Short-Term Efficacy of Pulsed Electromagnetic Field Therapy on Pain and Functional Level in Knee Osteoarthritis: A Randomized Controlled Study

Diz Osteoartiritinde Pulse Elektromanyetik Alan Tedavisinin Ağrı ve Fonksiyonellik Üzerine Kısa Dönemde Etkisi, Randomize Kontrollü Çalışma

Duygu Geler Külcü¹, Gülçin Gülşen¹, Elif Çiğdem Altunok²

¹Yeditepe Üniversitesi Tıp Fakültesi, Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, İstanbul, Türkiye ²Yeditepe Üniversitesi Tıp Fakültesi, Biyoistatistik Bilim Dalı, İstanbul, Türkiye

Abstract

Objective: We aimed to determine the efficacy of pulsed electromagnetic field therapy on pain and functional level in knee osteoarthritis when compared to therapeutic ultrasound (US) and controls.

Material and Methods: Forty-five patients with knee osteoarthritis (mean age: 63.5±10.2 years) were randomly assigned to three groups. The first group received pulsed electromagnetic field therapy (frequency: 2 Hz, 100 Hz, 25 Hz consecutively, 35 minutes/ session), the second group received therapeutic US (frequency: 1 MHz, power: 1.5 watt/cm² continuously, 10 minutes/session) and the third group served as the no- treatment control group. Evaluations were done at baseline and at the end of the treatment (third week). Assessment parameters were pain, stiffness and functional level scores of the Western Ontario and McMaster Universities (WOMAC) questionnaire and pain severity evaluated by Visual Analog Scale (VAS) (0-10).

Results: VAS (p=0.005), WOMAC pain score (p=0.001), WOMAC joint stiffness score (p=0.027) and WOMAC functional level score (p=0.003) significantly improved in the first group. VAS (p=0.001), WOMAC pain scores (p=0.008), WOMAC stiffness scores (p=0.012) and WOMAC functional level (p=0.004) scores significantly improved in the second group as well. No change was observed in any assessment parameter in the third group (p>0.05). There were differences between groups regarding the percent change in VAS scores (p<0.001), WOMAC pain scores (p<0.001), WOMAC joint stiffness scores (p=0.013) and WOMAC functional level scores (p<0.001) after the treatments.

Conclusion: Both the pulsed electromagnetic field and therapeutic US were significantly more effective than no treatment. The pulsed electromagnetic field may be applied as an effective and alternative therapy approach in knee osteoarthritis.

(Turk J Rheumatol 2009; 24: 144-8)

Key words: Pulsed electromagnetic field, knee, osteoarthritis, ultrasound

Received: 28.10.2008 Accepted: 10.03.2009

Özet

Amaç: Diz osteoartiritinde pulse elektromanyetik alan tedavisinin ağrı ve fonksiyonel düzey üzerine etkisini ultrason tedavisi ve kontrolle karşılaştırarak araştırmaktır.

Yöntem ve Gereçler: Kırkbeş diz osteoartiriti olan hasta randomize olarak üç gruba ayrıldı (ortalama yaş= 63.5 ±10.2 yıl). Birinci gruba pulse elektromantetik alan tedavisi (frekans: sırasıyla, 2 Hz, 100 Hz, 25 Hz, 35 dakika/seans), ikinci gruba ultrason tedavisi (frekans: 1 MHz, güc:1,5 watt/cm² devamlı,10 dakika/seans) uygulandı. Üçüncü grub kontrol grubu oldu. Değerlendirmeler başlangıçta ve tedavi sonunda (üç hafta sonra) yapıldı. Değerlendirme değişkenleri, Western Ontario ve McMaster Üniversiteleri Anketi'nin (WOMAC) ağrı, eklem sertliği ve fonksiyonel düzey skorları ve görsel ağrı skalalasına (GAS) göre (0-10) ağrı şiddeti idi.

Bulgular: Birinci grupta, GAS skoru (p=0.005), WOMAC-ağrı skoru (p=0.001), WOMAC eklem sertliği skoru (p=0.027), WOMAC fonksiyonel düzey skoru (p=0.003) açısından anlamlı iyleşme kaydedildi. İkinci grupta da WOMAC ağrı (p=0.008), WOMAC eklem sertliği (p=0.012), WOMAC fonksiyonel düzey skorları (p=0.004) ve GAS (p=0.001) skorlarında anlamlı düzelme saptandı, Üçüncü grupta hiçbir değerlendirme parametresi açısından anlamlı değisiklik gözlenmedi (p>0.05). Gruplar arasında değerlendirme parametrelerinin tedavi sonundaki yüzde değişimleri açısından GAS skoru (p<0.001), WOMAC ağrı skoru (p<0.001), WOMAC eklem sertliği skoru (p=0.013) ve WOMAC fonksiyonel düzey skoru (p<0.001) açısından fark saptandı.

Sonuç: Hem pulse elektromanyetik alan tedavisi hem töropatik ultrason tedavisi kontrol grubuna göre anlamlı olarak daha etkili bulunmuştur. Pulse elektromanyetik alan tedavisi diz osteoartriti tedavisinde etkili bir alternatif tedavi yaklaşımı olarak uygulanabilir. (*Turk J Rheumatol 2009; 24: 144-8*)

Anahtar sözcükler: Pulse elektromanyetik alan, diz, osteoartrit, ultrason

Alındığı Tarih: 28.10.2008 Kabul Tarihi: 10.03.2009

21. Ulusal FTR Kongresi

Address for Correspondence / Yazışma Adresi: Dr. Duygu Geler Külcü, Yeditepe Üniversitesi Tıp Fakültesi, Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, İstanbul, Türkiye Tel.: +90 216 578 40 38 Faks: +90 216 467 88 69 E-posta: d_geler@yahoo.com.tr

Introduction

Osteoarthritis (OA) is the most common rheumatologic disease and commonly affects the large weight-bearing joints, such as the hips and the knees (1). Decrease in the content of aggrecan and collagen, and increase in collagenases result with the breakdown and loss of the cartilage of the effected joint (2). Degeneration and inflammation of the cartilage can stimulate new bone outgrowths to form around the joints. These degenerative changes lead to joint pain, swelling and stiffness (1).

Since no treatment can stop osteoarthritic process, the treatment of knee OA (KOA) has been focused on symptom relief and function improvement. Physical agents such as superficial and deep heat, cold, electrotherapy and exercises have been used alone or in combination for many years (3. 4). However, an opthimal therapy for the management of KOA has not been developed yet. Therapeutic US is one of the most prefered physical agent for the treatment of KOA in routine daily clinical practice although it is not supported by clinical trials and not recommended by EULAR and OARSI guidelines. It is a kind of diathermy (deap heat) delivered by high-frequency sound waves (5). It relieves pain, decreases muscle spasm, increases collagen extensibility and accelerates metabolic processes (6) by providing temperature elevations up to 4 -5 degree at depths of 8 cm and by micromassage effect (7).

Pulsed electromagnetic field (PEMF) is rarely prefered in the treatment of KOA in clinical practice. The PEMF was initially used in the early 1970s for the treatment of soft tissue injuries (8). Its most accepted effect is promoting bone and cartilage repair, particularly in case of delayed healing such as non-union fractures (8). But it has also been used in the treatment of the non-fracture musculoskeletal conditions (9-14). The action of PEMF is based on creating small electrical fields in tissue and thereby promoting biological effects (15). Furthermore, PEMF has some advanteges such as non-contact with the skin, has few contrendications and complications, has no detectable thermal effect and it does not take time of the therapist. So it is suggested that, PEMF should be an alternative and attractive therapy choice for KOA. There are few studies investigated the effect of PEMF in KOA. The previous studies were either animal studies (2, 16) or sham controlled studies which reported positive effects (17-19). To our knowledge, the efficacy of PEMF in KOA has not been investigated by comparing it to any physical agent yet. The aim of this study is to investigate the effect of PEMF on pain intensity and functional level of the patients with KOA by comparing to that of therapeutic US therapy and to that of no ttreatment control group.

Material and Methods

Sample size

A power analysis indicated that a sample size of 45 patients would provide 80% power at an alpha level of 0.05 (effect size: 0.506).

Patient population

Fiftyfive patients, who admitted with knee pain lasted for at least 3 months were evaluated. Patients were assessed by one of the two authors by history and detailed physical examination. Laboratory tests (whole blood count, C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor and routine biochemical tests) were assessed to rule out secondary OA. All patients were initially guestioned for age, sex, weight and height. The diagnosis of KOA was based on the American Collage of Rheumatology criteria (20). Patients who had not responded adequately to treatment with nonsteroidal anti-inflammatory drugs, had grade II-III Kellgren-Lawrence (21) scores and had no limitation in range of motion were included to the study. Exclusion criteria were as follows: 1.secondary OA. 2. contraindications for PEMF and US therapy such as tuberculosis, pregnancy, malignancy, cardiac pacemaker or any implanted electrical device, atrophic skin or scar tissue on the knee region. bleeding disorders, insensitivity, edema and ischemia, 3. unable to understand the guestionnaires. Furthermore patients were excluded from the study if they had been on pyhsical therapy programme or had recieved intraarticular injections in the previous 6 months, had undergone an operation for any knee pathology previously. Eight patients were excluded from the study. Two patients did not participate because of inconsiderable reasons so 45 patients completed the study. All participants gave written informed constant. The study was approved by the ethics commitee of the university.

