

Session: 151. Viruses and Bacteria in Immunocompromised Patients

Friday, October 5, 2018: 12:30 PM

Background. Diarrhea is common among hematopoietic stem cell transplant (HSCT) recipients, but the etiology is rarely identified. Multiplexed PCR may increase the detection of diarrheal pathogens, but its role has not been evaluated in this population.

Methods. In June 2016, the FilmArray™ Gastrointestinal panel (GI PCR) was implemented at NewYork-Presbyterian Hospital/Weill Cornell Medical Center to diagnose infectious diarrhea, replacing stool culture and other conventional Methods. We reviewed all adult patients who received a HSCT at our center from June 2014–May 2015 (pre-GI PCR) and June 2016–March 2017 (post-GI PCR). *Clostridium difficile* infection was diagnosed by PCR for toxin B gene in both cohorts. Patients were followed for 1 year post-transplant. We compared the percentage of patients with an identified diarrheal pathogen, yield of testing per diarrheal episode, and number and cost of stool tests between cohorts.

Results. We identified 163 HSCT recipients in the pre-GI PCR cohort and 146 in the post-GI PCR cohort. Patients had a median of two diarrheal episodes during 1-year follow-up in both cohorts. The proportion of patients with at least one identified infectious etiology of diarrhea increased from 21.5 to 34.3% after implementation of GI PCR ($P = 0.01$). Only two patients (1.2%) in the pre-GI PCR cohort tested positive for a pathogen other than *C. difficile*, vs. 35 patients (24.0%) in the post-GI PCR cohort ($P < 0.001$). Post-GI PCR, patients were most likely to have the following pathogens: *C. difficile* ($n = 23$, 15.8%), diarrheagenic *Escherichia coli* ($n = 20$, 13.7%), and norovirus ($n = 10$, 6.8%). The percentage of diarrheal episodes for which an infectious etiology was identified increased from 11.7% (41/351) to 20.9% (74/354; $P = 0.001$) in the post-GI PCR period. The median number of stool tests performed per year per patient decreased from 12 (interquartile range [IQR] 7–20) to 5 (IQR 3–11; $P < 0.001$). Median costs of stool testing per patient during follow-up did not differ: (pre: \$473, IQR \$243–851) vs. (post: \$425, IQR 249–956; $P = 0.23$).

Conclusion. After introduction of GI PCR, infectious etiologies of diarrhea were identified in a higher proportion of HSCT recipients compared with traditional stool testing, without an increase in testing costs.

Disclosures. L. Westblade, BioFire Diagnostics, LLC.: Research Contractor, Grant recipient. C. Crawford, Merck: Scientific Advisor and Speaker's Bureau, Consulting fee; Redhill: Speaker's Bureau, Speaker honorarium. M. Satlin, Biomerieux: Grant Investigator, Grant recipient.

1590. A Hybrid CMV Prevention Strategy Is Effective in Preventing CMV Disease Outcomes in Pediatric Solid Organ Transplant Patients

Lucia Dalle Ore, BS¹, Derek Boothroyd, PhD², Hayley Gans, MD, FPIDS³ and Sharon F. Chen, MD, MS⁴; ¹University of Southern California, Los Angeles, California, ²Stanford University, Palo Alto, California, ³Pediatrics, Stanford University School of Medicine, Stanford, California and ⁴Pediatrics, Stanford University, Stanford, California

Session: 151. Viruses and Bacteria in Immunocompromised Patients

Friday, October 5, 2018: 12:30 PM

Background. Optimal CMV prevention strategies for pediatric solid-organ transplant (SOT) patients have not been clearly defined for early and late post-transplant periods.

Methods. We analyzed CMV prevention strategies in liver, kidney, heart, lung and intestinal SOT patients from 2005 to 2015 in our institution. A hybrid strategy was defined as prophylaxis for ≤ 6 months post-transplant and then transition to a pre-emptive strategy.

