500. Efficacy of 30-Day Fidaxomicin for Treatment of Acute Clostridium difficile Infection With History of Multiple Recurrences
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Background. Multiple recurrent Clostridium difficile (rCDI) infections pose major challenges to patients and to the healthcare system. rCDI is associated with multiply hospitalized and significantly higher costs. It can also lead to chronic, severe diarrhea, colectomy, or death. Fecal microbiota transplantation (FMT) is an effective treatment, but its long-term safety remains unknown, and approximately 10% of patients do not respond to multiple FMTs. A 30-day course of fidaxomicin was evaluated as a treatment of a new episode of rCDI superimposed on rCDI, including those who did not respond to multiple FMTs. Fidaxomicin was chosen because it disrupts the fecal microbiome less than vancomycin.

Methods. Twenty-nine adult patients with at least two episodes of recurrent CDI were initiated on fidaxomicin 200 mg when they experienced new episode of CDI (symptoms plus positive for CD toxin gene by polymerase chain reaction). These patients continued with fidaxomicin 200 mg twice daily for 10 days, and 200 mg once daily for 20 additional days in an open-label clinical trial. The primary endpoints were a clinical response at the completion of 30 day course of fidaxomicin and a sustained clinical response at time 8 weeks from the last dose of fidaxomicin. Patient-related quality of life was evaluated through the treatment using the RAND-36 Item Health Survey (copyright® the RAND Corporation).

Results. Twenty-four of the 29 patients (83%) experienced clinical resolution of CDI-related symptoms by the completion of 30-day fidaxomicin treatment. Twenty-two of the 29 patients had a sustained clinical response with the overall cure rate of 76% (22/29). Eleven of the 29 patients had multiple FMTs and were enrolled into this study as they failed FMTs. Eight of the 11 patients (73%) of these patients had a sustained clinical response. Statistically significant improvements (P < 0.05) in multiple dimensions of quality of life according to the RAND-36 Item Health Survey were also observed.

Conclusion. An extended regimen of fidaxomicin is an effective treatment for adults with multiple rCDI and in restoring quality of life, including those who failed FMTs.

501. Evaluation of Bezlotoxumab in Prevention of Recurrent C. difficile Infection: A Multicenter Single-Arm Study in Outpatient Infusion Centers
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Background. Bezlotoxumab (BEZ) was approved in October 2016 for the prevention of recurrent C. difficile (rCDI) infection in patients receiving standard-of-care (SoC) antibiotic therapy for active CDI who are at high risk for CDI recurrence. Presently, there are little real-world data on recurrence rates and factors associated with recurrence in patients receiving BEZ. This study describes characteristics of patients receiving BEZ in US Outpatient Infusion Centers (OCs) and analyzes subsequent CDI recurrence.

Methods. Medical records from 24 OCs were retrospectively reviewed of all patients treated with BEZ through December 2017. Data collected included demographics, comorbidities, and all therapy parameters, including SoC antibiotic therapy. Risk factors for rCDI were assessed and included age, immunocompromised status, prior number of CDI episodes, use of gastric acid suppressants, inflammatory bowel disease (IBD), and history of fecal microbiota transplant (FMT). rCDI defined as diarrhea lasting 22 days with treatment for CDI with or without a positive stool test for toxigenic C. difficile, as assessed through a follow-up visit post BEZ administration. Risk factors for rCDI were evaluated using Student's t-test and Pearson χ² test.

Results. Eighty patients received BEZ (10 mg/kg) with 78 available for follow-up evaluation for rCDI ≥90 days post treatment. Mean age was 65 ± 16 years with 51% female. Mean number of CDI episodes was 3 ± 1 with an immunocompromised status of 14% (66% of patients) with 41% on long-term taper, fidaxomicin (33% of patients), and metronidazole (25% of patients). Nineteen (24%) patients received more than one SoC antibiotic during their treatment course, most commonly with metronidazole and another SoC antibiotic. Of the 78 CDIs episodes, 17 (22%) developed rCDI with a mean time to recurrence of 33 ± 22 days. Risk factors for rCDI are shown in the table. The use of BEZ earlier in the disease course (first or second CDI episode) was associated with a decreased risk of rCDI (OR: 0.21; 95% CI: 0.04–0.98; P = 0.033).

Table 1. Antimicrobial Susceptibilities of C. difficile from I-CDI and R-CDI Patients.

| Group               | Phase          | Range (mg/L) | GM (mg/L) | % R | Range (mg/L) | GM (mg/L) | % R |
|---------------------|----------------|--------------|-----------|-----|--------------|-----------|-----|
| R-CDI               | Planktonic     | 0.25–4       | 1.69*     | 0.03–32 | 3.38*       | 34.8 (24/69) |     |
|                    | Biofilm        | 8–128        | 73.9*     | 100 (73/73) | 4–128   | 60.85*     | 98.5 (66/67) |     |
| R-CDI               | Planktonic     | 2.4          | 1.69*     | 273 (9/33) | 0.25–128 | 3.31*      | 35.1 (14/37) |     |
|                    | Biofilm        | 4–128        | 72.8*     | 100 (34/34) | 8–128    | 59.5*      | 93.5 (29/31) |     |

*Significant difference P < 0.05; GM: Geometric mean; %R: Resistant.

