy helps in order to regain mobility in patients with avascular necrosis of the femur. (4,13)

An expert panel has released evidence-based guidelines for the treatment of SCD, including a strong recommendation that hydroxyurea and long-term, periodic blood transfusions should be used more often to treat patients. Other recommendations include the following: (4,8,19)

- Use of daily oral prophylactic penicillin up to age 5.
- Annual transcranial Doppler examinations between the ages of 2 and 16 years in patients with sickle cell anaemia.

- Long-term transfusion therapy to prevent stroke in children with abnormal transcranial Doppler velocity (≥ 200 cm/s).
- In patients with sickle cell anaemia, preoperative transfusion therapy should be used to increase hemoglobin levels to 10 g/dL.
- Rapid initiation of opioids for the treatment of severe pain associated with a vaso-occlusive crisis.
- Use of analgesics and physical therapy for the treatment of avascular necrosis.

5. Peri-operative Management

This part aims at reviewing the general assessment and diagnostic measures, as well as the precautions to be adapted by the treating team when dealing with a SCD patient requiring a surgical intervention in order to minimise the risks of peri-operative complications. Even though the specifics of each patient and the wide clinical spectrum of this disease makes it difficult to establish a definitive applicable management.

5.1. Pre-operative Assessment

A general assessment of each patient is needed as early as possible in the pre-operative period in order to establish a general view of his condition. Laboratory tests and imaging studies are used depending on the clinical presentation and complaints of the patient.

5.1.1. Laboratory Tests

Laboratory tests used in patients with SCD include the following: (4,6)

- Haemoglobin electrophoresis confirms the diagnosis with the presence of homozygous Hb S.
- CBC count with differential and reticulocyte count
- Serum electrolytes
- Hemoglobin solubility testing
- Peripheral blood smear
- Pulmonary function tests including transcutaneous oxygen saturation. Preoperative evaluation of pulmonary damage is essential to predict perioperative risk of sickle events.
- Renal function such as creatine, BUN, and urinalysis.
- Hepatobiliary function tests such as ALT, AST, GGT and fractionated bilirubin.
- CSF examination should be considered after CT scanning in febrile children who appear toxic and in presenting with neurologic findings such as neck stiffness, Brudzinski or Kernig signs, and focal deficits.
- Blood cultures
- ABGs

- Secretory phospholipase A2 (sPLA2)
Based on the clinical presentation and these laboratory tests, the need for preoperative transfusion can be determined. (4)

5.1.2. Imaging studies

Imaging studies that aid in the assessment of sickle cell anemia in patients include the following: (4)

- Radiography such as a chest x-ray should be performed in patients presenting respiratory symptoms.
- MRI is useful for early detection of bone marrow changes due to acute and chronic bone marrow infarction, marrow hyperplasia, osteomyelitis, and osteonecrosis (9,13)
- CT scanning may demonstrate regions of osteonecrosis not apparent on plain radiographs in patients who are unable to have an MRI and to exclude renal medullary carcinoma in patients presenting with haematuria.^[20]
- Nuclear medicine scanning:^{99m}Tc bone scanning detects early stages of osteonecrosis;¹¹¹In WBC scanning is used for diagnosing osteomyelitis
- Trans-cranial Doppler ultrasonography can identify children with SCD at high risk for stroke. An abdominal ultrasonography is used to rule out cholecystitis, cholelithiasis, and to measure spleen and liver size.
- Echocardiography identifies patients with pulmonary hypertension and to exclude transfusional hemosiderosis by ventricular function assessment.
- Transcranial near-infrared spectroscopy or cerebral oximetry can be used for low cerebral venous oxygen saturation in children with SCD.(9)

5.2. Pre-operative Management:

Patients with SCD are usually admitted at least 48 to 72 hours before their elective procedure for hydration, packed red blood cell transfusion if needed and in order to teach and start incentive spirometry. (21)

