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Effects of extremely low frequency pulsed electromagnetic field added to kinesitherapy procedure on quality of life in patients with end stage renal disease on dialysis

Efekti primene elektromagnetnog polja niske frekvencije sa procedurama kineziterapije na kvalitet života bolesnika sa terminalnom bubrežnom slabošću na dijalizi

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Abstract

Background/Aim. Extremely Low Frequency Pulsed Electromagnetic Magnetic Field (ELF-PEMF) has a wide range of therapeutic applications which were expanding during the last decades. ELF-PEMF, as non-invasive, long-term safe method of physical therapy can influence a variety of aspects in chronic diseases including quality of life. Patients with chronic kidney disease (CKD), especially with end stage renal disease (ESRD), treated by dialysis, have lower health-related quality of life and changed normal way of living because of ESRD-related comorbid illnesses, associated conditions and complex dialysis procedures. The objective of this study was to assess the effectiveness of long-term ELF-PEMF in concordance with exercising on quality of life in ESRD patients on dialysis. **Methods.** A total of 124 patients (59 men and 65 women) with ESRD on dialysis program were divided into study group and control group. Patients included in the study group (n = 54) agreed to receive treatment with ELF-PEMF (18 Hz, 2 mT, applied during 40 minutes after ten consecutive dialysis procedures, four times through one year, 120 treatments in total) together with kinesitherapy over three years. The patients in the control group (n = 70) were subjected only to kinesitherapy as a physical therapy procedure. Quality of life was assessed through the Short Form Health Survey, version 2 (SF36v2) and the Functional Assessment of Chronic Illness Therapy, version 4 (FACIT Fatigue v4) questionnaires. **Results.** In the study group, treatment with ELF-PEMF significantly improved FACIT Fatigue v4 scale score as well as physical health, physical functioning, bodily pain and energy/fatigue domains of SF=36v2 scale. There were no effects on mental health domain, limitations due to physical health problems, limitations due to personal or emotional problems, emotional well-being, social functioning, and general health perceptions. In the control group, no beneficial effects on FACIT Fatigue v4 scale and SF36v2 scale item were noticed. **Conclusion.** ELF-PEMF could be a additional and safe strategy for improving quality of life in patients with ESRD on dialysis.

Key words:
electromagnetic fields; magnetic field therapy; kidney failure, chronic; dialysis; quality of life; surveys and questionnaires; treatment outcome.

Apstrakt

Uvod/Cilj. Pulsno elektromagnetno polje ekstremno niske frekvencije (ELF-PEMF) ima široki spektar terapeutske primene koji se povećava poslednjih godina. ELF-PEMF kao neinvazivna, dugoročno bezbedna metoda fizikalne terapije može povoljno uticati na različite aspekte u hroničnim bolestima. Bolesnici sa terminalnom bubrežnom slabošću, posebno oni na dijalizi, imaju nizak kvalitet života uslovljen komorbiditetima, pridruženim stanjima i kom-

