# Efficacy of low frequency pulsed electromagnetic field therapy on physical fitness in juvenile rheumatoid arthritis: a randomized, placebo-controlled study.

# S. M. El-Shamy<sup>1</sup>, A. A.Mohamed<sup>2</sup>,

<sup>1</sup> Lecturer Physical Therapy for Disturbance of Growth and Development

in Children and its Surgery, Faculty of Physical Therapy, Cairo University, Egypt.

- <sup>2</sup> Lecturer of Physical Therapy for Cardiovascular/ Respiratory Disorder and Geriatrics, Faculty of Physical Therapy, Cairo University, Egypt.
- racuity of r hysical Therapy, Cairo Universit

# ABSTRACT

Juvenile rheumatoid arthritis (JRA) is the most common rheumatic disease of childhood. This study was conducted to examine the effects of low frequency pulsed magnetic field therapy on physical fitness in children with polyarticular JRA. Thirty children, with polyarticular JRA, aged 8 to 12 years were included. Children were randomized for treatment in two groups. In the group A (study) received low frequency pulsed magnetic field therapy 3 times per week for successive 12 weeks. In the group B (control) received a placebo treatment. Evaluation of knee joint pain using the Visual Analogue Scale (VAS) and physical fitness using 6 Minute Walk Test (6MWT) were performed before and after the treatment. The result of this study revealed that there was a statistically significant improvement in physical fitness in children with JRA. Therefore, low frequency pulsed magnetic field is effective, innovative, non-invasive, non-expensive and can be used as a new trend physical therapy modality in the treatment of fatigue in JRA.

## INTRODUCTION

Juvenile rheumatoid arthritis (JRA) is a disease that occurs in children beginning before sixteen years of age [1]. Although JRA is a chronic disease of childhood, the actual cause of the disease is unknown [2]. Some common signs and symptoms of JRA are morning stiffness, joint guardian, fatigue, sleep disturbances and irritability [3, 4].

Fatigue in JRA is being increasingly recognized within pediatric practice. As in adult patients, it is characterized by longstanding, medically unexplained tiredness, functional disability and accompanied by a variety of physical and psychological complaints [5].

Functional impairment is a key aspect of the condition and it affects most areas in children's lives. Rangel et al., [6], reported that when the illness was at its worst, most children with chronic fatigue syndrome (CFS) had stopped socializing with their friends and family relationships had become strained in many instances. Half had been bedridden for prolonged periods and some were in wheelchairs. Most striking was the impairment caused in school attendance: two-thirds had been totally unable to attend school, with a mean time out of school for one year.

While juvenile arthritis is markedly different from adult rheumatoid arthritis, goals of management are similar, including reduction of joint inflammation, pain relief, prevention of disability and maintenance of function, the provision of education and attention to psychosocial, growth and development needs. A multidisciplinary approach is required to deliver a comprehensive and effective program [7]. In the short term, decreased physical fitness and activity levels can lead to further functional deterioration. In the longer term, decreased physical fitness and activity levels can lead to an increased risk for cardiovascular disease [8].

Pulsed electromagnetic field (PEMF) exposure is approved by the United States Food and Drug Administration for the treatment of problems associated with musculoskeletal disorders, including delayed union or non-union fractures, failed joint fusions, and congenital pseudoarthroses [9]. Specific joint disorders that have been investigated using this treatment modality include rheumatoid arthritis (RA) [10], osteoarthritis and rotator cuff tendonitis [11, 12].

Pulsed electromagnetic field induces timevarying ionic currents in tissues, which stimulate changes in cellular calcium and cyclic adenosine monophosphate levels [13], as well as in the synthesis of collagen, proteoglycans, DNA, and RNA [14]. In addition, some of the enzymes and hormones involved in skeletal homeostasis are affected by PEMF and it increases nitric oxide production and levels of reactive oxygen species [15].

There is growing evidence in the literature of the beneficial effects of magnetic fields on different multiple sclerosis symptoms [16], and there have been reports that the technique can alleviate symptoms such as fatigue, bladder control, and spasticity, as well as improve quality of life. The aim of this study was to investigate the efficacy of PEMF on physical fitness in children with juvenile rheumatoid arthritis.

#### **MATERIALS AND METHODS**

## Study design

This was a randomized, placebo therapy controlled trial assessing the effects of low frequency magnetic fields versus placebo therapy on physical fitness in JRA children.

#### **Subjects**

Thirty children had polyarticular participated in the study ranged in age from 8 to 12 years. They were recruited for the study from an outpatient clinic of "Abo El-Rish pediatric Hospital-Cairo University Hospitals" according to the following criteria:

#### Inclusion criteria:

All patients should have fulfilled the American College of Rheumatology (ACR) criteria for polyarticular JRA: presence of arthritis in five or more joints during first 6 months of disease. Symmetry of arthritis however, the degree of involvement was varied. Cardinal hallmark signs and symptoms of joint involvement in JRA that generally were marked by pain, swelling and morning stiffness.

#### **Exclusion criteria:**

1 - The use of drugs that could potentially interfere with fatigue.

2 - Possible secondary causes of fatigue.3 - Psychiatric disorders, epilepsy and other chronic diseases that could cause fatigue.

4 - Patients who had advanced radiographic changes as bone destruction, bony ankylosis, knee joint subluxation, epiphyseal fractures, and growth abnormalities related to marked skeletal changes seen in JRA. All subjects gave written informed consent.

#### Randomization

After the baseline assessment and data collection, a computer-generated random number list was used to randomize patients into two equal groups, the PEMF and placebo group. Randomization was performed using sequential sealed envelopes prepared by an independent therapist before enrollment. The sealed envelopes contained a record of the allocation. The researchers and participants were all blind to the group allocation throughout the study.

