Biophysical Stimulation in Athletes' Joint Degeneration

Subjects: Orthopedics

Contributor: Davide Bizzoca

Biophysical stimulation is a non-invasive therapy currently employed in orthopaedics and traumatology practice to enhance the reparative abilities of the musculoskeletal system. Biophysical stimulation refers to the application of physical energy to a biological system to increase and facilitate tissue regeneration and anabolic activity.

Keywords: PEMF ; ESWT ; biophysical stimulation ; extracorporeal shock wave therapy ; cartilage ; bone ; osteoarthritis ; athletes

1. Introduction

Over time, bone edema can resolve if adequately treated or can evolve towards bone necrosis (spontaneous osteonecrosis of the knee, SONK), which, however, can also be secondary to vascular pathologies, or towards arthritic evolution.

Many conservative therapies are available, such as chondroprotective drugs and nonsteroidal anti-inflammatory drugs (NSAID), Hyaluronic-acid or Platelet Rich Plasma (PRP) or staminal cells' injection or biophysical stimulation.

Biophysical stimulation is a non-invasive therapy currently employed in orthopaedics and traumatology practice to enhance the reparative abilities of the musculoskeletal system. Biophysical stimulation refers to the application of physical energy to a biological system to increase and facilitate tissue regeneration and anabolic activity [1].

Several types of non-invasive electrical stimulation devices have received US FDA approval for orthopaedic application and are classified into: electrical energy applied directly to the tissue by adhesive electrodes (capacitively coupled electric field, CCEF), ultrasound energy (low-intensity pulsed ultrasound system LIPUS) and electromagnetic energy applied by coils (pulsed electromagnetic fields, PEMFs) or extracorporeal shock wave therapy (ESWT) or Low-Level Laser Therapy (LLLT) [2].

2. PEMF

Damage to articular cartilage is increasingly identified as a source of joint limitation and reduced athletic performance in athletes, whether isolated or in conjunction with ligament or meniscal or tendon tears [3]; therefore, surgical treatment must be supported by biophysical therapy to facilitate functional recovery and achieve better outcomes.

Later, Gobbi and colleagues also evaluated their use in the treatment of early osteoarthritis (Kellgren Lawrence < 2) and age < 60 for 2 years; the results were mixed as they showed an improvement in pain symptoms and KOOS and Tegner scores after one year of treatment and a worsening, instead, at two years [4]. The author concluded that an annual repetition of the treatment may result in sustained symptomatic improvement for the patient.

Some authors, such as Gremion et al. and Ozgüçlü et al., found that a different pulsed signal therapy improved the clinical state of treated patients but there was no significant statistical difference to other conservative treatments such as physiotherapy and therapeutic ultrasound [5][6].

Biophysical therapy, with specific and tested parameters of PEMF, must be considered a valid aid to arthroscopic surgical treatment considering the role of cell stimulation and the reduction of inflammation and pain after treatment. Its use would allow the athlete a more rapid functional recovery and therefore an early return to sporting activity. However, unlike the bone edematous pathology, in which it occupies a prominent place in association or not with bisphosphonates and load reduction, there are no studies in the literature on sportsmen that evaluate whether biophysical therapy alone can replace surgical treatment in the case of mild/moderate chondral damage.

3. ESWT

Human osteoblasts exposed to shock waves show a dose-dependent increase in differentiation and growth secondary to the increased expression of the Transforming Growth Factor β1 (TGF-β1), which plays a fundamental role in osteogenesis and osteoblastic lineage differentiation [7][8][9]; similarly, Hausdorf et al. demonstrated an increase in FGF-2 in human osteoblasts and fibroblasts. Lyon et al. showed a response to ESWT on a rabbit's knee with smaller denudation on cartilage and enhanced density and chondrocytes formation; a decreased level of TNF-α on chondrocytes after shockwave application may partially explain the mechanism by which ESWT improves cartilage repair and chondroprotection [10]. Another investigation by Moretti et al. confirmed the chondroprotective effects of shock waves stimulation by restoring normal levels of Il-10 and TNF-α [11]. Wang et al., in a series of studies on osteoarthritic knees in rats, confirmed the effect on cartilage through histochemical examinations with Hematoxylin-eosin and Safranin-O stains, showing less cartilage fissuring and better chondrocyte vitality and concentration in the ESWT group compared with the untreated ones [12].

Similar results were also found in rabbit models with osteochondral defects after ESWT showed improvements in the macroscopic characteristics of hyaline cartilage [13]. The application of ESWT to knee OA in rats results in the decline of urinary levels of cartilage degradation markers such as CTX and MMP [12][13][14]. Several studies focused on the effect of ESWT on MSCs; all of them have shown that shockwaves improve stem cell recruitment and differentiation into chondrocytes in mouse models [15]; an augmented proliferation rate was also observed in equine ASCs treated with ESWT [16][17].

