Poster 1376

Oral vancomycin as secondary prophylaxis against *Clostridioides difficile* infection in pediatric patients

Hongkai Bao, PharmD[1]; Jennifer Lighter, MD[2]; Yanina Dubrovskaya, PharmD[1,3]; Cristian Merchan, PharmD[1]; Justin Siegfried, PharmD[1]; John Papadopoulos, PharmD[1,3]; Shin-Pung Jen, PharmD[4]

[1]Department of Pharmacy, NYU Langone Health, New York, NY; [2]Department of Pediatrics; NYU School of Medicine, New York, NY; [3]Department of Medicine, NYU School of Medicine, New York, NY; [4]Department of Pharmacy, Newark Beth Israel Medical Center, Newark, NJ

Contact Information
Hongkai Bao, PharmD
NYU Langone Health
Department of Pharmacy
550 1st Avenue
New York, NY 10016
Hongkaibao@gmail.com

October 21-25 • Philadelphia, PA • www.idweek.org
IDWeek 2020
Advancing Science, Improving Care

BACKGROUND

- Oral vancomycin is employed as secondary prophylaxis in adults as a means to reduce the risk of *Clostridioides difficile* infection (CDI) recurrence during concomitant antibiotic therapy
- Retrospective studies have suggested that there may be a benefit to administering secondary oral vancomycin prophylaxis (OVP) in adult patients with prior CDI[1-4]
- This practice is poorly described in pediatric patients as infants are colonized with *C. difficile* and may be asymptomatic[5]
- Children with prior *C. difficile* are at a much higher risk for subsequent infections, and up to 30% of *C. difficile* patients experience recurrence[6]
- At NYU Langone Health (NYULH), guidelines for CDI management in pediatrics recommend the use of secondary OVP for any pediatric patient with a history of CDI while receiving systemic antibiotics
- The ultimate decision to institute OVP is determined on a case-by-case basis leading to heterogenous practice

Secondary OVP candidate
- Prior CDI history
- On systemic antibiotics

→ Initiate enteral vancomycin 10 mg/kg (up to 125 mg) twice daily → Continue while on antibiotics + 5 days after discontinuation

OBJECTIVE

To assess the efficacy and safety of OVP in pediatric patients with a history of CDI and receiving concomitant antibiotics

METHODS

Study Design

- Retrospective cohort study within NYULH system during January 2013 to December 2019
- Identified patients ≤18 years of age with positive diagnostic test for *C. difficile*[1] from electronic health record

Inclusion Criteria	Exclusion Criteria
Met clinical criteria for CDI during initial episode	<1 year of age
Required inpatient or outpatient visit after initial CDI episode (index encounter)[2]	Not treated for initial CDI episode
Prescribed ≥24 hr of systemic antibiotics during index encounter	Received active CDI treatment
	Died of non-CDI causes during follow-up

[1]By immunoassay or polymerase chain reaction-based assay
[2]If multiple encounters were eligible for secondary OVP, only the first encounter during the study period was included

ALLOCATION

Received OVP with systemic antibiotics during index encounter | **No OVP** with systemic antibiotics during index encounter

Outcomes

Primary	CDI recurrence within 8 weeks following antibiotic exposure
Secondary	• Severity of CDI recurrence • Time to CDI recurrence • Vancomycin-resistant enterococci (VRE) infection from any site within 8 weeks following initiation of OVP

RESULTS

Table 1. Patient Characteristics

	No OVP (n=47)	OVP (n=32)	*P* value
Age, years, median (IQR)	8.6 (3.1, 14.4)	9 (4.8, 16.9)	0.171
Gender, male	24 (51.1)	24 (75)	**0.032**
Comorbidities			
Malignancy	21 (44.7)	16 (50)	0.642
Stem cell transplant	2 (4.3)	6 (18.8)	0.056
Inflammatory bowel disease	4 (8.5)	2 (6.3)	1.000
Immunosuppressed	19 (40.4)	17 (53.1)	0.266
Feeding tube	16 (34)	14 (43.8)	0.383
Prior CDI episodes			
1	37 (78.7)	21 (65.6)	0.196
≥2	10 (21.3)	11 (34.4)	
NAP1 strain[a]	2 (22.2)	1 (9.1)	0.566
Time since last CDI[b]			
<6 months	29 (64.4)	21 (70)	0.617
6-12 months	9 (20)	5 (16.7)	0.717
≥12 months	7 (15.6)	4 (13.3)	1.000
Hospital length of stay, days, median (IQR)	5 (1, 10)	14 (5.3, 37.3)	**0.001**
Recent hospitalization within 30 days	19 (40.4)	13 (40.6)	0.986
Antibiotic use within 3 months[c]	29 (61.7)	23 (71.9)	0.349
High risk antibiotics	23 (48.9)	21 (65.6)	0.143
Number of classes received, median (IQR)	1 (0, 3)	3 (0, 4)	**0.001**
Concomitant metronidazole use	4 (8.5)	2 (6.3)	1.000
Concomitant PPI use	4 (8.5)	8 (25)	0.059
Concomitant H2RA use	14 (29.8)	11 (34.4)	0.667
Concomitant probiotic use	10 (21.3)	7 (21.9)	0.949
Antibiotic use during index encounter[c]			
High risk antibiotics	40 (85.1)	30 (93.8)	0.299
Classes of antibiotics received, median (IQR)	1 (1, 2)	2 (1.3, 3)	**0.001**
Duration of antibiotics, days, median (IQR)	8 (5, 12)	12.5 (9, 16)	**0.002**

