Journal of Osteoporosis & Physical Activity

Lad et al., J Osteopor Phys Act 2013, 1:2
DOI: 10.4172/2329-9509.1000106

Research Article Open Access

Is there any Role for Pulsed Electromagnetic Fields in the Treatment of Early Osteoarthritis of the Knee?

Dnyanesh Lad, Georgios Karnatzikos and Alberto Gobbi

OASI Bioresearch Foundation, Milan, Italy

Abstract

Objective: Pulsed Electromagnetic Fields (PEMFs) were introduced in the clinical setting in the 1970s. Proven to be a successful method of treating non-union and delayed union of fractures, its effects on cartilage has remained ambiguous. PEMFs have demonstrated a pro-anabolic and anti-catabolic activity on cartilage metabolism. We hypothesized that the use of PEMFs in patients with symptomatic cartilage lesions of the knee would lead to improved clinical outcomes in an observational study to evaluate the results after 2-years.

Methods: 25 patients between the age of 30 and 60 years who underwent treatment with PEMFs for symptomatic cartilage lesions of the knee (grade 1-2 as per ICRS classification) were included in this prospective case series. Patients were evaluated pre-treatment, at 12 months and 24 months using Visual Analogue Scale (VAS) scale for pain, Tegner and KOOS scores..

Results: A significant improvement in all scores was observed at 1-year follow-up (p=0.003). At 2-year follow-up, results deteriorated but were still superior to pre-treatment levels (p=0.04). No adverse reactions were seen.

Conclusions: PEMFs in patients with symptomatic isolated cartilage lesions of the knee can cause improvement in symptoms, knee function and activity in the short term. Repetition of treatment annually may improve the long term results.

Keywords: Cartilage lesions, Pulsed electromagnetic fields, Knee, Chondral injury

Introduction

Injuries to articular cartilage can lead to joint dysfunction and progressive joint degeneration with a considerable social impact related to high costs of treatment and loss of work days. Curl et al in a retrospective review of 31,516 arthroscopies identified cartilage lesions in 63% of cases [1]. Cartilage has a poor intrinsic healing potential and when left untreated, cartilage lesions can progress rapidly and lead to early onset of Osteoarthritis (OA) [2]. Given that the average life span of man has increased, and there is growing trend towards fitness and athleticism, we now must deal with a population which is either too young, or too fit to undergo a metal resurfacing procedure. The focus should be to delay this eventuality or avoid it altogether. Many conservative treatment modalities are available. These include oral and topical Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), intra-articular corticosteroids injections, visco-supplementation, Platelet-Rich Plasma (PRP) injections, bracing, and physical therapy [3-6].

In vitro and in vivo studies have demonstrated an influence on cartilage metabolism through pro-anabolic and anti-catabolic activity, which has generated interest in the use of PEMFs [7-12]. PEMFs were introduced in the clinical setting in the 1970s as a successful method for treatment of non-union and delayed union of fractures; the effects on focal cartilage lesions of the knee remain unknown while studies on OA are equivocal [13-19]. The aim of this observational study is to evaluate the outcomes of the treatment with PEMFs in patients presenting with symptomatic cartilage lesions of the knee. We hypothesized that the treatment would lead to relief of symptoms and improved clinical outcomes, and that the results would be better in a younger patient population.

Material And Methods

Study group

This is a prospective case series begun in January 2009 with institutional review board approval. A written, informed consent was obtained from all the patients.

53 patients with symptomatic cartilage lesions of the knee were treated with PEMFs at our institute. 28 of them (13 male and 15 female) met our study inclusion criteria and were prospectively followed up for a minimum of 2-years post treatment.

Inclusion criteria

- age between 30 and 60 years;
- grade 1-2 cartilage lesion according to the ICRS classification, evaluated by MRI and previous diagnostic arthroscopy ± lavage within 6 months prior to start of treatment (Table 1) (Figure 1-3)
- symptomatic patients with functional limitations

Exclusion Criteria

- radiographic findings of knee OA (of grade 2-4 as per Kellgren-Lawrence classification), ICRS classification 3 or 4 and degenerative changes involving hip and ankle in both lower extremities;

***Corresponding author:** Dr. Alberto Gobbi MD, President and Founder O.A.S.I. Bioresearch Foundation,Via Amadeo 24, 0133 Milan, Italy, Telephone: (+39)027610310, Fax: (+39)0270124931, E-mail: gobbi@cartilagedoctor.it

