PULSED ELECTROMAGNETIC FIELDS TREATMENT MEDIATES ANTI-INFLAMMATORY AND CHONDROPROTECTIVE EFFECTS THROUGH ADENOSINE RECEPTOR PATHWAY

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Several studies have explored the biological effects of low frequency low energy pulsed electromagnetic fields (PEMFs) on human joint reporting different functional changes. From the biophysical point of view, the PEMFs are characterized by different parameters of the signal as intensity, frequency and wave form of the magnetic and electric fields (IGEA, Carpi, Italy). It is well known that biophysical stimulation with PEMFs promotes anabolic activity resulting in an increase in chondrocyte and proteoglycan synthesis. Several experimental results support the hypothesis that PEMF treatment is chondroprotective and is accompanied by the control of inflammation. The effectiveness of the treatment has also been shown in patients where the control of joint microenvironment by PEMFs is an important therapeutic approach after arthroscopic treatment in the perspective of a new regenerative medicine for musculoskeletal disorders (Cadossi et al., 2014). A double role for PEMFs could be hypothesized in vitro by stimulating cell proliferation, colonization of the scaffold and production of tissue matrix (Fini et al., 2013). Another effect could be obtained in vivo after surgical implantation of the construct by favoring the anabolic activities of the implanted cells and surrounding tissues and protecting the construct from the catabolic effects of the inflammatory status (Veronesi et al., 2015).

Adenosine has been shown to affect various physiological and pathological processes acting with four cell surface G protein-coupled receptors named as A1, A2A, A2B and A3 adenosine receptors (ARs) (Borea et al., 2016). Much research activity has focused on the mechanisms of interaction between PEMFs and membrane receptors such as the involvement of ARs. In particular, PEMF exposure mediates a significant upregulation of A2A and A3ARs expressed in various cells such as chondrocytes, synoviocytes and osteoblasts involving a reduction in most of the pro-inflammatory cytokines. Of particular interest is the observation that PEMFs, acting as modulators of adenosine, are able to increase the functionality of the endogenous agonist. PEMFs through the increase of ARs enhance the working efficiency of adenosine, producing a more physiological effect than the use of drugs without the side effects, desensitization and receptor down-regulation often related to the use of agonists (Varani et al., 2017). In particular, a prolonged stimulation of the membrane receptors with an exogenous agonist can dampen the ability to transduce the signal which is followed by the process of the receptor internalization into specific vesicles inside the membrane. Therefore, the prolonged use of agonists decreases the receptor density by reducing the effect of the drug itself, while the PEMFs potentiate the effect of endogenous adenosine as an anti-inflammatory agent. This observation suggests the hypothesis that PEMFs may be an interesting approach as a non-invasive treatment with a low impact on daily life mediating a significant increase on the effect of the endogenous modulator. In conclusion, PEMFs represent an important approach in the pharmacological field providing encouraging therapeutic results in various inflammatory diseases and in the functional recovery of the damaged cartilage tissues.

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