Introduction

Osteoporosis is characterized by low bone mass and micro-architectural deterioration of bone structure, resulting in bone fragility and an increase in susceptibility to fracture and spinal fusions. OP-1 can be manipulated to enhance fusion rates and fracture healing with or without osteoporosis. Ovariectomized rats have been used as an osteoporotic model for posterolateral intertransverse process fusion in BMP experimental studies. Many studies have shown rhBMP-7 promotes spinal fusions in posterolateral fusion animal models. Not only is OP-1 able to promote spinal fusion in a standard animal model, but also it has been shown to overcome the inhibitory effects of nicotine in a rabbit posterolateral spinal fusion model. Moazzaz et al. reported in 2005 that there was no significant effect of rhBMP-7 to promote spinal fusion in an osteoporotic rat model. They concluded that OP-1 was unable to overcome the detrimental effects of oestrogen deficiency on spinal fusion. Posterolateral intertransverse process spinal fusion using recombinant human osteogenic protein (rhBMP-7) was performed in present study in ovariectomized female rats to investigate whether OP-1 device (rhBMP-7 and TCP-CMC) will enhance posterolateral spinal fusion in an osteoporotic rat model (estrogen deficiency).

Methods

A total of 42 ovariectomized Sprague-Dawley female rats were randomly assigned to two experimental and four control groups. 30 µg lactose + 400mg TCP-CMC, 2) 90 µg lactose + 400 mg TCP-CMC, 30 µg rhBMP-7 + 3) 400 mg TCP-CMC and 4) 90 µg rhBMP-7 + 400 mg TCP-CMC, 5) 400 mg TCP-CMC alone and 6) no TCP, no rhBMP. Spinal fusion was evaluated by manual motion testing as the definitive test and was supported by information from Faxitron digital X-ray CT scans, DEXA scans and histology.

Results

Ovariectomized rats receiving 30 µg lactose + 400mg TCP-CMC, 90 µg lactose + 400 mg TCP-CMC, and 400 mg TCP-CMC alone did not show spinal fusion. OVX rats receiving 90 µg rhBMP-7 + 400 mg TCP-CMC showed significantly higher fusion rates than the lactogen or TCP putty groups. (P <0.0001). The rats receiving 30 µg rhBMP-7 + 400 mg TCP-CMC did not show solid fusion either radiologically and histologically (Fig 1 and 2).

Discussion

The present study demonstrated that OP-1 can overcome the negative effects of oestrogen deficiency in rat posterolateral fusion model has been demonstrated in the present study. In present study, 42 rats underwent single level of posterolateral fusions at L5-6 using either TCP-CMC without/with 30, 90 µg lactose or with 30 or 90 µg rhBMP-7 (bovine type I collagen + CMC as a carrier). 21 days after surgery, all rats with TCP-CMC without/with lactose did not show any new bone formation and solid fusion on manual palpation, radiological, histological assessment, whereas the 90 µg OP-1-treated rats demonstrated predominantly mature new bone formation at the fusion sites (6 out 7) but not 30 µg OP-1-treated animals which was consistent with results presented by Moazzaz, et al. In our TCP-CMC, one of components, CMC is plant-derived fibre, can bind OP-1 molecules well and the tricalcium phosphate can be manipulated into a variety of shapes, and provide reasonably space maintenance and structural support. In the present study, the carrier, OP-1 device composed of TCP-CMC (TCP and CMC) and BMP-7, supplied by Stryker, is different from that used by Moazzaz, et al. CMC carrier may improve efficacy for OP-1 in osteoporotic animals. The TCP/CMC scaffold for the attachment and proliferation of mesenchymal cells, which, in response to OP-1, differentiate to form new bone at the fusion site. The TCP/CMC scaffold is temporary and is completely reabsorbed when the bone formation process is complete, whereas the TCP/CMC scaffold was reabsorbed slowly in which OP-1 was absent. The carrier used in Moazzaz et al’s study was not the same as in OP-1 device (Stryker, in present study) containing carboxymethylcellulose sodium (CMC) and tricalcium phosphate. This standard OP-1 device is somewhat different from the one Moazzaz et al used. The implication of OP-1 in osteoporotic model will open a new therapeutic window for osteoporotic or osteopenic patients for the requirements of spinal fusion.

Conclusion

The rhBMP-7 is able to overcome the inhibitory effects of estrogen deficiency on posterolateral spinal fusion and generate a relatively robust fusion but higher dose of OP-1 and modification of carrier are required compared with those in non-ovariectomized animals in spinal fusion. Therefore, effect of the OP-1 on osteoporotic spine is dose-dependent with/without carrier-dependent

References