Received September 30, 2013; **Accepted** November 16, 2013; **Published** November 22, 2013

Citation: Lad D, Karnatzikos G, Gobbi A (2013) Is there any Role for Pulsed Electromagnetic Fields in the Treatment of Early Osteoarthritis of the Knee? J Osteopor Phys Act 1: 106. doi:10.4172/2329-9509.1000106

Citation: Lad D, Karnatzikos G, Gobbi A (2013) Is there any Role for Pulsed Electromagnetic Fields in the Treatment of Early Osteoarthritis of the Knee? J Osteopor Phys Act 1: 106. doi:10.4172/2329-9509.1000106

Lesion Grade	International Cartilage Repair Society (ICRS) Classification
0	**Normal**
I	**Nearly Normal** Superficial Lesions. A – Soft Indentation B – Superficial Fissured and Cracks
II	**Abnormal** Lesion Extending down to <50% of the Cartilage Depth
III	**Severely Abnormal** Cartilage Defect A – Extending down >50% of the Cartilage Depth B – Down to Calcified Layer C – Down to but not through the Subchondral Bone D – Presence of Blisters
IV	**Severely Abnormal** Penetrating Subchondral Bone A – Penetrating Subchondral Bone but not Full Diameter B – Penetrating Subchondral Bone and Full Diameter

Table 1: International Cartilage Repair Society (ICRS) classification (Brittberg M, Aglietti P, Gambardella R, et al. The ICRS clinical cartilage injury evaluation system 2000; 3rd ICRS Meeting, Göteborg, Sweden, April 27-28)

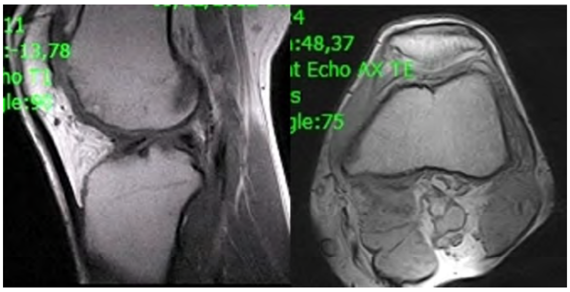

Figure 1: Coronal and axial MRI images showing cartilage lesion on the lateral femoral condyle and trochlea.

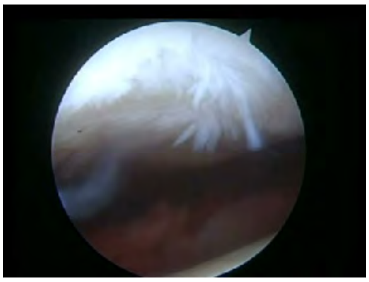

Figure 2: Arthroscopic image showing Grade 1 ICRS Classification cartilage lesion.

Figure 3: Arthroscopic image showing Grade 2 ICRS Classification cartilage lesion.

- malalignment of the lower limbs (varus-valgus greater than 8° from physiological);
- knee instability or patello-femoral maltracking;
- previous knee surgery for cartilage or ligaments when performed within 12 months prior to treatment (including microfracture, meniscectomy, ACL reconstruction, Bone Marrow Aspirate concentrate with scaffold);
- previous intra-articular injections with corticosteroid, PRP or hyaluronic acid (within 6 months prior to the study);
- inflammatory arthritis;
- smokers;
- severe cardiovascular disease.

Treatment protocol

All patients underwent biophysical treatment with PEMFs (I-ONE therapy, IGEA S.p.A., Carpi, Italy). The protocol included a 4-hour treatment per day, for a total of 45 days. The maximum intensity of magnetic field was 1.5 mT and frequency 75 Hz. (Figure 4). The treatment could be administered through a battery operated device allowing ambulation (25 patients) or through an electric device requiring the patient to be stationary (3 patients).

The patients would receive no other treatments (intra-articular injections, or oral medications) for the knee with the exception of acetaminophen on an 'as required' basis. Each patient was questioned regarding analgesic consumption and alternative treatments at each follow up. Need for more than 3 analgesic tablets per day for more than 3 days consecutively, more than twice in the follow up period was a clause for exclusion. All patients underwent physiotherapy at the same center, with the same protocol for 4 weeks beginning 1 week after the initiation of treatment to improve muscle strength and range of motion.