Results. Of 833 patients, 769 were prophylaxis and 62 were hybrid strategies. Compared with prophylaxis, hybrid patients were more likely to have a D–/R– CMV serology status, be ≤ 1 year old and have a heart transplant ($P < 0.001$). We found no significant differences in CMV disease frequency, rejection or mortality between hybrid and prophylaxis groups. In total, we found 13 cases of CMV disease, of which 1 was a hybrid and the rest a prophylaxis strategy. The median time to CMV disease was 1.5 years from transplant. We found more allograft rejection ($n = 9$) in patients with CMV disease compared with patients with CMV infection or no infection. For the same comparisons, no significant difference was found for age or type of organ transplant. Late rejection was frequent ($n = 6/13$, 67%) in patients with CMV disease, and the majority were not started on empiric anti-virals with the rejection episode. In contrast, no CMV disease was found in patients who had late rejection and received empiric anti-viral with the rejection episode, even though these patients had increasing CMV DNAemia ($P = 0.04$).

Conclusion. In the early post-transplant period, a hybrid CMV prevention strategy is effective with similar clinical outcomes compared with a prophylaxis strategy, even in younger CMV naive patients and relatively more immune suppressed heart transplant patients. A hybrid strategy may provide effective long-term control of intermittent CMV replication as suggested by the low frequency of CMV disease in this group compared with prophylaxis. In the late post-transplant period, administering episodic empiric anti-virals with a rejection diagnosis may be necessary to prevent CMV disease associated with late rejection episodes.

Disclosures. All authors: No reported disclosures.

1591. Infectious Outcomes of Levofloxacin Prophylaxis in Obese vs. Non-obese Patients with Hematologic Malignancies

Amanda Kurtz, PharmD¹; Kelly Fritz, PharmD, BCOP¹, Kathryn Eloffson, PharmD¹ and Russell Benefield, PharmD, BCPS (AQ-ID)¹; ¹Huntsman Cancer Institute at the University of Utah, Salt Lake City, Utah

Session: 151. Viruses and Bacteria in Immunocompromised Patients

Friday, October 5, 2018: 12:30 PM

Background. Levofloxacin given at a standard dose of 500 mg daily is recommended for antibacterial prophylaxis in patients receiving myelosuppressive chemotherapy. Obese patients have been shown to exhibit enhanced clearance of levofloxacin and may be at risk for prophylactic failure.

Methods. This was a single-center, retrospective cohort study evaluating the infectious outcomes of obese (BMI > 30 kg/m²) and non-obese (BMI ≤ 30 kg/m²) adult patients who received standard dose levofloxacin as primary prophylaxis after chemotherapy. Patients were included if they were treated at our institution from June 1, 2014 through May 31, 2017 and had National Comprehensive Cancer Network (NCCN) defined intermediate infection risk. Patients were excluded if they were lost to follow-up, treated at another institution for febrile neutropenia (FN), or had renal impairment (estimated creatinine clearance (CrCL) less than 50 mL/minute). The primary endpoint was incidence of FN as defined by NCCN guidelines. Secondary endpoints included 30-day mortality and the correlation between estimated levofloxacin AUC and rates of FN. Levofloxacin AUC was estimated from CrCL using the method of Pai *et al.*

Results. A total of 98 patients met the inclusion criteria (34 obese and 64 non-obese). Estimated CrCL was similar between obese and non-obese patients (mean 84.5 vs. 81.6 mL/minute, $P = 0.61$), as was estimated levofloxacin AUC (mean 115.1 mg hour/L vs. 107.8 mg hour/L, $P = 0.25$). FN occurred in 26 patients: 12 (35.3%) obese and 14 (21.9%) non-obese ($P = 0.16$). Bivariate comparisons between patients who did and did not experience FN found no significant associations with the weight-related variables total body weight (mean 84.7 vs. 82.0 kg, $P = 0.56$), BMI (mean 28.8 vs. 28.0 kg/m², $P = 0.51$), or body surface area (1.99 vs. 1.96 m², $P = 0.62$). Multivariate analysis identified presence of mucositis and diagnosis of multiple myeloma as variables independently associated with FN. No patients died within 30 days of the FN event.

Conclusion. There were no significant associations between body weight-related variables and FN in this cohort of patients with similar renal function. Obesity should not be a justification for more aggressive levofloxacin dosing schemes when used for FN prophylaxis.