Conclusion. C. difficile isolates in blood were 100-fold more resistant to vancomycin than planktonic cells. Isolates recovered from patients with R-CDI showed higher susceptibility compared to C. difficile isolated from C. difficile patients. These data suggest that biofilm formation ability may play a key role in the R-CDI by contributing to vancomycin resistance/tolerance. Further, C. difficile from recurrent episodes sporulated to a greater capacity which may facilitate prolonged C. difficile persistence in the gut following a follow-up visit for BEZ.
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Background. Clostridium difficile infection (CDI) is the most common nosocomial infection, representing 12% of all hospital acquired infections. The risk for CDI is clearly linked to antibiotic (abx) exposure. Several studies, including one from our institution, indicate prophylaxis of patients who recently had CDI with oral vancomycin decreases the risk of a relapse when exposed to abx. In an effort to further analyze this, we examined all patients with CDI in our inpatient population who received any abx after the CDI and determined how that modified their risk of relapse.

Methods. All patients with a positive PCR for C. difficile at our institution between 2012 and 2014 were examined for receipt of abx within 3 months of a positive PCR. Patients who received metronidazole were excluded to remove the potential confounding effect. The relapse rate for all patients, patients who received abx, and patients who did not receive abx were calculated. Timing of the relapse from the last episode of CDI and from receipt of abx were determined.

Results. A total of 6,636 patients were identified, representing 8,000 episodes of CDI. The relapse rates and timing based on prior CDI episodes and receipt of additional abx prior to relapse are shown in Table 1.

Table 1: Relapse Rates and Timing of Relapses Within 3 Months of CDI Episode

| Category                     | Relapse Rate | Days Since Last CDI | Days Since abx |
|------------------------------|--------------|---------------------|----------------|
| All episodes                 | 12.5%        | 38.4                | N/A            |
| Received abx prior to relapse| 11.8%        | 46                  | 73             |
| Received high-risk abx prior to relapse | 12.4% | 46.5 | 72 |
| Received no abx prior to relapse | 12.6% | 36.9 | N/A |

There were 1,375 episodes of CDI where abx were given within 3 months of the episode. Of these patients, 33 received prophylaxis with oral vancomycin, and none of these relapsed within 3 months.

Conclusion. While abx clearly are the major risk factor for CDI, the receipt of abx after a relapse of CDI does not change the overall rate of relapse. However, when the timing of the relapses after abx is examined, the relapses occur both later in those who received abx than relapses in patients who do not receive abx and shortly after abx. It is likely that abx trigger relapses in patients who otherwise would not have relapsed. Oral vancomycin prophylaxis appears to be effective in preventing relapses in patients given abx after CDI.

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504. Change in Clostridium difficile Strain-Type Distribution After Implementation of Diagnostic Stewardship

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Background. The aim of this study was to evaluate the change in strain-type distribution after eliminating testing of formalin lavage with toxigenic C. difficile.

Methods. Beginning in July 2013, all C. difficile-positive stool samples by Cepheid's GeneXpert were routinely typed using Multi-Locus Sequence Typing (MLST). MLST was performed as previously described (1). After implementation of rejection policy and re-education of staff, strain type (ST) distribution among tested samples was analyzed and compared with historic data.

Results. After evaluation of our historical typing data the 10 most frequent ST were identified. Diagnostic stewardship led to 40.0% reduction in testing volume, the positivity rate increased from 12.0% to 12.6%. The frequency distribution of threemost prevalent strain types (MLST-2, 8, and 42) declined by 38%, 60%, and 42%, respectively. The absolute number of epidemic strains, ST-1 and ST-11, remained unchanged and the frequency distribution increased from 9.6% to 14.0%. No clonal outbreaks were detected during this time.

Conclusion. Implementation of diagnostic stewardship led to a reduction in epidemic strains without substantial impact on detection of hypervirulent or epidemic strains.

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505. Bezlotoxumab Reduces Recurrence of Clostridium difficile Infection in Immunocompromised Patients: Early Experience at a Tertiary Care Center

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Background. Bezlotoxumab (BEZ) was approved in 2017 for prevention of recurrent C. difficile infection (CDI), with a number needed to treat (NNT) of 10 reported in the registration trials. Little information is available on its effectiveness in high-risk populations. BEZ was added to the institutional outpatient formulary in 2017 for use in patients with CDI at high-risk for recurrent CDI (rCDI), i.e., history of solid organ (SOT) or hematopoietic stem cell (HCT) transplantation, active malignancy, chronic steroid (prednisone equivalent 20 mg/day), and failed fecal microbiome transplant (FMT). Patients that met criteria were referred by the antimicrobial stewardship team to the infectious disease clinic for BEZ insurance approval and administration. The goal of this study was to evaluate the effectiveness and safety of BEZ in this high-risk population.

