In Vitro studies of Premixed, Injectable and Biodegradable Filler: Poly-(propylene fumarate)(PPF), α-tricalcium phosphate(α-TCP)and Hydroxyapatite Particle (HAP)Composite for Vertebroplasty and Kyphoplasty

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Introduction: Lots of filler materials have been applied in vertebroplasty and kyphoplasty for vertebral fractures, but no current material is perfect in all biomechanical and biological characteristics. The most commonly used injectable fillers are poly methylmethacrylate(PMMA) with shortages including exothermic reaction damaging adjacent soft tissues, non-biodegradability, adverse effects of MMA monomer and abnormally high mechanical strength. Other literature reported deaths are caused mainly by reactions of extravasated PMMA during procedures. Many novel injectable bone fillers introduced and commercialized in clinical uses are claimed to solve the current problems of PMMA. Although these cements do improve temperature, bio-degradability and biocompatibility problems, the mechanical strength are relatively low with subsequent problems including fixation collapse, early resorption and poor handling properties. The current study is meant to evaluate the in vitro properties of a novel composite of biphasic CPC, α-TCP/HAP and PPF in compare with PMMA and previously reported HAP and PPF composite cement for possible future applications in the vertebroplasty and kyphoplasty.

Materials and Methods: 1. PPF was fabricated by heating diethyl fumarate(Sigma-Aldrich) and propylene glycol(Sigma-Aldrich)and propylene γ-pyrrolidone (Sigma)and was mixed with calcium hydroxide (Baker) and calcium hydroxide (Baker). 2. PPF was cross-linked by N-α-tricalcium phosphate(HAP) and PMMA. But the cytotoxicity of PMMA immediately after cement curing were significantly higher than those of other groups at day 1, 3 and 7. 3. Significantly lower radio-opacities were observed only at day 1 and 3 with significances. 4. The radio-opacity by CT of 70% composite (1456HU) is lower than PMMA group (1461HU) with no significance (p=0.45). The HU of 50% HAP composite were higher than those of 50% α-TCP/HAP with significances (p<0.0001) and were higher than 60% α-TCP/HAP with no significances. 5. The compression strength of 70% composite was 58-60MPa more close to that of bone and did not decrease after emersion for 2 months. 6. The pH value changed more significantly in 50% α-TCP/HAP and 50% HAP composite and not significantly in 70%composite group. 7. The cell proliferations (WST-1 test) of all studied groups were lower than that of cell culture only group with significance (all p<0.0001). 8. The cytotoxicities of PMMA group were significantly higher than those of composites groups in first, third and seventh days. 9. The cytotoxicities of all the studied groups are higher significantly than those of cell only culture group. The cytotoxicities of PMMA immediately after cement curing were significantly higher than those of other groups (all p<0.0001), but scanty loss in HAP composite at 8th week. 10. Size of the blocks was kept constant by changing the size of the blocks. 11. Higher cytotoxicities of 50% and 60% α-TCP /HAP and HAP groups than 70% composite were observed only at day 1 and 3 with significances.

Discussion: 1. The curing temperatures of composites were lower than 45°C and cloud reduce possible exothermal damages. 2. Proper compression strength of composites was close to that of cancellous bone and may possibly reduce mechanic problems of stiff PMMA blocks. 3. The acidified surroundings induce bone absorption. The pH value change of 70% α-TCP /HAP composite significantly lower than other groups and also significantly slow dissociation of the blocks. 4. The radio-opacity by CT scanning in PMMA group was higher than 70% α-TCP /HAP group without significance. 50% HAP composite were higher than 50% and 60% α-TCP/HAP composites and the X-ray revealed some figuration differences of different blocks, it may due to the different setting mechanisms with volumetric changes. 5. It takes more than 3 months for the fractured bone to heal. Less weight loss (about 9%) and less mechanical strength loss of 70% α-TCP/HAP after 2 months would provide better support before bone union. The reduced weight loss could be caused by transformation of α-TCP into calcium deficient hydroxyapatite interlaced crystals observed by SEM pictures around the hydroxyapatite particles and stabilized the structures, these interlaced crystals cloud not found in SEM pictures of 50% HAP composite. 6. The biocompatibility tests of composite group were inferior to cell only culture and PMMA groups. This may be due to gradual destruction and release of products of the composites. But the cytotoxicities of PMMA immediately after cement curing were significantly higher and this may be cause by higher curing temperature and release of toxic monomers and reactants while setting of PMMA.