The role of subchondral bone throughout the early stages of OA showed that subchondral bone alteration might be a therapeutic focus in OA therapy [18][19]. Wang C. et al. observed improved tissue distributions, including cortical bone, cancellous bone, and fibrous tissue, in many studies using extracorporeal shockwaves to the subchondral bone of the medium tibia condyle. ESWT increased BMP-2 and osteocalcin expression in OA rats, which is usually linked with cell proliferation and extracellular matrix synthesis in healthy osteoblasts [20]. The immunohistochemical examination revealed that the expression of Dickkopf-related protein 1 (DKK-1)—a regulator of osteoblast activity—was considerably greater in OA and significantly decreased after ESWT therapy; these findings show that shock wave stimulation can boost subchondral bone anabolism and improve trabecular microarchitecture. Iannone et al. tests the effects of ESWT on subchondral osteoblasts in vitro and found a significant increase of IL-10 intracellular levels both in OA and healthy osteoblasts [21], in contrast to Moretti et al. who observed downregulation of IL-10 expression in human chondrocytes by applying the identical protocol of ESWT. The dissimilar responses of cartilage and subchondral bone in IL-10 expression after ESWT suggest that IL-10 may play a different role in each component of the OA joint. In a rat model, Hashimoto et al. proposed that ESWT might expedite the repair of meniscal injuries in avascular areas, which may contribute to OA development.

The beneficial effect on OA pain could be explained by nerve fibre responses to ESWT treatment. Ohtori et al. showed that ESWT caused nerve fibre degeneration and reduced the expression of calcitonin gene-related peptide (CGRP) in dorsal root ganglia (DGR) neurons. The analgesic effect and the functional ability enhancement may be time-limited because of nerve regeneration that occurs in fibres 14 days after ESWT [22][23]. The time limits of the benefits of ESWT were studied by Ochiai in rat models, showing an improvement in functional performance between 4 and 14 days after treatment; however, between 21 and 28 days, there were no differences compared to the placebo group [24].

4. Conclusions

Biophysical therapies with PEMF or ESWT can act to improve the symptoms and function of joints, such as the knee in patients with non-advanced OA or those who have suffered a trauma that has led to cartilage damage or subchondral edema. This can be very useful in athletes for an early return to sport and, above all, for preventing this damage from causing an arthritic evolution of the joint. However, in the literature, few studies use exclusively sportsmen or athletes as a sample to study. Particularly concerning the treatment with ESWT, studies that evaluate the effectiveness of the treatment are mainly on animal models while studies on human models focus on musculotendinous pathology.

Further high-quality studies on athletes are needed to draw stronger conclusions.

References

1. Massari, L.; Benazzo, F.; Falez, F.; Perugia, D.; Pietrogrande, L.; Setti, S.; Osti, R.; Vaienti, E.; Ruosi, C.; Cadossi, R. Biophysical stimulation of bone and cartilage: State of the art and future perspectives. Int. Orthop. 2019, 43, 539–551.

