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Effects of pulsed electromagnetic fields on patients' recovery after arthroscopic surgery: prospective, randomized and double-blind study

C. Zorzi · C. Dall'Oca · R. Cadossi · S. Setti

Abstract Severe joint inflammation following trauma, arthroscopic surgery or infection can damage articular cartilage, thus every effort should be made to protect cartilage from the catabolic effects of pro-inflammatory cytokines and stimulate cartilage anabolic activities. Previous pre-clinical studies have shown that pulsed electromagnetic fields (PEMFs) can protect articular cartilage from the catabolic effects of pro-inflammatory cytokines, and prevent its degeneration, finally resulting in chondroprotection. These findings provide the rational to support the study of the effect of PEMFs in humans after arthroscopic surgery. The purpose of this pilot, randomized, prospective and double-blind study was to evaluate the effects of PEMFs in patients undergoing arthroscopic treatment of knee cartilage. Patients with knee pain were recruited and treated by arthroscopy with chondroabrasion and/or perforations and/or radiofrequencies. They were randomized into two groups: a control group (magnetic field at 0.05 mT) and an active group (magnetic field of 1.5 mT). All patients were instructed to use PEMFs for 90 days, 6 h per day. The patients were evaluated by the Knee injury and Osteoarthritis Outcome Score (KOOS) test before arthroscopy, and after 45 and 90 days. The use of non-steroidal anti-inflammatory drugs (NSAIDs) to control pain was also recorded. Patients were interviewed for the long-term outcome 3 years after arthroscopic surgery. Thirty-one patients completed the treatment. KOOS values at 45 and 90 days were higher in the active group and the difference was significant at 90 days ($P < 0.05$). The percentage of patients who used NSAIDs was 26% in the active group and 75% in the control group ($P = 0.015$). At 3 years follow-up, the number of patients who completely recovered was higher in the active group compared to the control group ($P < 0.05$). Treatment with I-ONE aided patient recovery after arthroscopic surgery, reduced the use of NSAIDs, and also had a positive long-term effect.

Keywords Cartilage · Chondroprotection · Pulsed electromagnetic fields · Arthroscopy · Knee

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Introduction

Inflammatory processes may cause serious damage to joint cartilage [10, 12, 15]. The activity of inflammatory cells and the release of pro-inflammatory cytokines in the synovial fluid are responsible for catabolic effects on the cartilage matrix, which degenerates, subsequently leading to loss of mechanical function of the joint cartilage.

Inflammatory processes of the joint may be secondary to trauma, surgery, extreme joint torsion and infection [2, 13], and are often associated with synovial reaction.

To protect the joint cartilage from the catabolic effect of pro-inflammatory cytokines, exposure to inflammatory cells should be limited or prevented. Neutrophils, in small amounts, have been detected on the surface of the joint cartilage in the presence of inflammatory processes; they give rise to enzymatic activities, especially metalloproteinases that can degrade the cartilage matrix [17, 18].

An essential role in preserving the cartilage is played by drug therapy, whether administered to patients by general route, or used locally, e.g. by direct injection into the joint. To prevent the detrimental effect of the inflammation of the joint cartilage, studies have been performed to identify new molecules or techniques able to control the inflammatory processes. One up-to-date approach undoubtedly involves the study of the molecules having an adenosine agonist action on the A_{2A} receptors of the inflammatory cells. Activation of the A_{2A} receptors by adenosine is the mechanism by which the body controls inflammatory phenomena [11, 17]. Recently, molecules with A_{2A} agonist action have shown to prevent articular cartilage degeneration when experimental septic arthrosis is induced, thus these drugs are considered chondroprotectors [4].

In 2002, an in vitro study, with human neutrophils, showed that pulsed electromagnetic fields (PEMFs) of defined intensity and physical characteristics, demonstrated an adenosine agonist effect for A_{2A} receptors [19]. This observation suggests that these PEMFs might be used to control joint inflammation and ultimately protect articular cartilage [8].

