Use of Tedizolid for the Treatment of *Staphylococcus aureus* Bacteremia – an off labelled indication

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Abstract

Aims

We aim to share our experience in the successful use of tedizolid for the treatment of *Staphylococcus aureus* bacteremia in two of our patients.

Presentation of cases

Our first patient had methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia. The MRSA isolated was sensitive to linezolid and vancomycin (MIC=2), resistant to daptomycin (MIC=2). In view of the documented drug allergy to ceftriaxone and drug interaction with daptomycin, the patient was initially initiated on intravenous vancomycin but developed a breakthrough fever with rising inflammatory markers. However, upon initiation of tedizolid, fever lysed and the patient improved clinically.

Our second patient has end–stage renal failure on hemodialysis. The patient has methicillin-susceptible *Staphylococcus aureus* (MSSA) catheter-related bloodstream infection. The MSSA isolated was sensitive to vancomycin (MIC=2) and ceftaroline (MIC=0.50), but resistant to daptomycin (MIC=2). Vancomycin was initiated in view of documented drug allergy to ceftriaxone but repeated blood cultures showed the persistence of MSSA. Antibiotics were switched to linezolid for 3 days before switching to tedizolid due to previous neutropenia with linezolid. Blood cultures had documented clearance with tedizolid.

Discussion and conclusion

In both our patients, tedizolid was introduced after a few days of vancomycin therapy. Hence, the efficacy of tedizolid as the first-line therapy for the treatment of staphylococcus bacteremia remains unknown. Nevertheless, in both patients, there was no relapse of staphylococcus

bacteremia when tedizolid was used to complete the antibiotic therapy. The optimal treatment duration of staphylococcus bacteremia with tedizolid also remains unknown.

Introduction

For decades, vancomycin has been the cornerstone for treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections, but increasingly, creeping minimum inhibitory concentration (MIC) of MRSA has resulted in treatment failure [1 – 2]. In view of the lack of clinical experience in the use of tedizolid for off-labeled indications, we describe two patients with MRSA/MSSA bacteremia and were treated with tedizolid successfully.

Case Presentation

The first patient was a 51-year-old Chinese male. His medical history was significant for diabetes mellitus, depression and alcohol dependency with Child's B alcoholic liver cirrhosis. He presented with giddiness and was febrile (37.7°C) on admission. He was recently admitted for mild pancreatitis, was given ceftriaxone but developed fixed drug eruption (diagnosed by a dermatologist). MRSA screen came back positive and blood cultures subsequently grew MRSA – sensitive to linezolid and vancomycin (MIC=2), resistant to daptomycin (MIC=2). Heart echo revealed no vegetation.

Despite the high MIC, the patient was initiated on vancomycin due to limited therapeutic options – loading dose of 20mg/kg, followed by 20mg/kg Q12h. Despite receiving high doses of vancomycin (25mg/kg Q12h) after several titrations, serum vancomycin troughs remained persistently sub-therapeutic (4.4 – 13mg/L). Patient's renal function remained good throughout with no change in urine output. Blood cultures were negative on day 3 of vancomycin but on day 13 of vancomycin therapy, patient spiked fever (39.9°C) and repeated inflammatory markers

(pro–calcitonin, C–reactive protein, and white cell count) were up–trending. As the patient was taking escitalopram for depression, concurrent use with linezolid was not recommended due to the risk of serotonin syndrome. Ceftaroline was contraindicated as the patient is allergic to ceftriaxone. In light of the poor response to vancomycin with breakthrough fever and limited therapeutic options, intravenous tedizolid 200mg once-daily was initiated. Thereafter, fever normalized and inflammatory markers were down-trending. Repeated blood cultures remained negative, the patient completed one week of tedizolid, was discharged well without antibiotics and there was no relapse of infection on follow up.

Our second patient was a 58-year-old Chinese male who presented with fever (39°C), chills and rigors. The patient had end-stage renal failure; on thrice-weekly hemodialysis since 2010. Due to recurrent vascular access issues, the patient had been dialyzing through permanent catheters. He was recently admitted and given 1 week of intravenous vancomycin for catheter exit-site infection, and blood cultures were negative then. In this current admission, blood cultures sent on admission grew MSSA – sensitive to vancomycin (MIC=2), ceftaroline (MIC=0.50), resistant to daptomycin (MIC=2). Heart echo revealed no vegetation. Vancomycin was initiated as the patient had type I hypersensitivity reaction to ceftriaxone. The infected permanent catheter was removed on day 2 of admission but repeated blood cultures showed the persistence of MSSA up to day 6 of admission (two sets of blood cultures were repeated on a daily basis). Hence, in view of treatment failure with vancomycin and patient's drug allergy, linezolid was initiated but was later switched to tedizolid 200mg once-daily after 3 days – taking into account patient's previous history of known thrombocytopenia with linezolid. On the day of the switch from linezolid to tedizolid therapy, repeat blood cultures came back negative. While using tedizolid, the patient's

platelet count was monitored closely. Platelet counts were normal initially and the patient was planned for 2-weeks course of tedizolid. However, on day 11 of tedizolid therapy, platelet count dropped to <100 x 10^9/L and tedizolid was stopped. The patient was subsequently discharged well without antibiotics. Two weeks post-discharge, patient's platelet counts normalized and there was no relapse of infections.

Discussion

In both our patients, alternative anti-MRSA/anti-MSSA therapies (daptomycin, ceftaroline, linezolid) within our formulary were taken into consideration in view of therapeutic failure with vancomycin. Both our patients had severe allergic reactions to ceftriaxone and this prohibits the use of ceftaroline. Daptomycin could not be used both of MSSA/MRSA from our patients exhibit a high MIC of 2 to daptomycin (resistant). Linezolid was not used or continued in view of drug interactions and adverse drug effects observed [3 – 4].

Multiple studies have demonstrated tedizolid's potent *in-vitro* activity against MSSA/MRSA [5 – 6]. Tedizolid's long elimination half-life (10-12h) and its improved potency allow for a lower dose to be used. This contributes to a lower incidence of thrombocytopenia, when compared to linezolid [7]. In addition, tedizolid does not appear to have a significant drug interaction with serotonergic agents [8].

In both our patients, tedizolid was introduced after a few days of vancomycin therapy. Hence, the efficacy of tedizolid as the first-line therapy for the treatment of staphylococcus bacteremia remains unknown. Nevertheless, in both patients, there was no relapse of staphylococcus

bacteremia and infections when tedizolid was used to complete the antibiotic therapy. The optimal treatment duration of staphylococcus bacteremia with tedizolid also remains unknown.

Conclusion

To date, tedizolid is only licensed for the treatment of acute bacterial skin and skin structure infection (ABSSSI), with investigational use in nosocomial pneumonia. While evidence for its use in bacteremia is lacking, we reported that tedizolid is effective and safe in the treatment of *Staphylococcus aureus* bacteremia, with no relapse.

Declarations

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