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pleksnom procedurom dijalize. Cilj studije bio je ispitivanje efekata dugoročne primene ELF-PEMF uz kineziterapiju na kvalitet života bolesnika sa terminalnom bubrežnom slabošću na dijalizi. **Metode.** U studiju je bilo uključeno 124 bolesnika (59 muškaraca i 65 žena) sa terminalnom bubrežnom slabošću na programu hemodijalize. Formirane su dve grupe ispitanika: studijska grupa (n = 54), bolesnici koji su dobrovoljno pristali da uz kineziterapiju u naredne tri godine dobijaju i ELF-PEMF tretman (18 Hz, 2 mT, tokom 40 minuta posle deset uzastopnih procedura hemodijalize, četiri puta tokom jedne godine, ukupno 120 tretmana) i kontrolna grupa (n = 70) kod koje je od fizikalnih procedura primenjivana samo kineziterapija. Kvalitet života je procenjivan na osnovu *Short Form Health Survay, version 2* (F36v2) i *Functional Assessment of Chronic Illness Therapy, version 4* (FACIT) *Fatigue* v4 upitnika. **Rezultati.** U studijskoj grupi posle primene ELF-PEMF značajno su bili poboljšani skorovi FACIT Fatigue v4 skale, kao i domeni fizičkog zdravlja, fizičkog funkcionisanja, bola i energije SF = 36v2 skale. ELF-PEMF nije imala efekte na domene mentalnog zdravlja, ograničenja zbog fizičkog zdravtsvenog stanja, ograničenja zbog personalnih ili emocionalnih problema, emocionalog stanja, socijalnog funkcionisanja i utiska opšteg zdravlja. U kontrolnoj grupi nije primećeno poboljšanje skora FACIT Fatigue v4 skale ni skora bilo kojeg domena SF36v2 skale. **Zaključak.** ELF-PEMF bi mogla predstavljati dodatnu i bezbednu metodu u pokušaju poboljšanja kvaliteta života bolesnika sa terminalnom bubrežnom slabošću na dijalizi.

Ključne reči:
elektromagnetna polja; magnetoterapija; bubreg, hronična insuficijencija; dijaliza; kvalitet života; ankete i upitnici; lečenje, ishod.

Introduction

Based on experimental trials and early clinical findings, the United States Food and Drug Administration (FDA) approved pulsed electromagnetic fields (PEMF) for the treatment of delayed union or nonunion fractures, failed joint fusions, and congenital pseudarthroses [1, 2]. For therapeutic purposes, PEMF is typically applied at extremely low frequencies between 5 and 300 Hz – Extremely Low Frequency Pulsed Electromagnetic Magnetic Field (ELF-PEMF). ELF-PEMF has a wide range of other therapeutic applications. The scientific evidence for therapeutic effects of PEMF are proven in some indications while data in the others are mostly empiric, observational and insufficient. The review of four meta-analyses of randomized trials investigating the use of ELF-PEMF for fracture healing confirmed clinical validity of this method of physical therapy [3]. Also, in some observation and cross-sectional studies, beneficial effects of ELF-PEMF were found and this procedure is recommended as adjuvant therapy in osteoporosis and other conditions associated with accelerated bone loss or high bone turnover [4]. PEMF treatment was also regarded as a viable alternative for arthritis therapy by virtue of chondroprotective and anti-inflammatory effects [5]. The administration of ELF-PEMF is followed by the high variability in terms of magnetic flux density, signal type, frequency, duration, and number of treatment sessions [2]. Despite the lack of a proven biological mechanism and diversity of applied parameters, a number of indications for ELF-PEMF treatment increased during the last decades. The most frequently mentioned indications are musculoskeletal disorders, but other therapeutic areas include fixation of cementless implants, wound healing, skin ulcers, fibromyalgia, neurological diseases, chronic pain, insomnia, spasticity in multiple sclerosis and even cardiovascular disorders.

It is important that adverse effects of ELF-PEMF as non-invasive, long-term safe method was not reported. There is no discomfort or known risk associated with ELF-PEMF. The method is easy to apply and the cost is low. Some authors assert that ELF-PEMF is important in well-being [2, 6].