Furthermore, ex-vivo experimental observations, using full-thickness bovine articular cartilage explants, show that PEMFs prevent the cartilage matrix degeneration induced by the pro-inflammatory cytokine, IL-1. Under the same experimental conditions, PEMFs were able to increase proteoglycan synthesis and favour the anabolic effect of IGF-1 on cartilage explants [5, 6].

In in vivo studies, PEMFs increased the expression of TGF-β1 in articular cartilage and inhibited TNF-α synthesis [1, 3]. Finally, in a model of spontaneous osteoarthritis in Dunkin Hartley it was demonstrated that PEMFs can prevent cartilage degeneration and sclerosis of subchondral bone, thus preserving cartilage integrity and its mechanical properties [3, 9]. Finally, in sheep, PEMFs have been able to favour knee autologous osteochondral graft healing [16].

The pre-clinical studies above summarized provide the rational for the clinical use of PEMF stimulation to control inflammation and its catabolic effects on articular cartilage [8].

Every time a joint is subjected to surgical intervention—even a minimally invasive one, such as arthroscopy—the trauma produced is associated to an inflammatory response of varying intensity. In a group of patients undergoing knee arthroscopic surgery we sought to assess whether the treatment with PEMFs could be used to control inflammation and enhance functional recovery.

The aims of this pilot, prospective, randomized and double-blind study were to assess the tolerance to the treatment used for the first time within 1 week after an arthroscopic procedure and the effects on functional recovery at 45 and 90 days evaluated by Knee injury and Osteoarthritis Outcome Score (KOOS) clinical score [14].

Materials and methods

Patients, male and female, aged between 18 and 70, presenting painful symptoms at the knee were recruited at the Sacro Cuore Hospital (Negrar, Verona, Italy). Exclusion criteria were: rheumatoid arthritis, autoimmune disease, systemic disease, knee instability, severe axial deformity, body mass index > 32. All patients gave their consent to participate in the study.

Patients were treated in arthroscopy by chondroabrasion and/or perforation and/or radiofrequency. During arthroscopic surgery the severity of the cartilage lesion was scored as per Outerbridge.

The patients began PEMFs treatment within 5 days after arthroscopy with an I-ONE generator (IGEA, Carpi, Italy; Fig. 1). Half of the patients used a device that supplied the coil with electric pulses at 75 Hz; the coil generated a peak magnetic field of 1.5 mT (active group). The other patients (control group) used a device that supplied the coil at minimum current to allow device indicators to function, but the magnetic field generated by the coil was 0.05 mT (i.e. 300 times lower than the active device), well below the threshold value required for an adenosine agonist effect or to modulate proteoglycan synthesis in cartilage explants [7, 19]. The devices were fitted with a clock to memorize the hours of treatment, in order to monitor patients' compliance. Patients were advised to use the device 6 h per day for 90 days.

Patients were instructed to interrupt the treatment and to report to the hospital if any local effects, like burning sensation or skin irritation, was experienced.

The medical staff was unable to differentiate between them. The status of the stimulators was identified only after all patient evaluations were completed.
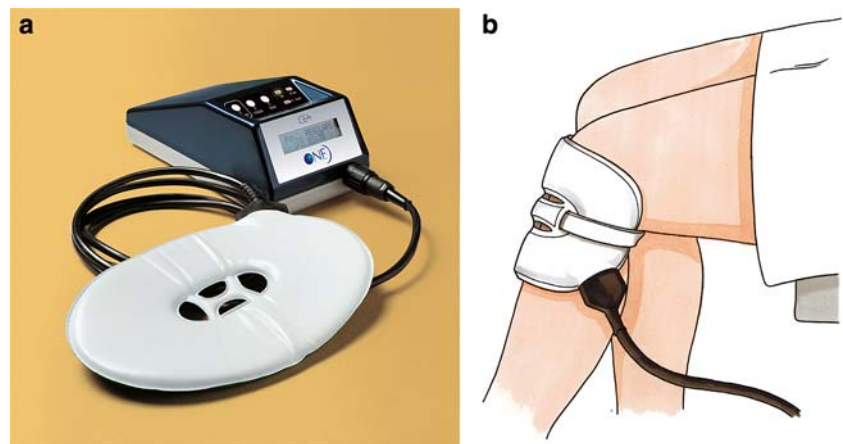
Patients were randomized to receive either active or control stimulators. To ensure uniformity between these two groups, the patients were divided into four categories based on the results of Outerbridge grading during arthroscopy. The patients were assigned either to the active or control group according to a computer generated schedule. A random number seed was entered into the computer to generate a list that assigned equal numbers of active and control stimulators (blocks of 4, 2 active and 2 control).

