Gelatin hydrogel with sustained cefazolin release as a novel treatment for pyogenic spondylitis

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INTRODUCTION:

The treatment of pyogenic spondylitis is difficult, and currently, most cases are treated conservatively, primarily with bed rest and long-term antimicrobial therapy[1,2]. Treatment is a lengthy process, and patients remain on extended bed rest, resulting in a decline in their QOL[2] and significant economic burdens on both the patient and the hospital[3].Thus, new treatment methods are needed.

We aimed to investigate the efficacy of sustained-release antimicrobial agents using gelatin hydrogel microspheres[4] (GM) in a pyogenic spondylitis model using rat tail vertebrae.

METHODS:

An established rat model[5] of caudal vertebral pyogenic spondylitis was used. First, the caudal disc (Co8) was manually punctured with a 27G needle to a depth of 5 mm, the approximate vertical distance from the skin to the center of the medullary nucleus, using a stopper, and 1.0×10^8 CFU/100 µl of luminous *Staphylococcus aureus* (MSSA, XEN29) were introduced[3]. After 3 days, the rats were divided into four groups: Group C (n = 4), local administration of GM-PBS; Group V (n = 4), intraperitoneal injection of free cefazolin solution (30 mg/kg); Group P (n = 4), local administration of free cefazolin solution (0.3 mg/kg); and Group G (n = 4), local administration of GM-cefazolin (0.3 mg/kg, calculated for cefazolin). GM-cefazolin was solubilized in collagen so that it could be administered by injection with a 20G needle.

The results were obtained for the amount of bacteria using an *in vivo* imaging system (IVIS), white cell count, Bone volume/Tissue volume (BV/TV) ratio with µCT imaging, and body weight. Results were evaluated at 7, 14, and 28 days after puncture. We used a one-way analysis of variance with Tukey's post-hoc test to compare degeneration between groups. Statistical significance was set at $P < 0.05$.

RESULTS:

Group G showed a significant decrease in luminance compared to the other three groups 7 days after puncture (Group C, $P < 0.001$; Group V, $P = 0.003$; Group P, $P = 0.035$). However, there were no significant differences among the four groups 14 and 28 days after puncture. The white blood cell count of group G was significantly lower than that of the other three groups 7 days after puncture (Group C, $P = 0.040$; Group V, $P = 0.024$; Group P, $P = 0.040$). However, at 14 and 28 days after puncture, there was no significant difference in the V group, although there was a significant difference in the C (day 14, $P = 0.004$; day 28, $P < 0.001$) and P (day 14, $P = 0.001$; day 28, $P < 0.001$) groups. In contrast, there was no difference in BV/TV among the four groups at 7 and 14 days after puncture; however, group G had significantly higher values than the other three groups at 28 days after puncture (Group C, $P = 0.01$; Group V, $P = 0.02$; Group P, $P = 0.03$). In addition, there was no significant difference in body weight between the four groups at 7, 14,and 28 days after puncture.

DISCUSSION:

We investigated the treatment of pyogenic spondylitis using GM with cefazolin in a rat model. We found that administering cefazolin along with GM in the center of the rat's tail could inhibit the progression of pyogenic spondylitis at an early stage and maintain its effect, leading to early improvement. Local administration of cefazolin via GM increased and maintained local concentrations of cefazolin significantly more rapidly than previous intravenous administration of cefazolin, suggesting that it promoted early healing of pyogenic spondylitis.

SIGNIFICANCE/CLINICAL RELEVANCE:

Studies involving *in vivo* models have suggested that gelatin hydrogels may provide early protection from pyogenic spondylitis because they increase and maintain local concentrations of cephazolin in a sustained-release manner. This study can be used effectively in the future to develop an early treatment for pyogenic spondylitis.

REFERENCES:

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FIGURES: