“Powder or liquid? What specific mixing method maximizes vancomycin elution from commercially available Bone Cement?”

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INTRODUCTION: Polymethylmethacrylate (PMMA) is commonly utilized to deliver antibiotics to the periprosthetic space in total joint arthroplasty (TJA) and is used to prevent and treat periprosthetic joint infection (PJI). Vancomycin powder is frequently added in the operating room to PMMA by orthopedic surgeons, but can be less predictable than commercially available pre-loaded aminoglycosides formulated PMMA. Differing recommendations exist for best practices on mixing vancomycin-loaded PMMA [1]. The purpose of this study was to determine if mixing vancomycin powder in the liquid monomer or polymer powder affects the antibacterial properties of vancomycin, if these two methods have different antibiotic elution rates, and if this differs in the two common commercially available PMMA formulations.

METHODS: A validated colorimetric assay [2] was utilized to create a Vancomycin hydrochloride powder (Fresenius Kahl, Hamburg, Germany) standard curve of concentration. Two commercially available PMMA products, Surgical Simplex P (Stryker, Mahwah, NJ) and Palacos R (Heraeus Medical, Hanau, Germany), were used for the two arms of comparison. 1g of vancomycin hydrochloride powder was ground in a mortar and pestle for 30 seconds and then added to either the liquid monomer of the PMMA product or the powered polymer. In the liquid monomer group, vancomycin powder was swirled together to create a homogenous suspension and then added to the polymer. In the polymer powder group, vancomycin powder was mixed in by hand with a spatula for 1 minute to ensure even distribution. Liquid monomer was then added to this mixed powder. The resulting compound was mixed by hand until a working consistency was reached. PMMA was then manually inserted into custom silicon molds and allowed to cure for 1 hour. The silicon mold created standard PMMA discs of 36mm diameter and 6mm thickness. Discs were retained if within 1 standard deviation of the mean weight, resulting in 8 qualifying discs for each treatment condition (N=32). Discs were submerged in 13ml of PBS in individual plastic dishes and incubated statically at 37°C. At 1, 2, 4, 24, 48 and 72 hours, eluate was collected and subjected to the colorimetric assay to quantify eluted vancomycin. Following each timepoint, discs were transferred into new dishes containing fresh PBS to maximize elution diffusion gradients. At 1, and 24 hours, a minimum inhibitory concentration (MIC) assay was performed with 1x10^8 MSSA (Xen 36, Perkin Elmer, Waltham, MA) planktonic bacteria. Using concentrations from the colorimetric assay, eluates were diluted to 4ug/mL and then serially diluted to 2ug/mL, 1ug/mL, and 0.5 ug/mL. Any bacterial growth at 1ug/mL or greater signifies an MIC failure [3]. Diluted eluates were confirmed using the aforementioned colorimetric assay.

RESULTS SECTION: Mixing vancomycin into the liquid monomer of Surgical Simplex P cement eluted the most vancomycin overall, followed by mixing vancomycin into the liquid monomer of Heraeus Palacos R. Mixing vancomycin into the PMMA powder provided similar overall elution in both commercial brands. A Two-Way ANOVA for mixing was performed, with significance shown (p<0.01). MIC data from both 1 hour and 24 hours further showed that eluted antibiotic did inhibit growth of staph aureus at 1ug/mL, but did not at 0.5 ug/mL. Regardless of variations in vancomycin elution, all trials released sufficient antibiotic to inhibit bacterial growth.

DISCUSSION: Mixing vancomycin hydrochloride powder into the liquid monomer of bone cement may provide better overall elution than vancomycin added to PMMA powder. Both mixing methods released sufficient antibiotic to inhibit bacterial growth.

SIGNIFICANCE/CLINICAL RELEVANCE: Mixing vancomycin hydrochloride powder into the liquid monomer of bone cement may provide better overall elution than vancomycin added to PMMA powder, however both iterations elute sufficient levels above the minimum inhibitory concentration for staph aureus at 1 hour and 24 hours. Clinicians should prioritize making sure that ingredients are mixed homogeneously, regardless of mixing order.

REFERENCES:

IMAGES AND TABLES:
Figure 1

Figure 1. Averaged Vancomycin Elution for all Mixing Methods. Unpaired Student T-Tests were also performed between mixing and brands (*p<0.05, **p<0.01, ***p<0.001).