Data collection and analysis

The standard radiographic pre-operative evaluation included a standing anteroposterior long-leg radiograph (including hips and ankles), standing antero posterior and 45° flexion views, lateral view of the knees, skyline patellofemoral view, and MRI. Visual analogue scale (VAS) for pain (0 = no pain at all, 10 = worst pain), Tegner, Knee Injury and Osteoarthritis Outcome Score (KOOS) scores were collected before treatment, and at 1 and 2 year follow-up and analyzed independently by another author. Primary outcomes of the study were range of motion (ROM), pain relief, improvement of symptoms and improvement of activity level. The level of patient satisfaction was also recorded.

Statistical analysis

SPSS software (SPSS 17.0, SPSS, Chicago, IL) was used for the statistical analysis. Mean values of KOOS, Tegner and VAS before treatment, at 1 and 2 year follow-up were compared and the statistical significance was calculated with the t-student test. The non parametric Mann-Whitney test was performed to analyze difference between subgroups based on age. A confidence interval of 95% was set with $p<0.05$ indicating significance.

Results

25 (12 Males, 13 females) patients were available at final follow-up. 3 patients were excluded at follow up: 1 underwent a microfracture procedure 5 months after initiating treatment due to re-injury at sport

Citation: Lad D, Karnatzikos G, Gobbi A (2013) Is there any Role for Pulsed Electromagnetic Fields in the Treatment of Early Osteoarthritis of the Knee? J Osteopor Phys Act 1: 106. doi:10.4172/2329-9509.1000106

Figure 4: PEMF with I-ONE therapy, IGEA applied to the knee.

Variables	Data
Number of patients	25 (12 male / 13 female)
Mean age	48.1 ± 2.6 (range: 30-60)
Mean follow-up (years)	2.1
Age ≥ 45 years	14
Age < 45 years	11
Single lesions	20 (8 PAT, 8 MFC, 1 MTP, 1 LFC, 2 LTP)
Multiple lesions	5 (3 LFC/LTP, 2 MFC/MTP)

PAT: Patella; MFC: Medial Femoral Condyle; LFC: Lateral Femoral Condyle; LTP: Lateral Tibial Plateau; MTP: Medial Tibial Plateau.

Table 2: Patient demographics and localization of cartilage lesions.

Age of Patient (in years)	Sex	Type of Procedure	Number of years prior to start of treatment
42	Female	ACL Reconstruction	10
34	Male	ACL Reconstruction	12
38	Male	ACL Reconstruction	7
53	Male	Partial Medial Meniscectomy	8
41	Female	Partial Medial Meniscectomy	5
39	Male	Arthroscopic Debridement	8

Table 3: Demographics of patients with prior surgery.

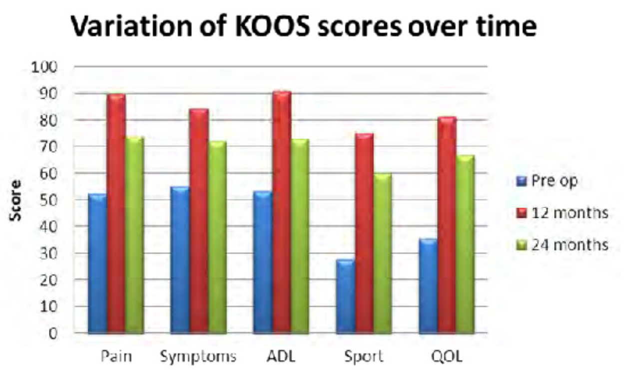

Figure 5: Trend of KOOS score improvement from pre-treatment to 1 and 2 year follow-up.

and worsening of symptoms; the second patient took 2 intra-articular corticosteroid injections after 3 months of initiating treatment while the third patient underwent arthroscopic debridement of the knee at another center. Mean age at the time of treatment was 42.2±2.1 years (range, 30-60 years) and average follow-up was 25 months (range, 24-30 months).

20 patients presented with a single cartilage lesion while 5 of them presented with multiple lesions. Demographic data is described in table 2 and 3. There was a significant improvement in all scores at 1-year follow-up (p=0.003). At 2 year follow-up, results deteriorated but were still better than the pre-treatment values (p=0.04) (Figures 5, 6, 7). The mean values obtained in KOOS, VAS and Tegner scores before treatment, at 1 and 2 year follow-up are presented in (Table 4). Average ROM was 4.5-120.0° ± 3.6° before treatment, 0-124.1° ± 4.1° at 1-year follow-up and 0.9-126.7° ± 5.3° at final follow-up.

