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BACKGROUND

- Antimicrobial stewardship programs (ASP) have primarily focused on the optimization of antibiotic therapy, while the use of antifungal therapy and antiviral therapy has been relatively ignored
- Antifungal and antiviral medications are often used in high-risk patients (i.e. immunocompromised, oncology, transplant), are costly, and are frequently associated with adverse drug effects
- Use of antifungal and antiviral therapy in children demands closer scrutiny to improve patient outcomes and potentially reduce hospital expenditures

OBJECTIVE

Compare the prescribing of antifungal and antivirals among a high-risk pediatric population of oncology, bone marrow transplant, and solid organ transplant patients across free-standing U.S. children's hospitals to identify potential targets for antimicrobial stewardship efforts.

METHODS

- Study Design:** Retrospective cohort study of antifungal and antiviral prescribing in high-risk hospitalized pediatric patients across 47 free standing children's hospitals
- Data Source:** Pediatric Health Information System database
- Study Population:**
 - Less than 18 years of age
 - Discharged between January 1 and December 31, 2015
 - High-risk patients: All Patient Refined Diagnosis Related Group (APR-DRG; version 32) for oncology, bone marrow transplant, or solid organ transplant
- Study Drugs:**
 - Antifungal therapy: fluconazole, voriconazole, posaconazole, itraconazole, amphotericin, caspofungin, micafungin, anidulafungin, flucytosine, or terbinafine
 - Antiviral therapy: acyclovir, cidofovir, famciclovir, foscarnet, ganciclovir, oseltamivir, peramivir, ribavirin, rimantadine, valacyclovir, valganciclovir, or zanamivir

METHODS

Data Collection:

- Antifungal and antiviral use: proportion of patients who received any antifungal or antiviral therapy within each APR-DRG; total days of antifungal or antiviral therapy (DOT) were standardized per 1,000 patient days

Statistical analysis:

- Frequencies and proportions for categorical data; medians and interquartile ranges for continuous variables
- Study deemed nonhuman subjects by the Children's Hospital of Philadelphia Institutional Review Board

RESULTS

Demographics: 784,240 total inpatient discharges; 35,211 (4.5%) of which were classified as oncology, bone marrow transplant, or solid organ transplant by APR-DRG. These high-risk patients were predominately male (56%) and Caucasian (63%), with a median age of 7.9 years (3.6-13.6 IQR).

Use: high-risk patients received 50% of all antifungal DOT and 46% of all antiviral DOT despite comprising less than 5% of all hospital discharges.

Variability: antifungal use ranged from 75 to 608 DOT/1000; median 371 (263-428) antiviral use ranged from 18 to 451 DOT/1000; median 230 (146-275)

RESULTS

TABLE 1. Antifungal Therapy (AFT) and Antiviral Therapy (AVT) Prescribing Among High-Risk Children

APR-DRG Title	Total Patients (N)	Patients Prescribed AFT (%)	AFT DOT/1000 days	Patients Prescribed AVT (%)	AVT DOT/1000 days
Chemotherapy	18884	12%	257	5%	70
Major hematologic/immunologic diagnosis except sickle cell crisis & coagulopathy	7474	20%	306	11%	148
Acute leukemia	2431	34%	460	11%	100
Bone marrow transplant	1323	93%	845	80%	685
Nervous system malignancy	772	6%	66	3%	25
Other OR prophylaxis for lymphatic/hematopoietic/other neoplasms	500	19%	434	7%	92
Musculoskeletal malignancy	488	4%	36	4%	45
Lymphoma, myeloma & non-acute leukemia	459	19%	279	10%	80
Major OR prophylaxis for lymphatic/hematopoietic/other neoplasms	434	26%	443	6%	94
Kidney transplant	363	21%	116	88%	656
Heart &/or lung transplant	362	41%	125	83%	308
Kidney & urinary tract procedures for malignancy	336	4%	41	0%	0
Liver transplant &/or intestinal transplant	332	71%	459	94%	626

CONCLUSION

- Antifungal and antiviral agents represent important stewardship targets because they:
 - Are used for the treatment or prevention of relatively high-risk infections
 - Can be associated with a relatively high rate of adverse drug effects
 - Often require challenging therapeutic drug monitoring
 - Are costly
- Prescribing of antifungals and antivirals is relatively high among this immune compromised population
- Variability in the use of these agents exists, even when examining this relatively homogenous cohort
- Guidelines exist to address antifungal and antiviral therapy in oncology and transplant patients and our data suggests that more can be done to standardize practice and minimize unnecessary use
- Benchmarking antifungal and antiviral is an important step in identifying targeted stewardship strategies to enhance judicious antimicrobial prescribing

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FIGURE 1. Variability in Antifungal Therapy and Antiviral Therapy Prescribing Among High-Risk Children in 47 Free Standing Children's Hospitals

