PART III: COMPREHENSIVE CARE

1. PERI-OPERATIVE MANAGEMENT

Principles

- To minimize the risk of morbidity and mortality in patients undergoing surgical procedures.

Recommendations

1. Pre-operative Care

- All patients should undergo consultation with an anesthesiologist prior to surgery.
- There should be close communication between the anesthesia, medical and surgical teams.
- The patient's treating hematologist, or another hematologist with expertise in sickle cell disease, should be directly notified of the upcoming surgery so that all important peri-operative factors are reviewed.
  - Pre-operative transfusion:
  - Decisions about the role and optimal method of pre-operative transfusion must take into account the risk category and individual patient factors (e.g., comorbidities and severity of sickle cell disease phenotype).
  - Patients undergoing moderate-risk surgery should typically receive prophylactic RBC transfusions to a target hemoglobin of 100 mg/L, or, if pre-transfusion hemoglobin is >=90 g/L, partial manual exchange to target HbS <60%.
  - Automated red cell exchange transfusion to target HbS <30% must be considered in high-risk procedures, and in patients with complex comorbidities or a history of post-operative complications.
- Cross-match compatible, phenotype-matched, Sickledex-negative units of red blood cells should be on hold in the blood bank (number based on risk of intra-operative blood loss).
- All patients should receive adequate hydration prior to surgery.
- If the patient is required to remain in NPO status prior to surgery, they should be admitted for intravenous hydration with isotonic solution during the NPO period.

2. Intra-operative Care

- The anesthesiologist should avoid regional anesthesia, when possible.
- Tourniquets or arterial clamping may be used when surgically required. but duration should be minimized.
- Intraoperative monitoring should include temperature, heart rate, blood pressure, and oxygenation.
- Temperature optimization may include use of warmed intravenous fluids and warming blankets.
- Careful attention should be paid to hydration and volume status.

3. Post-operative Care

- Isotonic intravenous fluids should be administered until the patient is drinking and eating well.
- Supplemental oxygen should be provided as needed.
- Consider involvement by respiratory therapy for deep breathing exercises and/or incentive spirometry.
- Clinical monitoring, including temperature, heart rate, blood pressure, oxygenation.
- Laboratory monitoring should be undertaken as indicated: hemoglobin, lactate dehydrogenase (LDH), reticulocyte count, bilirubin, arterial blood gas, chest x-ray.
- Pain control must be optimized. Patients with SCD may have increased opiate requirements compared with the general population. Good pain control will facilitate mobilization, and may help prevent splinting and atelectasis.
- Patients should receive post-operative thromboprophylaxis, as post-surgical bleeding risk permits.

Assessing and Managing Surgical Risk

Surgical procedures such as tonsillectomy, splenectomy, cholecystectomy or orthopedic surgery are commonly required in patients with sickle cell disease (SCD) because of hypersplenism, chronic hemolysis, or bone complications, respectively. In addition, patients with SCD may require unrelated surgeries during their lifetimes.

Patients with SCD have a higher risk of perioperative complications than the general population, for several reasons.

1. Anemia – Patients with SCD are already anemic, and procedural bleeding will further decrease hemoglobin levels, leading to more severe anemia, and decreasing the oxygen-carrying capacity of blood cells.
2. Hypoxemia – Intraoperative hypoxia, local tissue hypoxemia, or post-operative atelectasis can trigger sickling of red blood cells. Sickling of red blood cells can lead to a painful crisis or acute chest syndrome, among other SCD-related complications.
3. Dehydration – Several factors in the perioperative period can predispose the patient to dehydration, including pre-operative nothing-by-mouth (NPO) status and reduced oral intake following some surgeries (e.g., tonsillectomy or bowel surgery). Systemic dehydration can lead to dehydration of the red blood cells, and a subsequent increased rate of sickling.
4. Hypothermia – Intraoperative skin and tissue exposure, and the use of unwarmed intravenous infusions can lower body temperatures, leading to increased risk of red blood cell (RBC) sickling.
5. Acidemia – Use of prolonged tourniquets or arterial clamping required in some procedures can cause acidemia, leading to increased risk of RBC sickling.
6. Infection – Asplenia, either surgical or due to recurrent infarction, contributes to the risk of postoperative infection.
7. Chronic organ disease related to SCD can make certain patients more susceptible to organ-specific complications.

The risk of complications increases with the age of the SCD patient, and certain surgeries are known to be high-risk.[1] Risk must be assessed individually for each patient, however, depending on medical condition and the procedure to be undertaken. Tonsillectomy, for example, is classically a moderate-risk procedure in other patient populations; however, it may carry increased risk in an SCD patient because of the risk of airway compromise and hypoxia, the risk of excessive bleeding, and possible decreased oral intake during the post-operative recovery period.

The Cooperative Study of Sickle Cell Disease used the following classification for surgical risk:[1]

- Low-risk – Procedures of the eyes, skin, nose, ears, distal extremities, and also of the dental, perineal, and inguinal areas;
- Moderate-risk – Procedures of the throat, neck, spine, proximal extremities, genitourinary system, and intra-abdominal areas;
- High-risk – Procedures of the intracranial, cardiovascular, and intrathoracic systems.