Methods. The cohort of patients referred for BEZ were compared by those who received BEZ vs. those who did not receive BEZ (standard of care, SOC). The primary endpoint was rCDI at ≤100 days of BEZ infusion or end-of-treatment (EOT). Secondary endpoints were time to rCDI and insurance status. Safety of BEZ was evaluated as infusion reaction ≤24 hours and death ≤100 days.

Results. Twenty-nine patients were referred for BEZ; 14 (48%) received BEZ. Patients characteristics are in Table 1. rCDI at 100 days occurred in 14.3% BEZ vs. 28.6% SOC (P = 0.3654) with an NNT of 7. Average time to rCDI was longer in the BEZ group vs. SOC (49 vs. 27 days). No infusion reactions or death were noted in the BEZ group. Insurance approval for BEZ was denied in 26.7%, Medicaid coverage was common in SOC (46.7% vs. 7.1%; P = 0.0191) and Medicare coverage was more common in BEZ group (71.4% vs. 33.3%; P = 0.0438).

Conclusion. Early experience with BEZ appears promising in a high-risk, pre-dominantly immunocompromised population. The NNT to prevent rCDI was 7. Larger cost–benefit studies in immunocompromised and transplant populations are warranted.

Table 1: Characteristics of BEZ and SOC Patients

| Variable | BEZ (N = 14) | SOC (N = 15) | P-value |
|----------|--------------|--------------|---------|
| Age >60  | 57.1%        | 26.7%        | 0.1027  |
| ≥1 prior CDI episodes | 50.0% | 26.7% | 0.2042 |
| Average no. of prior CDI episodes | Immuno compromised | 87.5% | 78.6% | 0.5704 |
| SOT recipient | 42.8% | 33.3% | 0.4507 |
| HCT recipient | 21.4% | 13.3% | 0.6323 |
| Active cancer | 29.6% | 26.7% | 0.9667 |
| Failed FMT | 7.1% | 6.7% | 1.0000 |

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506. The Impact of Bowel Management System (BMS) on the Incidence of Hospital-Onset (HO) Clostridium difficile Infection Laboratory-ID Events Despite Diagnostic Stewardship

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Background. Clostridium difficile infection (CDI) Laboratory-identified events are reportable to CMS through the CDC's NHSN. Diagnostic stewardship has been shown to decrease the incidence by decreasing false-positive incident diagnostic BMS lab events. BMS (BMS) have been associated with transient loss of tone of anal sphincter muscles that result in diarrhea. These episodes of diarrhea may be misdiagnosed as CDI due to a false-positive test result. The objective of this study was to determine whether the use of BMS has resulted in false-positive CDI Lab-ID events.

Methods. We performed a retrospective review of all HO-CDI Lab ID events from October 1, 2016 to December 31, 2017 in a 1,157-bed tertiary academic medical center. Since 2013, several interventions were implemented to decrease the incidence of CDI Lab-ID events. These interventions have included: (i) enhanced environmental cleaning, (ii) CDI testing algorithm, (iii) use of hydrogen peroxide terminally cleaning of high-risk units, and (iv) computer-assisted decision support diagnostic stewardship. Poisson regression analysis was performed to compare incidence rates. A P-value of ≤0.05 was considered significant.

Results. A sustained low and decreasing HO-CDI incidence was observed from 2013 to 2017 (7.9, 6.0, 7.1, 6.5 and 5.2 CDI/10,000 patient days; P = 0.011). An incremental decrease was observed when comparing the annual incidence in 2016 to the YTD incidence in 2017 (6.5 vs. 5.2 CDI/10,000 patient days; P = 0.001). Comparing the five quarters before vs. after diagnostic stewardship was implemented to post-intervention, the CDI incidence decreased from 6.7 to 5.2 CDI events/10,000 patient days (P = 0.009).

Of the 180 HO-CDI Lab-ID events that occurred post-implementation of the diagnostic stewardship, 31 (17%) were cases in which the computer-assisted alerts were overridden and may have been false positives. An additional 12 (6.7%) cases occurred in patients who had BMS in place within 48 hours and 22 (12%) had BMS in place within 1 week.

Conclusion. Diagnostic stewardship through computer-assisted decision support is an effective method of reducing false-positive C. difficile Lab ID events. We found that an additional 12% of the HO-CDI are potentially false positives as these were obtained from patients who had BMS in place immediately before the positive test results. All authors: No reported disclosures.