REVIEW

Perioperative Management of Paediatric Patients with Sickle Cell Disease

KJ Sullivan[1, 2], J Dayan[1], M Reichenbach[3], M Irwin[2], A Pitkin[2], C Gauger[4], SR Goodwin[1], N Kissoon[5]

ABSTRACT

Patients with sickle cell disease (SCD) are prone to acute and chronic organ injuries that may necessitate surgical interventions earlier and with more frequency than non-SCD cohorts. They are also at an increased risk for perioperative morbidity and mortality because of the inherent pathophysiological derangements associated with SCD.

Perioperative outcomes are influenced by phenotype variability, end-organ injury and the variable risks of surgical procedures, as well as the availability of beneficial therapies, especially where resources may be limited. Safe and effective perioperative management relies on anticipation and avoidance of complications, which can be best achieved by collaboration among anaesthesiologists, intensivists, surgeons and haematologists. This review addresses potential perioperative complications and contemporary management to assist in the perioperative care of paediatric patients with SCD.

Keywords: Paediatric patients, perioperative management, sickle cell disease

Manejo perioperatorio de pacientes pediátricos con la enfermedad de células falciformes

KJ Sullivan[1, 2], J Dayan[1], M Reichenbach[3], M Irwin[2], A Pitkin[2], C Gauger[4], SR Goodwin[1], N Kissoon[5]

RESUMEN

Los pacientes con enfermedad de células falciformes (ECF) son propensos a lesiones agudas y crónicas de los órganos. Tales lesiones pueden requerir intervenciones quirúrgicas con mayor anticipación y más frecuencia que las cohortes sin ECF. Estos pacientes corren también un mayor riesgo de morbilidad y mortalidad perioperatorias debido a las inherentes alteraciones patofisiológicas asociadas con ECF. Los resultados perioperatorios son influenciados por la variabilidad del fenotipo, la lesión del órgano afectado, los riesgos variables en los procedimientos quirúrgicos, así como la disponibilidad de terapias beneficiosas, especialmente dónde pueda haber limitación de recursos. Un manejo perioperatorio seguro y eficaz tiene como base la capacidad para anticipar y evitar las complicaciones, lo que puede lograrse mejor mediante

From: [1]Department of Anesthesiology, Nemours Children Clinic and Wolfson Children Hospital, Jacksonville, Florida, United States of America, [2]Department of Anesthesiology and Congenital Heart Center, University of Florida, Gainesville, Florida, United States of America, [3]University of Central Florida, Orlando, Florida, United States of America, [4]Department of Hematology Oncology, Nemours Children Clinic and Wolfson Children Hospital, Jacksonville, Florida, United States of America and [5]Children's Hospital of British Columbia, University of British Columbia, Vancouver, Canada.

Correspondence: Dr KJ Sullivan, Department of Anesthesiology and Congenital Heart Center, University of Florida, 1600 SW Archer Road, PO Box 100254, Gainesville, FL 32610, United States of America. Email: ksullivan@anest.ufl.edu

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la colaboración entre anestesiólogos, intensivistas, cirujanos, y hematólogos. Este artículo aborda las posibles complicaciones perioperatorias y el manejo contemporáneo para ayudar a la atención perioperatoria de los pacientes con ECF.

Palabras clave: Pacientes pediátricos, manejo perioperatorio, enfermedad de células falciformes

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INTRODUCTION

Sickle cell disease (SCD), the most common inherited haemoglobinopathy, is associated globally with substantial morbidity and mortality. Further, the number of children born with SCD each year is expected to increase from 300 000 to 400 000 by 2050 (1). Surgery in children with SCD is hazardous regardless of the indication. The increased vulnerability compared with non-SCD patients postoperatively has been recognized for over 50 years (2–4).

The purpose of this review is to contextualize contemporary knowledge and assist the paediatric intensivist, anaesthesiologist, surgeon and haematologist in the management of paediatric patients with SCD in the perioperative period. We review the genetic defects in SCD, pathophysiologic derangements, acute and chronic complications of SCD, and perioperative assessment and management of children with SCD.