Randomization

Patients were randomly allocated to three groups by sequential assignment, according to their application turns. First group (1st, 4th, ...43rd) recieved PEMF therapy, second group (2nd, 5th, ...44th) recieved US therapy, third group (3rd, 6th, ...45th) recieved no treatment. Figure 1 shows the randomization and follow-up process of the groups. Neither the assessors nor the patients were blinded.

Therapy protocols: PEMF group

PEMF therapy was applied by a magnetotherapy device (BodyMag, manufactured by Eltech S.r.I, Treviso, Italy). Both knee of the patients were put in the middle portion of the big cycle solenoid applicator in supine position. The fre-



Figure 1. Flow-diagram of the patients

quency, intensity and application duration/session were selected according to the recommendations of the manufacturer. PEMF was applied in a frequency of 2 Hz, 100 Hz and 25 Hz, consecutively. Intensity variated between 2mT and 10 mT during the application. A therapy session lasted for 35 minutes and 15 sessions performed during 3 weeks (5 sessions/week).

US therapy group

The skin was coated with an acoustic gel not containing any pharmacologically active substance. US was then applied to the superomedial and lateral parts of the knee by the same therapist stroking the applicator in circular movements. The transducer head was applied to the knee at right angles to sustain maximal absorption of the ultrasound energy. Continuous ultrasonic waves with 1 MHz frequency and 1.5 watt/cm² power were applied with a 3 cm diameter applicator ultrasound equipment (Chattanooga, TN, USA.). US therapy lasted for 10 minutes/ session.

Third group served as control. Only the third group was allowed to receive paracetamol when needed during the study.

Outcome measures

Severity of joint pain, joint stiffness and physical function levels were evaluated as outcome measures. Assessment tools were Visual Analoge Scale (VAS) (from no pain=0 to unbearable pain=10) and Western Ontario and McMaster Universities (WOMAC) questionnaire. WOMAC is a validated, disease specific and sensitive measurement of symptom related to KOA (22). It has 3 parts which measures pain, stiffness and physical function. The validity of Turkish version of WOMAC questionnaire has been well documented (23). WOMAC scores were recorded on a Likert scale of 0 -4, where 0= no pain/ limitation and 4=very severe pain/limitation. Maximum scores for stiffness, pain and physical function were 8, 20 and 68 respectively.

Statistical analysis

Statistical tests were performed by SPSS program (version 11.0). All data was expressed as mean±standard

deviation or median (minimum-maximum). Demographic characteristics were compared by χ^2 test and ANOVA. Kruskal Wallis test was used in order to compare the differences between changes of scores during time among the groups. For the significant differences according to Kruskal Wallis variance analysis, Mann-Whitney U test was used to analyze which group is different from the other in terms of those parameters. Bonferroni correction was applied for all possible multiple comparisons. Differences within groups were analyzed by Wilcoxon signed rank test.

Results

All of the patients had bilateral KOA. The right knee was evaluated in all patients. 45 patients (63.5±10.2 vrs of age) completed the study. Demographic characteristics are presented in Table 1. No complication has been noted in group I and II. There were no significant differences with respect to age, gender, body mass index, and Kellgren-Lawrence scores among groups. All outcome parameters improved significantly within group I and group II. No change was observed in any outcome measure within group III (Table 2). There were differences among groups regarding the percent change of VAS scores (p<0.001), WOMAC pain scores (p<0.001), WOMAC joint stiffness scores (p=0.013) and WOMAC functional level scores (p<0.001) after the treatments (Table 3). There were no differences between first and second group regarding the improvements in VAS, WOMAC pain, joint stiffness and functional level scores (Table 3).

Discussion

In the present study, PEMF therapy has been found to be effective in reducing pain and stiffness and improving functional level in KOA.

