1.0 Introduction

The purpose of this document is to supplement the supportive care documents provided in the current COG AML protocol and to clarify the recommendations for The Hospital for Sick Children (SickKids) specifically. It is suggested that the reader refer to the current COG AML protocol, (a protocol link can be found in the patient summary section of the Hem/Onc database or on COG website) in conjunction with this document. The target users of this guideline are nurses, physicians, and pharmacists. These guidelines are intended for patients with de novo AML excluding acute promyelocytic leukemia.

2.0 Definitions

AML - acute myeloid leukemia

3.0 Clinical Practice Guideline

Statement of Evidence
A literature search was conducted using Medline from 1966 – 2016, using keywords acute myeloid leukemia and other terms specific to area of recommendation. Grade A evidence is available regarding fluconazole prophylaxis in patients with a high risk of invasive fungal infection. Recommendations regarding discharge and the association between corticosteroids and invasive fungal infection are derived from grade B evidence.

Table 1. Grades of Recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tr>
<td>A</td>
<td>Recommendation supported by at least one randomized controlled trial, systematic review or meta-analysis.</td>
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<tr>
<td>B</td>
<td>Recommendation supported by at least one cohort comparison, case study or other experimental study.</td>
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<tr>
<td>C</td>
<td>Recommendation supported by expert opinion or experience of a consensus panel.</td>
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3.1 Criteria for Discharge or Pass

3.1.1 It is suggested that families be informed at initial diagnosis that discharge home between cycles of chemotherapy may be possible depending on clinical course and individual factors. (Grade B)
3.1.2 Criteria for discharge or pass are identical and include all of the following:\(^{(1-3)}\) (Grade B)
- Bone marrow recovery is defined as an increasing absolute neutrophil count (ANC) (neutrophils plus bands) on at least two consecutive measurements following the nadir
- Minimum ANC of 0.1 x 10^9/L
- Clinically well and not in need of other inpatient care
- Consideration for the distance from hospital to home and the ability of the family to return to the hospital promptly
- Patients admitted for CLASP (higher dose cytarabine and L-asparaginase) cycles of therapy may be discharged on day 3 of therapy and readmitted for day 8 therapy provided that they meet all of the above criteria for discharge. Given the timing requirements for this cycle of therapy these patients will be given priority for bed assignment for readmission. Patients receiving a CLASP cycle of chemotherapy for relapsed leukemia will not be eligible for discharge between days 3 and 8 of this cycle of therapy.

The decision to discharge or send the patient on pass lies with the responsible physician on the inpatient unit.

3.2 Vital Sign Monitoring during Admission

3.2.1 Vital signs must be obtained q4h while hospitalized until criteria for discharge/pass are met. (Grade C)

3.3 Management of Fever

3.3.1 Refer to the SickKids’ Formulary Antimicrobial Guidelines for: Management of Haematology/Oncology & Haematopoietic Progenitor Cell Transplant Patients (HPCT) with Fever (Grades A & B)

3.4 Prophylaxis and Management of Invasive Fungal Infection

3.4.1 These patients should receive fluconazole or caspofungin prophylaxis.\(^{(4)}\) Caspofungin is reserved for use in patients who cannot receive fluconazole due to liver impairment, hypersensitivy or are receiving concurrent medication which interact with fluconazole (eg sorafenib). Although a CYP34A-mediated interaction between etoposide and fluconazole is theoretically possible, the clinical significance of this interaction is unknown. Therefore, we will give etoposide and fluconazole concurrently until more information becomes available. Following the last cycle of chemotherapy, fluconazole or caspofungin prophylaxis should be continued until an ANC of at least 0.1 x 10^9/L following the nadir has been achieved.

3.4.2 Empiric antifungal therapy should be initiated as per the SickKids’ Formulary Antimicrobial Guidelines for: Empiric Antifungal Use in Haematology/Oncology Patients. Given the high risk for invasive fungal infection in this patient population,\(^{(5)}\) initiation of empiric antifungal therapy on day 5 of persistent fever or in the event of a new fever after 5 days of empiric antibiotic therapy is encouraged (Grade A).

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3.5 Other Prophylaxis Against Infection

3.5.1 Refer to the SickKids’ Formulary Antimicrobial Guidelines for: Prophylaxis for *Pneumocystis pneumonia* (Grade A). Prophylaxis for *Pneumocystis pneumonia* should be continued for 3 months following completion of chemotherapy.

3.5.2 Prophylactic acyclovir should not be routinely administered prior to progenitor cell transplantation. (Grade A)

3.6 Corticosteroid Administration

3.6.1 Prolonged administration of corticosteroids is associated with an increased risk of invasive fungal infection (Grade B)

3.6.2 Corticosteroids should not be administered routinely as an anti-emetic unless the patient has failed ondansetron prophylaxis (i.e. 2 vomits and/or retched in 24 hours or significant nausea) (Grade C)

3.6.3 All attempts to minimize the duration of corticosteroid administration should be made. (Grade C)

3.6.4 Corticosteroid eye drops are not required prophylactically for courses of lower dose cytarabine (100 mg/m²) but should be given if conjunctivitis develops. Corticosteroids eye drops are required for cycles of therapy containing higher dose cytarabine (1000mg/m²) or greater (Grade C)

3.7 Menses Suppression

3.7.1 The need for menses suppression during treatment should be considered on an individual basis. If required, refer to the Sick Kids’ Formulary guidelines for: Menses Suppression in Girls Receiving Chemotherapy (Grade C)

4.0 Implementation of CPG

Organizational barriers to implementation

- Distance between home and hospital.

Facilitators to implementation

- Ronald McDonald House or alternative proximal housing

Potential economic impact

- Fewer days of hospitalization
Key review criteria/indicators for monitoring and audit purposes

- Morbidity and mortality

5.0 Related Documents

- AAML1031 (A protocol link can be found in the patient summary section of the Haem/Onc database or on the COG website)
- SickKids’ Formulary Antimicrobial Guideline for: Management of Haematology/Oncology & Haematopoietic Progenitor Cell Transplant Patients (HPCT) with Fever
- SickKids’ Formulary Antimicrobial Guideline for: Empiric Antifungal Use in Haematology/Oncology Patients
- SickKids’ Formulary Antimicrobial Guideline for: Prophylaxis for Pneumocystis pneumonia
- Menses Suppression in Girls Receiving Chemotherapy

6.0 References

7.0 Guideline Group and Reviewers

Guideline Group Membership:

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Revision History
Approved Haem/Onc QUPC April 11, 2011
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Approved by Haem/Onc/BMT/Imm/Allergy Quality, Utilization and Patient Care Committee: April 9, 2007
Approved by Section of Leukemia and Lymphoma: Dec. 13, 2006

Attachments:
Revision History.docx