Guideline

Sickle Cell Crisis: Emergency Management in Children

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Purpose

These guidelines are intended for use by clinicians providing care to children with Sickle Cell Disease (SCD) who present to the Emergency Department, to ensure that these children are expediently and correctly assessed and managed according to best practice guidelines.

Scope

This guideline applies to all patients with Sickle Cell Disease presenting to the Lady Cilento Children's Hospital Emergency Department.

Underlying Principles

SCD is an autosomal recessive disorder caused by a structurally abnormal haemoglobin (HbS) that polymerises with shape change when deoxygenated, resulting in obstruction of blood flow.

There are 3 common types of SCD

- Sickle Cell Anaemia (HbSS)
- Sickle Beta Thalassaemia
- Sickle haemoglobin C disease

Patients with SCD may present with the following acute problems:

- Painful Vaso-occlusive crisis (VOC)
- Fever
- Acute chest syndrome

- Acute splenic sequestration
- Aplastic crisis
- Stroke
- Priapism

Acute crises may occur spontaneously or may be precipitated by infection/ dehydration/ hypoxia or anaesthetic/ surgery.

ALERT : Almost all patients become **functionally asplenic** and are at risk for severe infection and sepsis (particularly by encapsulated organisms). **Infection is the most common cause of death in this group**. Commencement of antibiotic therapy should **not** be delayed if febrile or there is other clinical suspicion of infection.

Triage and Admission Guidelines

Children and young adults known to have SCD who present with pain or an acute intercurrent illness should receive a minimum **ATS Category 2 (review** within 10 minutes of presentation), and treatment should be undertaken with early Consultant or Senior Registrar consultation.

SCD patients with the following presentations **must** be referred for admission:

- Significant pain not responsive to simple analgesia
- Fever (>38°C) without clear focus or patients who are clearly unwell/systemic toxicity
- Fever in a child with a central venous line (CVL) or Port-a-cath
- New neurologic signs or symptoms
- Splenic sequestration (see below)
- Acute Chest Crisis (see below)
- Priapism

SCD patients with the following circumstances should be **strongly considered** for admission:

- Patients aged under 2 years presenting with any acute problem

Children with SCD are admitted under General Paediatrics as the primary team, with Haematology providing regular consultative support as required.

General Approach

Clinical Assessment

History

- Symptoms and duration - pain, dyspnoea, fever, pallor, lethargy, neurologic signs
- Nature of pain and whether it is in keeping with "usual" pain crises
- Provoking factors (fever, travel, procedures, recent hospital admission)
- Past history of chest crises and severity – particularly ICU admission/ previous need for ventilation
- Significant comorbidities – particularly asthma
- Immunisation status and use of prophylactic penicillin
- Usual therapy – hydroxyurea or chronic simple transfusion or exchange transfusion
- Management steps (e.g. oral analgesia / other strategies) already taken at home

Examination

- Vital signs
- Hydration status
- Pallor or jaundice
- Signs of infection
- Cardiopulmonary examination – new findings may indicate chest crisis
- Splenic examination – significant splenomegaly may indicate sequestration crisis
- Neurologic exam – new neurologic findings may indicate stroke

Investigation

- FBC including reticulocyte count
- Blood group and cross match (if suspected anaemia, acutely enlarged spleen, neurologic or respiratory symptoms). If new patient or has never had previous transfusion request **extended red cell phenotyping** given high incidence of alloimmunisation developing in this group.
- Blood and urine cultures if febrile
- ELFTs if dehydrated or jaundiced (or send if IV hydration required)
- CXR if respiratory signs / symptoms, hypoxia, or febrile / toxic appearance
- LP only if would be indicated as per usual work up of a child with "fever and no focus"
- Consider abdominal USS for RUQ or epigastric pain (risk of cholelithiasis and intrahepatic sickling)
- Urgent CT brain **without** contrast (or MRI if available without delay) in a child with new neurologic symptoms or signs

Management (see below for management of specific presentations)

