Impact of a pharmacist-driven probiotic protocol on *Clostridioides difficile* infection at a community hospital

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Background

- *Clostridioides difficile* (*C. difficile*) is a gram-positive anaerobic bacteria that is associated with significant morbidity and mortality that has been identified as an urgent antibiotic resistance threat by The Centers for Disease Control and Prevention (CDC).
- Decreasing the frequency, duration, and number of antibiotics is the only proven intervention to prevent *C. difficile* infections (CDI).
- There have been many studies examining the efficacy of probiotics for primary prevention in CDI, but results have been inconsistent.
- The 2017 IDSA Clinical Practice Guidelines for CDI did not make any recommendations on the use of probiotics for primary prevention due to insufficient evidence supporting its efficacy.
- In January 2018, Olathe Medical Center (OMC) implemented a protocol allowing pharmacists to order probiotics for at-risk patients in an effort to decrease CDI rates.

Purpose

- Compare the number of CDI in high-risk patients before and after the implementation of a protocol allowing pharmacists to order *lactobacillus/acidophilus/casei/rhamnosus* (Bio-K®).
- Analyze pharmacists' adherence to the probiotic protocol.

Study Endpoints

Primary endpoint

- CDI within six months of discharge

Secondary endpoints

- Number of probiotics ordered by pharmacists per protocol
- CDI in patients with a documented penicillin (PCN) allergy

Methods

- Retrospective chart review of patients receiving high-risk broad-spectrum antibiotics during admission at OMC pre- and post-protocol implementation, March 2015 to March 2016 and March 2018 to March 2019, respectively.
- Randomly evaluated patients for probiotics based on protocol criteria.
- Those who died within six months of discharge were excluded.
- Assessed baseline characteristics including CDI risk-factors, PCN allergy, and antimicrobial agents used in each group.
- 150 patients were included in each group for 80% power and α=0.05.
- Data from the National Healthcare Safety Network (NHSN) was used to determine CDI within six months.
- Nominal data were analyzed using X^2 test.
- Continuous data were analyzed using Mann-Whitney *U* test.

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Table 1 - Probiotic Protocol

Two or more CDI risk factors

- Age ≥ 65 years
- Hospitalization > 72 hours length of stay (LOS)
- Order for ceftriaxone, cefepime, ciprofloxacin, levofloxacin, piperacillin/tazobactam, meropenem, or ertapenem
- History of CDI`
- Proton pump inhibitor (PPI) or H2-receptor antagonist (H2RA)
- Recent or prolonged stay at hospital, long term care facility (LTCF) or rehabilitation facility

Plus

- Taking oral medications AND on at least clear liquid diet

WITHOUT any of the following comorbidities

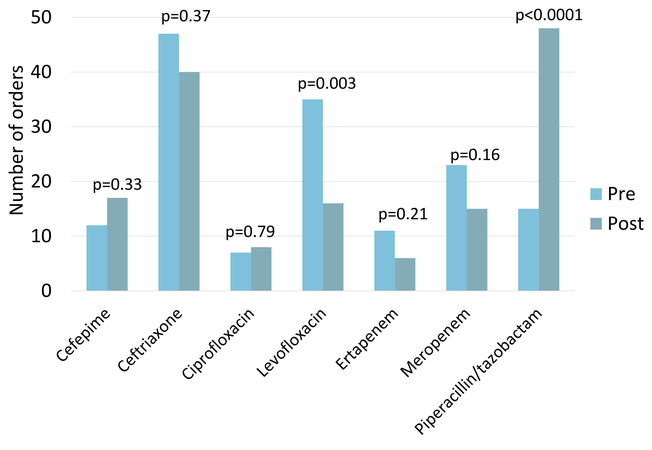
- Active chemotherapy
- Absolute neutrophil count (ANC) less than 1500
- Greater than prednisone 20 mg or equivalent per day
- Human immunodeficiency virus (HIV) with CD4 < 200
- Opportunistic or Acquired immunodeficiency syndrome (AIDS) defining illness present
- Any other immunocompromising condition

Population Characteristics (N=300)

Table 2 – Baseline Patient Characteristics

	Pre-protocol n (%)	Post-protocol n (%)	p-value
Average age, years	68	66	0.21
Sex, female	89 (59.3)	91 (60.7)	0.81
Age ≥ 65	88 (58.7)	87 (58)	0.91
> 72 hour LOS	95 (63.3)	104 (69.3)	0.27
CDI history	10 (6.7)	15 (10)	0.3
Recent hospitalization or LTCF in past 90 days	41 (27.3)	51 (34)	0.21
PPI/H2RA therapy	106 (70.7)	87 (58)	0.02
PCN Allergy	42 (28)	28 (18.7)	0.06

Figure 1 – Antibiotic Usage Before and After Protocol Implementation



Results

A total of 300 patients were included, 150 per group. 491 charts were reviewed. 79 patients were excluded due to death within six months of discharge and 112 patients did not meet protocol criteria.

Table 3 – CDI Cases and Number of Probiotic Orders

	Pre-protocol n (%)	Post-protocol n (%)	p-value
CDI cases	**7 (4.7)**	**4 (2.7)**	**0.36**
Probiotics	2	3	
PCN Allergy	1	0	
Probiotic orders	**26 (17.3)**	**55 (36.7)**	**<0.001**
Provider	26 (100)	19 (35)	
Pharmacist	0 (0)	36 (65)	

Table 4 – CDI in patients without PCN allergy

Pre-protocol (n)		Post-protocol (n)	
Cefepime	1	Ceftriaxone	1
Meropenem	2	Piperacillin/tazobactam	3
Levofloxacin	3		

Conclusions

- There was no significant difference in CDI due to the implementation of the pharmacist-driven probiotic protocol.
- Probiotic orders significantly increased with pharmacists initiating 65% of orders, but adherence to the protocol was low overall.
- There was no association between CDI and documented PCN allergy.
- Antimicrobial stewardship efforts to decrease fluoroquinolone and carbapenem use explains the trend in antibiotics seen.
- Another study should be conducted after the implementation of VigiLanz® in Spring 2020 to re-assess pharmacists' identification of patients and better understand the impact of probiotics on CDI.

Limitations

- NHSN data only includes patients who presented back to OMC with CDI which may under-estimate CDI occurrence.
- The adoption of ultraviolet-c (UV-c) emitting cleaning towers at OMC in March 2017, significant decrease in acid suppressive therapy, and change in levofloxacin and piperacillin/tazobactam use may have also impacted CDI.
- Timing of pharmacist intervention and administration of other broad-spectrum agents during admission was not analyzed.
- Protocol excludes patients with feeding tubes.
- Perceived risk of CDI may have been inflated in the implementation group as 30% of patients without a PCN allergy received levofloxacin.

References

1. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.
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