Efficacy of Dalbavancin and Telavancin in the Treatment of Acute Bacterial Skin and Skin Structure Infections

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ABSTRACT

Objectives: Two glycopeptide analogues, such as dalbavancin and telavancin, with improved pharmacokinetic/pharmacodynamic parameters have been developed. These two glycopeptide analogues are approved by Food and Drug Administration (FDA) for treatment of various Gram-positive bacterial skin infections.

Materials and Methods: We have conducted an open labelled prospective randomized study to compare the efficacy of these two drugs. A total of 200 patients diagnosed with acute bacterial skin and skin structure infections (ABSSSI) were recruited for the study. They were randomized to receive either a single dose of dalbavancin 1500 mg i.v (Group I) or telavancin 10 mg/kg intravenously (i.v.) every 24 hours for six days (Group II). The skin infection rating score (SIRS) was calculated on Day 0 for all patients at the time of diagnosis. Signs and symptoms of the lesions were assessed based on the following factors: blistering, exudate/pus, erythema/inflammation and itching/pain. Each factor was classified as one of the following: absent – 0, minimal – 1, moderate – 2 and severe – 3.

Outcomes: Clinically successful treatment was defined as complete resolution of clinically meaningful signs and symptoms of infection, including SIRS score of 0. The outcome measure was the percentage of patients with SIRS score of 0 on day 7 (clinical success). The third most common diagnosis at baseline was impetigo (13% in both groups). Patients who received dalbavancin had a higher clinical success rate than those receiving telavancin.

Conclusions: Findings of the present study show that single i.v dose of dalbavancin is better than telavancin repeated doses in treatment of ABSSSI.

Keywords: Dalbavancin, Telavancin, efficacy, acute bacterial skin, skin structure infections.

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INTRODUCTION

Skin infections account for a significant proportion of dermatologic disease, often resulting in or as a consequence of a disruption in skin integrity (1). Damage to skin integrity compromises its barrier function and allows bacteria to pass into the subdermal environment, where the moist, warm and nutritious conditions are conducive to microbial colonization and proliferation (2). *Staphylococcus* and *Streptococcus* are Gram-positive bacterial species that cause the majority of bacterial skin infections including impetigo, folliculitis and other minor soft tissue infections (3, 4). The increasing prevalence of resistant Gram-positive pathogens, especially methicillin-resistant *S. aureus* (MRSA), has intensified the search for novel treatment options.

Dalbavancin, a novel lipoglycopeptide, was approved by FDA for the treatment of MRSA skin infections. Dalbavancin is not well absorbed orally and thus requires intravenous administration. This glycopeptide has a very long half-life, it is administered once weekly as a two-dose regimen and is being marketed as a potential outpatient alternative to the existing therapies such as teicoplanin and vancomycin, which are common intravenous agents for skin infections associated with MRSA (5). Dalbavancin is administered via i.v. infusion over 30 minutes in a dose of 1500 mg. Dose adjustments are not necessary for mild to moderate renal impairment.

Telavancin is a semisynthetic lipoglycopeptide which was approved by the FDA for use against Gram-positive organisms including MRSA (6). The recommended dosage regimen for telavancin is 10 mg/kg body weight i.v. infused over a 60 minutes period every 24 hours, in patients with normal renal function.

To the best of our knowledge, there have been no studies on the efficacy of dalbavancin and telavancin in the treatment of acute bacterial skin and skin structure infections (ABSSSI) and hence, this study has been undertaken.

MATERIALS AND METHODS

Study conduct

The study was conducted in the Department of Dermatology at MNR Medical College and Hospital, Sangareddy with the approval of Institutional Review Board. The duration of the study was from January 2016 to May 2016. It is an open labelled, prospective, randomized, comparative study.

Study patients

Patients above 18 years with ABSSSI were included in the study. The diagnosis of ABSSSI required the presence of cellulitis, major abscess, or traumatic wound/surgical site infection, each associated with at least 75 cm² of erythema. Pregnant breast-feeding patients on systemic corticosteroid therapy, with signs and symptoms of a concurrent infection requiring additional antibiotic therapy, diabetes mellitus, HIV/AIDS, and history of hypersensitivity or allergy were excluded from the study. A total of 200 patients diagnosed with ABSSSI were recruited for the study after obtaining their informed consent.

Randomization and Intervention

Patients were randomly assigned, based on random number table, in a 1:1 fashion to each of the two groups (100 subjects per group). On day 0 (First visit), Random Blood Sugar (RBS) and HIV status were tested and baseline demographic data (age, sex, weight, associated diseases, habits, drug history, and allergy history) were collected. Group I received dalbavancin via i.v. infusion over 30 minutes in a dose of 1500 mg, and group II telavancin (10 mg/kg) i.v. infused over a 60-minute period every 24 hours for six days.

The skin infection rating score (SIRS) was calculated on Day 0 for all patients at the time of diagnosis. Signs and symptoms of the lesions were assessed based on the following factors: blistering, exudate/pus, erythema/inflammation and itching/pain. Each factor was classified as one of the following: absent – 0, minimal – 1, moderate – 2 and severe – 3. The parameters considered were SIRS for assessment of improvement in clinical symptoms. Clinically successful treatment was defined as complete resolution (SIRS score of 0) of clinically meaningful signs and symptoms of infection. The outcome measure was the percentage of patients with SIRS score of 0 on day 7 (clinical success). For all patients, SIRS score was noted on day 7. Patients were asked to report any adverse effects as well as symptomatic improvement during their visits.
They were also advised to record any adverse effects in a diary, which was evaluated during follow up visits.

