Towards safer surgery in patients with sickle cell disease

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ABSTRACT

Surgery in patients with sickle cell disease (SCD) has been associated with high morbidity and mortality. In recent years, a marked improvement in the safety of surgery and anesthesia in this high-risk group of patients has been witnessed; owing to the improvements in surgical and anesthetic care, greater awareness of pathophysiology of the disease, proper perioperative preparation, and attention to factors predisposing to vasoocclusive crises. However, this is not paralleled by similar improvement in countries where the disease is not prevalent. Greater population mobility in recent years makes close encounter with this disease more likely nowadays, even in areas of low SCD prevalence. Therefore, recognition of this disease and its surgical manifestations are of paramount importance in surgical practice worldwide if we are to aim towards safer surgery in this high-risk group of patients.

Preoperative preparation. Prior knowledge of the patient’s sickling history and the actual-S level indicated by electrophoresis, helps to estimate the individual perioperative risks, and facilitate safer anesthesia and surgery. Patients with SCD undergoing elective surgery are admitted 1-2 days earlier, and the predicted risk of postoperative complications is calculated. This is anticipated by the grade and complexity of the surgical procedure, and by the severity of SCD activity especially in the presence of frequent and recent complications.

Other factors that may predict high-risk postoperative complications include radiographic evidence of abnormal lung field indicating chronic sickle lung disease, pregnancy, pre-existing septic focus or infection, and African haplotypes, as they have more severe disease than the Asian haplotype. Such factors should be looked for and identified during the preoperative assessment. Moreover, it is imperative that co-morbid medical conditions are identified and treated promptly in order to optimize the patient’s general condition. Also, a decision on a preoperative transfusion regimen is made based on the frequency and severity of sickling crises. This is a key component of the comprehensive management of SCD patients undergoing major surgical procedures as it reduces the perioperative risks associated with surgery and anesthesia. It is recommended that every hospital should have its own protocol or guidelines on perioperative blood transfusion in SCD patients undergoing surgery.
Various transfusion regimens have been suggested from correcting the anemia by simple top up transfusion, regardless of the hemoglobin-S concentration (the conservative regimen), to more aggressive regimens, such as exchange transfusion. Exchange transfusion is commonly used to reduce hemoglobin-S to <35%, a level at which the risk of sickle cell crises is unlikely to occur, as this diminishes the blood viscosity, improves the circulation, and thus decreases the morbidity and mortality associated with surgery. Moreover, it is not associated with a rise in hematocrit, a problem that occurs with simple blood transfusion. Recent randomized trials have confirmed that a conservative transfusion regimen is as effective as the aggressive ones in decreasing perioperative complications in SCD patients, and is associated with only half as many transfusion-associated complications. The conservative regimen is, therefore, advocated for SCD patients undergoing minor surgical procedures, and exchange transfusion is reserved for those undergoing major surgeries especially in the presence of severe SCD as judged by frequent major crises and systemic SCD complications. Attempts must be made to avoid overtransfusion, and appropriate prophylactic antibiotics may be administered as indicated by the nature of the surgical procedure. Adequate intravenous hydration must be maintained especially on the night of the planned operation as the patient is kept nil by mouth from midnight. Also, strong preoperative sedation is avoided, and pharmacological thromboprophylaxis in the form of low molecular weight or standard heparin is prescribed, except for patients receiving preoperative transfusion to avoid troublesome intraoperative bleeding.