An analysis of the results in patients under 45 years old revealed better outcomes in this sub-group compared to patients over 45 years of age (Table 5). The difference in Tegner score between the two sub-groups was significant (p=0.028). While analyzing the collected data, it was observed that, a similar trend of significant improvement in KOOS, Tegner and VAS scale at 1-year follow-up (p=0.01) and a decline at 2-year follow-up (p = 0.04) was also seen in patients under 45 years of age. No adverse reactions or side effects were seen. At 2-year follow-up 80% of patients were satisfied with the results.

Discussion

In vivo studies conducted on Dunkin Hartley guinea pigs showed that PEMFs was able to reduce tissue fibrillation, preserve cartilage

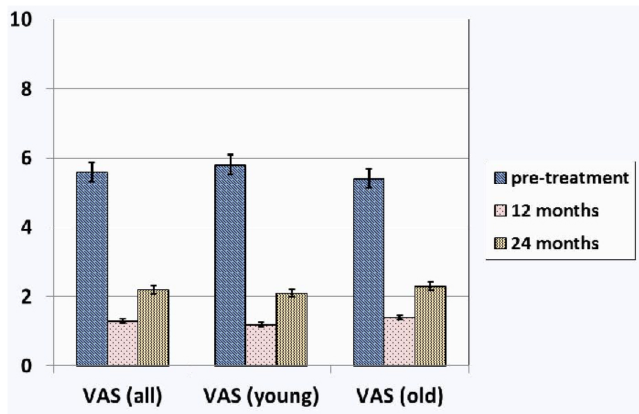

Figure 6: VAS scale before treatment, at 1 and 2 year follow-up: overall results, and results in the sub-groups of patients under 45 years old and over 45 years old.

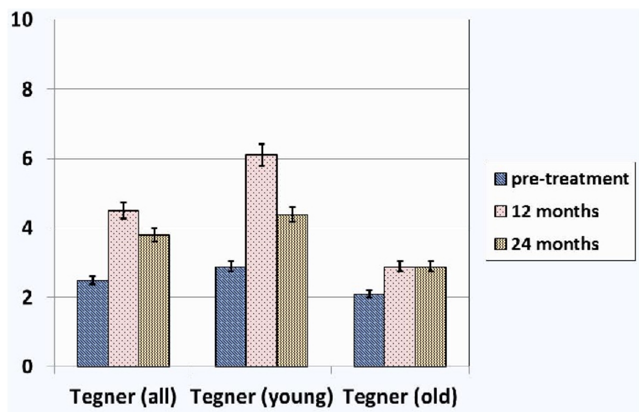

Figure 7: Tegner score before treatment, 1 and 2 year follow-up: overall results, and results in the sub-groups of patients under 45 years old and over 45 years old.

Scale	Pre-treatment (mean ± SEM*)	12-month follow-up (mean ± SEM*)	24-month follow-up (mean ± SEM*)
KOOS Pain	52.3 ± 4.8	89.7 ± 4.3	73.9 ± 3.4
KOOS Symptoms	55.4 ± 5.0	84.5 ± 3.6	72.2 ± 3.7
KOOS ADL	53.3 ± 5.6	90.8 ± 3.4	72.9 ± 3.9
KOOS Sport	28.0 ± 5.9	75.4 ± 6.2	60.3 ± 5.5
KOOS QOL	35.6 ± 4.5	81.3 ± 4.7	66.8 ± 6.1
Tegner	2.5 ± 0.5	4.5 ± 0.5	3.8 ± 0.5
VAS	5.5 ± 0.4	1.3 ± 0.4	2.2 ± 0.6

The variables are expressed as mean ± SEM (standard error of the mean).
Abbreviations: VAS: Visual Analog Scale; KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: Activities of Daily Loving; QOL: Quality of Life.

Table 4: Clinical outcome: overall results.

