Fungal Prophylaxis in all-type ALL patients at a Paediatric Hospital after the new guideline.

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BACKGROUND:

The publication of "*Australasian consensus guidelines for the management of invasive fungal disease and use of antifungal agents in the haematology/oncology setting"* in 2021 prompted a review of the local fungal prophylaxis guideline - *Primary Fungal Prophylaxis in Haematology and Oncology patients*.

This was done to ensure best outcomes for paediatric Acute Lymphoblastic Leukaemia (ALL) patients as part of the hospital's antimicrobial stewardship activities.

The requirements specific to the patient population group being evaluated in this study based on the local GL, are summarised below:

Induction Phase (approx. 4 weeks)

B-cell	T-cell
• For all High Risk (HR) patients • Not for Standard Risk (SR) patients	• For all patients

Consolidation Phase (approx. 8-9 weeks)

B-cell	T-cell
• For HR patients when Absolute Neutrophil Count (ANC) $< 0.5 \times 10^9$/L • Not for Standard Risk (SR) patients	• For all patients when ANC $< 0.5 \times 10^9$/L

Interim Maintenance (approx. 8 weeks)

T-cell and B-Cell
- No antifungal prophylaxis recommended (regardless of ANC)

Delayed Intensification (approx. 8 weeks)

T-cell and B-cell
- For all patients when ANC $< 0.5 \times 10^9$/L

Interim maintenance 2 /maintenance (approx. 20 months)

T-Cell and B-Cell
- No further antifungal prophylaxis recommended

All patients who require fungal prophylaxis for the three treatment protocols also receive Vinca Alkaloid therapy. Fungal prophylaxis constitutes IV caspofungin as first line and IV amphotericin B as second line agent.

AIM:

To audit the use of fungal prophylaxis in ALL patients and evaluate adherence to the updated "*Primary Fungal Prophylaxis in Haematology and Oncology patients"* WCH guideline.

METHODS:

A retrospective audit was conducted of the patients as per the inclusion criteria below. Paper case notes of eligible patients were reviewed

Inclusion Criteria
Age 0 – 18 years
B-cell ALL or T-cell ALL
Initiated treatment after 1st July 2021
Started maintenance treatment before 30th May 2023

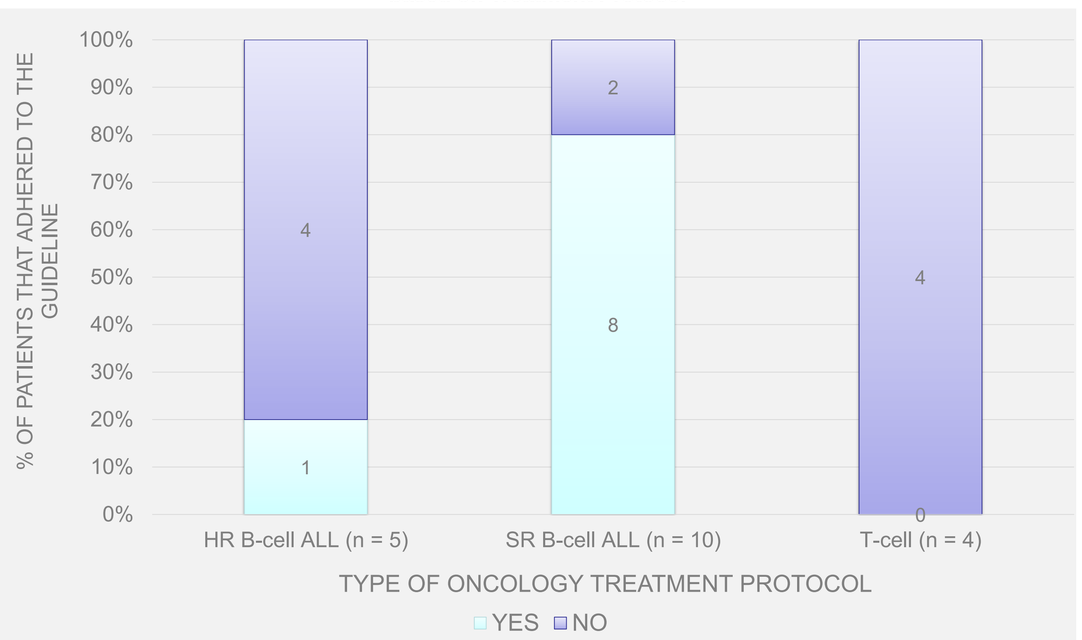
The data collected included;
- Oncology treatment protocol details
- Incidence of acute neutrophil count less then 0.5×10^9/L
- If and what fungal prophylaxis was provided
- Duration of fungal prophylaxis provided

Data was consolidated and compared against the updated antifungal guideline.

RESULTS:

19 patients met the inclusion criteria. They were grouped based on their oncology treatment protocol; 5 patients were HR B-cell ALL, 10 patients were SR B-cell ALL and 4 patients were T-cell ALL.

FIGURE 1: The Percentage of ALL patients who adhered to the Fungal Prophylaxis Guideline based on Treatment Protocol



HR B-cell ALL
- Four out of 5 patients received fungal prophylaxis in induction phase
- For 3 patients, treatment continued longer than necessary (often for an additional month) during the consolidation phase, when ANC was $> 0.5 \times 10^9$/L. Reason provided for one of these patients continuing therapy, was being admitted to the ward, regardless of ANC level .
- During delayed intensification phase, one patient received posaconazole instead of caspofungin for the ease of administration when travelling overseas.

SR B-cell ALL
- Eight out of 10 patients received fungal prophylaxis during the appropriate time periods.

T-cell ALL
- During the consolidation phase, all 4 patients received fungal prophylaxis despite having an ANC $> 0.5 \times 10^9$/L, often continuing for an additional month
- One patient received treatment for the first 4 of 8 weeks of the interim maintenance phase.

DISCUSSION:

At the time of this audit, WCH had paper medical records which offer poor documentation around when treatment was given and therefore relying on ANC blood results to interpret compliance to the guideline.

Fungal prophylaxis is crucial during ALL therapy to prevent invasive fungal disease in immunocompromised patients. The compliance to the current paediatric fungal prophylaxis guideline is sub-optimal.. Clinician discussion indicate that this maybe due to,
- An incorrect interpretation/evaluation of observed or expected low ANC by the auditor
- Continuing treatment expecting ANC to be low even when the levels were high
- Continuing treatment as the patients was admitted

Inappropriate use of antifungal medications could have side effects and pose logistical problems as below:.
- IV caspofungin infusion is given over 1 hour, requiring daily hospital in the home visits
- Liposomal amphotericin (3times a week) often leads to electrolyte imbalances
- Posaconazole and voriconazole require therapeutic drug monitoring to ensure therapeutic levels are achieved.

It is thereby important to not use antifungal medications when not indicated in this vulnerable group of patients.

CONCLUSION:

There needs to be education and awareness with respect to fungal prophylaxis in ALL paediatric patients to guide appropriate use. The guideline needs to elaborate on the interpretation of expected ANC levels to guide clinicians toward appropriate duration of therapy.

MOVING FORWARD:

- Now that WCH has EMR, a repeat audit should be conducted to check guideline compliance, as documentation is better and easier to access
- The WCH guideline "*Primary Fungal Prophylaxis in Haematology and Oncology patients"* needs to be amended to add in details of ANC interpretation

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