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Vancomycin Activity towards *Clostridioides difficile* Over Three Decades in Chicago

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Background

- In 2017, the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiologist of America (SHEA) updated the *C. difficile* (CD) treatment guidelines recommending vancomycin as the preferred therapy for *C. difficile* infections (CDI).
- Contrary to previous reports, recent data has indicated that the CD vancomycin minimum inhibitory concentration (MIC) have increased.

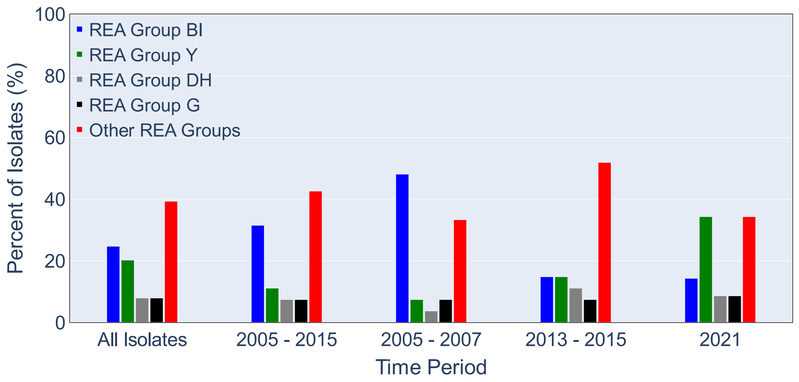
Objective

- To determine if the vancomycin MIC has increased significantly, we assessed the *in vitro* vancomycin minimum inhibitory concentration (MIC) for clinically relevant CD isolates collected across three decades to determine if there is a notable increase in the vancomycin MIC since these guidelines were published.

Methods

- We performed antimicrobial agar dilution susceptibility testing on 89 clinically relevant CD isolates collected within Chicagoland area.
- Isolates were selected from 3 separate time periods:
  - 2005 – 2007
  - 2013 – 2015
  - 2021
- Isolates were selected based on the prevalence of restriction endonuclease analysis (REA) strain types within each time period.
- Isolates within each REA group were selected randomly without knowledge of clinical outcome or additional antimicrobial susceptibility data
- Treatment response to vancomycin was reviewed for patients from the 2021 time period to assess clinical outcomes if CD isolates had a vancomycin MIC of ≥16 µg/ml.

REA Groups



Vancomycin MIC per Time Period

	No. Isolates	MIC (µg/ml)		Resistant Isolates		
		MIC_{50} (µg/ml)	MIC_{90} (µg/ml)	Range (µg/ml)	Resistant[a] (%)	Highly Resistant[b] (%)
All Isolates	89	2	4	1 - >16	8 (9.0%)	4 (4.5%)
2005 – 2007	27	2	4	2 – 8	2 (7.4%)	0
2013 – 2015	27	2	4	1 – 8	2 (7.4%)	0
2021	35	2	16	2 - >16	4 (11.1%)	4 (11.4%)

a. Vancomycin resistance defined as ≥8 µg/ml per CLSI m100 epidemiological cutoff
b. Highly resistance defined as ≥16 µg/ml

Vancomycin MIC per REA Group

	All Isolates		2005 – 2015		2021		
REA Group	**No. Isolates**	**Geometric Mean MIC (µg/ml)**	**No. Isolates**	**Geometric Mean MIC (µg/ml)**	**No. Isolates**	**Geometric Mean MIC (µg/ml)**	**p-value**
All Isolates	89	2.55	54	2.33	35	2.91	0.06
REA Group BI (RT027)	22 (24.7%)	3.53	17 (31.5%)	2.68	5 (14.3%)	12.13	<0.01
REA Group Y (RT014/020)	18 (20.2%)	2.33	6 (11.1%)	2.34	12 (34.3%)	2.38	0.23
REA Group DH (RT106)	7 (7.8%)	2.21	4 (7.4%)	2.31	3 (8.6%)	2	0.44
REA Group G (RT002)	7 (7.8%)	2	4 (7.4%)	2.31	3 (8.6%)	2	1
Other REA Groups	35 (64.8%)	2.34	23 (42.6%)	2.33	12 (34.3%)	2.38	0.56

Results

- The in vitro vancomycin geometric mean MIC against all 89 CD isolates was 2.53 µg/ml with a MIC_{50} of 2 µg/ml and MIC_{90} of 4 µg/ml.
- Comparing the 3 timeframes, the geometric mean vancomycin MICs from 2005-2007, 2013-2015, and 2021 were 2.39, 2.27, and 2.91, respectively (p=0.11).
- Comparison of the isolates collected from 2005 – 2015 to 2021, the in vitro vancomycin geometric mean MICs were 2.33 and 2.91, respectively (p = 0.06).
- REA group BI was the most common strain group to have an increased in vitro vancomycin MIC within the 2021 cohort as 4 of the 5 isolates tested had a MIC of 16 µg/ml.
- All 4 patients had a resolution of symptoms on vancomycin and two suffered from a recurrent infection within ≤4 weeks of the vancomycin treated primary infection.

Conclusion

- The vancomycin MIC against CD has trended upwards slightly over the past 20 years.
- We hypothesize that this increase is due to increased use of oral vancomycin for the treatment of CDI. However, these data indicate that the majority of isolates still have a MIC of ≤4 µg/ml and an elevated MIC does not appear to impact clinical outcomes.
- Further study is required to determine if this upward trend in vancomycin MIC continues and if this could have any potential clinical implications.

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