SCALE	Pre-treatment (mean ± SEM*)		1-year follow-up (mean ± SEM*)		2-year follow-up (mean ± SEM*)	
	Under 45	Over 45	Under 45	Over 45	Under 45	Over 45
KOOS Pain	52.6 ± 4.8	52.9 ± 3.8	93.8 ± 5.3	86.2 ± 5	78.8 ± 3.4	77.3 ± 34.4
KOOS Symptoms	53.6 ± 4.8	54.3 ± 4.8	89.1 ± 4	85.1 ± 3	71.9 ± 4.5	76 ± 3.5
KOOS ADL	54.8 ± 6	56.7 ± 4	96.2 ± 3.5	94.6 ± 2.5	80.7 ± 3.1	76.8 ± 2.1
KOOS Sport	31.8 ± 4.8	24.2 ± 5.8	80.8 ± 7.2	78.1 ± 4.2	73.3 ± 4.2	64.2 ± 2.4
KOOS QOL	37.7 ± 4.6	31.8 ± 4.6	83.3 ± 5.5	82.9 ± 2.5	72.5 ± 6	69.6 ± 4
VAS	5.8 ± 0.5	5.4 ± 0.3	1.2 ± 0.5	1.4 ± 0.3	2.1 ± 0.7	2.3 ± 0.6
Tegner	2.9 ± 0.4	2.1 ± 0.6	6.1 ± 0.5	2.9 ± 0.5	4.4 ± 0.5	3 ± 0.3

The variables are expressed as mean ± SEM (standard error of the mean).
Abbreviations: VAS: Visual Analog Scale; KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: Activities of Daily Loving; QOL: Quality of Life.

Table 5: Comparison of outcomes in patients under 45 years old versus over 45 years old: KOOS, VAS and Tegner.

thickness and prevent the sclerosis of the sub-chondral bone in the lateral and medial compartments of the knee.20,21 This pre-clinical data represents the rationale for the clinical application of PEMFs as an alternative to the use of NSAIDs or intra-articular injections (steroids, hyaluronic acid, PRP) in the symptomatic treatment of isolated cartilage lesions. Several investigations have been carried out to assess the efficacy of PEMFs in patients with OA but the results have been contradictory [20,22]. Thamsborg et al[18] conducted a Randomized Clinical Trial (RCT) including 83 patients and found no significant differences in the outcome scores in the group treated with PEMFs compared to a placebo group [18]. Their follow up however, was of only 6 weeks. This is in contrast to our findings, where we demonstrated a significant improvement in the results even at the 12 month follow up. We did experience, a decline in results between12 and 24 months, which we believe could be related to a reduction in the anti-inflammatory and chondroprotective action over time and that if treatment were repeated annually sustained improvement could be possible. In another RCT that included 86 patients treated with PEMFs versus placebo for knee OA, Trock et al. reported significant improvements in symptoms and Activities Of Daily Living (ADL) in the PEMFs group similar to the findings that we have demonstrated [19]. In 2009 Vavken et al. published their results of a systematic meta-analysis of RCT's dealing with treatment of OA using PEMFs. A total of 483 patients were included in their research, which concluded that there is evidence of a beneficial effect of PEMFs on functional outcomes in patients with knee OA [20].

PEMFs have also been applied in patients who have undergone knee arthroscopy for cartilage lesions. In a RCT evaluating the outcomes of arthroscopic chondro-abrasion or perforation followed by treatment with PEMF, Zorzi et al showed that PEMFs aided patient recovery by reducing the requirement of analgesics. The use of PEMFs was associated with improved functional outcomes associated with a long-term effects [22]. However, the cartilage procedure creates a confounding factor and questions the actual benefit of PEMF in the long run. In order to avoid this ambiguity, we excluded patients who had undergone a prior cartilage procedure from our study group, hoping to generate results specific to the use of PEMFs.

When analyzing the data, it was observed that relatively younger patients (below 45 years) showed better results. However, it can be speculated that this finding may be due to the fact that we were dealing with only Grade 1 and 2 cartilage lesions and that the baseline knee function in patients younger than 45 would be expected to be higher in any case. The finding however, is relevant as it reiterates a positive effect of the treatment in early stages of cartilage damage, making it a viable modality towards delaying the progression of the pathology. Thamsborg et al. concluded that there was a definite beneficial effect with respect to stiffness in patients below the age of 65 [18].

PEMFs have an anti-inflammatory effect associated with the up-regulation of adenosine A2A receptors. This has been demonstrated in both bovine and human chondrocytes and synovial fibroblasts [11,23]. The modulation of these receptors is possibly one of the mechanisms by which the PEMF counteracts the effect of pro-inflammatory cytokines in explants of cartilage and synovial fibroblasts and prevents the progression to OA [7,11,12]. On the other hand, bovine and human models have shown that PEMFs through a synergy with insulin-like Growth Factor 1 (IGF-1) exerts a pro-anabolic activity enhancing chondrogenic differentiation and synthesis of extra-cellular matrix component [9,10,24].

