Supplement 1: Formulation and Mixing Considerations for Antibiotic Loaded Bone Cement

Low-Dose formulations

Commercially prepared low-dose ALBC often contain one of the following antibiotics: gentamicin, tobramycin, clindamycin, colistin and erythromycin, and vancomycin[1]. Unlike antibiotics found in a hospital pharmacy, antibiotics manufactured specifically for use in cement are not lyophilized, giving them a non-clumpy consistency, which makes them easier to mix homogenously with polymethyl-methacrylate (PMMA) powder. The improved homogeneity of commercial low-dose ALBC has been associated with a significantly better mechanical strength compared to hand mixed low-dose ALBC, and has led to a general recommendation that commercial ALBC should be the only form of ALBC used in cases of primary arthroplasty [2]. This rule may depend on the type of antibiotic and type of cement used. Lee *et al.* found that hand-mixing low-dose (1 gram) vancomycin did not significantly decrease the mechanical strength (5%) of Simplex P cement (Stryker Orthopedics), but it did significantly reduce the strength of Palacos R cement (Heraus Medical)[3]. Lewis *et al.* found that mixing in gentamicin sulfate, either by hand or with an industrial blender, had no effect on the mechanical strength of Cemex XL cement (Tecres S.p.A.)[4]. Due to the disparity between products, we cannot universally state that commercial low-dose ALBCs more effectively retain mechanical strength compared to hand-mixed formulations.

Another criterion to evaluate commercial ALBC performance is antibiotic elution. When mixed following manufacturer instructions, commercial products have been shown to produce inferior elution profiles compared to hand-mixing at low doses [2; 4]. However, it is possible to improve elution profiles of some commercial products using mixing techniques that can be used

in the operating room. Meyer *et al.* demonstrated that vacuum mixing significantly improved antibiotic elution from commercial high viscosity PMMA (Cobalt G-HV [Zimmer Biomet], Palacos R+G and Simplex P)[5]. These results are somewhat unexpected given that vacuum mixing decreases cement porosity. The effect of vacuum mixing was reversed when low viscosity commercial ALBC (Cemex Genta) was used, a finding that was also confirmed by Neut *et al.*[6]. Mixing temperature has also been shown to affect elution from commercial ALBC. Sunblad *et al.* reported significantly higher cement porosity and 2-4 times greater antibiotic elution from low-dose ALBC discs mixed at different temperatures [7]. A critical note is that none of the studies of temperature-dependent elution enhancement [5-7], tested material strength of the ALBC. Therefore, it is unknown whether mixing temperature compromises load-bearing for low-dose ALBC. When considering the literature evaluating low-dose commercial ALBC, the variability in performance according to cement brand and antibiotic selection makes it difficult to definitively identify an overall advantage in efficacy that justifies the expense of commercial products.

References

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