The Elution Profile of a Cancellous Bone Allograft (OsteoSponge) Impregnated with Vancomycin and Tobramycin

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Statement of Purpose

Bone infections occur through different mechanisms, such as traumatic injury, surgery, or hematogenous spread. Biofilm formation from organism growth on the surface of an orthopaedic implant may result. In the case of a total hip replacement, the risk of infection increases from 1-2% for a primary implant to 3-4 % for revision surgery [1]. When an infection does occur, the implant must be removed along with the necrotic tissue, creating bone voids that need to be filled. Typically, bone allograft materials are used to fill the voids; however, if the infection has not been completely eradicated, the new allograft material is likely to become infected as well. Thus the need for allograft materials with anti-bacterial properties, able to resist infection, becomes apparent.

In a number of studies, researchers have impregnated bone by soaking it in an antibiotic solution [2-5]. In this study, a simple method for impregnating a demineralized cancellous allograft (OsteoSponge™) was investigated, and the resulting antibiotic elution characteristics are reported.

Methods

USP grade tobramycin (TBM) and vancomycin (VCM) were purchased from MP Biomedicals (Solon, OH, USA). OsteoSponge™ was manufactured from cancellous bone blocks using proprietary methods (Bacterin International, Belgrade, MT, USA).

A 5x5x5 mm block of dry OsteoSponge™ was submerged in a 1mL solution containing a combination of 100 mg/mL of VCM and 100 mg/mL TBM in deionized water. After soaking for 1 hour at 22 °C the block of OsteoSponge™ was rinsed 3 times with 4 mL of pH 7.4 phosphate buffered saline (PBS). Then the OsteoSponge™ block was placed in 2 mL of PBS and incubated in the dark at 37 °C. After 1 hour the OsteoSponge™ block was removed from the PBS and patted dry on a stack of Kimwipes® (to absorb excess PBS) and then placed in a new vial containing 2 mL of fresh PBS. After 4 hours and at the subsequent time points thereafter (see Figure 1) these steps were repeated. This method was repeated for a total of eight 5x5x5 mm blocks.

Concentrations of TBM and VCM eluted in each of the PBS solutions were determined using an Abbott Laboratories TDx analyzer (Abbott Laboratories, Diagnostics Division, Abbott Park, IL), which is based on fluorescence polarization immunoassay (FPIA) technology. The assay reagents kits for TBM and VCM were manufactured by Seradyn (Seradyn, Inc., Indianapolis, IN, USA) and the assay sensitivities are 0.2 µg/mL and 1 µg/mL respectively.

Results and Discussion

The elution characteristics of VCM and TBM are presented in Figure 1. Although their peak elution concentrations are similar, the TBM elution rate is faster than the VCM. Vancomycin eluted above the minimum inhibitory concentration (MIC) for *S. aureus* (1 µg/mL) [6] for 7 days, and the tobramycin concentration was above the MIC (0.5 µg/mL) [7] for 2-3 days (see horizontal lines in Figure 1). These results show that OsteoSponge™ can be successfully impregnated with vancomycin and tobramycin using a simple and rapid process.

The most common method of placing an antibiotic locally, in and around bone and orthopaedic implants, is through the use of poly(methyl methacrylates) bone cement that has been mixed with antibiotics. However, further clinical benefits are possible by using a material that is osteoinductive, osteoconductive, anti-bacterial and doesn't require additional surgery for removal upon clearance of the infection.

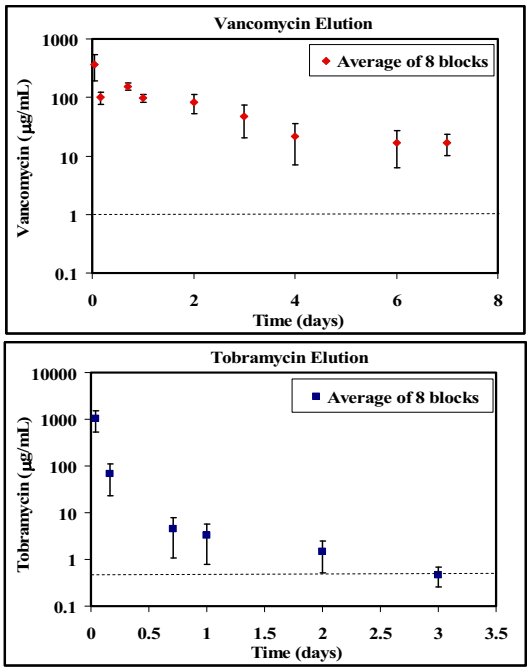

Figure 1. The dash line represents the MIC for *S. aureus*.

Conclusions

The combined osteoinductive, osteoconductive, and drug release properties of OsteoSponge™ make it an excellent allograft material able to promote bone growth and bone healing, but also able to serve as a depot for local antibiotic release.

References

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