**Perioperative care.** Although the risk of anesthesia in SCD patients is small, there are some reports of death in the perioperative period. General anesthesia and metabolic response to surgical trauma add additional risks as changes in temperature, oxygen tension, and fluid volume, all of which play an important role in predisposing to vasoocclusive sickling crises. Moreover, circulatory stasis or suboptimal ventilation allows the hemoglobin-S to polymerize in the capillaries with subsequent ischemic infarcts in many tissues. Therefore, special multidisciplinary care is needed in management of patients undergoing surgical interventions, and understanding the SCD pathophysiology is essential in minimizing complications from anesthesia and surgery, approaching 40% of SCD patients having major surgeries. It is imperative to assign an anesthetist who is experienced in dealing with SCD patients to handle the anesthesia. It is also important not to depress ventilation by preoperative sedation and the inspired oxygen concentration during surgery, and the postoperative period should be increased to maintain the arterial oxygen tension, to be monitored continuously by pulse oximetry. Moreover, circulatory stasis should be avoided by adequate hydration, and anticipation and prompt replacement of intraoperative fluid losses to avoid acute hypovolemia. It is also of paramount importance to keep the environmental temperature in the operating room as near normal as possible to avoid hypothermia or hyperthermia. The routine use of anti-deep venous thrombosis measures such as intermittent pneumatic calf compression is also advocated. Furthermore, an increasing number of evidence proved that minimally invasive surgery has more advantage than conventional surgery, and its safety in SCD patients is now well established. Therefore, minimally invasive surgery should be contemplated as much as possible in any surgical intervention in SCD patients due to its numerous advantages. However, it should be performed by an experienced laparoscopic surgeon to shorten the operative time.

**Postoperative care.** In the postoperative period, nursing of patients in the intensive care unit is rarely needed, and all patients should receive postoperative oxygen supplementation and adequate intravenous hydration, together with pharmacological thromboprophylaxis. Other factors such as hypothermia, sepsis, and acidosis that precipitate vasoocclusive crises should be avoided. It cannot be overemphasized that chest physiotherapy with incentive spirometry, early mobilization, and rapid discharge from hospital play a major role in reducing the rate of postoperative complications. Also, there is no doubt that proper and careful preoperative preparation helps minimize postoperative complications. The 2 most feared complications are acute chest syndrome (ACS) and vasoocclusive crisis (VOC), which are more commonly encountered in SCD patients undergoing laparotomy or thoracotomy. The ACS, a phenomenon of pulmonary sequestration that occurs in 0.4-10% of SCD patients undergoing surgery, is frequently missed in the postoperative period. Painful VOCs are often precipitated by the stress of surgery and poorly controlled postoperative pain. Effective postoperative pain control is, therefore, essential. Non-steroidal anti-inflammatory drugs can be an excellent adjunct to opioids, and epidural analgesia can minimize respiratory depression. The use of patient controlled self-administered analgesia devices is effective for improved narcotic delivery. Treatment of pain in SCD patients is one of the most daunting tasks that requires a comprehensive team strategy. It is unfortunate that successful pain control is often hampered by misperceptions of the care providers on the cause of the pain and the fear of addiction.

**New hopes.** Recently, more encouraging news for surgeons dealing with SCD patients is emerging. New preventive therapies have been recently introduced in...
an attempt to minimize the severity and frequency of sickle cell crises.\textsuperscript{18,19} The majority aim at increasing the synthesis of fetal hemoglobin (hemoglobin-F), which is believed to play a protective role against major crises.\textsuperscript{19} Such agents include hydroxyurea, inhaled nitric oxide and its precursor L-arginine, short-chain fatty acids, 5-azacytidine, and its safer analogue decitabine. Other therapies include newer drugs such as poloxamer 188 and fructose 1-6 diphosphate that have been tried, and found promising in decreasing sickling crises and reduces postoperative complications, and shorten hospital stay.\textsuperscript{20,21} Furthermore, bone marrow transplantation is now an accepted therapy for symptomatic children.\textsuperscript{22} However, progress in gene therapy has been slow due to inadequate gene transfer and low gene-expression.

The morbidity and mortality associated with surgery and anesthesia in patients with SCD have greatly improved in recent years. This is attributed to greater knowledge of the disease pathophysiology, better anesthetic techniques, and improvement in perioperative care and more recently, the introduction of minimally invasive surgery. A comprehensive perioperative management plan including preoperative blood transfusion and effective postoperative analgesia must be drawn by a multidisciplinary team for every SCD patient undergoing surgery. Protocols and guidelines should be readily available in every surgical department dealing with SCD patients. It is hoped that the increasing awareness of the surgical manifestations of SCD, and the introduction of new preventive therapies will further reduce the high mortality and morbidity associated with surgery in this high-risk population.\textsuperscript{1}

References