- Do not delay commencement of IV fluid or IV analgesics for topical anaesthetic cream
- Supplemental oxygen should be provided if O2 saturation <96%
- Start analgesics promptly (within 30 minutes of arrival):
    - **Mild pain** – oral paracetamol 15mg/kg (maximum 1g) every 6 hourly and ibuprofen 10mg/kg (maximum 400mg) every 8 hourly
    - **Moderate to severe pain** – oral paracetamol, ibuprofen, **and** morphine 0.1mg/kg intravenously (maximum 5mg) with reassessment within 30 minutes and early consideration of notification of the acute pain service and commencement of a PCA (Patient Controlled Analgesia), nurse controlled analgesia (NCA) or continuous opioid infusion for severe pain (particularly if a repeat bolus of opioid is required within 2 hours). See CHQ Opioid Infusion Guideline (ID CHQ-PROC-01003) and Opioid Intermittent Bolus Injection Guideline (ID CHQ-PROC- 01050)
    - **Intranasal** fentanyl 1 to 1.5micrograms/kg (maximum 100 micrograms per dose) may be considered for severe pain whilst IV access is being established
    - For moderate pain which responds rapidly to initial analgesia a combination of regular paracetamol orally and oxycodone orally 0.1-0.2mg/kg (maximum 5mg) every 4 to 6 hourly may be more appropriate than ongoing intravenous opioid therapy (regular reassessment is required).
    - Where intravenous opioids are used patients must have pulse oximetry applied and a sedation score monitored as per the paediatric analgesic infusion monitoring tool, or, when this is not available, according to local hospital policy (see ID 01003 & 01050 above)
- Fluids
    - Encourage oral fluids
    - May require IV fluids
        - Electrolytes should be ordered prior to IV fluid commencement
        - If clear signs of an acute chest crisis, abdominal or back pain, **do NOT give a bolus** and ensure a maximum total fluid intake of not greater than maintenance rate.
        - If there is clinically apparent dehydration a bolus of 10-20mL/kg of 0.9% sodium chloride (Maximum of 1L) may be considered, followed by maintenance IVF with 0.9% sodium chloride and 5% glucose
        - Fluid balance monitoring should be commenced for all patients
    - Blood transfusion
        - **Not** recommended to be given routinely during acute painful VOC
        - Is not required for severe anaemia that is chronic, asymptomatic and well-compensated (within 10 g/L of the patients normal baseline Hb)
        - "Over-transfusion" (Hb >100 g/L) should be avoided as higher Hb leads to increased plasma viscosity and potential for increased vaso-occlusion
        - **Standard products** are appropriate (irradiated or CMV negative blood product modifications are not required)

Specific Management

Fever

- All sickle cell patients should be treated as if they are functionally asplenic and at risk from invasive disease with encapsulated organisms
- If pain is also present treat concurrently as VOC
- If cough or dyspnoea also present look and treat for acute chest syndrome (see below)
- Commence antibiotics **without delay** if febrile or toxic:
    - Cefotaxime IV 50mg/kg (max 2g/dose) every 6 hours OR Ceftriaxone IV 100mg/kg (max 4g/day) once daily.
        - For patients with known or suspected cephalosporin allergy substitute with Ciprofloxacin 10mg/kg (maximum 400 mg per dose) 12 hourly and Vancomycin 15mg/kg IV 6 hourly (max 750mg per dose for initial dose), and consult Infectious Diseases
    - For severe illness add Vancomycin (15mg/kg IV (max 750mg per dose for initial dose) every 6 hours. Perform therapeutic drug monitoring (Paediatric Vancomycin TDM guideline: https://www.childrens.health.qld.gov.au/wp-content/uploads/PDF/ams/658201.pdf)
    - Consider addition of Azithromycin 10mg/kg (max 500mg) IV daily only if atypical pneumonia strongly suspected

Painful Vaso-occlusive Crisis (VOC)