Disclosures. All authors: No reported disclosures.

1592. Safety of Oral Trimethoprim/Sulfamethoxazole Prophylaxis in Renal Transplant Recipients

Courtney Horvat, PharmD; Thomas J. Dilworth, PharmD and Iram Nadeem, MD; Aurora St. Luke's Medical Center, Milwaukee, Wisconsin

Session: 151. Viruses and Bacteria in Immunocompromised Patients

Friday, October 5, 2018: 12:30 PM

Background. Trimethoprim/sulfamethoxazole (TMP/SMX) is the agent of choice for *Pneumocystis jirovecii* Pneumonia (PJP) prophylaxis in renal transplant (RT) recipients. All other prophylactic agents are considered second-line due to efficacy, drug intolerances, cost, administration requirements, and lack of coverage of *Toxoplasma*. Anecdotally, alternative agents are commonly used at our institution due to clinician hesitancy and perceived risk of adverse drug reactions (ADRs). Our objective was to assess the safety of TMP/SMX prophylaxis in RT recipients.

Methods. RT recipients transplanted at a tertiary US medical center between May 9, 2015 and November 30, 2017 were retrospectively identified. Patient charts were reviewed for antimicrobial agents used for PJP prophylaxis and ADRs due to TMP/SMX. ADRs were classified using the National Institutes of Health, Division of Microbiology and Infectious Diseases (DMID) criteria and were scored for probability of association with TMP/SMX using the Naranjo ADR probability scale.

Results. During the study period, 64 of 95 adult RT recipients (67.4%) received TMP/SMX for PJP prophylaxis. Of the patients who received TMP/SMX, 26 (40.6%) had a clinician-documented ADR attributed to TMP/SMX and 24 (37.5%) had the drug discontinued. The most frequent provider-reported ADRs due to TMP/SMX were hyperkalemia (10 patients, 15.6%), neutropenia (nine patients, 14.1%), and elevated liver function tests (LFTs) (three patients, 4.7%). However, when classified using DMID criteria, nine of the 26 ADRs were less severe than Grade 1. Two ADRs were Grade 3 (severe), including 1 case each of neutropenia and elevated LFTs. No ADRs were Grade 4 (life-threatening). All ADRs received a score ≤ 4 on the Naranjo ADR probability scale, indicating a possible ADR related to TMP/SMX. Often, ADRs did not resolve or other additional medication adjustments were needed following TMP/SMX discontinuation (19 of 26 patients, 73.1%). No cases of PJP occurred.

Conclusion. TMP/SMX is underutilized in RT recipients at our institution, despite being well-tolerated and efficacious. Clinician hesitancy with TMP/SMX in this population may be unfounded. Internal efforts are underway to increase the use of TMP/SMX in RT recipients.

Disclosures. All authors: No reported disclosures.

1593. Recurrence of *Clostridium difficile* Infection in Multiple Myeloma Patients Receiving Prophylactic Oral Vancomycin or Oral Metronidazole vs. No Prophylaxis

Gisele Moran, MPH¹; Naveen Yarlagadda, MD²; Sandra Susanibar, MD³; Atul Kothari, MD⁴; Juan Carlos Rico, MD⁴ and Mary J Burgess, MD⁴; ¹College of Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, ²Internal Medicine, UAMS, Little Rock, Arkansas, ³Myeloma Institute, University of Arkansas for Medical Sciences, Little Rock, Arkansas, ⁴Division of Infectious Diseases, UAMS, Little Rock, Arkansas

Session: 151. Viruses and Bacteria in Immunocompromised Patients
Friday, October 5, 2018: 12:30 PM

Background. Multiple myeloma (MM) patients are at increased risk of *Clostridium difficile* infection (CDI) compared with the general population. In prior studies, 12–14% were diagnosed with CDI, and ~16% had recurrent CDI during subsequent treatments. Recent studies have shown that oral vancomycin is effective secondary prophylaxis for the prevention of recurrent CDI in the general population. This retrospective study examined if secondary prophylaxis with oral vancomycin or metronidazole is effective to prevent recurrent CDI in MM patients.