Chronic kidney disease (CKD) affects 5%–10% of the world population and is associated with many adverse outcomes. It is progressive and leads to end stage renal disease (ESRD) which is treated mostly by dialysis [7]. According to the United Kingdom renal registry, about 90% of ESRD patients is on the maintenance dialysis program and data show that the incidence of new patients starting on hemodialysis increased by 1.2% in 2013 [8]. Beside the higher mortality rate of ESRD patients, the disease is also associated with greater health expenditures and lower health-related quality of life due to comorbid illnesses and frequent dialysis centers and hospital visits. It implies substantial changes in the patients' normal daily activities and suboptimal quality of life [9]. Also, numerous physical and mental symptoms affect quality of life. Dialysis-dependent patients have numerous physical symptoms, reporting fatigue, pain, cramps, poor nutrition, and inactivity, increased risk of falling and sexual dysfunction due to hypotension, myopathy and peripheral neuropathy [10]. On the other hand, depression, stress, anxiety and sleep disturbances are also very common [11]. Despite the relevance of symptoms, health care providers as well as patients themselves are not adept at recognizing these issues and they are usually underestimated. Additionally, evidence-based dialysis treatment interventions and symptom-targeted pharmaceutical therapies are flawed, except the use of erythropoiesis stimulating agents that can reduce fatigue [12]. Administration of nonpharmacologic steps including exercise and physical therapy that may contribute to improving quality of life is still rare. Physical activity is important aspect for prevention and treatment of chronic diseases, including ESRD. Exercise prescription for the CKD patients is less usual than for other chronic diseases considering that the CKD patients have low aerobic capacity [13]. Taking into account the benefits, in our hemodialysis center, exercise was pointed as an important component of treatment for all patients with ESRD on hemodialysis program.

Results of our previous prospective, controlled study[14], provided evidence for beneficial effect of three-years ELF-PEMF on bone mineral density (BMD) and risk of fracture in the ESRD patients on dialysis, suggesting, for the first time, that this physical procedure was of clinical relevance as a successful adjuvant option in the ESRD patients without reported side-effects. Due to the mentioned pleiotropic effects of ELF-PEMF and discovering positive effects of this treatment on bones, it can be presumed that this physical procedure may influence overall quality of life. So, the objective of this study was to assess the effectiveness of long-term ELF-PEMF in concordance with exercising on quality of life in the ESRD patients on dialysis.

Methods

Patients

Participants were selected according to the following criteria: diagnosis of ESRD, current hemodialysis treatment and volunteer participation. The patients who met the entry criteria were informed and gave their consent in accordance with ethical standards of the Helsinki Declaration from 1983 and International Conference on Harmonization Good Clinical Practice (ICH-GCP). The study was approved by the Independent Ethics Institutional Review Committee of the University Hospital "Zvezdara" being a part of the Faculty of Medicine, Belgrade University, Serbia on April 19, 2011.

Collection of demographic and case history data was made by reviewing case notes and treatment records. A total of 151 patients with ESRD on dialysis program were divided into a study group and a control group. The study group included the patients who agreed to receive treatment with ELF-PEMF (18 Hz, 2 mT, applied during 40 minutes after ten consecutive dialysis procedures, four times through one year, 120 treatments in total) together with kinesitherapy during three years. The control group involved the patients that were subjected only to kinesitherapy as a physical therapy procedure.

Out of 151 patients who were initially enrolled in the study (64 in the study group and 87 in the control group), a total of 124 patients (54 in the study group and 70 in the control group) completed all treatments and testing after three years. Ten patients in the study group and 17 in the control group were excluded from the study: 2 patients (one from each group) due to a change in concomitant therapy and 25 patients (9 from the study group and 16 from the control group) due to the death related to cardiovascular events. During the follow-up period, not a single patient underwent renal transplantation, nor he/she was transferred to another dialysis center, or changed the dialysis mode. Finally, there were 29 females and 25 males in the study group and 36 females and 34 males in the control group.

All patients had a chronic renal failure of a different origin (primary chronic glomerulonephritis, tubulointerstitial nephritis, nephroangiosclerosis, diabetic nephropathy) and were on dialysis program with hemodialysis product 36, for at least one year. Further inclusion criteria required the patients to be at least 25 years old. All patients have continued with their basic therapeutic regimen (vitamin D, calcium and phosphate binder supplementation) during the observation period. Exclusion criteria were: any relative or absolute contraindication for either ELF-PEMF or kinesitherapy treatment, any disorder affecting the bone metabolism (except renal failure and hyperparathyreoidism) and any medication affecting the bone metabolism (except vitamin D, calcium and heparin during hemodialysis).

Physical therapy procedures

We performed our own treatment protocol based on the fact that the best results are achieved with ELF-PEMF with low frequency (below 60 Hz), induction value between 1pT and 15mT as intermittent use of PEMF stimulation which has been shown to produce superior outcome responses to continuous use [2]. The magnetic field pad (35 × 27 × 13 cm) was a Magomil 2 (Electronic Design Medical, Belgrade, Serbia), with computed device for ELF-PEMF (18 Hz, 2 mT). The therapy was applied during 40 minutes after ten consecutive dialysis procedures, four times through one year (120 treatments in total during three years). The kinesitherapy treatment (active and passive-assisted exercises per segments in two series with ten repeats) was dosed individually, according to general shape during 30 minutes after every dialysis procedure and was carried out by the same physiotherapist who had been trained in the treatment scheme according to the usual program.

Biochemical analyzes were performed routinely using standard certified procedures for measuring the investigated parameters. Serum urea, creatinine, albumin, calcium, phosphate and intact PTH levels were measured and monitored using standard techniques.

Assessment of quality of life

The subjects filled out the following questionnaires at the beginning and once per year: the Short Form Health Survey, version 2 (SF36v2) and Fatigue v4 – the Functional Assessment of Chronic Illness Therapy, version 4 (FACIT) scales [15, 16]. Scores are calculated on line. Because functional capacity is usually impaired in the CKD patients, reaching 60%–65% of the age-predicted value [17], we could not administer some other explicit tests to our patients, except questionnaires.

Statistical analysis

For the statistical analysis, the patients' data were entered into a computer Excel® sheet (Microsoft Office) and subsequently analyzed with the Origin Pro 8.5 statistical software (Stata Corporation, College Station, TX, USA). Group data are expressed as mean ± SD. One-sample Kolmogorov-Smirnov test was used for testing a normal distribution of data. Summary statistics, including mean, standard deviation (SD), range and percentiles were calculated for the demographic data, SF36v2, FACIT Fatigue v4 scales results. One-way ANOVA and *t*-test for depended samples were used to investigate differences between groups for parametric variables and χ^2 test for nonparametric variables. Observations were considered significant if two-tailed *p*-values were below 0.05.

Results

Demographic and clinical data of the patients that completed the study are presented in Table 1 and 2. It is important to note that the patients in finally analyzed groups were comparable in relation to age, duration of dialysis, body mass index (BMI), smoking history, presence of bone fractures, parathyroid hormone (PTH) levels and primary cause of renal failure at the beginning of investigation.

The analyzed groups of the patients were at the beginning of the study also comparable in relation to the values of FACIT Fatigue v4 scale score and SF36v2 scale scores through two domains and eight subdomains (Table 3).

Table 1

Demographic and clinical data of female and male dialysis patients in the study and control groups at the beginning of investigation

Parameter	Female			Male		
	Study group (n = 29)	Control group (n = 36)	*p*	Study group (n = 25)	Control group (n = 34)	*p*
Age (years), mean ± SD	56.9 ± 6.4	61.2 ± 7.6	F = 1.89 $p = 0.13$	63.2 ± 7.4	61.2 ± 13.6	F = 0.55 $p = 0.85$
Duration of dyalisis (years), mean ± SD	9.3 ± 5.6	9.2 ± 6.6	F = 1.64, $p = 0.17$	8.8 ± 3.7	8.7 ± 3.4	F = 1.46 $p = 0.20$
BMI (kg/m^2), mean ± SD	23.7 ± 3.2	24.9 ± 5.4	F = 2.15 $p = 0.09$	25.9 ± 2.8	23.7 ± 3.5	F = 10.9 $p = 0.08$
Duration of menopause (years), mean ± SD	9.0 ± 4.5	10.8 ± 6.2	F=1.72 $p = 0.15$			
Early menopause (%)	20.7	16.7	$\chi^2 = 0.07$ $p = 0.98$			
Ever smoked (%)	44.8	47.2	$\chi^2 = 0.01$ $p = 0.99$	72.0	61.7	$\chi^2 = 0.13$ $p = 0.87$
Present smoking (%)	20.7	19.4	$\chi^2 = 0.01$ $p = 0.99$	40.0	41.1	$\chi^2 = 0.01$ $p = 0.99$
Bone fractures (%)	31.0	22.2	$\chi^2 = 0.26$ $p = 0.88$	24.0	20.5	$\chi^2 = 0.04$ $p = 0.99$
PTH (pg/mL), mean ± SD	761 ± 125	788 ± 147	F=1.08 $p = 0.61$	795 ± 119	774 ± 114	F = 1.18 $p = 0.55$

BMI – body mass index; BMD – bone mineral density; PTH – parathyroid hormone; SD – standard deviation.

Table 2

Frequency of causes of primary diagnosis of renal failure in the study and control groups

Diagnosis	Study group (n = 54) n (%)	Control group (n = 70) n (%)	*p*
Primary chronic glomerulonephritis	21 (38.9)	29 (41.4)	ns
Tubulointerstitial nephritis	4 (7.4)	6 (8.6)	ns
Nephroangiosclerosis	11 (20.4)	14 (20)	ns
Diabetic nephropathy	16 (29.6)	18 (25.7)	ns
Polycystic renal disease	2 (3.7)	3 (4.3)	ns

Table 3

The Functional Assessment of Chronic Illness Therapy, version 4 (FACIT Fatigue v4) and the Short Form Health Survey, version 2 (SF36v2) scores of patients in the study and the control groups at the beginning of investigation

Parameter	Study group (n = 54) mean ± SD	Control group (n = 70) mean ± SD	*p*
FACIT Fatigue v4	20.35 ± 9.54	21.36 ± 10.38	0.85
SF36v2 physical health	50.72 ± 10.33	48.75 ± 9.72	0.83
SF36v2 mental health	59.52 ± 17.05	62.58 ± 14.45	0.88
SF36v2 physical functioning	54.38 ± 16.19	52.35 ± 15.23	0.91
SF36v2 bodily pain	50.91 ± 7.55	52.12 ± 10.26	0.92
SF36v2 limitations due to physical health problems	43.61 ± 12.74	44.65 ± 13.24	0.89
SF36v2 limitations due to personal or emotional problems	65.18 ± 23.39	67.58 ± 25.22	0.83
SF36v2 emotional well-being	71.55 ± 19.37	70.25 ± 20.87	0.89
SF36v2 social functioning	49.02 ± 21.70	47.36 ± 22.32	0.87
SF36v2 energy/fatigue	51.55 ± 23.31	50.21 ± 19.27	0.92
SF36v2 general health perceptions	54.05 ± 12.91	55.58 ± 14.35	0.90

SD – standard deviation.

The changes of FACIT Fatigue v4 scale score and SF36v2 scale scores (calculated through physical and mental health domains and all eight subdomains, physical functioning, bodily pain, limitations due to physical health problems, limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions) after three-years treatment with ELF-PEMF in the study group are presented in Table 4. Treatment with ELF-PEMF significantly improved FACIT Fatigue v4 scale scores as well as physical health, physical functioning, bodily pain and energy/fatigue domains of SF = 36v2 scale. There were no effects on mental health domain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning and general health perceptions.

In the control group, three-years follow-up had no beneficial effects on any FACIT Fatigue v4 scale and SF36v2 scale item (Table 5).

During the study, ELF-PEMF administration was completed without any side-effects.

