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Departmental Clinical Protocol Manual

Clinical Protocol
CP.XX.xxx

This product is intended to be a resource, not a replacement for institutional protocols. Standard 1 of AmSECT's Standards and Guidelines for Perfusion Practice.1 These Standards and Guidelines may also be superseded by the healthcare professional's judgment considering the facts and circumstances of the individual case.

SUBJECT/TITLE: SICKLE CELL DISEASE

PURPOSE: To provide a guideline for pediatric patients diagnosed with Sickle Cell Disease (SCD) and to differentiate between SCD and Sickle Cell Trait (HbSC, Hb AS, SC trait). This disease affects approximately 2,600 births each year in the US.[6] SCD is a genetic disorder causing hemoglobinopathy, resulting in the formation of sickled red blood cells (RBC). This distortion in hemoglobin causes RBCs to become rigid and take on the pronounced sickling shape inherent to the disease.[6]

RBCs

RBCs are at risk of sickling when the patient is exposed to an altered environmental setting like hypoxia, acidosis, hypothermia, hypotension, increased viscosity, low flows, infection, and/or any rightward shift of the oxygen-dissociation curve. Sickling has negative clinical repercussions, including cellular injury, aggregation, inflammation, vascular occlusion and hemolysis due to increased membrane fragility, .[1,6]

These clinical manifestations can cause end-organ dysfunction, cerebral vascular accidents, inflammatory crises, pulmonary hypertension, and infarcts, thus increasing the risk of morbidity and mortality.[1,6] Sickled RBCs have a much shorter life span of 17 days, have a minimal capacity to load and unload oxygen, are associated with severe hemolytic anemia, and may lead to activation of the intrinsic clotting cascade.[6] Regardless of the disease state, homozygous or heterozygous, all cardiac team members should collaborate to ensure a safe and effective procedure for pediatric patients with SCD undergoing cardiac surgery.

TARGET POPULATION: Pediatric patients diagnosed with Sickle Cell Disease or Sickle Cell Trait.

DEFINITIONS:

Sickle cell disease is a hereditary, autosomal recessive hemoglobinopathy resulting from a mutant form of a β-globin gene. Instead of having the proper concentration of physiologically normal hemoglobin A (HgA), patients with this disease have a portion of their hemoglobin replaced with genetically defective hemoglobin S (HgS). HgS, compared to HgA, is insoluble, less pliable, and predisposed to crystallization and aggregation.[6]

Homozygous, or fulminant, SCD refers to patients having a concentration of over 70% HgS. This is also referred to as HbSS, HbSB-thalassemia, or sickle cell anemia. Patients with only partial genetic mutation for HgS, called sickle trait or HbSC, have less than 50% HgS.[2] The proportion and severity of sickling depend on the concentration of HgS in the patient's circulation. Sickling occurs when red blood cells become dysmorphic and dysfunctional.[2]

Clinical expression of sickle cell disease is variable, and even carriers of the trait (Hb AS) can produce manifestations as severe as those of patients who are homozygous for the disease (HbSS). It is crucial to recognize variables that play a role in sickling while on cardiopulmonary bypass. Any shift in the oxygen-dissociation curve to the right will increase the likelihood of

sickling, including hypoxemia, acidosis, hypothermia, infection, increase in 2,3 DPG. Other factors that increase the likelihood of sickling include hyper or hypotonicity, blood stagnation, and hemolysis.[4,6] As these manifest during cardiopulmonary bypass, it is essential to recognize which factors cause sickling and minimize these during bypass.[6]

IMPORTANT LIMITATIONS OF THIS DOCUMENT:

1. In emergency situations, immediate life support measures of whatever appropriate nature come first, with attention turning to measures described in this protocol/process as soon as possible and practical.
2. Considering all of the patient's circumstances, the healthcare professional's judgment should always take precedence over these protocols. This protocol/process encourages high-quality patient care but observing it cannot guarantee any specific patient outcome.
3. AmSECT reserves the right, but not the duty, to update this protocol from time to time. Review period: Review as changes occur or per institutional protocol.
4. The original hard copies and computer copies of this protocol are stored under the supervision of the Chief Perfusionist in the Department of Cardiovascular Perfusion.
5. Documents relating to patient care standards are developed according to the accepted hospital standards.

POLICY:

The following modifications must be considered to prevent the risk of sickling and sickling crisis:

1. **Pre-CPB:**
    a. Preoperative exchange transfusion to reduce HbS below 30%.[6]
    b. Temperature:
        i. Maintain normothermia[4,6]
            1. Warm fluids, warming blankets, and warm ambient room temperature.[4,9]
    c. Bypass set up:
        i. Hemolysis:
            1. Carefully set roller head occlusions to avoid unnecessary hemolysis.
            2. Consider using a centrifugal pump, if available.
            3. Judicious use of cell saver.[1]
        ii. Maintain a hyperoxic pump prime to prevent hypoxia during initiation of bypass until full flow CPB is achieved.[1,4]
        iii. Ensure physiologic primes, especially when priming with blood products or performing exchange transfusions.[3]
            1. Maintain an isotonic prime to avoid lysis (hypotonicity) or crenation (hypertonicity) due to RBC membrane fragility.
        iv. Maintain normothermic prime.[1]
    d. Exchange transfusion:
        i. Refer to Exchange Transfusion guideline for set-up.
        ii. Decrease the concentration of HgS below 30% for SCD patients.[3,6,9]
            1. Reduce HgS RBC concentration below 30% using one of the following calculations:
                a. $$\text{Exchange Volume (mL)} = \text{Blood Volume} \times \frac{\text{HbS}_{\text{initial}} - \text{HbS}_{\text{target}}}{\text{HbS}_{\text{initial}}}$$
                b. $V_1 \times C_1 = V_2 \times C_2$
                (V=Volume, C=concentration)
                V_1: Unknown (Pre-CPB blood volume)
                C_1: Initial Hb S+C