2. Vicenti, G.; Bizzoca, D.; Nappi, V.S.; Moretti, F.; Carrozzo, M.; Belviso, V.; Moretti, B. Biophysical stimulation of the knee with PEMFs: From bench to bedside. J. Biol. Regul. Homeost. Agents 2018, 32 (Suppl. 1), 23–28.
3. Mandelbaum, B.T.; Browne, J.E.; Fu, F.; Micheli, J.; Mosley, J.B.; Erggelet, C.; Anderson, A.F. Articular Cartilage lesions of the knee. Am. J. Sports Med. 2000, 26, 853–861.
4. Gobbi, A.; Lad, D.; Petrera, M.; Karnatzikos, G. Symptomatic Early Osteoarthritis of the Knee Treated with Pulsed Electromagnetic Fields: Two-Year Follow-up. Cartilage 2014, 5, 78–85.
5. Gremion, G.; Gaillard, D.; Leyvraz, P.F.; Jolles, B.M. Effect of biomagnetic therapy versus physiotherapy for treatment of knee osteoarthritis: A randomized controlled trial. J. Rehabil. Med. 2009, 41, 1090–1095.
6. Ozgüçlü, E.; Cetin, A.; Cetin, M.; Calp, E. Additional effect of pulsed electromagnetic field therapy on knee osteoarthritis treatment: A randomized, placebo-controlled study. Clin. Rheumatol. 2010, 29, 927–931.
7. Hofmann, A.; Ritz, U.; Hessmann, M.H.; Alini, M.; Rommens, P.M.; Rompe, J.-D. Extracorporeal shock wave-mediated changes in proliferation, differentiation, and gene expression of human osteoblasts. J. Trauma Acute Care Surg. 2008, 65, 1402–1410.
8. Hausdorf, J.; Sievers, B.; Schmitt-Sody, M.; Jansson, V.; Maier, M.; Mayer-Wagner, S. Stimulation of bone growth factor synthesis in human osteoblasts and fibroblasts after extracorporeal shock wave application. Arch. Orthop. Trauma Surg. 2011, 131, 303–309.
9. Cheng, J.H.; Wang, C.J. Biological mechanism of shockwave in bone. Int. J. Surg. 2015, 24, 143–146.
10. Lyon, R.; Liu, R.C.; Kubin, M.; Schwab, J. Does extracorporeal shock wave therapy enhance healing of osteochondritis dissecans of the rabbit knee?: A pilot study. Clin. Orthop. Relat. Res. 2013, 471, 1159–1165.
11. Moretti, B.; Iannone, F.; Notarnicola, A.; Lapadula, G.; Moretti, L.; Patella, V.; Garofalo, R. Extracorporeal shock waves downregulate the expression of interleukin-10 and tumor necrosis factor-alpha in osteoarthritic chondrocytes. BMC Musculoskelet. Disord. 2008, 9, 16.
12. Wang, C.-J.; Sun, Y.-C.; Wong, T.; Hsu, S.-L.; Chou, W.-Y.; Chang, H.-W. Extracorporeal shockwave therapy shows time-dependent chondroprotective effects in osteoarthritis of the knee in rats. J. Surg. Res. 2012, 178, 196–205.
13. Chu, C.-H.; Yen, Y.-S.; Chen, P.-L.; Wen, C.-Y. Repair of articular cartilage in rabbit osteochondral defects promoted by extracorporeal shock wave therapy. Shock Waves 2015, 25, 205–214.
14. Wang, C.-J.; Hsu, S.-L.; Weng, L.-H.; Sun, Y.-C.; Wang, F.-S. Extracorporeal shockwave therapy shows a number of treatment related chondroprotective effect in osteoarthritis of the knee in rats. BMC Musculoskelet. Disord. 2013, 14, 44.
15. Chen, Y.J.; Wurtz, T.; Wang, C.J.; Kuo, Y.R.; Yang, K.D.; Huan, H.C.; Wang, F.S. Recruitment of mesenchymal stem cells and expression of TGF-b1 and VEGF in the early stage of shock wave-promoted bone regeneration of segmental defect in rats. J. Orthop. Res. 2004, 22, 526–534.
16. Zhang, H.; Li, Z.L.; Yang, F.; Zhang, Q.; Su, X.Z.; Li, J.; Zhang, N.; Liu, C.H.; Mao, N.; Zhu, H. Radial shockwave treatment promotes human mesenchymal stem cell self-renewal and enhances cartilage healing. Stem Cell Res. Ther. 2018, 9, 54.
17. Raabe, O.; Shell, K.; Goessl, A.; Crispens, C.; Delhasse, Y.; Eva, A.; Scheiner-Bobis, G.; Wenisch, S.; Arnhold, S. Effect of extracorporeal shock wave on proliferation and differentiation of equine adipose tissue-derived mesenchymal stem cells in vitro. Am. J. Stem Cells 2013, 2, 62.
18. Li, G.; Yin, J.; Gao, J.; Cheng, T.S.; Pavlos, N.J.; Zhang, C.; Zheng, M.H. Subchondral bone in osteoarthritis: Insight into risk factors and microstructural changes. Arthritis Res. Ther. 2013, 15, 223.
19. Ji, Q.; Wang, P.; He, C. Extracorporeal shockwave therapy as a novel and potential treatment for degenerative cartilage and bone disease: Osteoarthritis. A qualitative analysis of the literature. Prog. Biophys. Mol. Biol. 2016, 121, 255–265.
20. Xu, Y.; Wu, K.; Liu, Y.; Geng, H.; Zhang, H.; Liu, S.; Qu, H.; Xing, G. The effect of extracorporeal shock wave therapy on the treatment of moderate to severe knee osteoarthritis and cartilage lesion. Medicine 2019, 98, e15523.
21. Iannone, F.; Moretti, B.; Notarnicola, A.; Moretti, L.; Patella, S.; Patella, V.; Lapadula, G. Extracorporeal shock waves increase interleukin-10 expression by human osteoarthritic and healthy osteoblasts in vitro. Clin. Exp. Rheumatol. 2009, 27, 794–799.
22. Ohtori, S.; Inoue, G.; Mannoji, C.; Saisu, T.; Takahashi, K.; Mitsuhashi, S.; Wada, Y.; Takahashi, K.; Yamagata, M.; Moriya, H. Shock wave application to rat skin induces degeneration and reinnervation of sensory nerve fibres. Neurosci. Lett. 2001, 315, 57–60.
23. Ochiai, N.; Ohtori, S.; Sasho, T.; Nakagawa, K.; Takahashi, K.; Takahashi, N.; Murata, R.; Takahashi, K.; Moriya, H.; Wada, Y.; et al. Extracorporeal shock wave therapy improves motor dysfunction and pain originating from knee

osteoarthritis in rats. Osteoarthr. Cartil. 2007, 15, 1093–1096.

24. Lizis, P.; Kobza, W.; Manko, G. Extracorporeal shockwave therapy vs. kinesiotherapy for osteoarthritis of the knee: A pilot randomized controlled trial. J. Back Musculoskelet. Rehabil. 2017, 30, 1121–1128.