

Antibacterial effect and biological reaction of calcium phosphate cement impregnated with iodine

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INTRODUCTION:

Calcium phosphate cement (CPC) has been used for bone defects such as bone tumor surgery and fracture treatment. Advantages of CPC were reported as following: CPC can be shaped easily to match the dimensions of a bone defect; CPC has good bone conduction and biocompatibility; CPC's chemical stability enables various classes of drugs to be added to CPC; CPC has an excellent sustained-release capacity.

The antibacterial spectrum of iodine is very broad, acting not only on general bacteria but also viruses, tubercle bacilli and fungi. In addition, iodine does not promote the development of drug-resistant bacteria unlike antibiotics.

Here, we developed CPC impregnated with iodine which had long-term and wide-spectrum antibacterial effect. Attenuation of iodine of the CPC, antibacterial effect, cytotoxicity, and bone conductivity were examined.

METHODS:

(1) Attenuation: Five-millimeter cubic CPC impregnated with iodine was immersed in 10 mL of phosphate-buffered saline (PBS). After the specified periods, the CPC was removed, the iodine content was measured by fluorescent X-ray analysis.

(2) Antibacterial effect: Using *S. aureus* and *E. coli*, 10⁶ colony-forming units were inoculated on the CPC, which was then covered with a slide glass and incubated at 37 °C for 2, 6, 24 hours. At each point, each CPC was washed with 5 mL of PBS. The washed elute was diluted 1:50 with PBS and 100µL of the dilute elute was incubated in tryptic soy broth for *S. aureus* and *E. coli* at 37 °C. The number of bacterial colonies was counted after 24 hours.

(3) Cytotoxicity: The V79 cell line (Chinese hamster fibroblasts) was used. Approximately 300 cells were seeded in the elute obtained by immersing iodine-containing CPC in 10 ml medium solution for 24 hours. After seeding, the dishes were gently shaken and cultured in the incubator. After 1 week, the cells were fixed with 10% formalin and stained with 0.15% methylene blue. Then, the number of colonies was measured. (4) Bone conductivity: Two-millimeter cubic CPC was inserted into the lateral condyle of the femoral bone of a rabbit. The femoral bone was removed at specific operative periods (2, 4, and 8 weeks). The presence of osteogenesis was measured using a scanning electron microscope.

RESULTS: The CPC with 5 % of iodine concentration had the highest iodine concentration after 1 week and 8 weeks (Figure. 1). The antibacterial effect was maintained until 8 weeks with the 5 % of iodine concentration (Figure. 2, 3). In addition, the 5% iodine concentration had no cytotoxicity (Figure. 4) and did not suppress bone conductivity (Figure. 5).

DISCUSSION AND CONCLUSION:

Osteomyelitis is defined as inflammation of bone and marrow cavity. It is severe infection to treat in orthopedic surgery. In general, antibiotic therapy for 6-8 weeks is needed. Intractable osteomyelitis may be treated with amputation. Several studies have shown that CPC could also be used as a delivery system for therapeutic peptides or antibiotics. It was reported that osteomyelitis was treated using CPC mixed with antibiotics and excellent results were obtained. Also, our group has shown the effectiveness of iodine-supported implants with a broad antibacterial spectrum. In addition, though there have been some reports of CPC containing antibiotics, no report of CPC with iodine has been described. The CPC impregnated with iodine may be useful for the treatment of patients with osteomyelitis and compromised patients with bone tumors.