Investigations such as a chest radiography, haemoglobin level, oxygen saturation, and pulmonary function tests give an idea of the degree of pulmonary pathology and whether it is a restrictive or reactive airway disease. (22) Renal assessment is an important preoperative objective since sickle patients have significantly lower blood pressure than the general population. We should then be aware of superimposed hypertension since it may result from renal failure. A rise in creatinine and proteinuria are suggestive of glomerular affection.(9)

After excluding any organ diseases, studies show that an important pre-operative measure is packed red blood cell transfusion in order to raise the haematocrit level and to increase the percentage of unaffected haemoglobin in blood before surgery. This measure contributes to better rheologic characteristics and increased oxygen carrying ability of erythrocytes resulting in the prevention of hypoxia and therefore prevent the occurrence of sickling crisis. (5,1) Although patients with SCD who receive blood transfusions are at increased risk of developing complications from allo-immunization, delayed hemolytic transfusion reactions and hyperhaemolysis. (23) Therefore, all blood transfusions should consist of sickle-negative blood. And patients with a history of febrile transfusion reactions should have leukocyte-reduced blood and should be given phenotypically matched blood peri-operatively to decrease the formation of new alloantibodies. (24)

The need for pre-operative transfusion is based on the overall clinical history of the patient and the type of surgery itself. There are two common techniques for preoperative transfusion: conservative and aggressive transfusion regimens. Conservative or simple transfusion aims to increase the haemoglobin level to 10 g/dL only. Whereas aggressive transfusion aims at decreasing the haemoglobin S level to less than 30% and to increase the haemoglobin concentration to approximately 10 g/dL. (1,5,25)

Simple or partial exchange transfusion should be strongly considered for patient with acute chest syndrome, priapism and organ damage prior to any procedure requiring general anaesthesia although the need for pre-operative transfusions must be individualised. (1,4)

Multicenter studies reported by Vichinsky *et al.* show that when aggressive transfusion was compared with the simple transfusion, it did not offer overall benefits, and by using a simple transfusion therapy complications related to transfusions in patients were decreased.⁹

Since dehydration represents an important risk factor for sickling crisis patients scheduled for surgery should be started on intra-venous fluids at least 12 hours prior to surgery. SCD patients should at least receive one and a half times the maintenance fluids while taking in consideration any additional losses. (1,9,13)

5.2. Intraoperative Management

During the operative period a good organisation of the surgical team is crucial. Additionally, the surgical procedure should be prepared meticulously by the multidisciplinary team which include a hematologist, pulmonologist, anesthesiologist, surgeon, and blood bank should be done in a centre specialised in sickle cell disease.

The most common intraoperative complications noted are excessive blood loss, followed by hypothermia. (5) That's why patients require extensive monitoring of cardiac rhythm, blood pressure, temperature, and continuous oxygen saturation measurement. (1)

Intraoperative care is focused on preventing potential sickling crisis, therefore hypoxemia, hypercarbia, hypovolemia (dehydration), hypervolemia (over-hydration) acidosis, and hypothermia should be avoided.

Proper hydration of the patient should be adjusted according to the procedure and to any pre-existing renal pathologies. (1) On another hand, patients with history of acute chest syndrome, asthma or with other respiratory pathologies should receive oxygen with or without bronchodilators in order to maintain blood oxygen saturation superior to 90% given that affected patients usually live with a relatively lower oxygen saturation than the general population. (22)

For patients with SCD, there are no absolute contraindications for sedations but anaesthesia care may be complex because of a risk of oxygen desaturation during intubation, which may induce sickling, therefore a minimum of 50% oxygen should be administered along with the anaesthetic agent. (1,26)

Studies demonstrate that the type of anaesthesia during surgery result in different outcomes. In fact, SCD related complications in the post-operative period were more frequent in patients who received regional anesthesia compared with those who received general anesthesia. (13) Surgical procedures are more difficult in patients with sickle cell disease since a meticulous control of oxygenation and fluid administration is needed. General anesthesia often is administered for these patients during surgical procedures resulting in a 10% risk of sickle cell crisis. (5) Another technique is found in medical literature using a combination of regional anesthesia for intraoperative and postoperative pain control and general anesthesia for surgery. (13)