GENETICS

Normal human haemoglobin consists of two alpha (α) and two non-α globin chains, with each attached to an iron-containing heme complex. Patients homozygous for the mutant β^S gene have sickle cell anaemia (HbSS: α_2, $\beta^S{}_2$). There are multiple haplotypes of the β^S gene (four African and one Arab/Indian) associated with different phenotype severity. Patients heterozygous for the β^S gene have the sickle cell trait (HbAS: α_2, $\beta^A\beta^S$), a generally benign condition.

Patients heterozygous at the β-globin gene locus for the mutant β^S and β^C genes have haemoglobin SC (HbSC: α_2, $\beta^S\beta^C$) disease, a condition of intermittent clinical severity. Other mutations and deletions in the β-globin gene locus result in decreased (β^+) or absent (β^0) production of β-globin chains. In HbSβ^0, there is absent β-globin chain production, resulting in a clinical phenotype of similar severity to HbSS disease. HbSβ^+ is associated with variable β-globin chain production and moderate clinical manifestations, similar to HbSC disease. These four genotypes (HbSS, HbSC, HbSβ^0 and HbSβ^+) express the sickle cell phenotype and are collectively termed 'sickle cell disease'. Gamma (γ) chains are present in fetal and early post-natal life and are a component of HbF (α_2, γ_2). In sickle haemoglobinopathies, HbF (8–30%, depending on genotype and haplotype) exerts a protective effect against expression of the SCD phenotype and is increased with the disease-modifying therapy, hydroxyurea.

PATHOPHYSIOLOGY

Sickle cell disease is characterized by the destabilization of oxygenated haemoglobin and diminished solubility of deoxygenated haemoglobin (5) which leads to oxidant stress that interferes with cell membrane structure and maintenance of ion gradients. Intracellular dehydration, haemoglobin polymerization and accelerated oxidant stress result in the creation of a cycle that irreversibly deforms the red cell membrane leading to sickling, microvasculature obstruction and ischaemic injury.

Endothelial cells in SCD are activated and bind erythrocytes, reticulocytes, platelets and leukocytes (6–8). Endothelial cells liberate vasoconstrictor endothelin-1 in response to vascular injury and systemic inflammation (9). Leukocytes liberate inflammatory cytokines and express adhesion molecules with affinity for the endothelium (10). Platelet activity is amplified in SCD, coagulant factors are consumed, and there is decreased activity of endogenous anticoagulant and fibrinolysis pathways (11, 12). Taken together, these findings support the presence of widespread endothelial inflammation and dysfunction.

Nitric oxide (NO) plays a critical role in modulating vascular tone and exerts a modulatory effect on endothelial adhesion molecule expression, platelet inhibition and leukocyte adhesion. Cell-free haemoglobin liberated during haemolysis scavenges NO, while arginase liberated from red blood cells consumes an essential substrate (arginine) required for the production of NO (13).

Decreased NO activity is present in patients with SCD with acute chest syndrome (ACS) and vaso-occlusive crisis (VOC), thus supporting the observation that

dysregulation of NO metabolism contributes to the SCD inflammatory cascade (14).

ACUTE SICKLE CELL DISEASE MORBIDITIES

The pathophysiological derangements outlined above cause the acute complications of SCD, including VOC, ACS, stroke, acute sequestration crisis, aplastic crisis, sepsis and priapism.

Vaso-occlusive crisis

Vaso-occlusive crisis is the most common acute complication of SCD. It affects bone and viscera and causes moderate to severe pain. Bone pain commonly affects the ribs, spine and long bones. Visceral abdominal pain may mimic surgical pathology such as appendicitis or cholecystitis. Vaso-occlusive crisis is treated with intravenous hydration, analgesia, oxygen (when required) and, rarely, transfusion therapy for severe or recalcitrant symptoms. Severe complications such as ACS or stroke may occur during VOC.

