Release of Vancomycin and Tobramycin from PMMA Cements Impregnated with Calcium Polyphosphate Hydrogel

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Purpose: The goals of this study were to determine the release of vancomycin (Vanco) and tobramycin (Tob) from calcium polyphosphate (CPP) gel-doped PMMA (Simplex P, SP), and investigate the influence of the impregnation of CPP gel on the mechanical strength, handling and cellular growth of SP cement.

Methods: The SP powder was mixed with liquid, followed by the addition of 10% CPP gel (w/w) to form SP/CPP composite (SPC). A combination of 0.225 g of Vanco and 0.27 g of Tob per 3.0 g of SP were mixed with the SP powder prior to adding the liquid (SP + VT). For SPC, the same amounts of antibiotics were mixed with CPP gel prior to mixing with the SP powder for setting (SPC + VT). The antibacterial activity of eluted antibioticsA was measured. The interaction of antibiotics with CPP was investigated using Raman. The surface roughness and pore sizes were analyzed by microCT, AFM and SEM. The handling and compressive strength were tested. MC3T3 cells were used to evaluate in vitro biocompatibility.

Results: Adding 10% CPP gel to SP led to a much lower burst release of Vanco and considerably extended release of both Vanco and Tob up to 24 weeks. At the end of 24 weeks, the release of Tob (68.8 ± 12%) and Vanco (92.7 ± 5.5%) from SPC is higher than that of SP (52.5 ± 3.3% and 85.6 ± 13%, respectively). Antibiotics released from SPC retain their bactericidal activity. The improvement in the antibiotic release kinetics is mainly due to the molecular interactions of antibiotics with embedded CPP polyphosphate chains as confirmed by Raman analysis. The inclusion of CPP hydrogel also increased the SP surface roughness, hydrophilicity, and pore sizes, leading to a higher release rate of antibiotics. The SPC cement is biocompatible and has similar handling properties and mechanical strength as compared to SP cements.

Conclusion: In this work, we found that the SPC significantly reduced the burst release of Vanco/Tob, and sustained the antibiotic release for up to 24 weeks. Our data suggest that the improvement in antibiotic release of SPC is mainly due to the intermolecular interaction of antibiotics with embedded CPP polyphosphate chains (reduction of burst release and sustained release coupled with slow degradation of CPP). In addition, the higher release rate of antibiotics from SPC may be due to the increase of surface roughness, hydrophilicity, and pore sizes in the presence of CPP. Furthermore, SPC is biocompatible and the handling properties and mechanical strength of SP are not sacrificed. We believe that SPC represents a better drug carrier of PMMA cement. Its long-term mechanical performance warrants further investigation in vivo.

See pages 401 - 442 for financial disclosure information.