Table 4

Effects of three-years treatment with Extremely Frequency Pulsed Electromagnetic Filed (ELMF) on values of FACIT Fatigue v4 scale score and SF36v2 scale scores of dialysis patients in the study group (n = 54)

Parameter	Before treatment mean ± SD	After treatment mean ± SD	*p*
FACIT Fatigue v4	20.35 ± 9.54	41.35 ± 12.35	$p < 0.05$
SF36v2 physical health	50.72 ± 10.33	68.13 ± 11.54	$p < 0.05$
SF36v2 mental health	59.52 ± 17.05	59.33 ± 15.39	$p = 0.98$
SF36v2 physical functioning	54.38 ± 16.19	65.33 ± 16.57	$p < 0.05$
SF36v2 bodily pain	50.91 ± 7.55	69.77 ± 12.87	$p < 0.05$
SF36v2 limitations due to physical health problems	43.61 ± 12.74	51.11 ± 15.86	$p = 0.25$
SF36v2 limitations due to personal or emotional problems	65.18 ± 23.39	63.32 ± 13.41	$p = 0.85$
SF36v2 emotional well-being	71.55 ± 19.37	71.28 ± 18.10	$p = 0.82$
SF36v2 social functioning	49.02 ± 21.70	52.36 ± 19.78	$p = 0.93$
SF36v2 energy/fatigue	51.55 ± 23.31	61.22 ± 21.13	$p < 0.05$
SF36v2 general health perceptions	54.05 ± 12.91	56.05 ± 10.56	$p = 0.89$

FACIT Fatigue v4 – the Functional Assessment of Chronic Illness Therapy, version 4; SF36v2 – The Short Form Health Survey, version 2; SD – standard deviation.

Table 5

Effects of three year treatment with Extremely Low Frequency Pulsed Electromagnetic Filed (ELMF) on values of the Functional Assessment of Chronic Illness Therapy, version 4 (FACIT Fatigue v4) scale score and the Short Form Health Survey, version 2 (SF36v2) scale scores of dialysis patients in the control group (n = 70)

Parameter	Before treatment mean ± SD	After treatment mean ± SD	*p*
FACIT Fatigue v4	21.36 ± 10.38	22.74 ± 12.54	$p = 0.88$
SF36v2 physical health	48.75 ± 9.72	48.75 ± 15.58	$p = 0.99$
SF36v2 mental health	62.58 ± 14.45	59.14 ± 17.65	$p = 0.78$
SF36v2 physical functioning	52.35 ± 15.23	45.33 ± 20.33	$p = 0.25$
SF36v2 bodily pain	52.12 ± 10.26	59.58 ± 14.53	$p = 0.19$
SF36v2 limitations due to physical health problems	44.65 ± 13.24	41.85 ± 14.20	$p = 0.85$
SF36v2 limitations due to personal or emotional problems	67.58 ± 25.22	65.32 ± 13.96	$p = 0.82$
SF36v2 emotional well-being	70.25 ± 20.87	71.28 ± 14.52	$p = 0.96$
SF36v2 social functioning	47.36 ± 22.32	45.95 ± 15.24	$p = 0.84$
SF36v2 energy/fatigue	50.21 ± 19.27	51.55 ± 19.58	$p = 0.87$
SF36v2 general health perceptions	55.58 ± 14.35	52.25 ± 17.97	$p = 0.78$

SD – standard deviation.

Discussion

In this paper we report the improvement of some aspects of quality of life in the ESRD patients on dialysis subjected to ELF-PEMF in twelve sessions over three years. In our previous article [14], we presented positive effects of this physical procedure on BMD and risk of fracture in the ESRD patients on dialysis without reported side-effects. Also, there was a slight but not significant effect on a patient's overall survival [14]. However, as it was expected, this therapy did not have effects on urea, creatinine and parathormone levels nor on ESRD and dialysis outcome, due to irreversible kidney damage.