Acute chest syndrome

Acute chest syndrome is characterized by the presence of one or more lobar pulmonary infiltrates associated with dyspnoea, fever, chest pain, hypoxaemia and cough. This syndrome may be provoked by pulmonary fat emboli from long bone infarction, vaso-occlusion in the pulmonary circulation, bacterial or viral pneumonia, or systemic inflammation from VOC or surgery itself. Its severity varies from mild respiratory infection to a life-threatening syndrome indistinguishable from acute respiratory distress syndrome. Treatment involves oxygen therapy, positive pressure ventilation (when required), ambulation (when able), pulmonary toilet, antibiotics, bronchodilators and occasionally corticosteroids. Transfusion therapy is not always needed, but is often administered as a simple transfusion for moderate disease (15) and an exchange transfusion for rapidly progressive disease (16). Acute chest syndrome has historically been a leading cause of premature death in patients with SCD and is a risk factor for acute stroke (17).

Stroke

Stroke is a leading cause of morbidity among patients with SCD. Stroke affects 10% of young adults by the time they reach the age of 20 years, and one-quarter of patients by the time they are 45 years old (18). Stroke results from disease of large intracranial arteries rather than vaso-occlusion. Measurements of transcranial Doppler flow rates in the large arteries of the brain predict future stroke and are used in comprehensive sickle cell centres to identify patients at high risk for future stroke. These children may be candidates for chronic transfusion therapy, which substantially reduces the incidence of stroke (19), a risk that returns with cessation of chronic transfusion therapy (20). Treatment of acute stroke includes supportive critical care and exchange transfusion followed by chronic transfusion therapy to keep the haemoglobin S percentage below 30%. Recent evidence suggests ischaemic stroke in adult patients with SCD can be treated with thrombolytic therapy (21).

Acute sequestration crisis

Acute sequestration crisis presents with splenomegaly, hypovolaemia and anaemia due to trapping of the circulating blood volume in the splenic sinusoids. This crisis occurs in preschool children before splenic autoinfarction occurs. Aggressive red blood cell transfusion is required to restore haemoglobin concentration and circulating blood volume. Haemoglobin concentration must be monitored closely, as sequestered red cells may return to the circulation with treatment. Haemoglobin concentration should be kept below 10 to 11 g/dL because acute viscosity increases at this level in patients with SCD and is associated with an increased risk for stroke.

Aplastic crisis

Aplastic crisis is a more compensated reduction in haemoglobin concentration due to viral-mediated decrease in reticulocyte production that fails to keep pace with accelerated red cell destruction. Transfusion with small aliquots of packed red blood cells is administered to increase haemoglobin concentration while avoiding circulatory overload.

Sepsis

Sepsis has historically been a leading cause of death in patients with SCD, and they are functionally splenectomized early in life and prone to infection with encapsulated organisms. Advances in immunization practices and routine use of penicillin prophylaxis have decreased the frequency of severe or fatal bacteraemia in developed countries, but fever in patients with SCD should prompt immediate evaluation for a potential infectious source, and antibiotics effective against the most likely bacterial organisms should be instituted. The surgeon and anaesthesiologist should be mindful of the vulnerability of patients with SCD to bacterial infection, including those caused by encapsulated bacteria, and

must be even more vigilant in the prevention of surgical site infection.

Priapism

Priapism is a medical emergency that may complicate postoperative management of patients with SCD. Young men experience the sudden, painful onset of penile tumescence that may wax and wane (*ie* stuttering priapism) or may be unremitting. Ischaemic priapism in SCD results from impaired venous outflow from the corpora cavernosa, and persistence of this condition results in fibrosis and irreversible erectile dysfunction. Treatment includes hydration, pain management, transfusion, and aspiration and irrigation of blood from the corpora cavernosa, with or without instillation of adrenergic medications (*ie* phenylephrine). Exchange transfusion to reduce haemoglobin S to below 30% and surgical placement of a shunt to divert blood may be required in refractory cases.

PERIOPERATIVE MANAGEMENT

Preoperative management and assessment

Preoperative assessment for patients with SCD begins by identifying patients with relevant haemoglobinopathies. In the United States of America, most patients will have been identified through universal newborn screening. Haemoglobin separation techniques (*ie* high-pressure liquid chromatography or haemoglobin electrophoresis) are commonly used to delineate specific SCD genotypes. Genetic testing is available to haematologists and is usually beyond the purview of anaesthesiologists and surgeons. Preoperative screening of at-risk populations has yielded a clinically insignificant detection rate (22, 23).