In our experience, the use PEMFs is a valid and cost-effective therapeutic approach; it has advantages over the chronic use of NSAIDs or cortisone injections related to the absence of potential side effects [25,26].Moreover, it is a non-invasive treatment, free of complications, and it is well accepted by the patients. However, there are varieties of PEMFs protocols available, which differ for device characteristics (intensity and frequency of the magnetic field), application intervals and duration of treatment.

A long-term follow-up represents a point of strength in this investigation. All the published articles that investigated the use of PEMF in the past have a shorter follow-up (between 6 and 12 weeks) [14-19]. Moreover, we used several validated scoring systems in order to obtain information about all aspects of daily living and sport participation.

This study has a few limitations - the first being the relatively small sample size; the second is the absence a control group and randomization. We were unable to perform a post treatment arthroscopy or MRI in all the patients to assess progression of the lesion if any. We have attempted to limit any bias by performing a systematic prospective data collection with an independent reviewer of the data. We have been strict with the inclusion criterion which has reduced the number of patients we could follow.

In the future it will be useful to compare the outcomes of the treatment with PEMFs with other conservative therapeutic approaches such as oral medication (NSAIDs, glucosamine, chondroitin sulfate) or intra-articular injections (steroids, hyaluronic acid, PRP platelet-rich plasma). Also, an MRI study comparing pre-treatment and post-treatment findings would be useful in order to investigate if changes

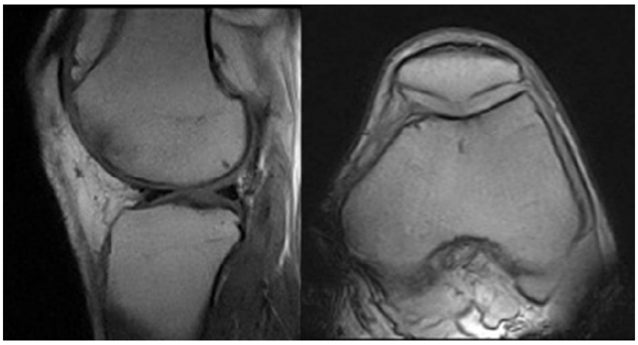

Figure 8: Coronal and axial MRI images of the knee showing improvement in the cartilage appearance at the lateral femoral condyle and trochlea as compared to Figure 1.

occur on a macroscopic level. Figure 8 show a post treatment MRI of the same patient (Figure 1 and 2) taken at final follow up with definite radiologic improvement.

Conclusions

In an era where cartilage lesions are being treated with regenerative techniques and stem cells, PEMF is a valid and useful conservative modality in the early stages of osteoarthritis. It can offer good symptomatic improvement but with ill sustained long term benefits; annual repetition of treatment may improve outcomes further. Follow up MRI and more randomized control trials, with a longer follow up period are required to ascertain its role vis-a-vis other conservative treatment options.