In chronic diseases, over the past few decades, quality of life research endpoints developed as valuable research tools in assessing the outcome of therapeutic interventions. Quality of life, as defined by the World Health Organization in 1994, is the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [18]. It comprehends a wide range of indicators covering overall satisfaction with life in areas such as health, housing conditions, employment, safety, education, and leisure [18]. ESRD is a chronic disease causing a high level of disability in different domains of the patients' lives, leading to impaired quality of life. In the ESRD patients, the physical, social and emotional impacts of quality of life are affected by the disease itself and also by its treatment. Dialysis therapy is time intensive and expensive, and requires fluid and dietary restrictions, resulting in a loss of freedom, dependence on caregivers, disruption of marital, family, and social life, and reduced or loss of financial income, and thus compromising quality of life.

Some physical procedures, such as exercises, were shown in CKD patients to improve quality of their lives with regard to positive effects on physical fitness, muscular strength, muscular functioning, walking capacity and cardiovascular function [13]. ELF-PEMF delivered by whole-body mass are promoted in many countries for a wide range of therapeutic applications and for enhancing well-being [6]. The mechanism of biophysical interactions between ELF-PEMF and tissue is still not completely understood. It is suggested that external magnetic stimuli interact with cells either via transmembrane receptors or ion channels, thereby initiating one or more signal transduction cascades or cell functions [19]. ELF-PEM showed that it can increase blood supply [20]. It can mimic and potentiate effects of physical activity on osteogenesis [21]. The application of ELF-PEMF as a physical stress promotes the formation of very small electric currents and piezoelectric potentials. Piezoelectric potentials are primarily due to movement of fluid-containing electrolytes. When these electrolytes move, they generate streaming potentials transforming mechanical stress into an electrical phenomenon capable of stimulating synthesis of tissue components. Time-varying ELF-PEMF also generates changes in metabolic activity. Interaction between cell membrane and ELF-PEMF modulates critical events in signal transduction mechanisms such as Ca^{2+} influx and mobilization, surface receptors redistribution and protein kinase C activity. PEMF can produce a modification of membrane cytoskeleton organization, together with an alteration of protein kinase activity, modify membrane structure and interfere with initiation of signal cascade pathway. Significant reduction of proinflammatory cytokines such as tumor necrosis factor alpha (TNFα) and interleukin-6 (IL-6) and inflammatory mediators like prostaglandin E2 (PGE2) are noticed. In mice models the expression levels of angiopoietin-2 and fibroblast growth factor-2 are increased and angiogenesis acceleration is suggested as a possible mechanism of the ELF/PEMF action.

In our study, the effects of ELF-PEMF on quality of life of patients with CKD on dialysis were assessed for the first time. We used the SF36v2 scale. The SF 36v2 scale is 36-item generic health-related quality of life questionnaire that consists of 36 questions related to physical and mental health status and an proven objective mean to measure aspects of quality of life such as physical, psychological, social, and cultural conditions from the perspective of patients with chronic diseases. Although some other instruments as self-report measure of quality of life are developed for ESRD patients on dialysis like The Kidney Disease Quality of Life (KDQOL), many investigators are reluctant to use it because of its length (43 kidney-disease targeted items as well as 36 items from SF36v2 scale that provide generic core of instrument) [22].

We found that treatment with ELF-PEMF, combined with exercise, significantly improve FACIT Fatigue v4 scale scores as well as physical health, physical functioning, bodily pain and energy/fatigue domains of SF = 36v2 scale. In the control group, exercise applied as only physical procedure did not show significant effects on these domains, although some slight but not significant effects were reached in physical functioning and bodily pain domains. The effects of exercise on quality of life in ESRD patients on dialysis are often inconsistent. Barcellos et al. [13] analyzed results of 18 studies and in 11 of them an increase of quality of life was found in the exercise group both in aerobic and resistance training. However, 4 of this studies found improvement only in the physical component. The Dialysis Morbidity and Mortality Study, a cohort study, found that dialysis patients engaged in more frequent exercise presented a significantly reduced mortality rate versus less active peers [23].