The patients' pre-existing co-morbidities are then considered, with an emphasis on the respiratory, cardiovascular and central nervous systems (CNS). History of cardiac disease, pulmonary hypertension and echocardiographic data, if any, should be reviewed. Any pulmonary morbidities should be sought, including the presence or absence of asthma, obstructive sleep apnoea and chronic lung disease. Spirometry results should be evaluated, if they are available or clinically indicated. The patient's history of stroke, silent cerebral infarction, and CNS imaging and transcranial Doppler flow rates should be reviewed to identify patients at risk for perioperative CNS injury. Finally, renal function, history of hepatic disease, and chronic pain burden should be assessed.

The use of disease-modifying therapies and current haemoglobin concentration should be reviewed. Physiologic insults that may provoke vaso-occlusion (such as fever, systemic inflammation, dehydration and intercurrent infection) should be sought and treated. Further preoperative evaluation should be dictated by the history and physical examination.

Preoperative transfusion therapy, including chronic transfusion participation and the timing of recent isolated transfusions, should be reviewed. Reasons for participation in chronic transfusion therapy are usually significant and imply significant incurred or threatened morbidity. Compliance with chronic transfusion therapy or recent transfusion for treatment of complications of SCD may provide an optimized haemoglobin concentration or reduced haemoglobin S percentage (patients on chronic transfusion). Compliance with hydroxyurea therapy increases HbF concentration, which improves solubility of haemoglobin and decreases endothelial interactions with cellular components of the blood.

Preoperative hydration is essential for optimization of surgical candidates, and the care team must decide how best to minimize the dehydration associated with preoperative fasting. Preoperative admission and intravenous hydration providing maintenance fluid requirements are common practice and must be tailored for the presence of renal and cardiac disease. Data are lacking to support the safety of oral preoperative hydration as an outpatient, although some centres and clinicians permit this for low-risk patients undergoing low-risk procedures. Cholecystectomy, splenectomy, appendectomy, tonsillectomy and adenoidectomy, myringotomy, and umbilical hernia repair are the most commonly performed surgical procedures in children with SCD (4). Common procedures in older patients with SCD include Caesarean section, dilatation and curettage, and orthopeadic procedures for hip core decompression or replacement procedures (3, 4, 24–31). Estimation of relative risk of surgical procedures has been derived from a variety of prospective (3, 24–27, 31) and retrospective (4, 28–30) studies of perioperative outcomes in predominantly paediatric (4, 24, 28, 29), predominantly adult (25) and mixed cohorts (3). In some studies, investigators were primarily assessing the benefit of exchange *versus* simple transfusion for preoperative optimization (31).

Complications reported in most studies of perioperative outcome include those relevant to SCD itself (stroke, death, ACS and VOC), those secondary to transfusion therapy (alloimmunization, viral infection, febrile

transfusion reactions, and delayed or acute haemolytic reactions), and those common to the procedures performed (fever, haemorrhage, atelectesis and infection). Taken together, the collective literature and clinical experience suggest CNS, cardiac and thoracic surgery procedures represent the highest-risk tier. Moderate-risk procedures include upper abdominal procedures (cholecystectomy and splenectomy), hip replacement, and ear, nose, and throat interventions (tonsillectomy and adenoidectomy in some studies), as well as Caesarean section and dilatation and curettage. Finally, minor procedures (hernia repair, dental, oral-maxillofacial surgery, urologic surgery, orthopaedic, ophthalmologic, central line placement, and tympanostomy tube placement) are associated with a decreased risk of serious postoperative complications.

The most intensely debated question in the preoperative management of patients with SCD is whether prophylactic preoperative transfusion therapy should be applied to all patients. Consensus is lacking, and variability exists in preoperative transfusion practices (32). Retrospective and prospective observational studies suggest that SCD-related complications were less common in certain patients and procedures. These observations led authors to call for prospective, randomized controlled trials to identify those patients most likely to benefit from preoperative transfusion, as well as those who might safely forego it.

