Parathyroid hormone (1-34) improved knee osteoarthritis and function in rats with anterior cruciate ligament transection

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Introduction:
Osteoarthritis (OA) is an increasingly common joint disease as the numbers of elderly people grow in many countries. In the United States, for example, ten percent of the over-60 population suffer from OA. Current treatments for OA primarily involve the use of anti-inflammatory drugs, analgesics, and lubricating supplements. Therefore, it is a priority to develop agents that can suppress the progression of OA at an early stage of the disease. Our previous study showed parathyroid hormone (1-34) (PTH) treatment reversed papain-induced OA changes (decreasing GAG and Col II, and increasing Col X and chondrocytic apoptosis) in the knee joints of the rats [1]. In this study, we propose that PTH also can improve knee osteoarthritis in anterior cruciate ligament transection (ACLT) induced OA animal. We will evaluate the effects of PTH in ACLT induced OA animal in the rats.

Methods:
The animal experiment was approved by the Animal Care and Use Committee of Kaohsiung Medical University. Ten 12-week-old male SD rats were divided into the control group (n=5) and the PTH treatment group (n=5). The rats received ACLT on the right knee. Each left knee, which served as the contralateral control joint, received the vehicle without PTH treatment or OA-induction. The right knees were the study joints. The right knees were injected intra-articularly with 40 μl of 10nM PTH (1-34) every three days for 5 weeks until sacrifice. The time of the rats can withstand in the treadmill were evaluated before sacrifice. After sacrifice, the knees of each rat were harvested, and the tibia plateaus, with articular cartilage were collected for histological study. The amount of GAG and the Mankin score were evaluated. Data are presented as mean and standard error. Statistical significance was evaluated by one-way analysis of variance (ANOVA). A p<0.05 was considered significant.

Results:
The amount of GAG decreased and the Mankin score increased after the induction of OA. The GAG increased about 52% after the treatment of PTH (Fig.1). The Mankin score decreased from about 6 to 3 after the treatment of PTH (Fig.2). With the treatment of PTH, the GAG increased and the Mankin score decreased. Besides, PTH treatment also increased the endurance of rats in the treadmill test about 3 times (from 1.5 min to 4.5 min) (Fig.3).

Discussion:
The 1-34 amino acid fragments of both PTH and PTHrP contain the functional sub-domains for PTHR1 signaling. PTHrP is an important growth factor in the regulation of endochondral ossification in the epiphyseal growth plate. PTHrP down-regulates the expression of Ihh produced by prehypertrophic chondrocytes of growth plates. PTHrP plays a role in maintaining the survival and chondrogenesis of proliferating chondrocytes of growth plates and slowing the terminal differentiation during endochondral ossification. Reports have indicated that the biological changes in articular chondrocytes during OA progression are similar to that of endochondral ossification. We previously demonstrated that PTH(1-34) could rescue AzaC-induced terminal differentiation in cultured human articular chondrocytes and suppress papain-induced OA changes in articular cartilage in rat knees. In this study, we further found PTH(1-34) could improve knee OA in ACLT model both in histology by increasing GAG and decreasing Mankin score and knee function by increasing the endurance in the treadmill test. PTH(1-34) could potentially be a therapeutic choose for OA.

Reference: