The Effect Of BMP-7 With Gelatin Hydrogel Sheets On Rotator Cuff Repair

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Disclosures:

Introduction: For the better clinical results after rotator cuff repair, it is important to promote the remodeling of humeral tendon-bone insertion. Bone Morphogenetic Protein-7 (BMP-7), which is one of the BMP families, has not only the ability of bone formation but also the abilities of growth stimulation and differentiation for chondrocyte and tendon cell. BMP-7 injection to the humeral tendon-bone insertion may promote repair of tendon-bone insertion. However, half life of BMP-7 activity is very short, and it is difficult to keep the effective concentration at the tendon-bone insertion. Gelatin hydrogel sheets (GHS) have been used for the sustained release of growth factor, to keep local concentration. The purpose of this study is to analyze the curative effect of BMP-7 with GHS on rotator cuff repair.

Methods: Twelve-week-old Sprague-Dawley (SD) wild-type male rats of the same strain (n=66) were used. The animals were housed in our institution’s animal facility in accordance with the policies and procedures set out in the Guide for the Care and Use of Laboratory Animals by the National Institutes of Health. Bilateral supraspinatus tendons were transected and sutured at the insertion on the greater tuberosity by the Mason-Allen technique. First, we evaluated whether GHS release sustainedly BMP-7 at the tendon-bone insertion. BMP-7 was labelled by \(^{125}\text{I}\) iodine using the method of Greenwood et al. \(^{125}\text{I}\)-labelled BMP-7 was injected into subacromial bursa (\(^{125}\text{I}\)-BMP-7 group) and GHS with \(^{125}\text{I}\)-labelled BMP-7 was set on the tendon-bone insertion (\(^{125}\text{I}\)-BMP-7 - GHS group). At 1, 3, 7, 14, and 21 days after surgery (n=3), \(^{125}\text{I}\)-labelled BMP-7 concentration at the tendon-bone insertion were measured by PACKARD COBRA E5002 Auto-Gamma Counting Systems (PerkinElmer Japan Co., Ltd., Kanagawa, Japan). Statistical analysis by two-way factorial analysis of variance and the Tukey’s post hoc test using Kruskal Wallis rank was performed.

Secondly, we evaluated the effect of GHS with BMP-7 on rotator cuff repair. Phosphate buffered saline (PBS) or BMP-7 was injected into subacromial bursa (PBS group, BMP-7 group), GHS with PBS or BMP-7 (Fig.1) was set on the tendon-bone insertion (PBS - GHS group, BMP-7 - GHS group). At 2, 4, and 8 weeks after surgery, the rats were sacrificed and harvested from their shoulders (n=3). Heterotopic ossification was evaluated by micro computed tomography (\(\mu\)CT) (micro focus 2D/3D, ScanXmate-E090S40, Comscantecno Co., Ltd., Kanagawa, Japan). Sections were stained with hematoxylin and eosin, safranin O for light microscopic examination. Tissue repair was evaluated by The tendon-to-bone maturing score reported by Ide et al. They evaluated histologic parameters including cellularity, vascularity, proportion of fibers oriented parallel, proportion of fibers of large diameter, continuity, bone ingrowth, fibrocartilage cells, and tidemark. The first two parameters were classified into Marked, Moderate, Mild, Minimal and the last six parameters were classified into 25%>, 25-50%, 50-75%, 75%< as compared to control (unoperated) group. They were scored each 1, 2, 3, 4 points. A perfect score in this scoring system is 32 points. Statistical analysis by three-way factorial analysis of variance using Kruskal Wallis rank was
performed. All values were expressed as mean ± standard deviation.

**Results:**
The BMP-7 residual rate in $^{125}$I-BMP-7-GHS group was significantly higher than that in $^{125}$I-BMP-7 group for 21 days after surgery (P<0.05) (Fig. 2). Heterotopic ossification was not observed by μCT in any groups. Cellularity was gradually reduced in all groups. Many inflammatory and mesenchymal cells were observed in three groups except PBS group at the bone tendon insertion at 2 weeks after surgery. Proportion of fibers oriented parallel increased in BMP-7-GHS group more than the other groups at 4 weeks after surgery. BMP-7 - GHS group had highest score about proportion of fibers oriented parallel at 8 weeks after surgery. Fibrocartilage was observed in BMP-7 group and BMP-7-GHS group at 4 weeks after surgery. Cartilage formation in all groups and the columnar arrangement of chondrocytes in BMP-7 - GHS group were observed at 8 weeks after surgery. The tendon-to-bone maturing score was almost same in PBS group (19±4.6), BMP-7 group(18.3±4.5) and PBS-GHS group (16.3±4.7) and was the highest in BMP-7-GHS group (23±1) at 8 weeks after surgery (Table.1).

**Discussion:** Tendon-bone insertion of rotator cuff consists of bone, cartilage and tendon. The results of this study showed that GHS facilitate sustained release of BMP-7 for 3 weeks at the tendon-bone insertion. In BMP-7-GHS group, Many inflammatory and mesenchymal cells were observed at the at the tendon-bone insertion at 2 weeks after surgery and rotator cuff repair was most obvious at 8 weeks after surgery, thus GHS with BMP-7 may promote rotator cuff repair.

**Significance:** GHS including BMP-7 may promote rotator cuff repair and shorten duration of rehabilitation after surgery.

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**References:**