Transfusion imposes risk of adverse sequelae, including immediate and delayed haemolytic reactions, transmission of viral pathogens, expense, iron burden, and especially alloimmunization. The difficulty in preventing alloimmunization requires extended cross-matching of red cell antigens. Alloimmunization prevalence of between 18% and 76% has been reported in patients with SCD when only A, B, O and D groups are matched (*versus* approximately 1% in non-SCD patients). Alloantibodies to the Rh (primarily C and E groups) and Kell systems account for two-thirds of alloantibodies seen in patients with SCD (33, 34). The magnitude, severity, expense and clinical hardship imposed by accumulated red cell antigen immunity are probably not appreciated by most anaesthesiologists, intensivists and surgeons.

To date, there have been only two randomized, controlled trials comparing preoperative transfusion to no transfusion, and they provide conflicting guidance (35, 36). The study of Al-Jaouni and colleagues included a large number of patients who were quasi-randomized to different transfusion strategies (simple, partial exchange), involved all SCD genotypes and was conducted exclusively in a geographic region associated with the mildest haplotype of the β^S mutation. In this series, preoperative transfusion was associated with more perioperative complications (35). Conversely, the recently published TAPS (Transfusion Alternatives Preoperatively in Sickle Cell Disease) study included children and adults undergoing low- and moderate-risk procedures with or without preoperative simple transfusion (36). Enrolled patients were almost exclusively of the HbSS genotype (97% of the patients), and 81% of the patients underwent moderate-risk procedures. The study was halted after an interim analysis of only 67 patients because of adverse events in 39% of the patients in the non-transfusion arm *versus* 15% in the transfusion arm, and a preponderance of ACS (9/10 patients) in the non-transfusion arm.

Estcourt *et al* conducted a Cochrane review of the efficacy of preoperative transfusion for patients with SCD and concluded that there was very low-quality evidence that preoperative transfusion was effective in reducing the occurrence of ACS (37). In addition, they were unable to make any recommendations regarding the utility of preoperative transfusion in HbSC, HbSβ^+, and other patients with high baseline haemoglobin concentrations (37). Further guidance came in 2014 when an expert panel summarized the recommendations for the management of perioperative patients with SCD (38). The panel recommended that: (a) all adults and children with HbSS and HbSβ^0 undergoing surgical procedures with general anaesthesia should be transfused preoperatively to bring the haemoglobin concentration to 10 g/dL; (b) an expert in SCD should be consulted to determine the best method of transfusion for patients with HbSS with a haemoglobin concentration of > 8.5 g/dL without transfusion, patients who are receiving hydroxyurea therapy, or require high-risk surgical procedures; and (c) an expert in SCD be consulted to determine if full or partial exchange transfusion is required for adults and children with HbSC and HbSβ^+ before surgical procedures that require general anaesthesia.

Based on these findings and the above expert recommendations, clinicians should strongly consider preoperative transfusion for all children with the HbSS and HbSβ^0 genotypes undergoing surgical procedures under general anaesthesia. We do not believe future trials are likely to clarify this important clinical question, thus the existing data should be viewed with the following modifying considerations: (a) none of the studies was done exclusively in children; (b) mortality and morbidity are reduced (though not absent) in the

paediatric population; and (c) alloimmunization early in life may hinder future transfusion therapy. The expense, safety of blood supply, alloimmunization status, patient genotype, phenotype and surgical procedure are all factors to be considered thoughtfully with the patient, parent and haematologist when considering the potential omission of preoperative transfusion. If preoperative transfusion is selected, simple transfusion (haemoglobin target of 10 g/dL) is as effective as exchange transfusion (haemoglobin target of 10 g/dL and haemoglobin S < 30%) for the prevention of perioperative SCD complications and is associated with fewer transfusion-related complications (31).

Intraoperative management

Surgical procedures represent the controlled cause of tissue injury that sparks inflammation and may provoke SCD complications. The majority of the efforts to optimize perioperative outcomes actually occur before the patient comes to the operating room. Because of this, there are basic tenets of anaesthetic management that, when violated, may help to promote vaso-occlusion and systemic inflammation. It is paramount to prevent conditions that promote delays in tissue-lung transit, haemoglobin desaturation and vascular stasis.