Methods. MM patients who tested positive for their first episode of CDI from January 2014–December 2016 were included, and the 3 months following the CDI diagnosis was reviewed. Patients who died, and those who did not receive additional chemotherapy or antibiotics during the 3-month review period were excluded. The patients were divided into 3 cohorts: (1) oral vancomycin as secondary prophylaxis, (2) oral metronidazole as secondary prophylaxis, and (3) no *C. difficile* prophylaxis.

Results. A total of 110 MM patients with a first episode of CDI were reviewed, six were excluded due to death and four were excluded due to no subsequent chemotherapy or antibiotics. This left 100 patients included for analysis. The median age was 62 years, range 34–81. 92 subjects (92%) had exposure to antibiotics and 76 (76%) received chemotherapy. A total of 38 (38%) received secondary prophylaxis: 16 (42%) with oral metronidazole and 22 (58%) with oral vancomycin. There was no significant difference in recurrent CDI in patients who received any secondary prophylaxis (7/38, 18.4%) and in those who received none (15/62, 24.2%), $P = 0.46$. Incidence of recurrent CDI in patients receiving oral vancomycin (3/22, 13.6%) was not significantly different from patients receiving oral metronidazole (4/16, 25%), $P = 0.56$. An analysis of risk factors for recurrent CDI showed no difference in recurrence in patients who received metronidazole vs. vancomycin as treatment for the initial CDI. Similar recurrent CDI occurred in patients who received antibiotics and those who received chemotherapy.

Conclusion. Secondary prophylaxis with either oral metronidazole or oral vancomycin did not reduce the incidence of recurrent CDI in MM patients.

Disclosures. All authors: No reported disclosures.

1594. Evaluating Clinical Outcomes of an Alternative Cefepime Dosing Regimen as Empiric Antibiotic Therapy in Hospitalized Adults with Febrile Neutropenia

Manuela Haiduc, PharmD; Derek Bremmer, PharmD, BCPS; Monank Patel, PharmD, BCPS, BCOP; Thomas Walsh, MD and Matthew Moffa, DO; Allegheny Health Network, Pittsburgh, Pennsylvania

Session: 151. Viruses and Bacteria in Immunocompromised Patients
Friday, October 5, 2018: 12:30 PM

Background. A cefepime dosing regimen of 1 g every 6 hours (1 g Q6h) has shown to provide similar exposure above the target minimum inhibitory concentration than the higher FDA-approved regimen of 2 g Q8h for febrile neutropenia. We hypothesize clinical outcomes among patients receiving either dosing strategy will be similar.

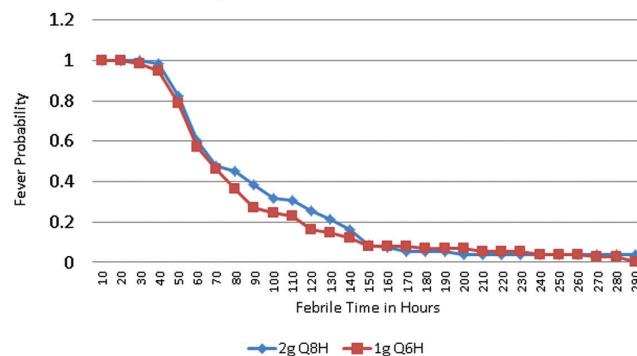
Methods. A retrospective chart review of hospitalized patients who received cefepime for documented febrile neutropenia over a two-year period was performed. Patients were grouped based on cefepime dosing strategy: 1 g Q6h vs. 2 g Q8h. The primary objective was to compare time to defervescence after cefepime initiation. Secondary objectives looked at all-cause and infection-related 30-day mortality, duration of therapy, and length of stay (LOS).

Results. Seventy-five patients in each arm were included. There were no differences in baseline age or severity of illness between groups. There was no difference in the primary objective as average time to defervescence was similar between the 1 g Q6h and 2 g Q8h groups (85.9 hours vs. 89.7 hours; $P = 0.206$), respectively. Additionally, no differences were found in the secondary objectives including all-cause 30-day mortality (6.7% vs. 9.3%; $P = 0.547$), duration of therapy (95.7 hours vs. 99.1 h; $P = 0.174$), or LOS (9 vs. 7 days; $P = 0.251$).