References

1. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, et al. (1997) Cartilage injuries: a review of 31,516 knee arthroscopies. Arthroscopy 13: 456-460.
2. Mankin HJ (1982) The response of articular cartilage to mechanical injury. J Bone Joint Surg Am 64: 460-466.
3. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G (2006) Intraarticular corticosteroid for treatment of osteoarthritis of the knee. Cochrane Database Syst Rev 2.
4. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, et al. (2006) Viscosupplementation for the treatment of osteoarthritis of the knee. Cochrane Database Syst Rev 2.
5. Gobbi A, Karnatzikos G, Mahajan V, Malchira S (2012) Platelet-rich plasma treatment in symptomatic patients with knee osteoarthritis: preliminary results in a group of active patients. Sports Health 4: 162-172.
6. Vangsness CT Jr, Spiker W, Erickson J (2009) A review of evidence-based medicine for glucosamine and chondroitin sulfate use in knee osteoarthritis. Arthroscopy 25: 86-94.
7. Ciombor DM, Aaron RK, Wang S, Simon B (2003) Modification of osteoarthritis by pulsed electromagnetic field--a morphological study. Osteoarthritis Cartilage 11: 455-462.
8. De Mattei M, Caruso A, Pezzetti F, Pellati A, Stabellini G, et al. (2001) Effects of pulsed electromagnetic fields on human articular chondrocyte proliferation. Connect Tissue Res 42: 269-279.
9. De Mattei M, Pasello M, Pellati A, Stabellini G, Massari L, et al. (2003) Effects of electromagnetic fields on proteoglycan metabolism of bovine articular cartilage explants. Connect Tissue Res 44: 154-159.
10. De Mattei M, Pellati A, Pasello M, Ongaro A, Setti S, et al. (2004) Effects of physical stimulation with electromagnetic field and insulin growth factor-I treatment on proteoglycan synthesis of bovine articular cartilage. Osteoarthritis Cartilage 12: 793-800.
11. De Mattei M, Varani K, Masieri FF, Pellati A, Ongaro A, et al. (2009) Adenosine analogs and electromagnetic fields inhibit prostaglandin E2 release in bovine synovial fibroblasts. Osteoarthritis Cartilage 17: 252-262.
12. Fini M, Giavaresi G, Torricelli P, Cavani F, Setti S, et al. (2005) Pulsed electromagnetic fields reduce knee osteoarthritic lesion progression in the aged Dunkin Hartley guinea pig. J Orthop Res 23: 899-908.
13. Sharrard WJ (1990) A double-blind trial of pulsed electromagnetic fields for delayed union of tibial fractures. J Bone Joint Surg Br 72: 347-355.
14. Callaghan MJ, Whittaker PE, Grimes S, Smith L (2005) An evaluation of pulsed shortwave on knee osteoarthritis using radioleucoscintigraphy: a randomised, double blind, controlled trial. Joint Bone Spine 72: 150-155.
15. Laufer Y, Zilberman R, Porat R, Nahir AM (2005) Effect of pulsed short-wave diathermy on pain and function of subjects with osteoarthritis of the knee: a placebo-controlled double-blind clinical trial. Clin Rehabil 19: 255-263.
16. Nicolakis P, Kollmitzer J, Crevenna R, Bittner C, Erdogmus CB, et al. (2002) Pulsed magnetic field therapy for osteoarthritis of the knee--a double-blind sham-controlled trial. Wien Klin Wochenschr 114: 678-684.
17. Pipitone N, Scott DL (2001) Magnetic pulse treatment for knee osteoarthritis: a randomised, double-blind, placebo-controlled study. Curr Med Res Opin 17: 190-196.
18. Thamsborg G, Florescu A, Oturai P, Fallentin E, Tritsaris K, et al. (2005) Treatment of knee osteoarthritis with pulsed electromagnetic fields: a randomized, double-blind, placebo-controlled study. Osteoarthritis Cartilage 13: 575-581.
19. Trock DH, Bollet AJ, Markoll R (1994) The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee and cervical spine. Report of randomized, double blind, placebo controlled trials. J Rheumatol 21: 1903-1911.
20. Vavken P, Arrich F, Schuhfried O, Dorotka R (2009) Effectiveness of pulsed electromagnetic field therapy in the management of osteoarthritis of the knee: a meta-analysis of randomized controlled trials. J Rehabil Med 41: 406-411.
21. Zorzi C, Dall'oca C, Cadossi R, Setti S (2007) Effects of pulsed electromagnetic fields on patients' recovery after arthroscopic surgery: prospective, randomized and double-blind study. Knee Surg Sports Traumatol Arthrosc 15: 830-834.
22. Varani K, De Mattei M, Vincenzi F, Gessi S, Merighi S, et al. (2008) Characterization of adenosine receptors in bovine chondrocytes and fibroblast-like synoviocytes exposed to low frequency low energy pulsed electromagnetic fields. Osteoarthritis Cartilage 16: 292-304.
23. Ongaro A, Pellati A, Masieri FF, Caruso A, Setti S, et al. (2011) Chondroprotective effects of pulsed electromagnetic fields on human cartilage explants. Bioelectromagnetics 32: 543-551.
24. Fini M, Torricelli P, Giavaresi G, Aldini NN, Cavani F, et al. (2008) Effect of pulsed electromagnetic field stimulation on knee cartilage, subchondral and epyphiseal trabecular bone of aged Dunkin Hartley guinea pigs. Biomed Pharmacother 62: 709-715.
25. Habib GS (2009) Systemic effects of intra-articular corticosteroids. Clin Rheumatol 28: 749-756.
26. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, et al. (2010) OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage 18: 476-499.