Hypoxaemia has traditionally been recognized as a key instigator in the exacerbation of SCD complications. Despite this basic recognition, examples of persistent or prolonged hypoxaemia (*ie* cyanotic congenital heart disease, high altitude exposure) have not always resulted in the development of SCD complications, and perioperative complications still occur despite the avoidance of intraoperative and postoperative hypoxaemia. Airway management, oxygen administration and mechanical ventilator manipulations should be performed with the goal of maintaining functional residual capacity and ensuring adequate arterial oxygen saturation and minute ventilation. Pulse oximetry tends to slightly underestimate the true oxygen saturation in patients with SCD.

The maintenance of tissue oxygen delivery with normal transit through capillary beds is critical to preventing excessive oxygen extraction and irreversible sickling of erythrocytes. As oxygen delivery is the product of cardiac output and arterial oxygen content, it is imperative to maintain optimal values for contractility, preload and afterload, as well as haemoglobin concentration and oxygen tension. Supplemental oxygen should be administered to keep arterial oxygen tension and saturation within the normal range. Both non-invasive and invasive measures of cardiac output and filling conditions may be used based on the patient's cardiovascular reserve and the proposed surgical procedure.

The preservation of intravascular volume status is guided by an estimation of ongoing maintenance fluid requirements in addition to insensible losses and blood loss. Failure to replace intravascular volume can result in vasoconstriction and stasis of blood flow through the microcirculation – optimal conditions for the promotion of sickle cell complications. While maintaining intravascular circulating volume, it is important to consider the type of fluid to administer. Fluid used for volume replacement is optimally isotonic crystalloids such as Lactated Ringers or normal saline, and consideration should be given to the balanced administration of these preparations to prevent excessive hyperchloraemia and the metabolic acidosis commonly seen with an exclusive administration of large quantities of normal saline.

The administration of hypotonic fluid has been advocated for patients with SCD with the intent to augment erythrocyte hydration. Hypotonic fluid administration cannot be recommended for patients with or without SCD, as this may promote dangerous iatrogenic hyponatraemia. It should be noted that erythrocyte dehydration is a consequence of the following intracellular events: (a) prolonged haemoglobin desaturation; (b) haemoglobin polymerization; (c) intracellular oxidant injury; (d) cell membrane dysfunction and loss of control of ion gradients; and (e) red cell dehydration.

As with any other surgical haemorrhage, circulating blood volume and haemoglobin concentration are preserved through red blood cell transfusion. The maintenance of adequate preload, cardiac output and oxygen-carrying capacity are necessary to minimize reflex capillary vasoconstriction, oxygen extraction and capillary bed transit time. Given the complexities of extended cross-matching in some patients with SCD, it is prudent to confirm preoperatively that red blood cells are available in the blood bank for elective procedures. For emergency procedures in which appropriate extended cross-matched blood is not available, the patient's haematologist should be consulted to discuss transfusion strategies that minimize the chances of haemolytic reactions and alloimmunization. Likewise, the maximum haemoglobin concentration allowable during surgery should be determined, as blood viscosity and the risk for stroke increase steeply in sickle cell patients as haemoglobin concentration exceeds 10 to 11 g/dL. Patients who had been receiving chronic transfusion therapy prior to surgery, with low HbS percentage, may tolerate a higher haemoglobin concentration.

Metabolic acidosis shifts the oxyhaemoglobin dissociation curve to the right, promoting the desaturation of oxyhaemoglobin. The effects of metabolic acidosis are often difficult to separate from their underlying cause (impaired arterial oxygen content, diminished cardiac output, increased tissue demands for oxygen, and dysregulated oxygen supply and demand as seen in sepsis). Although some early anecdotal experimental evidence supported a beneficial effect of an alkaline plasma environment on erythrocyte sickling and painful crisis severity, the administration of sodium bicarbonate has not been shown to prevent sickle complications in a significant manner during acute or chronic clinical scenarios (39, 40). The maintenance of pH in a relatively normal physiologic range is recommended.

Hypothermia also promotes cutaneous vasoconstriction, delays vascular transit and may promote vaso-occlusion. Patients and clinicians have noted, anecdotally, a correlation between cold exposure and SCD activity (41). However, neurosurgical and cardiac surgery procedures utilizing deep hypothermia have been safely performed. Hyperthermia, on the other hand, promotes cutaneous vasodilation, but also promotes haemoglobin unloading and could theoretically promote haemoglobin polymerization.

