

Pilot Study Comparing Daptomycin And Telavancin In The Treatment Of Skin And Soft Tissue Infections

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Citation

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Abstract

This is a prospective controlled, single blinded, randomized study comparing the efficacy and side effects of daptomycin and telavancin in patients with lower extremity skin and soft tissue infections (SSTI). Forty patients were enrolled with similar SSTI of the lower extremities and received either daptomycin or telavancin. Clinical cure was determined by resolution of their cellulitis. There did not appear to be any significant difference in clinical outcomes, rapidity of improvement, adverse events nor relapse rates. The duration of treatment was shorter in the telavancin arm than in the daptomycin arm of the study.

INTRODUCTION

Daptomycin is a novel lipopeptide antibiotic used for the management of SSTI, gram-positive bacteremia and right sided endocarditis [6]. It acts by interfering with the calcium-potassium channel mechanisms resulting in cell death. It has been studied extensively in SSTI and is generally well tolerated. Telavancin, a derivative of vancomycin, is a lipoglycopeptide whose bactericidal activity comes from its ability to simultaneously inhibit peptidoglycan synthesis and cause membrane depolarization. It is most commonly used against Methicillin-Resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *S. aureus* and linezolid-resistant *S. aureus* [7]. Telavancin's primary side effect, like its vancomycin derivative, is nephrotoxicity. Daptomycin and telavancin were both approved based on non-inferiority studies against vancomycin [10].

OBJECTIVE

This pilot study was conducted to establish if there was a significant difference in the clinical outcomes in patients treated for similar SSTI's with daptomycin versus telavancin. In addition the study also attempted to determine if there was a difference in the adverse effects of the two drugs and whether there was a pharmaco-economic difference between the two antibiotics.

MATERIALS AND METHODS

There were forty patients enrolled in the study- twenty in the daptomycin arm and twenty patients in the telavancin arm.

Patients were randomized to either the daptomycin or telavancin wings of the study. Approval was obtained from all the patients prior to enrollment and administration of the antibiotics. In addition, all patients in the study were treated and followed up by the same Infectious Disease's consultant. All patients in the study had lower extremity SSTI's below the knee without deep abscesses.

In the daptomycin treated group the average age was 69 years; gender ratio was 50% males and 50% females. The dose of daptomycin was 4mg/kg/day (average 5.6mg/kg/day) for an average of 10-14 days. The telavancin group had an average age of 65 years old with a gender ratio of 40% males and 60% females. The dosage of telavancin administered was 10mg/kg/day (average 8.2mg/kg/day) for 10-14 days.

Clinical cures were defined as resolution of the cellulitis and reduction of the pain and erythema. Relapse was defined as a reoccurrence of the pain and cellulitis at the previous site of treatment and was reassessed by the same Infectious Disease consultant at the 2-4 week follow up. In addition, co-morbid conditions such as diabetes mellitus, cancer and prior traumas were also noted in each patient prior to antibiotic administration.

Microbiology:

No tissue biopsies were obtained as all the patients presented with only clinical cellulitis and SSTI's.

RESULTS

Daptomycin:

Patients in the daptomycin arm of the study were treated for an average of 10-14 days at 4mg/kg/day. Fifty percent (10) of the patients had diabetes but did not have significant vascular insufficiency as observed by palpable bilateral dorsalis pedis pulses. Average white blood cell (WBC) count was 7.5 cells/cu/L and serum Creatine Phosphokinase (CPK) preformed at the end of the treatment was within normal limits. Eighty five percent of the patients treated with daptomycin showed resolution of the cellulitis/SSTI at the end of therapy and were determined as cured. During follow up, 2-4 weeks after the cessation of treatment, patients showed no evidence of relapse. The 15% of refractory cases that did not respond adequately were successfully retreated with daptomycin or another antibiotic.

