Fungal Infection Prophylaxis and Incidence of Fungal Infections in Children With Cancer

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Background

- Invasive fungal infections (IFI) contribute to morbidity and mortality in children with cancer
- Children with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and allogeneic hematopoietic stem cell transplantation (HSCT) are at increased risk for IFI
- Incidence of IFI ranges between 5-15% and varies based on geographical region and institution[1, 2]
- Most common pathogens: [3]
  - *Candida* species: mortality 20-40%
  - *Aspergillus* species: mortality 50-90%
- Although fungal prophylaxis is recommended in children at risk of IFI, there is no consensus on choice of agent, duration of prophylaxis, and population due to the limited evidence available

Objectives

- **Primary -** To describe inpatient antifungal prophylaxis in AML, relapsed ALL, and post-HSCT at BC Children's Hospital (BCCH)
- **Secondary -** To describe:
  - Indication for fungal prophylaxis
  - Antifungal used, dosage, and duration
  - Prevalence of proven, probable, or possible fungal infections
  - Prevalence and type of adverse effect

Methods

- **Design:** Retrospective cohort
- **Inclusion:** Children admitted to BCCH, aged 0 to 19, diagnosis of AML, relapsed AML, relapsed ALL, and post-HSCT
  - Longitudinal analysis: Data collected for all eligible diagnoses during the study period
- **Study Period**: January 2015 and June 2019
- **Adverse Effects:** Adverse effects associated Naranjo score

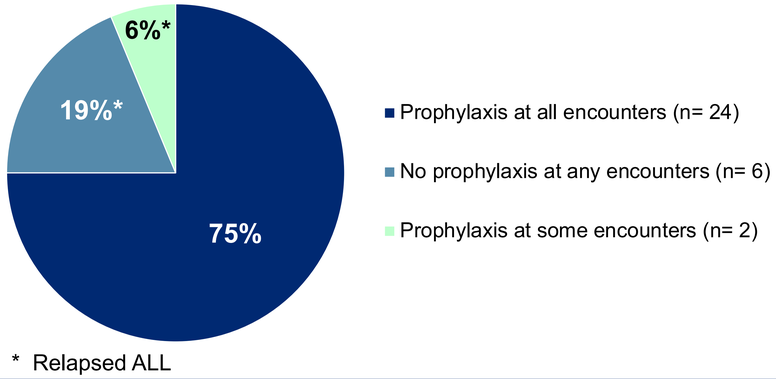
Results

Table 1. Baseline Characteristics

	N= 32
Age at Treatment, years [median (range)]	5 (1 – 19)
Male [n (%)]	22 (69)
Underlying Primary Diagnosis [n (%)]	
AML [a]	7 (22)
Relapsed AML [b]	1 (3)
Relapsed ALL [c]	9 (28)
Allogeneic HSCT	6 (19)
Autologous HSCT	9 (28)
Risk Factors [n (%)]	
Age at Diagnosis ≥10 years	7 (22)
Allogeneic HSCT	12 (38)
Central Line	32 (100)
ANC ≤ 0.5 for ≥ 10 days	20 (63)
Antibiotics ≥ 10 days	21 (66)
High dose steroids	25 (78)
TPN	11 (34)

[a] *Relapsed + received HSCT (n= 3)*
[b] *Received HSCT during study period*
[c] *Received HSCT (n= 1)*

Figure 1. Fungal Prophylaxis



* Relapsed ALL

Table 2. Fungal Prophylaxis

	N= 32
Caspofungin [n (%)]	22 (69)
▪ Dose, mg/m^2/day [median (range)]	47.6 (28 - 52)
▪ Duration, days [median (range)]	25 (6 – 63)
Fluconazole [n (%)]	2 (6)
▪ Dose, mg/kg/day [median (range)]	4.85 (4.8 – 4.9)
▪ Duration, days [median (range)]	12.5 (5 – 20)
Multiple [n (%)]	2 (6)
▪ Caspofungin + Fluconazole	
None [n (%)]	6 (19)

Prevalence of Fungal Infection

- No proven or probable fungal infections
- One possible fungal infection: participant receiving caspofungin prophylaxis
  - Relapsed ALL
  - Risk factors: 5
  - Treated and recovered with voriconazole

Table 3. Adverse Effects

	N= 26 n (%)	Naranjo Score [median (range)]
CNS Toxicity	1 (4)	1
Nephrotoxicity	5 (19)	1
Skin Reaction	16 (62)	1 (1 – 2)
Increase in Liver Enzymes	12 (46)	1 (1 – 2)
Hypokalemia	21 (81)	1 (1 – 2)

Limitations

- Retrospective chart review
- Small sample size, 86 participants not collected
- Only described inpatient prophylaxis

Conclusions

- Majority of participants received fungal prophylaxis with caspofungin
- Low incidence of IFI at BCCH
- Adverse effects had low likelihood of being related to fungal prophylaxis ("possible" score)

References

[1] Lehrnbecher T, Schoening S, Poyer F, Georg J, Becker A, Gordon K, Attarbaschi A, Groll AH. Incidence and outcome of invasive fungal diseases in children with hematological malignancies and/or allogeneic hematopoietic stem cell transplantation: results of a prospective multicenter study. Front Microbiol. 2019 Apr;10(681)

[2] Groll AH, Castagnola E, Cesaro S, Dalle JH, Engelhard D, Hope W, Roilides E, Styczynski J, Warris A, Lehrnbecher T. Fourth European Conference on Infections in Leukaemia (ECIL-4): Guidelines for diagnosis, prevention, and treatment of invasive fungal diseases in paediatric patients with cancer or allogeneic haemopoietic stem-cell transplantation. Lancet Oncol. 2014 Jul 1;15(8): 327-40

[3] Tragiannidis A, Dokos C, Lehrnbecher T, Groll AH. Antifungal chemoprophylaxis in children and adolescents with haematological malignancies and following allogeneic haematopoietic stem cell transplantation. Drugs. 2012 Mar 1;72(5):685-704