

CHONDROPROTECTION OF ARTICULAR CARTILAGE IN ATHLETES: I-ONE THERAPY

Massari L

*Dipartimento di Scienze Biomediche e Terapie Avanzate, Clinica Ortopedica
Ospedale S. Anna, Ferrara, Italy*

Articular cartilage has minimal reparative capability: "when destroyed it is never recovered". The possibility to prevent the degeneration of articular cartilage is a major challenge for modern orthopaedic surgery and regenerative medicine. Regenerative medicine foresees the replacement or repair of the damaged cartilage using mesenchymal stem cell implantation, microfractures or tissue engineering procedures, such as autologous chondrocyte transplantation with or without scaffolds. The different steps of these procedures have been defined with great details: i) tissue substitute preparation or "tissue-engineering phase"; ii) preparation of the recipient tissue, iii) surgical procedure. Nevertheless, a central role is played by the "wound healing phase"; the local environment influences the metabolic activity and the phenotypic expression of the cells in the treated area. Inflammation in the joint space favours the onset of fibrotic phenotype versus a more specialized phenotype. Furthermore, the presence of pro-inflammatory cytokines, such as IL-1 β and TNF- α , favours an extracellular matrix degradation and the release by synoviocytes of PGE2 that may induce chondrocyte apoptosis.

In the last years, several studies have shown that biophysical stimulation, with I-ONE therapy (IGEA, Carpi, Italy), has been able to modulate articular cartilage metabolism treating the whole cartilage surface and thickness, and the underlying subchondral bone homogeneously (1). In vitro, I-ONE therapy increases the binding between adenosine and A2A adenosine receptor on human neutrophil cell membrane, on bovine chondrocytes and fibroblast-like synoviocytes. It has been shown that drugs with A2A adenosine receptor agonist activity prevent articular cartilage degeneration in animals. I-ONE therapy inhibits PGE2 release from synoviocytes.

We hypothesized that the adenosine agonist effect of I-ONE therapy can also prevent cartilage degeneration. Ex vitro, in bovine full thickness articular cartilage explants, I-ONE therapy induces the largest increase in proteoglycan synthesis and in IGF-1 synthesis, when cartilage is exposed to specific I-ONE parameters. These effective parameters were subsequently used in in vivo experiments.

The effect of I-ONE therapy was investigated on Dunkin Hartley osteoarthritic knee by Mankin score and by histomorphometric and densitometric analysis; I-ONE therapy prevented cartilage degeneration and subchondral bone sclerosis. Osteochondral grafts were performed in the knees of sheep; I-ONE therapy favoured osteochondral grafts integration and prevented cyst-like resorption area formation, that can compromise the stability of graft and the success of the technique.

To support the in vitro results histological analysis of the synovial fluid were also performed in this animal model. The amount of inflammatory catabolic cytokines (IL-1 β and TNF- α) in the synovial fluid of I-ONE treated animals was significantly lower than in control animals. On the contrary, TGF- β 1 was significantly higher in stimulated animals than it was in controls. These results demonstrate not only the capability of I-ONE therapy to control the inflammatory reaction, but also its capability to favour cartilage anabolic activity.

Preclinical studies have shown that I-ONE therapy controls inflammation, protects extracellular matrix and favours chondrocytes metabolic activity. These results provide the rationale to design clinical studies to demonstrate the possibility to transfer the treatment to humans. We hypothesized that patients undergoing arthroscopic treatment could benefit from the use of I-ONE therapy. The results of two randomized, prospective, double-blind studies demonstrated that I-ONE therapy favours patients' recovery both in the short (90 days) and in the long term (3 years).

The percentage of patients with complete functional recovery is significantly higher among of the active group compared to the control (2,3).

We think that the long term benefit results from I-ONE chondroprotection of articular cartilage and from prevention of the fibrotic stimuli exerted by pro-inflammatory cytokines on wound tissue. Biophysical stimulation can play a central role in regenerative medicine, protecting the repair tissue from the catabolic effect of the inflammatory reaction elicited by the surgical implantation procedure.

References

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