Vancomycin and Telavancin Activity and Impact on Mechanical Properties When Added to Orthopedic Bone Cement

Sun Jung Kim¹, Aaron R. Bishop², Matthew Squire³, Heidi-Lynn Ploege¹,²,³, Warren E. Rose³,⁴
¹University of Wisconsin – Madison, Mechanical Engineering, ²University of Wisconsin – Madison, Biomedical Engineering, ³University of Wisconsin School of Medicine and Public, ⁴University of Wisconsin – Madison, School of Pharmacy

BACKGROUND

Periprosthetic joint infection (PJI) is one of the most challenging problems in orthopedic surgery. Infection in PJI involves the adhesion of bacteria to the implant and the production of a biofilm from the bacterial strains [1,2]. Some bacterial strains such as staphylococci and gram-positive bacteria cannot be completely eliminated by antibiotics and may result in the emergence of tissues surrounding an implant. Antibiotic-loaded bone cement (ALBC) is an effective treatment against infection at the implant site. With ALBC a higher level of drug concentration is delivered to the infection site, than can be reached by venous administration. However, the addition of antibiotics may weaken the cement’s mechanical properties. Vancomycin (VAN) loaded in Palacos R bone cement has shown antibiotic efficacy against main pathogens with sufficient drug elution in vitro, and mechanical properties [3]. Telavancin (TLV) is an investigational lipoglycopeptide antibiotic that is active against gram-positive pathogens, and is anticipated to have similar results as VAN when added to cement. In this study, two different antibiotics (VAN and TLV) with two types of cements (Palacos R and Simplex P) were compared in vitro for drug elution, efficacy and cement mechanical properties.

METHODS

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<th>Bone Cements</th>
<th>Composition</th>
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<td>Palacos R</td>
<td>Polymer powder: Poly(methyl acrylate, methyl methacrylate) 33.8 g</td>
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<tr>
<td>Simplex P</td>
<td>Polymer powder: Methyl methacrylate-styrene-copolymer 29.5 g</td>
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Sample Preparation
- Drug Elution: Disc 6 mm diameter × 4.5 mm height
- 4-point bending: Beam 75 mm × 10 mm × 3.3 mm
- Compression: Cylinder 6 mm diameter × 12 mm height
- Fracture toughness: Beam 44 mm × 10 mm × 5mm with crack length between 4.5 mm and 5.5 mm

Antibiotic Elution
- 60-day elution into 5mL potassium phosphate buffer
- Incubated (37°C) and shaken (100 rpm)
- Drug concentration determined with HPLC and CP column

Antibiotic Activity
- 2-week activity with daily sampling in tryptic soy broth

Bacterial Strains
- MRSA: K315 and ATCC 33591; MSSA ATCC 29213; S. epidermidis ATCC 35864

Mechanical Testing
- Performed on MTS Criterion, MTS Systems Corp., Eden Prairie, MN
- 21-day wet curing of samples in phosphate buffer solution at 21°C before testing
- Testing condition and methods followed ISO 5833

RESULTS

Figure 1. To 60 days of elution data of Vancomycin (VAN) and Telavancin (TLV) from Palacos and Simplex bone cement disk. N=15 at each time point. VAN + Palacos [1a], VAN + Simplex [1b], TLV + Palacos [1c], TLV + Simplex [1d]

Figure 2. Two weeks activity data from Vancomycin (VAN) and Telavancin (TLV) at 2.0 g per packet of Palacos and Simplex cement with 10⁴ initial CFU. VAN + Palacos [2a], VAN + Simplex [2b], TLV + Palacos [2c], TLV + Simplex [2d]

Figure 3. Mechanical testing with Vancomycin and Telavancin in Palacos and Simplex after 21 days of wet curing. A significance level of 5% was used for all tests. An * indicates a significant (p < 0.05) difference from Palacos R and Simplex P for each environmental condition.

CONCLUSION

- The samples with 1.0 g of VAN in Palacos R produced the highest mass of eluted antibiotic.
- Both TLV and VAN had significantly less elution from Simplex P than Palacos R.
- 0.5 – 2.0 g of VAN in Palacos R or Simplex P fully eliminated three S. aureus strains within 2 days.
- 2.0 g of TLV in Palacos R eliminated S. aureus strains but not when added to Simplex P.
- The cement's mechanical properties were degraded by added antibiotics and 21-day wet curing.
- VAN and TLV loads of 1.0 g or greater reduced compressive yield strength of Palacos R cement below the ISO minimum.
- TLV samples tended to have larger pore sizes, and lower mechanical properties than VAN samples.

REFERENCES