- All episodes of pain should be treated initially as a VOC
- Note that chest pain may indicate an acute chest syndrome rather than a simple VOC if associated with respiratory symptoms or signs
- Common sites include bone (extremities, dactylitis or hand/foot syndrome, back), and abdomen
    - Bone pain (most common type of pain crisis) may or may not be accompanied by swelling, low-grade fever, redness, and warmth. It may be symmetrical, asymmetrical, or migratory.
    - Dactylitis is a common presentation in infants and toddlers; back and abdominal pain are more common in older children.
    - Abdominal pain is **usually** a simple VOC, but other diagnoses may present similarly (splenic sequestration, liver sequestration, appendicitis, pancreatitis, biliary colic and cholecystitis, urinary tract infection, pelvic inflammatory disease, etc.) and should be ruled out.
- Pain may be very severe and should receive urgent attention
- Analgesia should be provided as per **general management** above
- Assessment of pain should use a validated developmentally-appropriate pain assessment tool - FLACC for **15 days to 3 years**, The Faces Pain Scale – Revised (FPS-R) for **age 4+**, Numbers Rating Scale (NRS) for **age 7+** and Verbal Rating Scale (VRS) for **age 12+.**

Acute chest syndrome (ACS)

- SCD can produce an acute respiratory illness related to infarction of lung tissue
- Chest pain and hypoxia may be the only signs

ALERT : Acute Chest Syndrome can be a life threatening condition and patients can deteriorate quickly.

- **Acute Chest Syndrome (ACS) is defined as a new pulmonary infiltrate AND any one of :**
  - **fever**
  - **tachypnoea**
  - **cough**
  - **hypoxia (O2 Sats<96%)**
  - **increased work of breathing**
  - **chest pain**
- Patients with a history of reactive airway disease/ asthma or previous chest crises are at higher risk
- See **General management** above
- **Supplemental oxygen should be provided to maintain saturations >96%**
- Chest x-ray should be performed (but should not delay prompt therapy).
- Pulse oximetry monitoring is mandatory and venous gas should be performed if hypoxic
- Commence intravenous antibiotics **promptly**
  - Cefotaxime 50mg/kg IV (maximum 2g/dose) every 6 hours
  - Consider addition of Azithromycin 10mg/kg (max 500mg) IV daily only if atypical pneumonia strongly suspected
  - **Addition of Vancomycin (15mg/kg IV (max 750mg per dose for initial dose) every 6 hourly may be considered for severe illness.** Perform therapeutic drug monitoring (Paediatric Vancomycin TDM guideline: https://www.childrens.health.qld.gov.au/wp-content/uploads/PDF/ams/658201.pdf)
- Trial inhaled bronchodilators (reactive airway disease / asthma is common in SCD)
- Oral steroids (prednisone 1mg/kg daily (Maximum 50mg/day) may be considered where clinical features are consistent with a significant reactive airways/ asthma component
- Small volume simple transfusion (10mL/kg) may be appropriate to improve oxygenation (avoid haematocrit, > 30% or Hb > 100 g/L post transfusion) or as a temporising measure whilst exchange is being arranged – Consult Haematology Service for advice
- Intensive Care referral for urgent exchange transfusion (with Haematology consultation) is imperative if there is rapid progression of ACS as manifested by:

- Impending or actual respiratory failure
- Marked clinical deterioration with progressive radiologic findings (particularly if there is deterioration after a simple transfusion)
- For patients with progressive chest crisis where Hb is >100 g/L (or Hct >30%) where simple transfusion not appropriate due to risk of increased viscosity

Acute splenic sequestration

- Defined as a Hb drop of at least 20g/L below baseline in a patient with an acutely enlarged spleen
- Occasionally may be the presenting feature of Sickle Cell Disease (new diagnosis)

ALERT : Acute Splenic Sequestration may present with hypovolaemic shock in the absence of overt bleeding symptoms

- Thrombocytopenia and reticulocytosis is usually present (unless co-existent aplastic crisis)
- While waiting for blood give 0.9% sodium chloride 10-20mL/kg to treat hypovolaemia
- Initial transfusion to aim for a Hb of 50-60g/L initially to ameliorate shock/ haemodynamic instability (10mls/kg)
- Do not raise the Hb above baseline as the spleen will shrink and autotransfusion will occur which can raise the Hb excessively with increased risk of stroke due to hyperviscosity.
- Commence IV antibiotics if febrile – Cefotaxime as above.