There are a few studies which investigated the effectiveness of PEMF in KOA. Benefical effects of PEMF have been presented by either clinical studies (17-19) or animal experiments (2, 16) but its efficacy has not been compared to that of another physcial agent yet. Jacobson et al. (19) found 46% improvement in pain reduction in a

		Group I (PEMF)	Group II (US)	Group III (control)	Р
		n=15	n=15	n=15	
Age (years)		65.8±10.3	63.1±13.6	62.0±6.0	0.656
Gender	Female	n=10	n=13	n=12	0.400
	Male	n=5	n=2	n=3	
Weight (kg)		71.6±8.2	68.5±16.0	68.5±5.1	0.462
Height(cm)		165.0±8.7	162.5±6.8	161.7±3.3	0.755
BMI (kg/m ²)		0.43±0.01	0.42±0.1	0.42±0.02	0.987
Kellgren-	Grade 2	n=7 (47%)	n=7 (47%)	n=10 (67%)	0.397
Lawrence score	Grade 3	n=8 (53%)	n=8 (53%)	n=5 (33%)	

	Group I (PEMF) (n=15)			Group II (US) (n=15)		Group III (control) (n=15)			P**	
	Pre- treatment	Post- treatment	P*	Pre- treatment	Post- treatment	Р*	Pre- treatment	Post- treatment	Р*	
VAS	5 (2-10)	3 (0-6)	0.005	7 (5-10)	2 (0-6)	0.001	7 (4-9)	5 (2-10)	0.344	< 0.000
WOMAC-pain	7 (2-16)	4 (0-8)	0.001	9.5 (1-17)	4.5 (0-11)	0.008	7 (5-9)	8 (5-9)	0.059	<0.000
WOMAC-stiffness	4 (0-7)	1 (0-5)	0.027	3.5 (2-11)	2 (0-7)	0.012	4 (2-7)	3 (2-6)	0.609	0.013
WOMAC- functional level	27 (6-42)	16 (0-26)	0.003	31 (6-41)	11.5 (0-26)	0.004	25 (17-35)	24 (18-30)	0.675	<0.000

PEMF: Pulsed electromagnetic field, VAS visual analog scale, WOMAC: Western Ontario Macmaster Questionnaire, *within groups, **between groups

		VAS-percent change	WOMAC-pain- percent change	WOMAC-stiffness- percent change	WOMAC-functional level-percent change
Group l (PEMF)	Group II (US)	0.183	0.979	0.536	0.244
	Group III (control)	0.008	<0.000	0.005	0.001
Group II (US)	Group III (control)	<0.000	0.001	0.003	0.001

similar sample size of the patients with KOA. Nicolacis et al. (18) also used WOMAC, and reported that PEMF reduced pain and improved daily living activities. Fischer et al. (15) and Thamsborg et al. (17) reported similar results on pain reduction even for the long-term. The results of the present study are similar to those of recent studies. However the frequency, duration of each session and total number of sessions are different from each other among these studies.

The PEMF has been shown to increase upregulation of gene expression for aggrecan, type II collagen synthesis (24, 25) and TGF β (26-28). TGF β stimulates the aggrecan and collagen synthesis, suppresses the pro-enzyme forms of collagenase and interleukin-1 (29), which may result with pain reduction. The opthimal frequency, intensity and duration required for the completion of these biological effects and for total recovery in human tissues, are unknown. Recent studies have suggested that PEMF activates cellular signaling process rapidly within few minutes (30, 31) and signaling is largely blunted after 30 minutes. So, 35 minutes/session may be sufficient for this process. Further histopathological analysis are needed to find out the opthimal dosage and duration.

In the present study, the improvements in pain relief, joint stiffness and functional level in the PEMF group have not been found superior to those of the US therapy group. Our US application form has been recommended for the restricted movements (32) and pain relief (33). Improvement in stiffness level of PEMF group should be due to enhanced blood circulation in the periarticular compartment. PEMF has been shown to activate synthesis of nitric oxide (34) which may enhance blood flow. Further studies should analyze long-term results in severe OA with restricted movements.

The effect of US therapy on pain relief in KOA has been documented by several studies (35-37). The US therapy has been compared to other physical agents such as shortwave diathermy, galvanic or interferancial current (36, 38). According to a meta-analysis, most of them have been reported that therapeutic US is effective but not superior to other physical agents (37). In the present study, PEMF has been compared to US therapy and similar results for pain relief have been found. There are several limitations of these recent studies such as heterogenous groups, untrastfull validty and reliability of the outcome measures, or lack of a control group. Only one study compared therapeutic US to that of placebo in KOA (38). US therapy has been found effective on pain and stiffness level but they have found no difference compared to sham (37). Similar to the others (35, 36), dosages were unclear in their study, too.