Conclusion. The regimen of cefepime 1 g Q6h provides similar clinical outcomes as the traditional FDA-approved 2 g Q8h regimen in the treatment of febrile

neutropenia. The lower total daily dose will result in less drug exposure and a potential decreased risk of cefepime-related adverse drug events.

Figure 1. Time to Defervescence



Disclosures. All authors: No reported disclosures.

1595. Impact of Levofloxacin for the Prophylaxis of Bloodstream Infection on the Gut Microbiome in Patients with Hematologic Malignancy

Matthew Ziegler, MD¹; Jennifer H. Han, MD, MSCE²; Daniel Landsburg, MD³; David Pegues, MD, FIDSA, FSHEA⁴; Emily Reese, MS⁵; Cheryl Gilmar, MS, MT, CIC⁶; Theresa Gorman, MSN, RN, AOCNS⁷; Kristen Bink, MSN, RN, AGCNS-BC³; Amy Moore, MSN, RN, ACNS-BC³; Brendan J. Kelly, MD, MS⁷ and CDC Prevention Epicenters Program; ¹Division of Infectious Diseases, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, ²Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, ³Division of Hematology and Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, ⁴Healthcare Epidemiology, Infection Prevention and Control, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, ⁵University of Pennsylvania, Philadelphia, Pennsylvania, ⁶Infection Prevention and Control, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, ⁷Division of Infectious Diseases, Dept. of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Session: 151. Viruses and Bacteria in Immunocompromised Patients
Friday, October 5, 2018: 12:30 PM

Background. Prophylactic antibiotics for the prevention of bloodstream infections (BSIs) during neutropenia (NTP) may reduce the incidence of BSIs, NTP fever, and mortality. However, antibiotics may also result in dysbiosis of the gut microbiome. We aimed to study the impact of levofloxacin prophylaxis compared with broad-spectrum β -lactam (BSBL) antibiotics used for the treatment of NTP fever on gut microbiome features in patients with hematologic malignancy.

Methods. Stool specimens from hematologic malignancy patients admitted for chemotherapy or stem cell transplant (SCT) in the setting of the evaluation of diarrhea were collected from September 2017 to November 2017. Levofloxacin prophylaxis was standard of care for patients undergoing autologous SCT or induction chemotherapy for acute myeloid leukemia (AML). 16S rRNA (V1–V2 amplicon) sequencing was performed using the Illumina HiSeq platform, formation of operational taxonomic units (OTUs) was performed using QIIME 1.9.1, and taxonomic assignment was performed via the GreenGenes database (13.8). Descriptive statistics were used to compare microbiome features.

Results. A total of 57 samples from 44 patients were included, most with AML (42%), multiple myeloma (33%), or non-Hodgkin's lymphoma (12%). In the 7 days prior to sample collection, 28 (49%) patients received a BSBL and 17 (29%) received levofloxacin. The gut microbiome of patients with BSBL exposure had significantly reduced Shannon alpha diversity compared with those without: median 1.96 (IQR 1.08–2.57) vs. 2.58 (IQR 2.05–2.93); $P < 0.01$. However, those with and without levofloxacin exposure showed no difference: median 2.37 (IQR 2.19–2.75) vs. 2.22 (IQR 1.71–2.81), respectively; $P = 0.48$. Additionally, those with BSBL exposure trended toward increased dominance with non-Bacteroidetes taxa: 14 (60%) vs. 14 (41%); $P = 0.14$. In contrast, levofloxacin exposure was associated with a lower risk of dominance: 2 (8%) vs. 15 (55%); $P < 0.01$ and was associated with a greater proportion of Bacteroidetes taxa: 75% vs. 27% ($P < 0.01$).

Conclusion. Our findings suggest that the impact of antibiotics on the gut microbiome vary by class, and that levofloxacin may have limited impact on the gut microbiome in this patient population. Further studies are needed to investigate this potential differential impact of antibiotic classes.

Disclosures. D. Pegues, DaVita / Total Renal Care: Consultant, Consulting fee.