Suspected Stroke

- Acute neurologic events occur in ~10% of patients with SCD
- Can occur in isolation, or a complication of acute chest syndrome / aplastic crisis
- See **General Management (above)**
- Airway, breathing and circulation must be addressed first
- Assessment of consciousness (AVPU or GCS) and neurologic examination
- Give high flow oxygen
- If symptoms suggestive of meningitis – urgent blood cultures, lumbar puncture and prompt antibiotic therapy required
- Early consultation with Neurology and Haematology Service is required
- MRI is modality of choice, if not available CT (without contrast – hyperviscosity risk); imaging should not delay appropriate treatment
- Transfusion support (in consultation with Haematology) may be required; early liaison with PICU to prepare for red cell exchange (goal HbS <30% and Hb <100g/L) is recommended; Simple transfusion to Hb 100g/L followed by exchange may be appropriate.

Priapism

- Prolonged painful erection of the penis, can occur in males at any age but increases after puberty
- Common, serious and frequency underdiagnosed complication of SCD – can lead to cavernosal fibrosis and impotence.
- Priapism lasting >3 hours is considered a surgical emergency
- Assess duration of current episode and any associated symptoms – fever, dysuria, dehydration or pain at other locations
- Assess history of prior episodes and previous treatments/ effectiveness
- Encourage emptying of bladder, catheterise if unable to empty
- Simple measures – moderate exercise, shower
- Do **not** use ice as cold may exacerbate sickling
- Hydration, oxygen, analgesia and early consultation with Urology and Haematology

Prepare for urgent exchange transfusion in patient with fulminant priapism > 4 hours despite other measures

Aplastic crisis

- Acute illness associated with Hb below baseline for that patient associated with a substantially low reticulocyte count (usually <1%)
- Associated with acute infection (including Parvovirus)
- See General Management above including attention to management of pain or fever
- Exclude splenic sequestration clinically
- Intravenous fluids and oral intake to a total of maintenance
- If symptomatic anaemia or Hb <50g/L give a blood transfusion (10mL/kg) over 4 hours (do not increase Hb by > 30g/L

Consultation

Key stakeholders who reviewed this version:

- Dr Katie Reeves, Staff Specialist, Emergency Department, Lady Cilento Children's Hospital (CHQ)
- Dr Pasquale Barbaro, Paediatric Haematologist (CHQ)
- Dr John Roy, Paediatric Haematologist (CHQ)
- Dr Clare Nourse, Paediatric Infection Specialist (CHQ)
- Dr Julia Clark, Medical Lead AMS, Service Group Director (Infection Management and Prevention service, Rheumatology and Immunology)
- Dr David Levitt, Director, General Paediatrics (CHQ)
- Nicolette Graham, Antimicrobial Stewardship Pharmacist (CHQ)

References and suggested reading

CHQ-PROC-01003 - Intravenous Opioid Infusions - Patient Controlled Analgesia (PCA), Nurse Controlled Analgesia (NCA), Continuous Opioid Infusion

CHQ-PROC- 01050 - Opioid Intermittent Intravenous (IV) Bolus Injection

CHQ-GDL-01202 - CHQ Paediatric Antibiocard: Empirical Antibiotic Guidelines

Spleen Australia Asplenia/Hyposplenism – Paediatric Guidelines (2016) Age 0 to 18 years
http://www.mvec.vic.edu.au/wp-content/uploads/2016/03/Asplenia-March-2016_children.pdf

Guideline revision and approval history

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1.0	Jeremy Robertson	Haematology Consultant team	Executive Director Medical Services

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