On their first visit, exudate or pus were collected from each patient’s skin lesions and inoculated onto Blood agar and MacConkey agar. By observing pigment production and performing coagulase test, isolates were identified as *S. aureus*. Isolates were classified as MRSA by testing them on Mueller-Hinton agar plates containing 6 μg/mL of oxacillin, supplemented with 4% NaCl.

**Statistical analysis**

All results are presented as mean ± SD and those regarding categorical measurements are presented in Number (%). Student *t* test (two tailed, independent) has been used to find the significance of study parameters on a continuous scale between two groups (inter group analysis) on metric parameters. Chi-square test was used to find the significance of study parameters on a categorical scale between two groups. *P* values of less than 0.05 were regarded as significant.

**RESULTS**

The age and gender distribution of patients in both groups was well matched, without any significant difference, as shown in Table 1 and Figures 1 and 2. Most patients were in the age group of 20-40 years. All 200 randomized subjects received one of the two study drugs and completed the study. None of them discontinued the study prematurely.

The most common condition diagnosed at baseline was furuncle (40% in Group I and 36% in Group II), followed by folliculitis (26% in Group I and 28% in Group II). The third most common diagnosis at baseline was impetigo (13% in both groups). Details of the diagnosis at baseline in both groups of patients are summarized in Figure 3.

*TABLE 1. Patient age distribution*

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Group I (Dalbavancin 1500 mg i.v.)</th>
<th>Group II (Telavancin 10 mg/kg i.v.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>3</td>
<td>3.0</td>
</tr>
<tr>
<td>20-30</td>
<td>34</td>
<td>34.0</td>
</tr>
<tr>
<td>31-40</td>
<td>39</td>
<td>39.0</td>
</tr>
<tr>
<td>41-50</td>
<td>14</td>
<td>14.0</td>
</tr>
<tr>
<td>51-60</td>
<td>9</td>
<td>9.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>33.86±9.98</td>
<td>33.96±9.63</td>
</tr>
</tbody>
</table>

*FIGURE 1. Gender distribution of studied patients (Group I)*

*FIGURE 2. Gender distribution of studied patients (Group II)*

*FIGURE 3. Diagnosis in each of the two studied groups of patients*
higher clinical success rate than those receiving telavancin. Both treatment regimens were well tolerated during the study. Two patients in Group I (2.17%) and one in Group I (1.11%) reported nausea and headache but all three completed the study as per protocol. The reported events were mild in intensity and were explained as being due to the study medication. There were no serious adverse events observed during the study period.

**DISCUSSION**

This study was designed to compare the efficacy of dalbavancin versus telavancin in the treatment of ABSSSI. Infections caused by Gram-positive microorganisms have changed dramatically over the past decade (7). The incidence of hospital acquired infections due to MRSA has been increasing worldwide (8).

Telavancin is a bactericidal lipoglycopeptide with multifunctional mechanism of action. Telavancin inhibits bacterial cell wall synthesis and disrupts bacterial membrane function (9), resulting in bacterial death. Telavancin is active against virtually all Gram-positive bacteria, including drug resistant organisms, such as MRSA and vancomycin – intermediate and resistant strains of *S. aureus* (10). With a half-life of 7-9 h and a prolonged post antibiotic effect (4–6 h), telavancin can be administered intravenously once daily (11). In many previous studies, intravenous telavancin therapy was shown to have a significant efficacy in complicated skin and skin structure infections (12).

Dalbavancin is a novel, semisynthetic lipoglycopeptide antibacterial agent with a better pharmacokinetic profile that allows weekly dosing. It has a potent *in vitro* activity against Gram-positive bacteria, including MRSA, and it is superior to most of the other antibiotics used to treat Gram-positive bacterial infections, including vancomycin (13). In addition, dalbavancin has demonstrated superior *in vivo* activity against infection due to MRSA and other bacteria in animal infection models (14). Its spectrum of activity suggests that dalbavancin has the potential to be useful for the treatment of skin and skin structure infections. Gram-positive bacteria, particularly *S. aureus* and *Streptococcus pyogenes*, are among the most common pathogens implicated in skin and skin structure infections (15). The half-life of dalbavancin in humans (eight days) allows a weekly administration of the drug, with therapeutic concentrations in plasma maintained for the entire seven-day period between doses. A recent study has demonstrated that a single 1500 mg infusion of dalbavancin is non-inferior to a two-dose regimen, has a similar safety profile, and removes logistical constraints related to delivery of the second dose (16).

**CONCLUSION**

The goal of the present study was to compare the efficacy of dalbavancin to that of telavancin for the treatment of patients with ABSSSI. Results show that a single i.v. dose of dalbavancin was better than telavancin repeated doses in the treatment of acute bacterial skin infections. At the end of treatment on day 7, the percentage of patients with a SIRS score of 0 was higher in the dalbavancin group (86%) compared to the telavancin group (81%).

Overall, findings from the present study demonstrated that dalbavancin appeared to be effective and to ensure more therapeutic success than telavancin for the treatment of patients with acute bacterial skin infections. Therefore, considering the current MRSA epidemic, dalbavancin could provide a timely and useful alternative for the treatment of complicated skin and skin structure infections. However, further research is needed to establish the safety and efficacy of dalbavancin over telavancin in the treatment of acute bacterial skin infections in studies with larger sample sizes and advanced clinical settings.

**Conflicts of interest:** none declared.

**Financial support:** none declared.
REFERENCES