Adverse outcomes may be minimized by optimal selection of anesthetic methods. Higher rates of postoperative painful crisis are associated with regional anesthesia than with local or general anesthesia.[1]

Use of tourniquets or arterial clamping are thought to increase the risk of sickling, because of hypoxia, acidosis, and venous stasis in the distal tissues. There have been several case series and case reports of generally successful outcomes with these surgical techniques, however.[2-4] Surgeons and anesthesiologists should be made aware of a patient's diagnosis of SCD and his or her pre-operative condition. Informed decisions about surgical technique and anesthetic approach must aim to best balance risks and benefits for the individual patient. The patient's treating hematologist, or another hematologist with expertise in sickle cell disease, should be directly notified of the upcoming surgery so that all important peri-operative factors are reviewed.

Role of Pre-operative Transfusion

Regarding pre-operative transfusion, the following questions must be considered for each patient:

1. Should this patient receive transfusion pre-operatively?
2. If so, what will be the transfusion parameters (i.e., target Hb and/or target sickle hemoglobin (HbS) concentration) and optimal method (i.e., simple vs. exchange)?

The risk category of the planned surgery plays an important role in risk stratification. As with all medical decision-making, individual patient factors (e.g., comorbidities and severity of sickle cell disease phenotype) must be considered in decisions about pre-operative transfusion.

Moderate-risk surgeries

The majority of surgeries performed on SCD patients are moderate-risk, including cholecystectomy, splenectomy, orthopedic and gynecologic surgeries.[1] Compared with low-risk procedures, moderate-risk surgeries are associated with higher rates of development of complications, including acute chest syndrome.[5]

In a randomized controlled trial of patients with sickle cell anemia (HbSS) undergoing a total of 604 operations, the Preoperative Transfusion in Sickle Cell Disease Study found that a pre-operative simple transfusion regimen (target pre-operative hemoglobin level of 100 g/L) offered outcomes equivalent to those of a pre-operative exchange transfusion regimen (target sickle hemoglobin [HbS] level <30%), specifically a similar incidence of serious peri-operative complications (31% vs. 35%) and acute chest syndrome (10% in both study groups). Furthermore, there was a higher rate of transfusion-related complications in the exchange transfusion group (14% vs. 7%, odds ratio [OR] 2.15, 95% confidence interval [CI] 1.23 to 3.77).[5] Seventy-five percent of the procedures were moderate-risk, with only one high-risk surgery, and the remaining classified as low-risk. The odds ratio for development of acute chest syndrome in moderate- and high-risk procedure categories was 2.97 (95% CI, 1.30 to 6.81). Equivalent outcomes were also seen in a cohort study of children receiving simple *versus* exchange transfusion prior to tonsillectomy and/or adenoidectomy.[6]

More recently the TAPS trial (Transfusion Alternatives Perioperatively in Sickle Cell Disease) assessed 67 patients with HbSS or HbS-beta^0-thalassemia who had been randomized to receive no pre-operative transfusion or to be transfused to a target pre-operative hemoglobin of 100 g/L.[7] Patients in the transfusion group who had pre-transfusion hemoglobin <90 g/L had simple transfusion, whereas those with hemoglobin ≥90 g/L received partial manual-exchange transfusion, targeting HbS level <60%. Exclusion criteria included: baseline hemoglobin <65 g/L, recent transfusion (within 3 months), history of acute chest syndrome within 6 months, any history of intubation and mechanical ventilation for treatment of acute chest syndrome, oxygen saturation <90%, current renal dialysis or history of stroke in children. In the study population, 13 (39%) patients in the no-transfusion group had clinically important complications, compared with five (15%) in the pre-operative-transfusion group (P=0.023), giving an OR of 3.8 (95% CI, 1.2 to 12.2, P=0.027). Of these complications, there were 10 (30%) serious adverse events in the non-transfusion group versus one (3%) in the transfusion group. Most events in this category were episodes of acute chest syndrome. Duration of hospital stay and readmission rates did not differ between study groups. Over 80% of patients in this study were scheduled for a moderate-risk procedure.

Low-risk surgeries

In a natural history study of 1,079 procedures performed in 717 patients with SCD, peri-operative transfusion in patients with HbSS undergoing low-risk procedures was associated with a lower rate of SCD-related post-operative complications (4.8% vs. 12.9% without transfusion).[1] Subsequent prospective observational studies in patients with SCD, however, have suggested that prophylactic transfusion is not required prior to low-risk procedures.[8,9] Given the lack of consensus from observational studies, and the fact that low-risk procedures accounted for a small proportion of patients enrolled in the Preoperative Transfusion in Sickle Cell Disease Study and TAPS trials (results outlined above), pre-operative transfusion may still be considered in patients with major comorbidities or history of severe sickle cell disease phenotype.

High-risk surgeries

No major studies have formally assessed transfusion strategies in high-risk surgeries. Expert opinion suggests that a pre-operative exchange transfusion be considered in most SCD patients, based on the complexity and/or duration of high-risk procedures.

Peri-operative Supportive Care

In addition to prophylactic transfusion, attentive peri-operative care is important, including: pre-operative anesthesiology consultation and hydration, intra-operative monitoring of cardiorespiratory paraemeters, and post-operative monitoring with administration of supplemental oxygen and intravenous hydration.

It is prudent to keep several units of crossmatched RBCs on hold, depending on the surgical risk of bleeding, because of the high prevalence of RBC alloantibodies in the SCD population.

To prevent dehydration, careful attention must be paid to volume status, with the patient receiving intravenous hydration while NPO (pre-, intra- and post-operatively). Selection of isotonic fluids will minimize the risk of RBC dehydration with hypertonic solutions and the risk of hyponatremia with hypotonic solutions.

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