Antibiotic Elution from a Structural, Resorbable Polyurethane Cement compounded with Tobramycin/Vancocymcin

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Introduction Infection risk is endemic to all surgical procedures and particularly relevant to orthopaedic trauma1. From this need, a number of applications have been emerged that weigh the value in rapid release with for the need for structural integrity – in many respects the trade-off has offered an inadequate therapeutic option – rapid release compromises structural integrity, and inert materials such as PMMA have a slow release and are not biologically integrated. An optimized treatment option would deliver high doses of antibiotic to a site of injury, maintain levels above normal therapeutic values, and avoid toxicity to sensitive body tissues.

Previous work has shown that a resorbable polyurethane cement compounded with either vancomycin, or tobramycin can effectively offer sustained release, maintain geometric stability, and still contain systemic release under what might be injurious2. The goal of this study was to evaluate in vitro elution of vancomycin and tobramycin that had been compounded into a closed-pore, bioabsorbable, polyurethane foam. This foam differs from currently available material in that it can be delivered as a liquid, has low exothermic in situ curing properties, demonstrates a long resorption profile, and when cured extends material characteristics similar to bone.

Methods The polyurethane cement was prepared from three separate ingredients, and antibiotics were mixed into the calcium carbonate to yield the final formulation of the material (Kryptonite, Doctors Research Group, Southbury, CT). Antibiotics were compounded at 0.5g and 1.25g per 10cc of biomaterial. The materials were allowed to polymerize in a UHMW Polyethylene mold to produce 2-mm discs. Discs of PMMA were similarly prepared from Simplex P Bone Cement with Tobramycin (1gm of tobramycin in 40g of PMMA) Stryker, Kalamazoo, MI. Once the wafers were prepared, they were placed into 5 ml of PBS and rocked continuously in 10-ml closed cap vials at 37 degrees. Elution readings were sampled at 11 intervals; 8, 16, 24, 48, 72, 96, 120, 144, 168, 204, and 240 hours after placement in saline. Evaluation of each time point consisted of 10 vials; 110 vials for each group including controls. As a commercially available vancomycin product was unavailable, the PMMA control is comparable to only the tobramycin.

When the elution time for a group was reached, vials were removed from the incubator and an aliquot of the saline solution was transferred to a separate vial. Wafers were retained for a later study of mechanical comparison. Concentrations of the vancomycin and tobramycin in each reaction tube were assessed on a Beckman Coulter Unicel DxC 6000 and dilutions assured that the measurements remained within the linear portion of the standard curve. Amounts are reported in µg/ml.

Results Each of the discs weighed approximately 0.05g, and accordingly a dose total of either .0025g (2500 µg), or .006g (6250 µg) would be expected per disc based on the compounding formulation. Vancomycin levels were dose related and as expected as its release kinetics have been reported to be much slower than tobramycin3. Release of vancomycin is shown in Figure 1 and demonstrates summative totals in solution at the specific time periods, reaching 12.7 and 40.2 µg/ml respectively for the two doses compounded.

Discussion The most important observations that could be made from this study were:

- Vancomycin and tobramycin demonstrated effective release kinetics when compounded with Kryptonite that surpassed PMMA in a head to head comparison.
- Release from 0.05g of polyurethane cement into 5ml of saline reached 2000g/ml at 10 days in the 1.25g/10g compounding.
- From a total of 6250ug calculated as the loading dose, at 10 days only 1000ug had been released.
- Net loss of the material at 10 days was 16%.

Discussions

References

3. Murphey J, Kolb E, Akkarapaka N, Franzus M; Moore T; Ganey TM. In vitro Antibiotic Elution Profile - Adhesive Polyurethane Bone Cement Compounded with Tobramycin/Vancocymcin. 26th Annual Meeting of the Orthopaedic Trauma Association, October 13 - 16, 2010. Baltimore, Maryland, USA

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