Management of children with acute leukemia and an elevated white blood cell count at diagnosis (hyperleukocytosis) in the Caribbean

Approved by the SickKids-Caribbean Initiative (SCI): June 23, 2015

1.0 Introduction

The SickKids-Caribbean Initiative (SCI) is a not-for-profit collaboration between the Hospital for Sick Children (SickKids), Toronto, Canada, and seven Caribbean health care institutions across six countries that strive to improve the outcomes and quality of life for children with cancer and blood disorders. The initiative has established a strong and formal partnership between SickKids, represented by key healthcare professionals, and six countries in the Caribbean: The Bahamas, Barbados, Jamaica, St. Lucia, St. Vincent and the Grenadines and Trinidad and Tobago. Inter-professional leaders from government, hospitals and academia are working collaboratively to implement a comprehensive strategy to build sustainable capacity in the identification and management of children with cancer and blood disorders in the Caribbean.

Newly diagnosed children with acute leukemia and hyperleukocytosis are at increased risk of early mortality due to severe cerebral, pulmonary and metabolic complications. Prompt reduction of the white blood cell count in these patients can be achieved by an early start of chemotherapy. The following guidance document is an empiric guideline for the management of children with acute leukemia presenting with hyperleukocytosis.

1.1 Disclaimer

This guidance document (“Guidance Document”) is intended solely for healthcare providers who are collaborators in the SickKids-Caribbean Initiative (“Collaborators”).

The Guidance Document is a general guide to appropriate practice, to be followed only subject to the judgment of a patient’s attending physician, taking into consideration all available information related to the condition of the patient and after review of the benefits and risks of the proposed course of action with the patient (if of an appropriate age) and/or the patient’s parents or guardians. The Guidance Document has been specifically tailored for use at Collaborators’ institutions taking into consideration available health care resources and other relevant contextual factors in Collaborators’ countries.

The Guidance Document is NOT intended for use by patients or their families and is not designed or intended to constitute medical advice or to be used for diagnosis. The Guidance Document is NOT a substitute for the personalized judgment and care provided by trained medical professionals.

Every effort has been made to ensure that the information provided in the Guidance Document is accurate and in accordance with the standards accepted at the time it was created, however new research and experience may result in changes to these standards. In all cases, you, in your role as the patient’s physician and the SCI lead physician for the relevant participating SCI country, are responsible for ensuring that the recommendations detailed below comply with all applicable local laws, statutes and regulations.

By viewing and using any information derived from the Guidance Document, you, in your role as the patient’s responsible physician, hereby waive any claims, causes of action and demands, whether in tort or contract, against any of the Collaborators (including their employees, physicians, directors and agents) in any way related to use of the Guidance Document or the information derived from it.
2.0 Definition and Abbreviations

**White Blood Cell**: WBC

**Hyperleukocytosis**: Initial WBC >100,000/mm$^3$

**Acute Lymphoblastic Leukemia**: ALL

**Acute Myeloid Leukemia**: AML

**Chronic Myelogenous Leukemia**: CML

**Acute Promyelocytic Leukemia**: APL

**Tumour Lysis Syndrome**: TLS

**Intravenous**: IV

**Fresh Frozen Plasma**: FFP

3.0 Guideline

3.1 Diagnosis of Hyperleukocytosis

Initial WBC > 100,000 /mm$^3$ at presentation or at relapse in children with ALL, AML or CML.

**Clinical symptoms**

- Neurologic: headache, seizure, decreased level of consciousness (ranging from mild confusion and somnolence to stupor and coma)$^1$
- Respiratory: cough, dyspnea, respiratory distress.
- Vascular: cerebral thrombosis (especially in AML), retinal vein haemorrhage/thrombosis, renal vein thrombosis, acute limb ischemia, myocardial infarction and priapism$^1$

**Investigations**

- NB: Platelets have to be counted manually since a high white blood cell count can result in the false elevation of automated platelet counts (depending on the machine used) due to the presence of white blood cell fragments.$^2$
- Chest radiographs may be normal or show diffuse infiltrates.
- Pulse oximetry may be helpful in demonstrating hypoxemia.$^1$
- Consider a head CT if there is a high suspicion of intracranial haemorrhage (ICH): use contrast with caution in case of renal failure.
Hyperleukocytosis is considered a medical emergency. Children with symptoms due to leukostasis or with an extremely elevated WBC (as indicated below) require urgent admission to the Pediatric floor or Pediatric Haematology/Oncology Unit. A Staff physician with experience in managing children with malignancies should be involved with the assessment and management of these children in the Emergency Department before transfer to a Hospital Ward.

