BIOLOGICAL PROPERTIES OF NANOSILVER-LOADED PMMA BONE CEMENT DOPED WITH BIOACTIVE GLASS

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Introduction

Bone cements are an attractive biomaterial group dedicated for the treatment of bone fractures and fixing implants. One of their main representatives is acrylic cement based on poly(methyl methacrylate) (PMMA). PMMA cement is a bioinert material without osseointegrative as well as antibacterial properties, which may result in limited integration with host bone tissue, implant-associated infections, or even future ineffective biofunctionality [1]. Hence, to obtain a fully bioactive biomaterial, commercially available bone cement was modified simultaneously with antibacterial and osteocondutive agents. In this work, the influence of such modification on the biological properties of cement was evaluated.

Materials and Methods

Acrylic bone cement Cemex (Tecres, Italy) was used as the base material, modified simultaneously with nanosilver (AgNPs; 1.5 wt.%; particle size ~50 nm; MkNano, USA) and one of the following bioactive glasses (BG; 5 wt.%): 45S5 or 1393-B3 obtained by the traditional melting method (particle size ≤40 μm). All cement specimens with/without modifications were prepared as described earlier [1-5]. Briefly, the powders of modifiers were manually mixed with cement powder, and then the liquid cement component were added and a paste was obtained. The cement paste was then placed into the mold and allowed to cure. The following tests of cement's biological properties were performed: 1) hemolysis assay, 2) platelet aggregation, 3) periodontal ligament cells (PDLCs) viability and morphology, 4) bacterial growth inhibition (*S. aureus* ATCC, *S. aureus* hospital strain and *E. coli* ATCC) and 5) bactericidal effectiveness (*S. aureus* hospital strain). All specimens before the research were sterilized with 75% ethanol followed by 30 min exposure to UV light.

Results and Discussion

PMMA bone cement, despite its advantages, still has some essential drawbacks and as a bioinert material does not meet the requirements for modern biomaterials. The proposed modification of cement using nanosilver and bioactive glass may be a valuable alternative to the currently used in clinic cements (mainly doped with antibiotic/s). The addition of nanosilver should protect against infections, while the addition of bioactive glass was aimed at inreasing the release of AgNPs and also improving cellular response.

The obtained results showed that the incorporation of various bioactive glasses had different effects on the biological properties of modified bone cement. For all tested specimens, the hemolysis rate did not exceed 5% and LDH in the supernatant 15.0 μmol/min/10^{12} RBC, hence no severe hemolytic reaction was found. Exposure of platelets to the specimens did not induce their spontaneous aggregation and there were no significant changes in thrombin-induced aggregation, expect 1393-B3 glass addition, for which a significant reduction in platelets viability and aggregation was also found. The viability of PDLCs cultured on the tested specimens significantly decreased compared to that on neat cement. The addition of 1393-B3 glass decreased cell viability drastically (about ~95%), while the 45S5 glass slightly higher viability compared to nanosilver-loaded cement. The neat cement,, nanosilver-loaded cement and nanosilver-loaded cement with 45S5 glass did not affect the PDLCs morphology, and the confluent monolayer was observed, however for the nanosilver-loaded cement with 1393-B3 BG most of the cells were rounded and not adhering well to the material. The applied nanosilver to bone cement significantly slowed down the growth of bacteria, compared to neat cement as well as antibiotic. Further, the addition of BG significantly improved the cement antibacterial effectiveness due to the increasing release of AgNPs, especially in the case of 1393-B3 BG. Moreover, the bactericidal effectiveness against *S. aureus* hospital strain was confirmed as in bacterial culture after exposure to specimens the number of bacteria was significantly reduced and the almost 100% killing of bacteria was found for nanosilver-loaded cement with 1393-B3 BG.

Conclusions

Nanosilver-loaded bone cement doped with various bioactive glasses has been successfully fabricated and displayed different biological properties. The addition of AgNPs allows for active antibacterial protection, and BG improves its release. Depending on the type of bioactive glass, a different cellular response for nanosilver-loaded cement was found. Based on the results for potential medical applications, we recommend the AgNp-loaded BC with the 45S5 BG as bone substitute and AgNp-loaded cement with 1393-B3 BG as a coating for spacers or drug delivery system in therapy.

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