A Comparative Analysis of In Vitro Susceptibilities of Vancomycin-Resistant Enterococci Against Doxycycline, Minocycline, Tigecycline, Eravacycline and Omadacycline

Mary Francine Chua, MD, MBA, Syeda Sara Nida MD, Jerry Lawhorn MS, and Vidya Sundareshan MD, MPH
Southern Illinois University, Division of Infectious Diseases, Springfield IL

BACKGROUND

- Vancomycin-resistant Enterococci (VRE) are nosocomial pathogens known to cause a gamut of infections that cause significant morbidity and mortality especially among patients with chronic medical conditions, critical illness and prolonged hospitalizations.
- Majority of human infections are caused by two species— *E. faecium* and *E. faecalis,* and which can acquire resistance to ampicillin, aminoglycosides, and vancomycin. Vancomycin-resistance present therapeutic difficulties, and are associated with both increased mortality and increased hospital & health care costs.
- Our aim was to study the susceptibility profile of the VRE strains to the tetracycline group of antibiotics on isolates collected from our local hospital (Memorial Medical Center, Springfield, IL). Both old tetracyclines (doxycycline and minocycline) and their novel derivatives (tigecycline, eravacycline and omadacycline) are included in this study.

METHODOLOGY

- Eighty preserved isolates of VRE from our research laboratory were tested against five tetracyclines, i.e. doxycycline, minocycline, tigecycline, eravacycline and omadacycline.
  - 54 of 80 isolates (67.5%) were vancomycin-resistant *E. faecium.*
  - 26 of 80 isolates (32.5%) were vancomycin-resistant *E. faecalis.*
- Antimicrobial susceptibility testing was performed using the E-test method in accordance to CLSI guidelines (CLSI M100, 2017).
- Isolates were initially classified as either susceptible, intermediately susceptible or resistant based on established CLSI breakpoints, when available. Then, isolates were classified as either susceptible or non susceptible; isolates that had intermediate susceptibility were classified as non susceptible.
- As established CLSI breakpoints for tigecycline, eravacycline and omadacycline are not available, isolates were classified as either susceptible or non-susceptible based on the available FDA interpretive criteria.

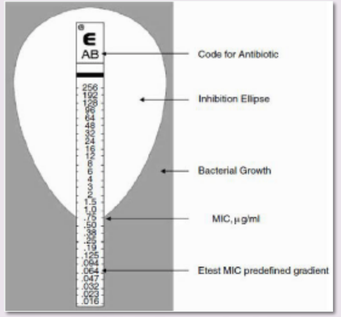
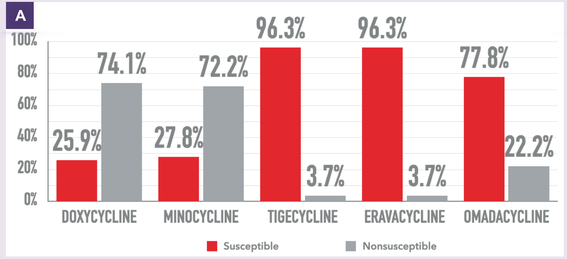


Figure 1. E-test (Epsilometer test) with inhibition ellipse showing the minimum inhibitory concentration (MIC) at the intersection of the bacterial growth and calibrated strip with predefined gradients. [Image credit: Nasir B et al, 2015. Austin Journal of Microbiology.]

RESULTS

- Out of 54 *E. faecium* isolates, 14 (25.9%) were susceptible to doxycycline, 15 (27.8%) were susceptible to minocycline, and 42 (77.8%) were susceptible to omadacycline. Tigecycline and eravacycline each had 52 (96.3%) susceptible isolates.

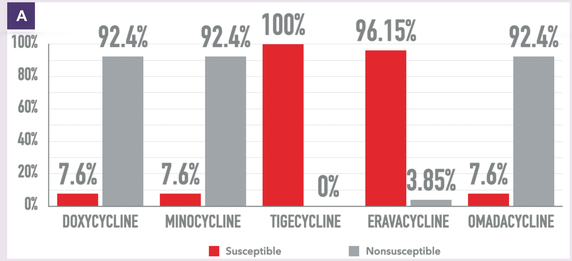


B — VR *E. faecium* (n=54)

Drug	Mean MIC (ug/mL)
Doxycycline	13.99
Minocycline	10.6
Tigecycline	0.1
Eravacycline	0.03
Omadacycline	0.28

Figure 2. A) Comparison of in vitro susceptibilities of 54 vancomycin-resistant Enterococcus faecium isolates against doxycycline, minocycline, tigecycline, eravacycline and omadacycline, and B) mean MICs in ug/mL for each drug.

- Out of 26 *E. faecalis* isolates, 26 (100%) were susceptible to tigecycline, while 25 (96.15%) were susceptible to eravacycline. Doxycycline, minocycline and omadacycline each had 2 (7.6%) susceptible isolates.



B — VR *E. faecalis* (n=26)

Drug	Mean MIC (ug/mL)
Doxycycline	15.62
Minocycline	14.73
Tigecycline	0.15
Eravacycline	0.05
Omadacycline	0.65

Figure 3. A) Comparison of in vitro susceptibilities of 26 vancomycin-resistant Enterococcus faecalis isolates against doxycycline, minocycline, tigecycline, eravacycline and omadacycline, and B) mean MICs in ug/mL for each drug.

CONCLUSION

- Tigecycline and eravacycline exhibited better *in vitro* antimicrobial activity against vancomycin-resistant *E. faecium* and *E. faecalis* when compared to doxycycline and minocycline.
- Omadacycline showed a relatively favorable susceptibility profile for vancomycin-resistant *E. faecium,* but less favorable for *E. faecalis;* this finding is unique to our local hospital. Results of this study will be useful to incorporate in the local antibiogram and will guide local antimicrobial stewardship efforts.
- The present study is limited by the unavailability of established CLSI breakpoints for tigecycline, eravacycline and omadacycline, therefore necessitating the use of available FDA interpretive criteria.

REFERENCES

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