3.2 Treatment

3.2.1 Supportive measures

- Prevention and treatment of acute TLS including: hydration with 0.9% sodium chloride IV at 3L/m²/day (or 200mL/kg/day if the child weighs less than or equal to 10kg). This is contraindicated if the child presents in acute renal failure.

- Mannitol or furosemide to maintain urine output of at least 80% of input (especially for children with a weight of less than or equal to 10kg).

- Avoid potassium, calcium and phosphate in IV fluids.

- Monitor serum creatinine, urea, urate, potassium, phosphate, calcium, sodium, albumin, and bicarbonate concentrations every 4 hours initially; glucose as needed.

- DIC and/or thrombocytopenia should be corrected aggressively: maintain the platelet count above 40 x 10⁹/L to reduce the risk of ICH (the combination of thrombocytopenia and hyperleukocytosis is a risk factor for CNS hemorrhage³).

  In cases of APL or AML, transfuse cryoprecipitate and FFP to keep fibrinogen > 1.5 g/L and INR < 1.3.

- Avoid the transfusion of packed RBC: RBC transfusions worsen hyperviscosity and have been associated with increased morbidity and mortality in patients with hyperleukocytosis⁴.⁵. In contrast, transfusion of platelets and fresh frozen plasma do not worsen the hematocrit. The judicious use of diuresis and gradual PRBC transfusion (e.g. slow transfusion of 3-5mL/kg of PRBC) is strongly recommended in case of congestive heart failure. Depending on the patient’s condition, this can be repeated until the hemoglobin level is satisfactory.

- If coagulation markers are not promptly available, consider giving pre-emptive FFP 10mL/kg. If FFP is not readily available, consider administering cryoprecipitate 1unit/10kg.
  If FFP was administered and fibrinogen was determined to be less than 1g/L thereafter, administer cryoprecipitate.

3.2.2 Reduction of the WBC

Early start of chemotherapy

- Start induction chemotherapy as soon as the diagnosis of leukemia has been confirmed. Keep in mind that in cases of leukemia with hyperleukocytosis diagnostic tests including morphology, flow cytometry,
molecular tests and cytogenetics can be performed on a sample of peripheral blood; an early start of therapy should not be postponed because of the delays associated with scheduling a diagnostic bone marrow aspirate.

- Be prepared for a prompt diagnosis and treatment of acute TLS associated with the chemotherapy-induced breakdown of large number of leukemic blasts in patients with hyperleukocytosis.

- In AML patients: consider starting hydroxyurea (25mg/kg/dose po once daily) or low dose cytarabine (100mg/m²/dose IV q12h) only for 1-2 days.

  In cases of AML M4/M4E0/M5 with respiratory distress, consider holding cytarabine and starting dexamethasone 6mg/m²/day divided bid (twice daily) for 3 days to treat pulmonary symptoms.

- In ALL patients: consider adding prednisone with allopurinol and hyperhydration for 1-2 days
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4.0 References


6.0 Guidance Document Group and Reviewers


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Strategic input to guide the development of this Guidance Document was solidified from and provided by clinical stakeholders the following Caribbean hospitals:

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- Milton Cato Memorial Hospital, Kingstown, St. Vincent and the Grenadines
- Victoria Hospital, St. Lucia
- Queen Elizabeth Hospital, Bridgetown, Barbados
- Princess Margaret Hospital, Nassau, The Bahamas
- Eric Williams Medical Sciences Complex, Trinidad and Tobago