The findings regarding pain reduction could be an important factor in improving quality of life in the ESRD patients treated with ELF-PEMF in combination with kinesitherapy. ELF-PEMF is a well-known physical agent which can influence chronic pain conditions, especially refractory pain. The investigation of analgesic effectiveness of ELF-PEMF administered twice daily over a 45-day period in 34 subjects with persistent or recurrent pain following back surgery showed that 33% reported a clinically meaningful (≥ 30%) reduction in pain intensity [24]. Improvements in pain intensity were paralleled to improvements in secondary outcomes. Very low-intensity magnetic stimulation may represent a safe and effective treatment for chronic pain and other symptoms associated with conditions without structural damages but with dysfunctional disorders like fibromyalgia [25, 26]. ELF-PEMF can also influence modification of pain in polyneuropathy which is common in the ESRD patients on dialysis [27, 28]. Not only nociception but also transduction, transmission, perception, interpretation and modulation of pain have been reported to be influenced by exposure to electromagnetic fields [29]. The mechanisms by which central nervous exposure to weak electromagnetic fields may have analgesic and antinociceptive effects remain to be explained. There is evidence that endogenous opioid systems are affected by magnetic fields [29].

According to our results there were no effects of ELF-PEMF on mental health domain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning and general health perceptions.

These domains of SF36v2 are narrowly associated with psychological symptoms in patients with ESRD on dialysis. There are many publications related to psychological symptoms in patients with ESRD on dialysis. Previous studies found that the psychological symptoms did affect quality of life and discussed the association between psychological symptoms with quality of life of dialysis patients [11, 30]. According to some reports, about 27%–36% of dialysis patients express depression, 38%–46% anxiety and about 20% chronic stress [11, 31]. Depression, anxiety and stress significantly contribute to reduced quality of life in dialysis patients' domains of physical health, psychological health, social impact, perceived environment and overall quality of life. Kousolula et al. [9] noticed that overall mood and emotional domains of quality of life correlated with age, higher education, shorter duration of dialysis and better family or social environment. Chronic renal failure affects both patients and their families. Beside socio-demographic variables, many others could be the reason for lower mood and emotional feeling, including health expenditures, frequent dialysis centers visits, ability to travel, financial issues, problems having access to dialysis, comorbid illness, poor nutrition, sexual dysfunction, fluid and dietary restrictions and social support [32]. In our study, ELF-PEMF did not express any significant changes in these domains. In the literature there are a very small number of papers investigating effects of ELF-PEMF on mental health. Martiny et al. [33] published that the transcranial PEMF treatment was superior to sham treatment in patients with ESRD treatment-resistant depression.

The other aspect is effects of ELF-PEMF on fatigue. Regenerative benefits of ELF-PEMF on fatigue in chronic diseases were confirmed in numerous conditions. In a long-term study, a beneficial effect of ELF-PEMF on multiple sclerosis fatigue was demonstrated indicating that it could be a useful therapeutic modality [34]. Evidence from this randomized, double-bind, placebo controlled trial is consistent with results from smaller studies suggesting that exposure to pulsing, weak electromagnetic fields can alleviate symptoms of multiple sclerosis [35].

However, our study had limitations that should be addressed in future research. Some aspects of mental health are assessed by questionnaires but not by mental health professionals. Therefore, the chances of false positive and false negative results are rather big. The other restrictions included the lack of analysis of some socio-demographic and clinical data which might interfere with patient quality of life and a lack of a possibility to study subgroups by energy levels or other parameters of treatment in order to produce recommendations for future studies. Finally, more controlled and double-blind studies, including more patients, might narrow down suspicions and show significant effects with the full support of our findings.

Conclusion

In conclusion, treatment with ELF-PEMF significantly improves physical health, physical functioning, bodily pain and energy/fatigue. Importantly, there have been no reports of side-effects of ELF-PEMF which had a clearly superior safety profile. Our results left enough space for improvement to significant values in forthcoming, larger studies. The time to onset and subsequent longevity of ELF-PEMF effects should be considered in future study design to achieve an accurate measurement. A clearer definition of the mechanisms might also help in choosing patients who are more likely to benefit from such a treatment.

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