At each visit, before arthroscopy, and 45 and 90 days after the start of PEMF treatment, with the assistance of the medical staff, the patients were requested to complete the KOOS test, which includes evaluation of joint rigidity and functional limitations. KOOS awards a maximum score of 100 points corresponding to an optimal state of health. All scores were calculated at the end of the study by a bio-statistician unaware of the experimental conditions. The administration of non-steroidal anti-inflammatory drugs (NSAIDs) is routinely recommended for 2 weeks following arthroscopy; patients were instructed to record if the use of NSAIDs was maintained after 3 weeks to control pain and joint swelling at the operated knee.

Three years after the end of the study, all patients were interviewed about their long-term satisfaction by hospital authorized staff, unaware whether the patient had used an active or control stimulator. The patients were asked if they returned to normal daily activity, if they could practice sport activity without pain or limitations, if the use of NSAIDs was not necessary for knee pain control, if the patient had not undergone or was not scheduled for further surgical procedure at the knee. Only when all responses were positive the outcome was scored as "positive."

Statistical analysis

Based on an expected difference of ten points between the two groups on KOOS test, we evaluated that to detect a significant difference, the number of subjects required per group was 15. Average data were compared by Student's t-test; comparisons between the two groups for the use of drugs and for long-term results was made by Chi square test and contingency table analysis.

Results

Thirty-four patients were enrolled, three patients of the control group (Outerbridge lesion IV two patients and Outerbridge II one patient) withdrew from the study within 2 weeks and were not included in the result analysis. We evaluated 31 patients (15 men, 16 women). Nineteen belong to the active group, 12 to the control group (Table 1). The average age in the control group was 47 ± 19 years and 51 ± 17 years in the active group. Chondroabrasion was performed on all patients; 6 patients also underwent perforations, and 16 also radiofrequencies. The stimulation with I-ONE started within 1 week after arthroscopic surgery in both groups.

With regards to the first aim of the study concerning tolerance to treatment, we did not observe any side effects that led to treatment interruption.

The mean length of treatment was 4.5 ± 2.2 h for patients in the active group and 4.2 ± 3.9 h for patients in the control group ($P = $ ns).

Figure 2 shows that changes in KOOS values in both groups. Before arthroscopy, the KOOS values were not significantly different between the two groups:

Table 1 In the table are reported all patients data recruited in the study

Patient	Outerbridge group	Sex	Previous surgery	Site[a]	Treatment[b]
Active group					
MG	I	M	None	F	1 + 2
DR	II	F	None	F	1 + 2
GG	II	M	None	F	1
SM	II	M	None	F, P	1 + 2
SL	II	M	None	F, T	1 + 2
VC	II	F	None	F, T	1 + 2
CG	II	M	None	F	2
AG	III	F	None	F, T, P	1 + 2 + 3
GR	III	M	None	F, T	1
LG	III	M	None	F, P	1
BG	III	F	None	F, T	1 + 2
PS	III	F	None	F, P	1 + 2
AA	III	M	None	F, T, P	1
RC	IV	F	None	F, T, P	1
SR	IV	M	None	F, T	1
AA	IV	F	1	P	1 + 2
ML	IV	F	None	F, T, P	1 + 2
PM	IV	F	None	F, T, P	1 + 3
VT	IV	F	1	F, T	1 + 2
Control group					
MF	I	F	None	F, P	1 + 2
BD	II	M	None	P	1
PE	II	M	None	P	1
SM	II	F	None	F	1 + 2
BR	II	M	None	F, T	1 + 2
CM	II	M	None	F	1 + 2
SG	III	M	None	F, T	1 + 2
BML	III	F	None	F	1 + 2 + 3
GG	III	M	None	F, T	1 + 3
NMC	IV	F	None	F, P	1 + 2 + 3
PR	IV	F	None	F, T	1 + 2
BL	IV	F	1	F, T	1