Telavancin:

Patients enrolled in the telavancin arm of the study had an average WBC count of 8.9 cell/cu/L and received an average of 8 days of therapy at 10mg/kg/day. Forty percent of these patients had diabetes. Eighty seven percent demonstrated resolution of the cellulitis/ SSTI by the end of treatment. The remaining patients were switched to an alternate antibiotic until the cellulitis resolved.

DISCUSSION

In recent years it has become increasingly difficult to adequately treat patients with acquired skin and soft tissue infections due to multi-resistant pathogens. Lui and Bayer suggested that vancomycin remains the mainstay of therapy in MRSA infections [4]. However there are increased reports of treatment failures with vancomycin with decreasing susceptibility to vancomycin [1]. According to this study, daptomycin was used as salvage therapy in patients with vancomycin failures. It has been noted that although vancomycin is the primary drug of choice, many studies including a study by Kapadia and Coyle demonstrated vancomycin's MIC creep from 0.25 microgram/ml in 1985 to 2.0 microgram/ml in 2004 [3]. In a study by Davis and McKinnon, patients received daptomycin or vancomycin for complicated SSTI with MRSA. They demonstrated that patients on the daptomycin achieved resolution of infection in 77% (41 patients) versus 42% (89 patients) for vancomycin. The average duration of therapy for daptomycin was 4-7 days [2]. It appears that daptomycin achieved a more rapid clinical cure and had a decreased

hospital stay than the vancomycin arm.

Since its approval for the treatment of skin and soft tissue infections in 2009, telavancin has been used as an alternative therapy for MRSA/MSSA infection. Stryjewski's study showed the non-inferiority of telavancin versus vancomycin/antistaphylococcal penicillin for the treatment of MRSA [8]. In patients with MSSA infections the cure rate was 80% (40/50) versus 77% (40/52) with telavancin and standard therapy respectively. In MRSA infections the cure rate was 82% (18/22) in the telavancin arm versus 69% (18/26) in the standard therapy arm. The overall test-of-cure evaluation was 79% (66/84) and 80% (66/83) for telavancin versus standard therapy with a failure rate of 7% (6/84) and 4% (3/83) respectively. The side effects between the drugs were not significant. In our study, we also noted similar statistics in respect to MRSA infections with a cure of 85% and 87% respectively with both telavancin and daptomycin.

Another in-vitro related study conducted by Steed and Vidaillac demonstrated the efficacy of telavancin versus daptomycin and vancomycin in daptomycin-nonsusceptible *S. aureus* strains. Daptomycin displayed initial bactericidal activity followed by regrowth and vancomycin did not exhibit any bactericidal activity against any strain [9]. However, no in-vivo studies were available to confirm this in patients. In their study, telavancin was significantly superior at reducing colony forming units against all three strains as opposed to vancomycin and more efficacious than daptomycin. Although a 120-hour window of observation limited this study, it suggests that telavancin has significant bactericidal activity when compared to the other two antibiotics [9].

Our study did not show statistically significant differences in the efficacy of telavancin and daptomycin in the treatment of skin and soft tissue infections. It appeared that telavancin was used for a shorter duration than daptomycin in the treatment of lower extremity cellulitis. This shorter duration of therapy may have resulted in a lower cost to the patient depending from where the drug was acquired.

Table 1

Patient data

	Daptomycin	Telavancin
Number of patients	20	20
Average Age	69	65
Sex (Male/Female)	50% / 50%	40% / 60%
Diabetics	50%	40%
Avg. WBC	7.5 cells/L	8.9 cells/L
Avg. Platelet	239 per L	224 per L
Duration of Treatment	15 Days	8 Days
Cure Rate	85%	87%
Relapse Rate	15%	13%

CONCLUSION

Despite the differences in the literature and the results of our pilot study, it appeared that both drugs are equally efficacious in the treatment of cellulitis although the patients in the telavancin arm required a shorter course. It is difficult to conclude with any certainty as to which drug may be more cost effective. Further studies to address the pharmacoeconomic aspect of both drugs can be done if one wishes to look at this comparative data.

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