Poster # 514

NYU Winthrop Hospital

The Effect of Probiotics on the Incidence of *Clostridium difficile*

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BACKGROUND

- *Clostridium difficile is* the most common cause of infectious diarrhea in healthcare settings [1]
- Antibiotic use is the most common risk factor for *Clostridium difficile infection* (CDI) especially β-lactams, Quinolones, and Clindamycin [1]
- According to the SHEA/IDSA guidelines, administration of probiotics is not recommended as prophylaxis for CDI as there is little supporting evidence for its use [2]
- In a 2012 prevalence study of 145 US hospitals, 96% of the hospitals administered probiotics in 2.6% of hospitalizations. Patients who received probiotics were more likely to have received antimicrobials and were 21 times more likely to have been diagnosed with CDI [7]
- The FDA approved indication for lactobacillus is, "probiotic to promote normal bacterial flora of the intestinal tract" [3]
- It is suggested that probiotics can be used as CDI prophylaxis due to the notion that lactobacilli remain in the colon after administration of probiotics [4]
- It is proposed that probiotics are more likely to be effective in primary prophylaxis of CDI as opposed to secondary prevention due to the significant alteration of the gut flora after recurrence of infection [4]

LITERATURE REVIEW

Allen et al.[4]:
- The PLACIDE study evaluated the use of lactobacilli and bifidobacteria compared to placebo on the occurrence of antibiotic associated diarrhea and *Clostridium difficile* diarrhea which demonstrated a lack of evidence for efficacy of probiotics in CDI

Cochrane review[8]:
- Indicated that there is moderate quality evidence to support the use of probiotics for preventing CDI

Shen et al.[5]:
- A systematic review evaluating the use of probiotics as prevention for CDI
- Concluded that the administration of probiotics closer to the first dose of antibiotics decreases the risk of CDI by greater than 50% in hospitalized patients
- Variation in probiotic species did not indicate any statistical significance

Lau et al.[6]:
- A meta analysis that evaluated the use of probiotics on the incidence of CDI in patients receiving antimicrobial therapy
- 26 randomized controlled trials including 7,957 patients either on probiotics or placebo showed a significant decrease in the risk of developing CDI by 60.5%

DISCLOSURES

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
Temima Saltzman, Sharon Blum, Burke A. Cunha, Melissa Fazzari: Nothing to disclose

OBJECTIVES

- Primary Objective: Evaluate whether the administration of probiotics is effective at precluding *Clostridium difficile* infection (CDI)
- Secondary Objective: Evaluate which historic risk factors were associated with increased incidence of CDI

METHODS

Study Design

IRB Exempt, Single-Centered Retrospective Cohort Analysis from August 1, 2015- August 1, 2017
Interim Analysis

Current Sample Size

1,502 Patients

Data Collection

- Patient demographics
- Antibiotic choice and start date
- Probiotic choice and start date
- CDI course and treatment

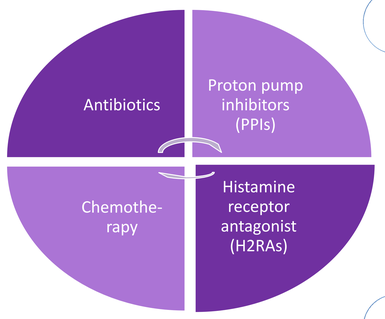
Inclusion Criteria:

- Patients at NYU Winthrop Hospital who are 18 years or older that received at least one dose of antibiotics that are high risk for inducing CDI
- Patients with multiple admissions: only the first admission included

Exclusion Criteria:

- Patients with CDI in the past 3 months prior to receipt of antibiotic
- Patients infected with another pathogen in the stool
- Patients with antibiotics and/or probiotics started <24 hours from incident of CDI

Risk Factors

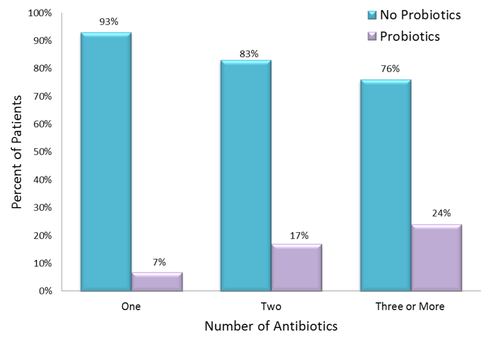


- Microbiology reports checked up to 12 weeks after initiation of antibiotics to determine if there was an incidence of CDI
- The relative risk of CDI with 95% confidence interval and corresponding p-value computed
- Baseline patient characteristics compared between probiotics groups via chi-square, Fisher's exact or t-tests
- A logistic regression model for incident CDI estimated to examine the effect of probiotics while adjusting for potential confounders
- Assuming 75 incident CDI cases will be observed, we will have >80% power

Baseline Characteristics

	No probiotics use [1,367(91%)]	Probiotics use [135(9%)]	P-value
Female [n(%)]	847 (90%)	90 (10%)	0.28
Male [n(%)]	520 (92%)	45 (8%)	
Age [mean(SD)]	72.4 (15.6)	75.8 (14.9)	0.02
Without PPI [n(%)]	1218 (91%)	117 (9%)	0.39
With PPI [n(%)]	149 (89%)	18 (11%)	
Without Chemo [n(%)]	1358 (91%)	134 (9%)	0.61
With Chemo [n(%)]	9 (90%)	1 (10%)	
Without H2RA [n(%)]	1225 (91%)	119 (9%)	0.56
With H2RA [n(%)]	142 (90%)	16 (10%)	
Without Colitis [n(%)]	1359 (91%)	131 (9%)	0.02
With Colitis [n(%)]	8 (67%)	4 (33%)	

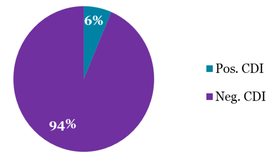
Relationship of Number of Antibiotics and Probiotics



p<0.0001

RESULTS

CDI Within 12 Weeks of Antibiotic Initiation



RR = 1.88; 95% Confidence Interval (1.11, 3.16)

	Probiotics [n=135]	No Probiotics [n=1,367]	P-value
Incidence of CDI	11.1%	5.9%	0.02

Logistic regression model for incident CDI within 12 weeks

Parameter	Point Estimate	95% Confidence Limits		P-value
Probiotics Use	1.48	0.77	2.83	0.24

Logistic regression model for incident CDI within 12 weeks

Parameter	Point Estimate	95% Confidence Limits		P-value
Age (years)	0.90	0.975	1.004	0.16
Number of high risk antibiotics taken concurrently, Ref: One				
Two	3.1	1.82	5.25	0.46
Three	6.27	3.13	12.68	0.0003
PPI	7.10	4.32	11.67	<0.0001
Female	0.62	0.39	0.98	0.04
H2RA	5.49	3.26	9.20	<0.0001

DISCUSSION/ CONCLUSION

- The results are similar to the PLACIDE study indicating a lack of support for the use of probiotics to prevent CDI
- Based on the interim analysis, probiotics were associated with increased incidence of CDI in patients who received concurrent antibiotics
- There was an increased incidence of CDI in patients who were on multiple antibiotics, PPIs or H2RAs

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