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AUDIT OF INVASIVE FUNGAL DISEASE (IFD) IN PAEDIATRIC HAEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) RECIPIENTS AND COMPLIANCE WITH A NATIONAL GUIDELINE FOR THE DIAGNOSIS, PREVENTION AND TREATMENT OF FUNGAL INFECTIONS DURING PAEDIATRIC HSCT; THE ROYAL MARSDEN HOSPITAL (RMH) EXPERIENCE 2018 – 2019.

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INTRODUCTION

Invasive fungal disease (IFD) in paediatric patients undergoing allogeneic stem cell transplant remains a recognised cause of morbidity and mortality. The national UK paediatric bone marrow transplant group agreed consensus guidelines for individual centre use in 2017.

AIM

A national multi-centre prospective audit is in progress with the aim to harmonise practice and to collect data on IFD incidence and effectiveness of current prophylaxis, diagnosis and treatment strategies.

We report single centre data for the Royal Marsden Hospital (RMH) over a one year period 2018 – 2019.

The local aims of the study were to assess IFD incidence, assess heterogeneity of practice in reference to the national guidelines and identify areas for local quality improvement.

METHOD

A prospective multi-centre data collection tool was used (REDCap) to capture antifungal use and IFD incidence. RMH data was collected for 27 paediatric HSCT patients (2-18 years, median 7 years) on a weekly basis with the median follow-up of 27 weeks (1-66).

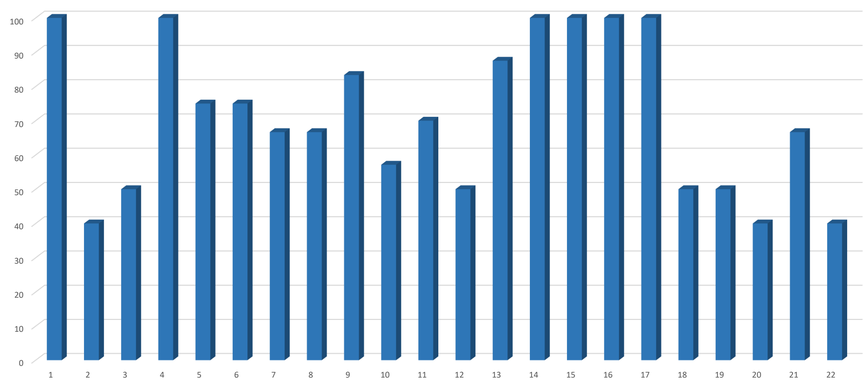
RESULTS

The antifungal primary prophylaxis used in the first month following HSCT was liposomal amphotericin (12), itraconazole (10) and caspofungin (2). 3 patients had a probable/proven IFD before transplant and were given antifungal treatment or secondary prophylaxis throughout the transplant including 1 patient who had active probable pulmonary IFD at time of transplant.

At last follow-up, 22/27 patients were alive, while 4 children died of transplant-related complications (no IFD) and one child died of leukaemia relapse. There were 28 episodes required empirical or pre-emptive antifungal treatment in 16 patients. 8/28 cases were suggestive of IFD (6 pulmonary, 1 hepatic, 1 central nervous system) in the period from day +7 until day +369 after HSCT and 1 case of proven Candida parapsilosis-associated sepsis was diagnosed on day +58 after HSCT.

Antifungal treatment occurred in line with the national guideline in all cases with liposomal amphotericin, caspofungin, voriconazole, posaconazole and anidulafungin used as agents. However, a moderate rate of none compliance with investigations in the cases of suspected IFD was identified 8/28 cases (28%) missing either diagnostic radiology or microbiology investigations. Out of 8 cases suggestive of IFD, there were 3 cases of potential probable IFD, for which the necessary diagnostic investigations had not been completed. Out of 6 pulmonary IFD cases, 3 patients underwent bronchoscopy but only 1/3 had 18s PCR testing. Therapeutic drug monitoring (TDM) occurred in all cases of azole prophylaxis but did not always occur with recommended frequency (weekly while inpatient and every outpatient appointment). Compliant azoles TDM rate was 68.3% in inpatient and 83.8% in the outpatient settings (Fig. 1). Appropriate dose adjustment following the level occurred in 40% of inpatient and 39% outpatient cases (Fig. 2). There were 12 cases of liposomal amphotericin renal toxicity (5 on the prophylactic dose and 7 on treatment dose) and 5 cases of azoles hepatotoxicity.

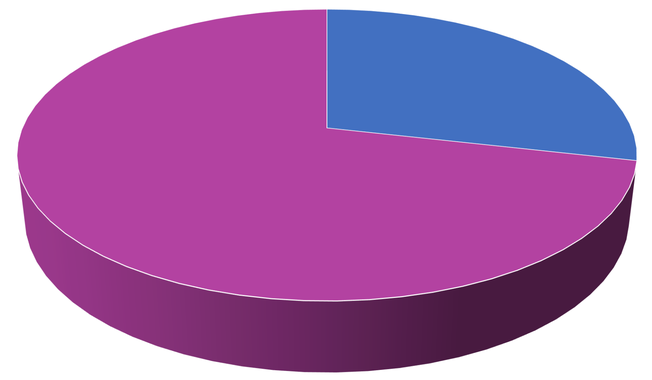
Azoles TDM weekly for inpatients, N of weeks from the start of azoles when the level checked out of N weeks on azole while inpatient in %



Azoles TDM every appointment for outpatients but not more than once weekly, N of episodes when the level was checked out of episodes when level check is appropriate and indicated, %

Figure 1

Azoles dose adjustment following TDM for inpatients



Azoles dose adjustment following TDM for outpatients

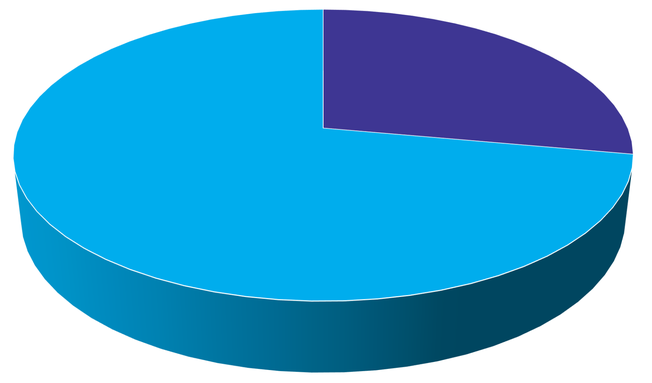


Figure 2

CONCLUSIONS

This single centre data confirms expected incidence of fungal infection in a paediatric allogeneic population and when multi-centre data is available will provide a new national benchmark for current morbidity and mortality related to fungal infections in UK allogeneic transplant recipients. Assessment of compliance with the national guideline highlighted areas for quality improvement and re-audit in relation to diagnostic pathways and TDM.

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