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Tedizolid for Treatment of Enterococcal Bacteremia

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ABSTRACT

Background: Due to the high prevalence of vancomycin-resistant enterococci (VRE) and emergence of daptomycin-nonsusceptible enterococci (DNSE) in the US hospital settings, tedizolid provides an alternative choice for the treatment of serious infections caused by VRE and DNSE. We share our experience in treatment of enterococcal bacteremia with a focus on DNSE using tedizolid as salvage antibiotic therapy.

Methods: DNSE and VRE isolates were identified on the basis of colony morphology, conventional biochemical tests, and were confirmed by analysis of 16S rRNA gene sequence or by the MALDI Biobiotyper CA System (Bruker). DNSE was defined as an enterococci isolate with a daptomycin minimum inhibitory concentration (MIC) of >4 µg/ml as determined by MicroScan System (Siemens)) and confirmed by Etest (bioMérieux). *In vitro* susceptibility of tedizolid and linezolid for these isolates were performed by broth microdilution using the Sensititre™ panel (Thermo Fisher Scientific) in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI).

Results: 4 patients with *E. faecium* bacteremia were treated and cured using tedizolid 200 mg once a day in a medical center in suburban New York City from November 2014 through June 2015.

Tedizolid was used as salvage therapy in these patients who had multiple contraindications for treatment with other antibiotics based on susceptibility data, existing laboratory abnormalities and potential drug interactions.

Conclusion: Our clinical data confirms the microbiological and pharmacological basis for potential use of tedizolid as salvage therapy in patients with infections caused by daptomycin-nonsusceptible enterococci.

INTRODUCTION

Westchester Medical Center (WMC) is a tertiary care, academic teaching hospital located in suburban New York City, where a high occurrence rate of vancomycin resistant enterococci (VRE) and daptomycin non-susceptible enterococci (DNSE) has been observed. With a patient population inclusive of those who have undergone solid organ transplantation and hematopoeitic stem cell transplantation (HSCT), the immunocompromised patients at our hospital are at high risk for colonization and infections with resistant gram positive organisms, thereby incurring limitations to treatment.

In 2014, the VRE rate at WMC was noted to be 27.1% hospital wide. The daptomycin non-susceptibility rates amongst VRE isolates and non-VRE isolates were observed to be 27%, and 2%, respectively. Tedizolid is a novel oxazolidinone antimicrobial agent with potent activity against a broad range of Gram-positive organisms. Advantages of tedizolid includes a more favorable toxicity profile when compared to linezolid. Due to the high prevalence of VRE and emergence of DNSE in the US hospital settings, tedizolid may provide an alternative to linezolid for the treatment of infections caused by VRE and DNSE. The aim of this study was to evaluate the safety and efficacy of Tedizolid in treatment of enterococcal bacteremia with a focus on DNSE infections.

MATERIALS AND METHODS

DNSE and VRE isolates were identified on the basis of colony morphology, conventional biochemical tests, and were confirmed by analysis of 16S rRNA gene sequence or by the MALDI Biobiotyper CA System (Bruker). DNSE was defined as an enterococci isolate with a daptomycin minimum inhibitory concentration (MIC) of >4 µg/ml as determined by MicroScan System (Siemens)) and confirmed by Etest (bioMérieux). *In vitro* susceptibility of tedizolid and linezolid for these isolates were performed by broth microdilution using the Sensititre™ panel (Thermo Fisher Scientific) in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI).

Cure was defined as clinical improvement and microbiological eradication of infection. Serial daily follow up blood cultures were drawn till negative

RESULTS

4 patients with *E. faecium* bacteremia were treated with tedizolid 200 mg once a day in a medical center in suburban New York City from November 2014 through June 2015. Tedizolid was used as salvage therapy in these patients who had multiple contraindications for treatment with other antibiotics based on susceptibility data, existing laboratory abnormalities and potential drug interactions.

Case	Patient Characteristics	Indication of treatment	DAP MIC µg/ml	LIN MIC µg/ml	TED MIC µg/ml	Duration of Treatment (Days)	Outcome
1	60/M Renal transplantation	VRE bacteremia rhabdomyolysis, thrombocytopenia, concomitant SSRI	4	1	0.25	14	Cure
2	75/M Burkitt's lymphoma	DNSE bacteremia	16	2	0.25	14	Cure
3	49/M Cirrhosis	DNSE bacteremia	6	2	0.25	10	Cure
4	54/F Acute Leukemia	DNSE bacteremia	32	2	0.25	7	Cure

DISCUSSION

Enterococcus is one of the leading cause of nosocomial infection including bacteremia, intra-abdominal infections and urinary tract infections in immunocompromised patients.

Attributable mortality, when isolated from blood, is up to 36%.

Daptomycin has being increasingly used for treatment of serious VRE infections. This has been associated with emergence of rising daptomycin MIC s(2-4mcg/ml) and daptomycin non-susceptibility

(MIC > 4 mcg/ml)

In the recent past, in-vitro susceptibility of DNSE and DSE isolates that were tested in our healthcare facility, have showed that resistance of tedizolid against daptomycin-nonsusceptible enterococci is rare with with DNSE and DSE in-vitro susceptibility reaching 96.7% and 92.9%, respectively.

The greater potency, improved resistance and safety profile of tedizolid compared with linezolid provides the microbiological basis for its potential use in patients with infections caused by daptomycin-nonsusceptible enterococci

For this study, we selected patients, who had very limited antibiotic choices for treatment of enterococcal bacteremia.

In the treatment of a limited number of patients, Tedizolid was safe and efficacious.

All (4/4) the patients were cured.

When used at longer duration (>6 days), no obvious side effects of myelosuppression, drug interaction and neuropathy were noted.

CONCLUSION

Our clinical data confirms the microbiological and pharmacological basis for potential use of tedizolid as salvage therapy in patients with infections caused by daptomycin-nonsusceptible enterococci. Tedizolid could also be considered as and as step down therapy for treatment of other enterococcal infections including bacteremia.

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