The impact of ambient temperature and the impact of wind speed are conflicting, with flares in SCD activity associated with increased and decreased ambient temperature (42, 43), as well as studies that show an absence of correlation (44). The impact of ambient temperature on SCD activity in anaesthetized patients with anaesthetic-induced impairment of thermoregulatory reflexes is unclear. The role of wind speed and skin cooling in the precipitation of SCD complications has recently gained increased appreciation (45) and may be applicable in the operating room where convective heating (and cooling) blankets are commonly used. The maintenance of core and extremity temperature within a normal physiologic range is recommended.

High-risk cardiovascular procedures that have required cardiopulmonary bypass and deep hypothermic circulatory arrest have been performed successfully without exchange transfusion (46), although most patients receive an exchange transfusion preoperatively or during the initiation of cardiopulmonary bypass (47). Similarly, CNS procedures using deep hypothermia, the administration of hypertonic contrast, and mannitol have all been done with success in patients with SCD. In countries with a safe and durable blood supply, most clinicians perform preoperative exchange transfusion before undertaking these high-risk procedures.

The use of tourniquets in orthopaedic procedures promotes acidosis, hypoxaemia, hypothermia and vascular stasis. In patients with SCD, these conditions may promote erythrocyte sickling and vaso-occlusion. Despite these concerns, tourniquets have been used successfully in patients with SCD for orthopaedic procedures. It seems intuitively prudent to minimize tourniquet time and to carefully exsanguinate the operative limb prior to tourniquet inflation. A recent literature review emphasized that although complications from the use of tourniquets were not commonly reported in the literature, the risks and benefits of their use should be carefully considered for each patient and procedure (48).

Postoperative management

The postoperative management of patients with SCD represents a continuation of the principles and practices applied in the preparation and operative management of these patients. Serious complications of surgery and anaesthesia occur most commonly in the first three days following surgery (ACS) and, when they occur, often prolong hospitalization significantly. Postoperative management should emphasize aggressive analgesia and pulmonary toilet. Analgesia is provided in the form of peripheral nerve blockade, neuraxial blockade, patient-controlled opioid analgesia and non-steroidal anti-inflammatory drugs (when not contraindicated). Analgesia is optimized to facilitate respiratory function without excessively depressing respiratory drive. Pulmonary toilet is optimized with incentive spirometry for older children and age-appropriate activities for younger children. Supplemental oxygen should be administered to maintain oxygen saturation in the normal (or patient's baseline) range, and early ambulation should be encouraged. Intravenous hydration is continued postoperatively, with careful attention to fluid intake and output, including insensible losses, urine output and all losses from drains and catheters. There is a paucity of data as to whether patients with SCD should be candidates for outpatient surgery. If the patient is allowed to go home, adequate pain management, ability to maintain adequate hydration, parental reliability, access to telephone, ambulance services, and proximity to the emergency department and intensive care unit must be considered.

CONCLUSION AND FUTURE DIRECTIONS

Sickle cell disease is the most common haemoglobinopathy, and it has global health implications. Surgery is common in children with SCD, and perioperative complications can inflict substantial morbidity and mortality. Advances in the longitudinal care of patients with SCD have improved longevity through the prevention and management of acute complications and chronic complications of SCD. Penicillin prophylaxis, transcranial Doppler screening, chronic transfusion therapy and hydroxyurea administration have been effective in the prevention and attenuation of acute and chronic morbidities. Despite these advances, SCD continues to inflict substantial suffering upon patients.

Perioperative management of patients with SCD is predicated upon a sound understanding of the genetic underpinnings of the disorders, an appreciation of the multiple facets of the pathophysiology of SCD, and the ability to prevent, recognize and treat associated complications. Management of patients with SCD must consider the accumulation of morbidity with age, the variability of disease expression across and within genotypes, the differential relative risk associated with various surgical procedures, and the ongoing evolution of evidence and guidance for optimal perioperative management of these patients. While the hazards of perioperative management of patients with SCD must be acknowledged, it is important to view the overall risk in the context of what is generally a safe perioperative experience. Optimal results occur when preoperative preparation is meticulous, collaboration between surgeons, critical care physicians, anaesthesiologists and haematologists is emphasized, and attention to the basic tenets of anaesthetic management is maintained.

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