

organization. Therefore, it may provide additional, important information compared to conventional section-based histology. Moreover, analyzing patients with medial compartment knee OA, we found that the medial OA menisci had higher histopathological scores than both reference medial menisci, as well as the lateral meniscus from the same knee.

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FRI0510 THE EFFECT AND MECHANISM OF HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS-DERIVED EXOSOMES ON BONE DESTRUCTION OF COLLAGEN INDUCED ARTHRITIS RATS

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Background: Rheumatoid arthritis (RA) is a highly disabling autoimmune disease, characterized by destruction of the cartilage and bone, which is difficult to reverse. mesenchymal stem cells-derived exosomes (Mesenchymal stem cells-derived Exos) is a kind of extracellular vesicle, produced by MSCs in resting or stress state, which can simulate the tissue repair effect of its maternal cells and may be a new breakthrough point in the treatment of RA bone destruction.

Objectives: Study the effect of human umbilical cord mesenchymal stem cells derived exosomes(hUCMSC-exos) on bone destruction in Collagen induced arthritis (CIA) rats.

Methods: 1. After isolated by differential centrifugation, hUCMSCs was cultured in vitro, which was identified by morphology and surface markers.2. Grouping: The CIA rats were randomly divided into CIA group, MTX group, hUCMSCs group, hUCMSC-exos low concentration group, hUCMSC-exos medium concentration group, hUCMSC-exos high concentration group, and a healthy control group.3. Efficacy evaluation: the efficacy of hUCMSC-exos on CIA rats was evaluated by measuring joint swelling, arthritis index, micro-ct scanning and pathological score. The expression levels of RANKL and OPG in the serum of rats in each group were detected by high-throughput flow, multi-factor detection technique or ELISA method, and the levels of the above factors in the synovial tissue of the ankle were detected by immunohistochemical detection technique, and the mRNA levels were detected by RT-PCR.

Results: 1. Effect evaluation: hUCMSC-exos can improve the arthritis index (AI) of CIA rats, and no definite side effect been found. In addition to hUCMSC-exos low concentration group, the joint synovial hyperplasia and inflammatory cell infiltration degree of each treatment group were significantly improved, comparing with that of CIA group. The Results of Micro-ct scanning suggested that the degree of osteoporosis in each intervention group was significantly improved comparing with that in the CIA group, and the improvement degree of hUCMSCs groups, MTX groups and hUCMSC-exos high concentration group was similar.2. The detection of bone metabolism factor in Serum and synovial tissue: medium and high concentrations of hUCMSC-exos, hUCMSCs group and MTX group could down-regulate the level of RANKL in serum and synovial tissues of CIA rats, and raise the level of OPG, and the effect of hUCMSC-exos in high concentration group was slightly obvious.

Conclusion: hUCMSC-exos can improve bone destruction in CIA rats, and it is safe. hUCMSC-exos can mimic its mother cells and exert an inhibitory effect on bone destruction by regulating the imbalance of RANKL/OPG, and the effect is equal or better than its mother cells, and the high concentration group is superior to the low concentration group.

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FRI0511 LOW Ω 6- Ω 3 RATIOS CAUSED REDUCTION IN CELLULAR INFLAMMATION IN HUMAN SYNOVIOCYTES CELL LINE (SW982): GENE EXPRESSION STUDY

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Background: Alarming global increase in osteoarthritis (OA), coupled with off target existing palliative care poses nutraceuticals an extremely attractive alternative in this respect. Beyond meeting the basic nutritional demands, nutrition is thought to play a beneficial role in the management of chronic diseases. Interestingly, the off target effects of nutraceuticals are beneficial in reducing co-morbidities. Skewed ratio of ω -6: ω -3 fatty acids (FAs) in modern diets has been shown associated with increased number of inflammatory diseases including bone and cartilage metabolism. Considering this, due to their disease modifying actions, ω -3 FAs are thought to serve better in OA management.

Objectives: We here investigated the effect of different ω -6: ω -3 ratios on synovitis, a prominent OA pathology. The selected ratios are generally found in global diet.

Methods: Selected ω -6FAs - arachidonic acid (AA), eicosadienoic acid (EDA), linolic acid (LA) and dihomo gamma linoleic acid (DGLA) along with selected ω -3 FAs docosapentaenoic acid 5 (DPA) and α -linolenic acid (ALA) were tested on induced SW-982 cells, in common dietary ratios of 16:1, 8:1, 4:1, 2:1 and 1:1 for their effect on synovial inflammation. For induction, 50ng/ml tumor necrosis factor- α (TNF- α) was used for 72 hrs and the PUFAs were added in the culture media in the selected ratios (concentration of each PUFA - 50 μ M). Finally, isolated cDNA was used to run quantitative RT-PCR for superoxide dismutase (SOD), interleukin-15 (IL-15), matrix metalloproteinase-1 (MMP-1) and vascular endothelial growth factor (VEGF).

Results: All the ratios LA:ALA of caused a remarkable reduction in MMP-1(P<0.001). Marginal reduction in VEGF was noted with 1:1, 4:1 and 8:1 ratios (P<0.005); 8:1 and 16:1 showed a significant increase (P<0.001). SOD did not show any particular trend but noteworthy increase was observed with 2:1, 8:1 and 16:1 ratios (P<0.001) while reduction with 1:1 and 4:1 ratios (P<0.001). IL-15 remained low for 1:1, 2:1 and 4:1 while a marked up-regulation was noted for 8:1 and 16:1 ratios (P<0.001). In case of EDA:DPA, a consistent down-regulation of MMP-1 was found with all the ratios excluding 4:1. The selected ratios were efficient against VEGF (P<0.001). A consistent high SOD was revealed by all the ratios of EDA:DPA, which remained comparable to control. Marginal reduction in IL-15 was noted with 1:1, 8:1 and 16:1 (P<0.05). Lastly, a significant MMP-1 reduction was caused by all the ratios of DGLA:DPA, except 2:1. Excluding 2:1, all the ratios were efficient against VEGF (P<0.001). Increased levels of SOD remained comparable with TNF- α for 1:1 and 4:1; a trivial drop was noted with 2:1 and 8:1, followed by a noticeable reduction with 16:1. IL-15 showed a down-regulation with 1:1, 4:1, 8:1 ratios of DGLA: DPA.

Conclusion: Consequence of synovial inflammation in typical and atypical forms results in cartilage-loss, osteophytes and pain. FA ratios when used in equivalent, was found highly effective against IL 15, MMP1 and VEGF, whereas inflammation increases with increase in their proportions. Low SOD indicated lower oxidative-stress while it was up-regulated in response to high stress. FAs work in two distinct ways, membrane incorporation and metabolic modulation. Unsaturated fatty acid increase membrane fluidity and thus improves cell signaling. Analysis of treated and untreated cells showed incorporation of FAs in cell membrane, which improves membrane fluidity and status of signal transduction.

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