All data in tables expressed as n (%) unless otherwise noted
[a]NAP1 strain only evaluable for 20 patients (no OVP group 9 patients, OVP group 11 patients) due to missing data
[b]Time since last CDI only evaluable for 75 patients (no OVP group 45 patients, OVP group 30 patients) due to missing data
[c]Patients may have received more than one class of antibiotics

Figure 1. Breakdown of Concomitant High Risk Antibiotics During Index Encounter

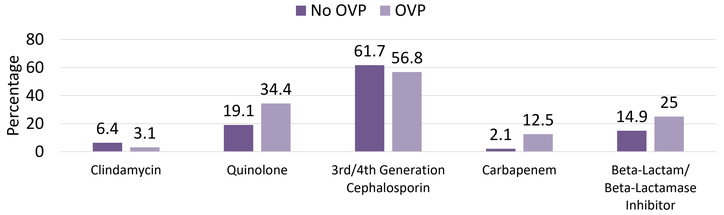

Table 2. Outcomes

	No OVP (n=47)	OVP (n=32)	*P* value
CDI recurrence[a]	11 (23.4)	1 (3.1)	**0.022**
Severity of recurrence			
Severe	1	1	-
Non-severe	10	0	-
Time to recurrence, days, median (IQR)	19 (5, 25)	6	0.667
Isolation of VRE[a]	0	0	-

[a]Within 8 weeks of systemic antibiotic exposure

Table 3. OVP Details (n=32)

Duration, days, median (IQR)	12 (8, 16.8)
Location of OVP initiation	
Inpatient	30 (93.8)
Outpatient	2 (6.3)
Location of OVP completion	
Inpatient	14 (43.8)
Outpatient	18 (56.3)
Days to OVP start, days, median (IQR)	1 (0, 1.8)
Received OVP after completing antibiotics	12 (37.5)

Table 4. Predictors of Recurrence

	Recurrence (n=12)	No Recurrence (n=67)	Multivariate OR (95% CI)	*P* value
Receipt of OVP	1 (8.3)	31 (46.3)	0.1 (0.01-0.75)	**0.027**
Malignancy	8 (66.7)	29 (43.3)	2.2 (0.41-11.34)	0.364
Immunosuppressed	6 (50)	30 (44.8)		
Feeding tube	4 (33.3)	26 (38.8)		
Recent hospitalization within 30 days	7 (58.3)	25 (37.3)	1.3 (0.21-7.87)	0.776
≥2 prior CDI episodes	4 (33.3)	17 (25.4)		
<6 months since last CDI[a]	8 (66.7)	42 (66.7)		
Concomitant metronidazole use	2 (16.7)	4 (6)	1.7 (0.18-16.27)	0.638
Concomitant PPI use	1 (8.3)	11 (16.4)		
Concomitant H2RA use	4 (33.3)	21 (31.3)		
Concomitant probiotic use	2 (16.7)	15 (22.4)		
Receipt of high risk antibiotics, prior	9 (75)	35 (52.2)	1.4 (0.15-13.60)	0.751
Receipt of high risk antibiotics, current	10 (83.3)	60 (89.6)		
≥3 classes of antibiotics received, prior	7 (58.3)	26 (38.8)	1.7 (0.21-14.56)	0.611
≥3 classes of antibiotics received, current	2 (16.7)	15 (22.4)		

[a]Time since last CDI only evaluable for 75 pts due to missing data

CONCLUSION

Discussion

- Included **high risk** population
- Patients in OVP group were at **greater risk** for recurrence
- Inclusion criteria not restricted to specific timeframe respective to prior CDI
- Patients were not excluded if they received metronidazole, PPI, H2RA, probiotics – logistic regression did not show any as risk factors
- Relatively low OVP dose and frequency were utilized

Limitations

- Retrospective, small sample size, patients outside network
- Possibility of concomitant diarrheal illness with asymptomatic *C. difficile* colonization
- Half of patients completed OVP as outpatients so could not confirm completion of doses

Conclusion

- OVP was clinically efficacious and well tolerated for pediatric patients at high risk for CDI recurrence using recommended practices at our institution
- Findings from this study should be validated by conducting randomized controlled trials

REFERENCES

1. Carignan A, et al. *Am J Gastroenterol*. 2016;111(12):1834-40.
2. Caroff DA, et al. *Infect Control Hosp Epidemiol*. 2019;40(6):662-7.
3. Van Hise NW, et al. *Clin Infect Dis*. 2016;63(5):651-3.
4. Knight EM, et al. *J Pharm Pract*. 2019:897190019825994.
5. Jangi S, Lamont JT. *J Pediatr Gastroenterol Nutr*. 2010;51(1):2-7.
6. Nicholson MR, et al. 2015;60(1):18-22.