## PROTECTIVE ACTION OF CLODRONATE ON OSTEOARTHRITIC CARTILAGE

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Bisphosphonates enhance bone mass and prevent bone resorption in patients affected by chronic inflammatory and degenerative arthropaties. In details, in animal models, clodronate shows an anti-inflammatory effect and decreases cartilage damage. In patients with rheumatoid arthritis, clodronate decreases plasma levels of proinflammatory factors secreted by synovial macrophages.

Since a few informations about clodronate action on chondrocytes are available, we studied the effect of clodronate (1 µM - 1 mM) on human articular chondrocytes from cartilage of osteoarthritic parients B ological and molecular effects of clodronate have been evaluated as follows: - Proliferation and liability by cell counting and Trypan Blue staining. - Apoptosi: by c. romosome ladder and lysis and Hoechst 33342 nuclear staining. - Mucopolysaccarides production by PAS reaction. - Actallep otemases 9 (MMP9) and TIMP-1 expression by quantitative Rea Tim 3-PCR. - Intravellular ATP evaluation by chemoluminescent luciferase assay. - Osteoprolege in OPG) and RAN'C-Ligarid (NANK-L) release by ELISA test on culture media. - Collagen I a to II capres sion by Rere se T a cri, tase-PCR and Real Time-PCR. Higher doses of clodronate in nibit cellular proliferation and ha a nation >80% cell viability along 6 days of incubation. Cell number decrease was due to app otic avents, as evidenced by chromosomic ladder and picnotic nuclear reamen ation (10% for 10) µ M and 13% for 1 mM clodronate versus 5% of control). MMP9 expression is s'rongly reduced while CPG and RANK-L release is not altered. Clodronate doesn't affect mucopolysaccarid is production. Intracellular ATP significantly increases in the presence of 10 µM of clodronate, when compared to control (26.92±0.23% of increase). Collagen I and mainly collagen II expression are significantly enhanced after incubation with clodronate. These results show that clodronate acts on chondrocytes promoting a protective and regenerative action on osteoarthrtitic cartilage.

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