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Short- and long-term effects of vertebroplastic bone cement on cancellous bone

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ABSTRACT

Vertebroplasty using poly(methyl methacrylate) (PMMA) bone cement is the most common method to treat osteoporotic vertebral fractures. However, several questions of interest remain to be clarified, including how does PMMA affect the cement-bone interface area and surrounding bone tissue, can damaged bone tissues be repaired, how will PMMA change the bone interface over the long-term, and what happens to PMMA itself? The purpose of this study is to investigate these concerns and provide a basis for clinical evaluation. We made bone defects in the lumbar vertebrae of New Zealand rabbits as a model of osteoporosis and injected them with bone cement. A mechanical testing machine was used to perform axial compression, three-point bending, and twisting resistance tests to observe and investigate the short- and long-term biomechanical properties of PMMA after implantation. Optical, fluorescence, scanning electron microscopy, and nanoindentation were used to observe the changes in the interface microstructure. PMMA can rapidly establish the strong support with stable function in the near future. Biomechanical experiments showed that biomechanical property of bone cement group was significantly higher than those in the other two groups ($P<0.05$) biomechanical property of bone cement group may decline with the time, but it's still better than that of OP in the control group ($P<0.05$). Histomorphological observation result shows that under osteoporosis state the bone grows slower, also bone's rebuilding time extended. And in the later period, main bone's continuous osteoporosis has some impact on the interface. Nano-indentation testing shows that the young modulus and stiffness of the interface among bone, material and interface were significantly differences ($P<0.05$). Bone cement had gave the best nano indentation hardness, then was interface and bone tissue. PMMA bone cement was able to quickly support and stabilize the defect in the short term, and bone growth restarted at the bone interface and was tightly integrated. However, over the long-term, fluorescent signal was weakened, osteoclasts appeared, the mechanical indicators for both the interface and the whole vertebra decreased, and bone resorption was eventually greater than bone

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formation, resulting in bone loss. Therefore, vertebroplasty is not the end of treatment, and we need to further study ways to improve the bone cement material, which is crucial for long-term vertebroplasty efficacy, to better treat osteoporosis.

1. Introduction

Osteoporosis (OP) is one of the most common metabolic bone diseases, with relatively high prevalence and features including decreased bone mass, deteriorated bone microstructure, increased bone fragility, and decreased bone strength. The prevalence of osteoporosis is increasing significantly with the aging population. According to incomplete statistics, there are currently nearly 200 million OP patients in the world and about 84 million in China (Meng, 2005). The most serious complication is osteoporotic fracture (also known as brittle fractures), and the most frequently affected positions, in order, are the spine, the centrum, and the distal radius. Because spine is rich in cancellous bone, mild violence can cause vertebral compression fractures (VCF). VCFs cause patients with incapacitating back pain for several months or longer, so the primary goal of treatments are pain relief. Percutaneous vertebroplasty (PVP) is a minimally invasive technique for spine treatment that uses transcutaneous puncture to inject artificial bone into the vertebral body directly or through the pedicle to enhance vertebral strength and stability, alleviate lumbar and back pain, and improve the quality of life quicker than conservative treatments just like analgesics, bed rest, and brace. Nowadays, PVP is widely used in the treatment of painful osteoporotic vertebral compression fractures with the injection of polymethylmethacrylate (PMMA) cement, although poly(methyl methacrylate) (PMMA) is widely used, several questions remain to be clarified after bone cement is implanted in the vertebral body, including how will the bone-bone cement-interface contact method, contact area, and the surrounding bone tissue alter the PMMA, can damaged bone tissues be repaired, how will PMMA change the bone interface over the long term, and what are the effects of implantation on PMMA itself? These are of great concern to scientists and clinicians. In this study, we used PMMA bone cement to conduct vertebroplasty in rabbits to simulate human PVP. We injected bone cement into the vertebral bodies of New Zealand rabbits and observed the bone-PMMA interface biomechanical properties, morphological changes, and the reactions and repair environment of the surrounding bone tissues at different time points to provide theoretical and experimental bases for the clinical evaluation of the long-term effects of PMMA bone cement on the bone interface after PVP. This work also provides solid experimental evidence for future researches to improve the bone-PMMA interface.

2. Materials and methods

2.1. Experimental animals

One hundred and five female adult New Zealand rabbits ($n=105$; age: 0.7–1.1 years, mean: 1.0 year; weight: 2.3–2.8 kg, mean: 2.5 kg) were used. All experimental studies followed the NC3Rs guidelines and were approved by our local animal experimental ethics committee. We randomly selected, castrated, and intramuscularly injected 70 rabbits with dexamethasone (Sniekers et al., 2008) to model osteoporosis, and the results of Dual Energy Absorptiometry (Schneider et al., 2010) showed that they met the diagnostic criteria for osteoporosis. The 70 OP animals were randomized and average into osteoporosis group and bone cement group, and the other 35 normal New Zealand rabbits were included in normal control group. Each group was divided into 2, 4, 8, 12, 16, 24, and 48-week subgroups. The OP and normal control groups only received the surgical operation to cause bone defects, but no bone cement was injected. In bone cement group, after the bone defect was created, PMMA bone cement III (Shanghai Synthetic Material Research Institute, China) was implanted. Surgical procedures were performed as described previously (Hadley et al., 2010). (1) Anesthetization: Anesthesia was induced with a 4% pentobarbital sodium (1 mg/kg) injection into the ear vein. (2) Surgery: After anesthetization, we placed the rabbits on the operating table in a prone position, positioned L7 (the highest points of the two bones), cut in from the center of the back, cut the skin, subcutaneous tissues, and fascia open in turn, separated the paravertebral muscle at one side, and exposed the front half of the L1–L6 vertebrae. We inserted a needle 1 mm behind the point of intersection of the pedicle centerline and the connection line of the front edges of the transverse processes 35–40° to the horizontal plane and 0–5° to the coronal plane, to a depth of 4–6 mm. We prepared PMMA as a low-viscosity bone cement (bone cement monomerto powder ratio=1 mL:4 g). Two minutes into the cement curing, then we drew injectable thin paste into a 1 mL syringe, slowly inserted it using an epidural puncture needle, pulled out the puncture needle before injection, injected 0.5–0.6 mL, and hold the rabbits in the position for 10 min for the PMMA completely set. Two vertebrae on each rabbit were randomly selected for operation, and five rabbits were operated on for each group. (3) Postoperative management: After surgery, 1 million U/rabbit of penicillin was intramuscularly injected daily for 7 consecutive days. On the 14th, 13th, 4th, and 3rd days before sampling at 4, 8, 12, 16, 24, and 48 weeks, we randomly selected a rabbit from Group C (bone cement group) and injected tetracycline hydrochloride intramuscularly for fluorescence labeling. Tetracycline hydrochloride solution was prepared before the injection and diluted with 0.9% normal saline (20 mg/mL tetracycline hydrochloride solution 25 mg/kg).

2.2. Biomechanical testing

After sacrificing the rabbits by injecting air embolism into auricular marginal veins, we took out the fresh vertebral