Prophylactic Oral Vancomycin for *Clostridioides difficile* in Allogeneic Hematopoietic Stem Cell Transplant Recipients

Lauren Ogawa, DO, MSPH, Kaylor Wright, MD, and Alfred Luk, MD
Tulane University School of Medicine, New Orleans, LA

Introduction

- Allogeneic hematopoietic stem cell transplant (alloHSCT) recipients are at increased risk for *Clostridioides difficile* infection (CDI) due to prolonged hospitalization, neutropenia, and alteration of the intestinal mucosa and gut microbiota from conditioning regimens, antimicrobials, and immunosuppressants[1]
- CDI in alloHSCT recipients is associated with higher rates of acute graft versus host disease (aGVHD)[2]
- Literature review revealed three institutions demonstrated oral vancomycin prophylaxis prevents CDI[3, 4, 5]
  - More studies are needed to evaluate the impact of prophylaxis on incidence of CDI, resistant infections, and other transplant-related outcomes

Methods

- Retrospective review comparing effectiveness of primary prophylactic oral vancomycin versus no prophylaxis in alloHSCT recipients in the prevention of hospital acquired CDI (N= 40)
- A control group consisted of consecutive alloHSCT recipients prior to initiation of the intervention (N=20)
- Prophylactic intervention was initiated June 2020
  - Twice daily vancomycin 125mg PO starting day of admission for transplant until discharge (N=20)
- Primary outcome: incidence of CDI
- Secondary outcomes: incidence of vancomycin resistant enterococcus (VRE) infection and incidence of aGVHD
- Baseline characteristics were compared using the chi-square test (p-value <0.05)
- Primary and secondary outcomes were compared using the Fischer exact test (p-value <0.05)

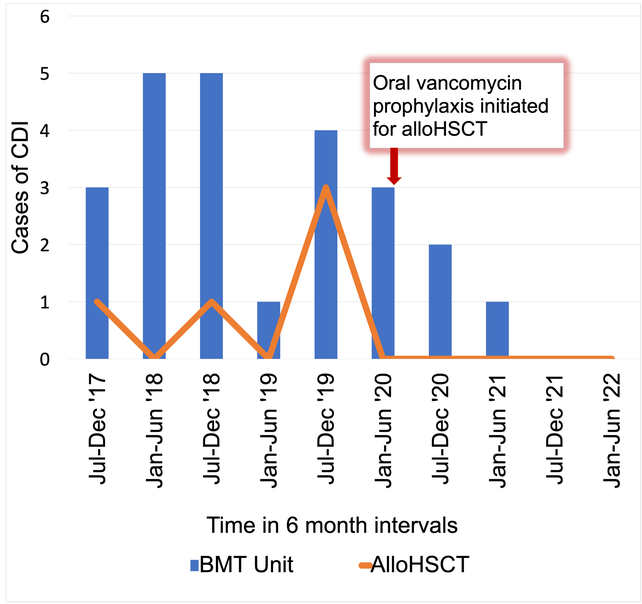
Results

Baseline characteristics of the control (no prophylaxis) and intervention groups are provided in Table 1. There were no significant differences between the groups. Since initiation of vancomycin prophylaxis in June 2020 there have been zero cases of hospital acquired CDI in alloHSCT patients compared to all patients in the bone marrow transplant (BMT) unit (Figure 1).

Table 1. Baseline characteristics of alloHSCT recipients

Characteristic	Control (N=20)	Oral vancomycin prophylaxis (N=20)	p-value
Recipient sex, n			1.0
Female	9	9	
Male	11	11	
Recipient age, mean in years	47	48	
Underlying diagnosis, n			0.350
ALL	2	1	
AML	10	14	
CLL	0	0	
CML	1	1	
MDS	6	1	
Other	1	3	
Graft source, n			1.0
Peripheral blood	18	18	
Bone marrow	2	2	
Conditioning regimen, n			0.057
Myeloablative	15	20	
Nonmyeloablative	2	0	
Reduced intensity	3	0	
Donor, n			0.292
Matched unrelated	13	8	
Mismatched unrelated	0	2	
Matched related	3	4	
Haploidentical	4	6	
Levofloxacin prophylaxis, n	12	16	0.301

Figure 1. Cases of CDI in alloHSCT compared to entire BMT



During admission for transplant and at day +100 post-transplant, 5/20 (25%) patients in the control group developed CDI compared to 0/20 (0%) in the prophylaxis group (p=0.0471, Table 2). Use of prophylaxis was not associated with higher rates of VRE infection through day +100 post-transplant. There was no significant difference in incidence of aGVHD.

Table 2. Primary and secondary outcomes

Outcome	Control (N=20)	Oral vancomycin prophylaxis (N=20)	p-value
CDI during admission for transplant, n (%)	5 (25)	0 (0)	0.0471
CDI by day +100, n (%)	5 (25)	0 (0)	0.0471
VRE infection during admission for transplant, n (%)	0 (0)	0	1
VRE infection by day +100, n (%)	2 (10)	0 (0)	0.487
aGVHD, n (%)	10 (50)	7 (35)	0.523

Discussion

- AlloHSCT recipients remain at risk for CDI
- CDI has a significant impact on morbidity and mortality in the United States[6]
- Prophylaxis with oral vancomycin was associated with a significant reduction in CDI
  - No cases of CDI in alloHSCT recipients in the past 2 years
  - Effective prevention strategy
- Use of prophylaxis was not associated with an increased risk for VRE infection
- No change in incidence of aGVHD
- In concordance with three other institutions, our study supports the use of vancomycin prophylaxis
  - No other new quality measures during this study that could influence CDI rates; no confounders
  - Limited by sample size
- Next steps:
  - Reassess as sample size increases
  - Continue to monitor for resistant infections and evaluate the impact on survival
  - Evaluate impact of prior antibiotic exposure
  - Changes in duration of hospitalization
  - Dosing optimization (daily vs twice a day)
  - Multicenter prospective controlled study and potential practice changing impact

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