Additionally, the circulating nurse should meticulously document and communicate with the surgeon and the anaesthesiologist regarding blood loss, even if the procedure is minor. Because SCD is a haematological disease, it is important to track blood loss and to watch the patient's haemoglobin closely in case he or she requires an intra-operative or post-operative blood transfusion, thus in order to avoid hypovolemia and shock. (1)

The circulating nurse should as well increase the ambient temperature in the OR to prevent hypothermia, which leads to a higher risk for blood sickling to occur. (24)

These patients also need active intraoperative warming, which usually consists of a combination of a warming blanket, humidifier, blood and fluid warmer, and heat lamp. Tourniquets should be minimised if not avoided to prevent aggregation of the sickled RBC's causing severe pain and venous occlusions. (1)

5.3. Post-operative Management

Similarly to the pre-operative period, post-operative management mainly consists of intravenous hydration, supplemental oxygen to prevent hypoxemia, intravenous antibiotics, chest physiotherapy, incentive spirometry and early mobilisation. Common complications noted in the early postoperative period with patients affected by sickle cell disease include acute chest syndrome (12%), vaso-occlusive crisis (9%), and less commonly, neurological and renal events. (5,13)

Laboratory test values including CBC count with differential and reticulocyte count, serum electrolytes, renal functions (creatinine, BUN) and hepatobiliary functions(ALT, fractionated bilirubin) should be evaluated and compared with the previous results obtained preoperatively and repeated daily. ABG's and blood cultures should be assessed in order to detect any abnormalities.

The nurse should continually monitor the patient's vital signs after surgery for hypothermia, infections, and dehydration. meticulous pain scoring and documentation should be done as well. (1)

Since sickle cell is commonly associated with painful crisis, close monitoring and pain scoring is an important aspect of post operative care. Effective and powerful analgesia such as morphine (regional analgesia in surgeries on upper and lower limbs could be considered) should be administered as early as possible in this period of care. (27) Pharmacological therapies such as non-steroidal anti-inflammatory drugs or acetaminophen should be given as well. Suitable antibiotic course should be started as prophylaxis and when infections occur. (1)

Additionally two litres per minute of oxygen administered by nasal cannula or by face mask should be given for at least eighteen to twenty-four hours post operatively and close pulse oximetry to keep saturation superior to ninety-two percent.

One and half times maintenance fluids should be administered intravenously or orally if tolerated while avoiding excessive hydration which may precipitate acute chest syndrome.(13)

Surgical patients should be encouraged to use incentive spirometry every 2hours, deep breathing, and early ambulation when it is allowed. (1)

As in the pre-operative and intra-operative period the room's ambient temperature should be monitored closely and increased to avoid

hypothermia. Thick blankets and stockings could be given to the patient as well. (1)

Affected patients remain psychologically fragile in periods requiring hospitalisation and surgeries, therefor close psychological support of the patient and his relatives should be organised, along with care education in order to prevent complications, ideally prior the patient's discharge back home. (1,4)

6. Conclusion

Sickle cell disease remains an important disease in some areas where proper management is crucial for the patient's well being and survival. Due to the clinical broad spectrum of this genetic disease a multi-disciplinary team is needed to manage this case with the best outcomes. Some serious complications of the disease require surgical intervention, electively or urgently, therefor this review aims at providing valuable informations and precautions in order to prevent and minimise complications occurring in the peri-operative period. Based on the current literature, adapted hydration, extensive oxygenation, avoiding temperature extremes, aggressive analgesia and adequate blood transfusions remain the major guidelines for the well-being of these vulnerable patients. There are still controversies regarding the types of blood transfusions, either simple or aggressive, and the best anaesthesia, either regional or general, that present the best outcomes and advantages for the patients. Ongoing studies will provide medical care givers with useful answer in the future.

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