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Reinforcing effect of calcium sulfate cement bovine bone morphogenetic protein on vertebral in the rabbit model of osteoporosis

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ABSTRACT

Objective: To observe reinforcing effect of calcium sulfate cement (CSC) bovine bone morphogenetic protein (bBMP) on vertebral in the rabbit model of osteoporosis. **Methods:** A total of 48 New Zealand white rabbits were randomly divided into group Ⅰ (blank control group), group Ⅱ (CSC injection group), group Ⅲ (CSC/bBMP injection group) and control group. White rabbit osteoporosis model was established rapidly by using castration method+methylprednisolone candidate. After modeling, groups Ⅱ, Ⅲ were given corresponding vertebral body injection material, and 4 animals were sacrificed respectively at 24 h, 6 weeks, 12 weeks after vertebral plasty. Tissue pathological status, vertebral mineral density and vertebral body bone mechanical strength were observed. **Results:** Vertebral body structure form was normal in the groups Ⅱ and Ⅲ. Trabecular bone coarsens, connection and repair were observed in micro fracture and bone defects, bone trabecular connectivity was superior to group Ⅰ significantly; vertebral body compression strength in the group Ⅰ was on the decline, vertebral compression strength in the groups Ⅱ and Ⅲ was on the rise, the largest vertebra. Postoperative BMC and BMD in groups Ⅱ and Ⅲ were incresed, and significantly higher than group Ⅰ after 6 weeks ($P<0.05$), BMC and BMD in group Ⅲ after 12 weeks were higher than the other three groups. **Conclusion:** Compound bBMP CSC has good bone induction. It can improve the three-dimensional construction effect for osteoporosis vertebral trabecula, and can significantly improve the vertebral strength, as a vertebral packing material with good application prospect.

1. Introduction

With the change of the living environment and diet, osteoporosis (OP) has become the main health problems of old people[1]. Vertebral compression fracture is common complication of OP. Vertebral plasty (VP) is commonly used in the treatment of vertebral compression fractures with curative effect, and has become an important approach to minimally invasive interventional treatment of the spine[3-5]. Packing material commonly used in VP is polymethyl methacrylate (PMMA). But the postoperative vertebral lesion has different strength from adjacent vertebral bodies, it will lead to adjacent vertebral fractures, it also has poor histocompatibility[6]. Because of its good biocompatibility, calcium sulfate cement (CSC) can be completely degradated in the body, with certain strength. It can promote the OP bone growth and renovation, and is widely used in bone defect filling[7]. Bovine bone morphogenetic protein (bBMP) is compound of cytokines, it can promote bone formation[8]. To observe the effect of CSC composite bBMP on OP vertebral strengthening effect, we used the castration method+methylprednisolone candidate to establish New Zealand white rabbit OP model, and observe reinforcing effect of CSC bovine bBMP on vertebral.

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2. Materials and methods

2.1. Experimental animal

A total of 60 healthy adult New Zealand white female rabbits were elected, aged 5 to 7 months, weighting 2.1-2.7 kg. They were provided by Experimental Animal Center of Xinjiang Medical University. Experiments were in accordance with Guidance on Treating Experimental Animals.

2.2. Instrument and reagent

S-3000N scanning electron microscope, HITACHI company (Japan); MTS 858 mini (System IncMinneapolis,U.S.A); Dual-energy X-ray absorptiometry bone mineral density instrument (Discovery Wi, Hologic Inc, Bedford MA, U.S.A.). Speed sleep new Ⅱ number provided by the southwest pharmaceutical co., LTD.; Methylprednisolone (methyl prednisone Long Hupo acid sodium), CSC, CSC/bBMP reagents were purchased from Army Orthopaedic Institute.

2.3. Model establishment

A total of 48 New Zealand white rabbits were randomly divided into group Ⅰ (blank control group), group Ⅱ (CSC injection group), group Ⅲ (CSC/bBMP injection group) and control group. OP model was established by castration method + methylprednisolone candidate. BMD was measured by dual-energy X-ray absorptiometry bone mineral density instrument 2 days before surgery. All animals were in fasting for 12 h, and group Ⅱ was injected with 0.25 mg/kg anesthesia drug intramuscularly. Abdominal bilateral ovary was resected and fallopian tubes were ligated. Animals in control group only had bilateral ovaries resection. White rabbit were given antibiotics preoperative and postoperative to prevent infection. After wound healing, methylprednisolone 1 mg/kg·d was given for 4 weeks. Two months postoperatively, significantly decreased lumbar BMD, vertebral BMC and BMD showed successful modeling. All animals were under the same feed conditions of low calcium.

2.4. Methods

After modeling, rabbits in groups Ⅱ, Ⅲ were given CSC, CSC/bBMP injection within vertebral body. CSC and CSC/bBMP was packed separately to make preparation for different vertebral injection. After anesthesia, animals underwent midline incision at prone position, tissues were cut and separated. Junction between L2, L4, L6 pedicle and transverse was exposed, periosteal was stripped to expose the bone marker. #12 needle was pierced into the vertebral body bone in 5-7 mm depth. After no breakthrough around the bone cortex was confirmed, 0.2 mL required material was injected to vertebral body till solidification. Without leakage, the needle was pulled out, and bleeding was stopped. Then layered suture was performed after washing the wound, and antibiotics was given after surgery postoperative to prevent infection.

2.5. Indexes observation

Four animals were sacrificed after the experiment after 6 weeks, L2 and L4, L6 vertebral body specimens were fixed in neutral formaldehyde and decalcified. All were soaked in plastic liquid after dehydration, tissues were embedded after 3 weeks. Tissues were cut along the horizontal section of vertebral body bone, sliced into 30 microns thickness specimen, to observe the bone trabecular microstructure morphology under light microscopy. Vertebral body bone structure mechanical strength was evaluated. L2, L4, L6 vertebral specimen was taken vertically in the MTS 858 mini System. Between the mold and axial, they were pressed gradually (5 mm/min), until a compression fracture bone occurred. According to the collect data the structure mechanical strength of the vertebral body bone was evaluated, and he mineral density of vertebral bones in groups was calculated.

2.6. Statistical analysis

Data were analyzed by t test using SPSS19.0 statistical software, and were expressed as mean±sd. $P<0.05$ was considered as statistically significant difference.

3. Results

3.1. Histological observation of vertebral body

Normal trabecular bones form was the circular or elliptic arch structure in the control group. Mutual connection between the trabecular bones showed uniform degree of thickness, rare trabecular bone fracture or the defects. Compared with the control group, group Ⅰ showed sparse vertebral body bone trabecular, decreased bone trabecular thickness, and bone defect after absorption of micro fractures and fracture forms. In group Ⅱ trabecular bone structure showed apparent high density, a lot of blue new bone along the trabeculae, repaired connection at trabecular bone splits, with a complete ring of trabecular bone. Group Ⅲ became coarsen, and showed apparent high density, a lot of new bone along the bone trabecular, and a lot of repair links were observed at bone trabecular splits, with a