[a] *F* femur, *T* tibia, *P* patella

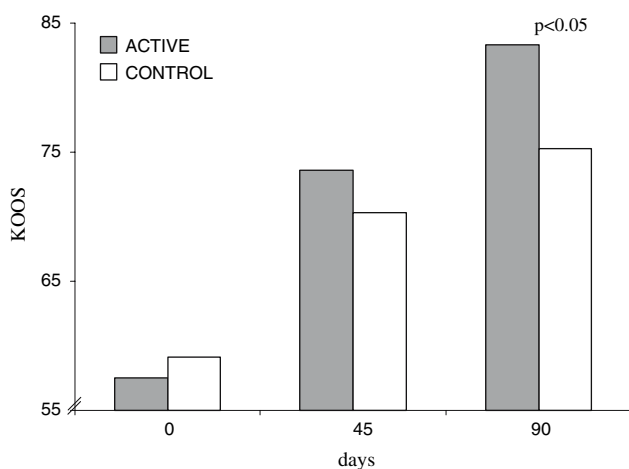[b] 1 represents chondroabrasion, 2 represents radiofrequency, 3 represents perforation

Fig. 2 Average KOOS test points before, 45 and 90 days after arthroscopic surgery

57.5 ± 8.5 active and 59.0 ± 10.3 control. The KOOS values were higher in the active group than in the control group both at 45 days (73.6 ± 10.3 vs 70.3 ± 14.9, ns) and at 90 days (83.6 ± 7.3 vs 74.7 ± 13.6, $P < 0.05$). More patients used NSAIDs in the control group (75%) than in the active group (26%), $P = 0.015$.

Table 2 shows the results of the interview at 3 years follow-up; the number of patients that returned to the normal daily and sport activity (positive outcome) was significantly higher in the active group ($P < 0.05$).

Discussion

Inflammatory response in a joint following surgery represents a potentially harmful event for the articular cartilage, which ultimately may jeopardize the positive effects expected by surgery [10]. We hypothesized that patients, undergoing arthroscopic surgery, could benefit of the treatment with PEMFs leading to early inflammation control and return to normal activity [8].

This pilot, randomized, prospective and double-blind study was designed to investigate the tolerance of the treatment, immediately after arthroscopic surgery, and to study the effect on the functional recovery of the patients.

Concerning tolerance to treatment, we did not observe any side effects that led to treatment interruption. Overall, the patient compliance was good, suggesting that the treatment was well accepted. The three drop-out patients belong to the control group; after a few days the patients decided to return the device and to interrupt the treatment for personal reasons.

Patients were allowed to use NSAIDs within the first 45 days to control pain. Three weeks after arthroscopy 26% patients in the active group and 75% in the control group were using NSAIDs. Not only the KOOS score was significantly higher in the active group at 90 days, but also it showed an effective benefit for the patients: scores were higher by almost ten points on average.

Table 2 Long-term results at 3 year follow-up

	Return to normal activities	Functional limitation	Not available
Active	10	6	3
Control	1	7	4

$P < 0.05$

Not all patients could be reached at long-term follow-up (84% active group, 66% control group); nevertheless, the results of the interview confirmed a more favourable outcome for patients in the active group than those in the control one. On the basis of the pre-clinical work, we can hypothesize that the PEMF treatment was able to control effectively inflammation, ultimately resulting in chondroprotection.

In this pilot study, we did not attempt to quantify the effect of PEMFs on the cartilage itself, although we could expect a positive effect from pre-clinical data [5, 8, 19]. A long-term instrumental investigation on a larger group of patients would be required to quantify the effect on articular cartilage, this was not the scope of this first pilot study. Although the number of patients in our study is not large, the study design, active vs sham-control, is adequate for the investigation of the effects of PEMFs in this cohort of patients undergoing arthroscopic surgery.

In conclusion, our finding demonstrates that patients' acceptance of I-ONE PEMF treatment is high and it can be applied immediately after arthroscopic surgery, without side effects, to improve functional recovery.

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