In the present study, both US and PEMF have been found effective compared to control group. The control group did not recieve sham either for US or PEMF. So, the placebo effect of both therapies should not be taken into consideration in the present study.

In conclusion, both therapy approaches were considered effective and PEMF should be used in higher rates in routine clinical practice as an alternative therapy method. For a more definitive answer on the use of PEMF in KOA, larger randomized studies are needed.

Conflict of Interest

No conflict of interest is declared by authors.

References

- Mankin H.J, Brandt K.D. Pathogenesis of osteoarthritis. In: Ruddy S, Haris ED, Sledge CB (eds). Kelley's Textbook of Rheumatology (vol II). Philadelphia: WB Saunders Company, 2001; 1391-407.
- Ciombor DM, Aaron RK, Wang S, Simon B. Modification of osteoarthritis by pulsed electromagnetic field a morphological study. Osteoarthritis Cartilage 2003; 11: 455-62.
- Hough AJ. Pathology of Osteoarthritis. In: Koopman WJ (ed). Arthritis and Allied Conditions. Baltimore:Williams & Wilkins, 1997; 1945-68.
- 4. Recommendations for the medical management of osteoarthritis of the hip and knee. American College of Rheumatology subcommittee on osteoarthritis guidelines. 2000 update. Arthritis Rheum 2000; 43: 1905-15.
- 5. Puett DW, Griffin MR. Published trials of nonmedicinal and noninvasive therapies for hip and knee osteoarthritis. Ann Intern Med 1994; 121: 133-40.
- 6. Kozanoglu E, Basaran S, Guzel R, Guler-Uysal F. Short term efficacy of ibuprofen phonophoresis versus continuous ultrasound therapy in knee osteoarthritis. Swiss Med Wkly 2003; 133: 333-8.
- Basford JR. Physical Agents. In: DeLisa JA, Gans BM (eds). Rehabilitation Medicine: Principles and Practice. Philadelphia: Lippincott-Raven, 1998; 483-503.
- 8. Wilson DH. Treatment of soft-tissue injuries by pulsed electrical energy. Br Med J 1972; 2: 269-70.
- Trock DH, Bollet AJ, Markoll R. The effect of pulsed electromagnetic fields in the treatment ofosteoarthritis of the knee and cervical spine: report of randomized, double blind, placebocontrolled trials. J Rheumatol 1994; 21: 1903-11.
- Binder A, Parr G, Hazleman B, Fitton-Jackson S. Pulsed electromagnetic field therapy of persistent rotator cuff tendinitis: A double-blind controlled assessment. Lancet 1984; 31: 695-8.
- 11. Bassett CAL. Beneficial effects of electromagnetic fields. J Cell Biochem 1993; 51: 387-93.
- Trock DH, Bollet AJ, Dyer RH Jr, Fielding LP, Miner WK, Markoll R. A double-blind trial of the clinical effects of pulsed electromagnetic fields in osteoarthritis. J Rheumatol 1993; 20: 456-60.
- 13. Bassett AL, Schink-Ascani M, Lewis SM. Effects of pulsed electromagnetic fields on Steinberg ratings of femoral head osteonecrosis. Clin Orthop 1989; 246: 172-85.
- Aaron RK, Lennox D, Bunce GE, Ebert T. The conservative treatment of osteonecrosis of the femoral head: a comparison of core decompression and pulsing electromagnetic fields. Clin Orthop 1989; 249: 209-18.
- Thamsborg G, Florescu A, Oturai P, Fallentin E, Tritsaris K, Dissing S. Treatment of knee osteoarthritis with pulsed electromagnetic fields: a randomized, double-blind, placebocontrolled study. Osteoarthritis Cartilage 2005; 13: 575-81.
- Kumar VS, Kumar DA, Kalaivani K, Gangadharan AC, Raju KV, Thejomoorthy P, et al. Optimization of pulsed electromagnetic field therapy for management of arthritis in rats. Bioelectromagnetics 2005; 26: 431-9.
- 17. Fischer G, Pelka RB, Barovic J. Adjuvant treatment of knee osteoarthritis with weak pulsing magnetic fields. Results of a placebo-controlled trial prospective clinical trial. Z Orthop Ihre Grenzgeb 2005; 143: 544-50.
- Nicolakis P, Kollmitzer J, Crevenna R, Bittner C, Erdogmus CB, Nicolakis J. Pulsed magnetic field therapy for osteoarthritis of the knee-a double-blind sham-controlled trial. Wien Klin Wochenschr 2002; 30: 953.
- 19. Jacobson JI, Gorman R, Yamanashi WS, Saxena BB, Clayton L. Low-amplitude, extremely low frequency magnetic fields for

the treatment of osteoarthritic knees: a double-blind clinical study. Altern Ther Health Med 2001; 7: 54-64.

- Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 1986; 29: 1039-49.
- 21. Ravaud P, Auleley GR, Amor B, Dougados M. Radiographic assessment of progression in knee osteoarthritis. J Rheumatol 1995; 24: 129-31.
- 22. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): A Review of Its Utility and Measurement Properties. Arthritis Care Res 2001; 45: 453-61.
- 23. Tuzun EH, Eker L, Aytar A, Daskapan A, Bayramoglu M. Acceptability, reliability, validity and responsiveness of the Turkish version of WOMAC osteoarthritis index. Osteoarthritis Cartilage 2005; 13: 28-33.
- 24. Aaron RK, Ciombor DM. Acceleration of experimental endochondral ossification by biophysical stimulation of the progenitor cell pool. J Orthop Res 1996; 14: 582-9.
- Ciombor DM, Lester G, Aaron RK, Neame P, Caterson B. Low frequency EMF regulates chondrocyte differentiation and expression of matrix proteins. J Orthop Res 2002; 20: 40-50.
- Aaron RK, Ciombor DM, Keeping H, Wang S, Capuano A, Polk C. Power frequency fields promote cell differentiation coincident with an increase in transforming growth factorbeta(1) expression. Bioelectromagnetics 2000; 21: 73.
- Lohmann CH, Schwartz Z, Liu Y, Guerkov H, Dean DD, Simon B, et al. Pulsed electromagnetic field stimulation of MG63 osteoblast-like cells affects differentiation and local factor production. J Orthop Res 2000; 18: 637-46.
- Aaron RK, Wang S, Ciombor DM. Upregulation of basal TGFbeta1 levels by EMF coincident with chondrogenesis-implications for skeletal repair and tissue engineering. J Orthop Res 2002; 20: 233-40.
- 29. Chandrasekhar S, Harvey AK. Transforming growth factorbeta is a potent inhibitor of IL-1 induced protease activity and cartilage proteoglycan degradation. Biochem Biophys Res Commun 1988; 157: 1352-9.
- Kristupaitis D, Dibirdik I, Vassilev A, Mahajan S, Kurosaki T, Chu A, et al. Electromagnetic field-induced stimulation of Bruton's tyrosine kinase. J Biol Chem 1998; 273: 12397-401.
- 31. Dibirdik I, Kristupaitis D, Kurosaki T, Tuel-Ahlgren L, Chu A, Pond D, et al. Stimulation of Src family protein-tyrosine kinases as a proximal and mandatory step for SYK kinasedependent phospholipase Cgamma2 activation in lymphoma B cells exposed to low energy electromagnetic fields. J Biol Chem 1998; 273: 4035-9.
- 32. Sharma L. Nonpharmacologic management of osteoarthritis. Curr Opin Rheumatol 2002; 14: 603-7.
- Klaiman MD, Shrader JA, Danoff JV, Hicks JE, Pesce WJ, Ferland J. Phonophoresis versus ultrasound in the treatment of common musculoskeletal conditions. Med Sci Sports Exerc 1998; 30: 1349-55.
- Diniz P, Soejima K, Ito G. Nitric oxide mediates the effects of pulsed electromagnetic field stimulation on the osteoblast proliferation and differentiation. Nitric Oxide 2002; 7: 18-23.
- Svarcová J, Trnavskÿ K, Zvárová J. The influence of ultrasound, galvanic currents and shortwave diathermy on pain intensity in patients with osteoarthritis. Scand J Rheumatol 1987; 67: 83-5.
- 36. Jan MH, Lai JS.The effects of physiotherapy on osteoarthritic knees of females.J Formos Med Assoc 1991; 90: 1008-13.
- Falconer J, Hayes KW, Chang RW. Effect of ultrasound on mobility in osteoarthritis of the knee. A randomized clinical trial. Arthritis Care Res 1992; 5: 29-35.
- Marks R, Ghanagaraja S, Ghassemi M. Ultrasound for osteoarthritis of the knee: a systematic review. Physiotherapy 2000; 86: 452-63.