

# The Use of Antibiotic Impregnated, Implanted Synthetic Calcium Sulfate Tablets in the Treatment of Soft Tissue, Vancomycin Resistant Enterococcus Infections

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## Introduction

Enterococci are facultative anaerobic, gram negative cocci that are known to thrive in extreme conditions such as high and low pH and a wide range of temperatures(1). They are naturally found in soil and water as well as in the human gastro-intestinal and female genito-urinary tracts (1,2). Although they were initially classified as Streptococcus, they originated as a separate species in the mid -1980's (3). Traditionally not a particularly virulent bacteria, vancomycin-resistant strains of Enterococcus have developed in the last two decades. In many ways this is attributable to their ability to develop resistance to other antimicrobial classes, such as the cephalosporins (4).

Vancomycin resistant Enterococcus (VRE) infections were previously reported only in patients with certain risk factors such as hospitalization, recent antibiotic treatment, those with known colonization of other highly resistant strains (such as MRSA or VRSA), immunosuppression, recent abdominal or thoracic surgery, indwelling catheters/central line and/or the presence of a feeding tube or pressure sore (2). Antimicrobial resistance is more likely to be seen in Enterococcus faecium than Enterococcus faecalis infections (1).

VRE infections are often difficult to treat and may require multiple antimicrobial agents based on anecdotal evidence of in-vitro studies (3). Treatment options often include antimicrobial agents which do not have a specific VRE indication. Although several of these combinations have shown in-vitro, animal model and anecdotal success, no standardization has been established (5,6). Combination therapies that have shown success have included linezolid, daptomycin, quinupristin-dalfopristin, ceftriaxone, gentamicin, vancomycin and tigecycline (5-7)

Other complicating factors include; 1- Medical co-morbidities such as peripheral vascular disease and diabetes 2- biofilm formation and 3- tissue concentration of antimicrobial agents, particularly in end-organs such as the lower extremity. These would all benefit from direct implantation of the antimicrobial agent rather than systemic introduction and limited bioavailability.

## Methodology

Five patients presented to the author's outpatient clinic with a chief concern of soft tissue infection to the foot. Each had been treated in a similar manner with oral antibiotics, surgical debridement, and subsequent hospitalization with intravenous antibiotics, and none showed significant improvement. Digital, trans-metatarsal or below-knee amputations were offered to each as a treatment of last resort.

None of the patients presented with a clinical history normally associated with VRE infections. Although two were diabetics, they were both in their fourth decade and were well controlled with no other co-morbidities. None of the five reported any known trauma however each reported either a recent tinea pedis infection (3/5) or a suspected "spider bite" (2/5). All five had intact pedal perfusion, verified by palpable pedal pulses and TCOM measurements above 50 mmHg within one centimeter of the wound.

Each was consented for surgical procedure and brought to the operating room. Under appropriate anesthesia the wounds were debrided of devitalized tissue and thoroughly flushed with sterile saline. None was noted to have exposed bone or other evidence of osteomyelitis. At the onset of the procedure, synthetic calcium sulfate was prepared and mixed with linezolid and ceftriaxone. Once the tablets hardened, they were implanted in the wound(s). A primary, non-adherent layer was applied, the secondary dressing was dependent on the amount of drainage from the wound. Patients were followed in the clinic at post op day 2, 7, 14, 21, 28 and 42 (+/- 2 days).



24 year-old male with history of "spider bite"



21 days post debridement and implantation

## Results

Within 24 hours of surgical debridement and antibiotic tablet implantation, all five patients responded with a reduction of both clinical signs of infection and wound drainage. Within four days none had any clinical, laboratory or radiographical signs of infection. The tablets dissolved in 15-25 days. By day 28 all wounds had re-surfaced with no clinical or radiographical signs of infection, and all the patients had returned to work and all their other pre-incident activities and shoe gear.



53 year-old female with history of "athletes feet"



28 days post debridement and implantation



71 year old Diabetic male with a history of "athletes feet"



28 days post debridement and implantation

## Discussion

Vancomycin-Resistant Enterococcus infections are becoming more prevalent and treatment options are becoming less definitive. High doses of antimicrobial agents have shown promise in the treatment of such infections (3). The author has successfully treated five patients with VRE infections in the soft tissue that had become refractory to other standard treatments initiated. In addition to the antimicrobial agent itself, it is felt that the high level of antibiotic achieved at the site of infection is a contributing factor to its success.

Synthetic calcium sulfate offers the advantages of predictability in the elution of antibiotic agents over a three to four-week period, buffering the local wound pH (towards physiologic), elimination/reduction of dead-space and compatibility with a number of antimicrobial agents.

The author has mixed synthetic calcium sulfate with vancomycin, gentamicin, linezolid, cefazolin, ceftriaxone, daptomycin, tobramycin, amphotericin, cefotaxime, amikacin and ciprofloxacin. This allows a clinician to choose appropriate antibiotics to mix with the synthetic calcium sulfate and optimally avoiding intravenous administration of antibiotics, in certain cases.

The limitations to this study are that it has a small sample size and that no placebo or other treatment arm was targeted; however, it does show that by taking advantage of the high local concentration of antibiotics achieved, that the implantation of synthetic calcium sulfate is a viable option for the treatment of VRE soft tissue infections.

## References

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