BACKGROUND

- Neutropenia and antibiotic use put patients at risk for Clostridium difficile infection (CDI) following allogenic hematopoietic cell transplant (alloHCT)
- Factors that increase the risk of CDI in patients include hospitalization, older age, exposure to antibiotics, immunosuppression, source of stem cells, and type of conditioning regimen
- CDI following alloHCT has been associated with acute graft versus host disease (GVHD), a significant cause of morbidity and mortality in this population
- A single center study looking at vancomycin prophylaxis in alloHCT patients was conducted in 145 patients at the University of Pennsylvania
- They found that vancomycin was highly effective at reducing the incidence of CDI in alloHCT patients and was not associated with a higher risk of acute GVHD at day 180 post-transplant.
- Effective strategies to reduce the risk of CDI in alloHCT patients are needed due to the incidence and potential detrimental effects of infection.

OBJECTIVES

- Evaluate if prophylactic oral vancomycin reduces the incidence of CDI in alloHCT recipients and add to the current knowledge on this topic
- Primary outcome: Incidence of CDI in patients with oral vancomycin prophylaxis compared to those who did not receive prophylaxis during hospital admission for alloHCT
- Secondary outcomes: Incidence of grade 2-4 GVHD, Incidence of vancomycin resistant enterococcus (VRE), Incidence of bloodstream infections, Length if Stay, Event Free Survival

METHODS

Study Design: Single center retrospective chart review

Time Frame: May 2017 through January 2019

Inclusion Criteria: All patients who underwent alloHCT at TUKHS aged ≥ 18 years and were admitted on day 0 to the hospital

Exclusion Criteria: Active CDI at Day 0, Underwent autoHCT, Post implementation group: no vancomycin on Day 0 and/or not continued for ≥ 7 days

Interventions:
- CDI prophylaxis was implemented in all alloHCT patients starting in March 2018
- Oral vancomycin 125 mg twice daily starting on the day of inpatient admission for alloHCT and continued until discharge
- Compared 200 consecutive adults (100 alloHCT patients pre-implementation vs 100 alloHCT patients post-implementation)

Data Collected:
- Sex, Disease Type, Degree of HLA Match, GVHD Prophylaxis, CIBMTR 1-Year Survival Score, Sex, Age, Donor Source, Conditioning Intensity, CIBMTR 1-Year Survival Score, Incidence of CDI, Incidence of GVHD, Antibiotic Exposure

RESULTS

Baseline Characteristics and Disease Demographics

- 52 years average age
- 65% Male
- 39.5% AML
- 24.5% MDS/MPN
- Average CIBMTR 1 Year survival: 69.5%
- 63% Peripheral Blood graft source no prophylaxis group
- 62% Bone Marrow graft source prophylaxis group

Primary Outcome

Incidence of CDI

<table>
<thead>
<tr>
<th>Vanc Ppx</th>
<th>Incidence of CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>98</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No Ppx</th>
<th>Incidence of CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>89 P = 0.018</td>
</tr>
</tbody>
</table>

Secondary Outcomes

Clinical Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Oral Vancomycin Prophylaxis (N=100)</th>
<th>No Prophylaxis (N=100)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of aGVHD grade 2-4</td>
<td>35</td>
<td>36</td>
<td>0.77</td>
</tr>
<tr>
<td>Length of Hospital Stay, average days (SD)</td>
<td>26.5 (14.1)</td>
<td>25.6 (11.2)</td>
<td>0.825</td>
</tr>
<tr>
<td>Incidence of VRE, n</td>
<td>11</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Incidence of Bloodstream infection, n</td>
<td>13</td>
<td>9</td>
<td>0.366</td>
</tr>
<tr>
<td>Event Free Survival at one year</td>
<td>59%</td>
<td>68%</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Highest Grade GVHD Organ Involvement

<table>
<thead>
<tr>
<th>No prophylaxis group</th>
<th>Vancomycin prophylaxis group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>23</td>
</tr>
<tr>
<td>Liver without TBI rise</td>
<td>45</td>
</tr>
<tr>
<td>Intestine</td>
<td>1</td>
</tr>
<tr>
<td>Liver</td>
<td>2</td>
</tr>
</tbody>
</table>

DISCUSSION

- Oral vancomycin is effective at preventing C.difficile infections in patients that underwent an alloHCT
- Gut flora and GVHD
- No association between oral vancomycin prophylaxis and aGVHD at 100 days post-alloHCT as well as relapse or death at one year
- No increase in VRE colonization
- Type of graft source
  - Donor source changed significantly between the pre-intervention group and post intervention group, with 63% and 38% receiving a peripheral blood stem cell transplantation (PBSCT), respectively (p=0.001).
  - We do not expect this to negatively affect the results of this study given that hematological recovery is more rapid and graft rejection less frequent after PBSCT compared to bone marrow transplantation (BM HSCT). Patients receiving a BM HSCT have an increased risk of CDI due to prolonged neutropenia, and therefore prolonged antibiotic use for prophylaxis or treatment, as compared to PBSCT.
  - However, this could potentially confound our GVHD results since our prophylaxis group has more BM HSCT

CONCLUSION

- Oral vancomycin is effective in preventing CDI in alloHCT recipients without increasing the risk of GVHD or disease relapse
- Has maintained our ongoing standard of practice

LIMITATIONS

- Single center retrospective study
- Descriptive statistics
- Data collected largely dependent on appropriate provider documentation and patient follow-up
- Change in room cleaning practice
- Similar rates of CDI were documented before and after this change and does not alter the results (6 cases vs 5 cases in the pre-intervention group).
- Did not collect VRE colonization vs. invasive VRE infection.
- Potential for increased gram-negative infections through selective pressure and gut dysbiosis

FUTURE DIRECTIONS

- Larger sample size
- Use of chronic C.diff prophylaxis for autoHCT patients
- Fidaxomicin vs. oral vancomycin for prophylaxis

CONTACT INFORMATION

Olivia Altemeier, PharmD, PGY1 Pharmacy Resident; oaltemeier@kumc.edu

Authors have no disclosures to report

Scan QR code for complete baseline characteristics and results. References available upon request.