V_2: Final CPB Prime Volume (V_1 + Known Prime Volume)
C_2: Final Hb S+C (30-35%)[8]

iii. Verify appropriately decreased HgS concentrations.

e. Anesthesia Management:
   i. Preoperative:
      1. Consider admission the night prior to surgery to prevent dehydration.
      2. It is advisable to hold administrations of blood pressure medications, particularly diuretics and ACE inhibitors.[14]
   ii. Perioperative:
      1. The efficacy of anti-fibrinolytics in SCD patients is not well documented.[4]
      2. Antibiotics to prevent infection.
      3. Nitric oxide to reduce the risk of sickling.
      4. Avoid the following medications, as they are known to induce hemolysis:
         a. Salicylates, quinidine, vitamin K, chloromycetin.
      5. Pre-bypass hemodilution and hydration via anesthesia fluids[3]
      6. Preoperative transfusion[4,7]

2. CPB:

a. Blood gas monitoring:
   i. Maintain a pH 7.35 – 7.45 to prevent acidosis.[3,6]
   ii. Continuous monitoring is recommended.
   iii. If continuous monitoring is unavailable, perform intermittent arterial and continuous venous blood gas analysis to verify and ensure high oxygen saturation and treat any acidosis.[4]
   iv. SVO_2, should be maintained >80% to ensure proper hemoglobin saturation.[6,9]
b. Hematocrit:
   i. Maintain between 25-30% to maintain proper oxygen delivery[6,7,10] while also decreasing viscosity to prevent RBC sludging and subsequent microvascular occlusion.[1,6,10]
c. Temperature management:
   i. Normothermia above 34°C[6,9]
d. Reduce hemolysis:
   i. Minimize usage of pump suckers.
e. Flow:
   i. Maintain high flows of at least 2.4 Cardiac Index (CI) to prevent hypotension and intravascular stagnation.[9]
   ii. Avoid low output and/or blood flow states.[9]
   iii. Use vasodilators, if clinically appropriate, to maintain a higher CI.
   iv. Minimize the use of vasoconstrictors to prevent areas of stagnation.
f. MAP's:
   i. Maintain on the higher end of established institutional protocol ranges to optimize perfusion.[6]
g. Cardioplegia:
   i. There is no consensus on the safest method of cardioplegia (CDPG) delivery.[6]
   ii. Fibrillatory arrest, asanguinous, and warm blood CDPG are alternative options that could be considered in place of cold cardioplegia administration, when applicable/warranted.[6]

iii. If HgS levels lowered to < 30% via exchange transfusions, cold CDPG may be tolerated.[9]
iv. Cold CDPG (4:1 ratio):
1. Initial warm antegrade/retrograde induction dose(s) to wash out HgS from the coronaries before switching to cold CPDG delivery (if cold CPDG is indicated) to decrease risk of sickling within coronaries.[6,9]
a. Washout with warm cardioplegia until full arrest occurs, then switch to cold cardioplegia.[9]
2. Administer subsequent CPDG doses at an initial warm temperature to wash out any stagnant coronary blood before switching to cold CPDG delivery to decrease the risk of sickling in the coronaries.
3. Consider more frequent CPDG doses to avoid prolonged stasis periods in the coronary arteries during the cross-clamp period.
4. Scavenge cold CDPG returning to the right atrium.
5. Due to the potential for sickled cells in the coronaries from stasis of sanguineous CPG delivery, consider flushing the coronaries with warm blood and sending it to wall waste before cross-clamp removal.

h. Anticoagulation:
i. Ensure full anticoagulation for the entirety of the case with ACT's greater than 480 seconds or level established by institutional protocols.
i. Fluids:
i. Preferentially administer isotonic fluids.[12,13]
j. Hemofiltration during and after bypass:
i. Zero-balance ultrafiltration may be performed to reverse high potassium, attributed to additional cardioplegia dosing.[3]
ii. Ultrafiltration, whether it be DUF, CUF, and/or MUF may be utilized[4] with hypervigilance for the following:
1. Dehydration promotes sickling.[11]
2. Maintain euvolemia.[13]
iii. Preferentially use a heat exchanger if performing MUF to maintain perfusate normothermia.
k. DHCA:
i. If necessary, ensure HgS levels are below 30% before the arrest period.[3,6]
l. Cell Saver:
i. AABB denotes that the use of an autotransfusion device in this patient population is a relative contraindication.[5]

3. Post-CPB

a. Minimize stagnation in the bypass circuit by continuously recirculating through all shunts and AV loop.
b. Maintain normothermia:[4,6,9]
i. Warm fluids, warming blankets, and warm ambient room temperature.

CLINICAL ASSESSMENT/SCREENING:

A. Contraindications: None.

RELATED DOCUMENTS:

A. Exchange Transfusion
B. Cardioplegia Solution Delivery System Set-Up and Administration
C. Exchange Transfusion Volume Calculator[8]

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