#### Materials

The ASA magnetic field is a device for magneto-therapy, its model is (Automatic PMT Quattro pro). It consists of an appliance, motorized bed and solenoids. The appliance was connected to electrical mains supplying 230 v  $\pm$  10% at a frequency of 50 or 60 Hz with earth connection. The intensity and spatial layout of the generated magnetic field depend on the type of solenoid used.

#### Assessment

All children (control and study) received the standard physical therapy treatment for JRA , regardless of treatment allocation. The standard physical therapy program consisted of muscle stretching, strengthening exercises, proprioceptive training, gait and balance training for (one hour /day, 3 sessions/week) for successive 12 weeks. The study group underwent additional PEMF with the standard physical therapy treatment.

All patients were assessed at baseline and at the end of therapy (after 12 weeks) by the same assessor who was blinded to treatment.

1 - Visual analogue scale (VAS) was used to assess levels of pain and anxiety, both before (pre) and after (post) magnetic field or placebo exposure. The pain scale ranged from no pain to worst (from no pain=0 to unbearable pain=10) [17].

2 - The six minute walk test (6MWT) was performed individually with standardized encouragements during the test. An indoor quiet corridor distance of 20 meters between turning points was used. Each child was instructed to cover as many laps of the course as possible in 6 minutes without running. The test was performed with no 'pacer' (a therapist who walks behind the patient) except when there is a high risk of falling [18].

## Magnetic field application:

The child was asked to remove metal objects or anything sensitive to magnetic field such as chains, belts, watches, etc....before lying on the bed. Then the child was placed in a comfortable supine lying position over the motorized bed. During application, the child was asked not to move and remain stable as much as possible. The appliance was connected to electrical mains supplying  $230V\pm 10\%$ . The solenoids were adjusted to be over both knee joints. The options of the appliance were adjusted with very low frequency (15 HZ), very low intensity (20 G) for 20 minutes, 3 sessions / week for successive 12 weeks [19].

#### **Statistical analysis**

Statistical analysis was performed using SPSS version 16.0. Descriptive statistics of mean and standard deviation presented the child's age, weight, height and body mass index. Pain and physical fitness results pre- and post-treatment values were assessed using the ANOVA test. The significance level was set at (0.05).

Character	Study group (A) Mean ± SD	Placebo control group (B) Mean ± SD	F-Value	P-Value
Age (years)	12.22 ± 2.33	11.90 ± 2.74	0.145	**0.707
Height (Cm)	145.9 ± 10.76	146.03±11.38	0.001	**0.974
Weight (Kg)	44.03 ± 10.2	44.47±9.87	0.014	**0.907
BMI (kg/m2)	20.16 ± 2.24	20.55±1.65	0.285	**0.598
Right Knee joint Pain	5.53 ± 0.83	5.53 ± 0.64	0.000	**1.000
Left Knee joint Pain	5.6 ± 0.83	5.67 ± 0.62	0.063	**0.804
Functional Capacity (6MWT)(m)	543.93 ± 18.65	544.87± 24.04	0.014	**0.906

Table 1: The pre-test values of both groups

Level of significance at P<0.05. \*= significant \*\*= non-significant

Character	Study g Mean ± SD	roup (A) Mean ± SD	T-Value	P-Value	Placebo cont Pre	rol group (B) Post	T-Value	P-Value
Right Knee joint Pain	5.53 ± 0.83	2.87 ± 0.64	16.73	0.00	5.53 ± 0.64	3.67 ± 0.82	14.00	*0.00
Left Knee joint Pain	5.6 ± 0.83	2.93 ± 0.59	16.73	0.00	5.67 ± 0.62	3.60 ± 0.63	31.00	*0.00
Functional Capacity (6MWT) (m)	543.93 ± 18.65	570.00 ± 21.29	- 23.67	0.00	544.87 ± 24.04	552.33 ± 24.09	- 13.35	*0.00

Table 2: Comparison between pre and post-test values of both groups

Level of significance at P<0.05. \*= significant \*\*= non-significant

#### RESULTS

Thirty children with juvenile arthritis (22 boys and 8 girls) commenced the 12-week low frequency pulsed electromagnetic therapy and underwent final analysis at the end of the 12-week period. In the baseline evaluation, the results of this study revealed that there were nonsignificant differences between the two groups (study group A and placebo control group B) before treatment (pre-test values) in the demographic characteristics including age, height, weight and body mass index. Also; results of this study revealed that there were non-significant differences between the two groups before treatment (pre-test values) in the measured variables including right knee joint pain, left knee joint pain evaluated via visual analogue scale (VAS) and functional exercise capacity evaluated via 6 minute walk test (6MWT) (Table 1).

When comparing the mean changes in levels of right knee pain, left knee pain between the two groups. Results revealed that there was significant reduction in levels of right and left knee pain. Furthermore, there are significant differences between both groups in levels of knee pain reduction in favor of group A. (P-value < 0.05) (Table 2). Also when comparing the mean changes in the levels of functional exercise capacity between the two groups; this revealed that there was a significant increase in levels of functional exercise capacity in both groups. Furthermore, there is a significant difference between both groups in functional exercise capacity improvement in favor of group A. (P-value < 0.05) ( Table 2).

The result of this study also revealed that after 3 months of pulsed electromagnetic field treatment; the percentages of change in right & left knee pain levels and functional exercise capacity for study group A were more than those in group B. (Table 3).

#### DISCUSSION

This study was done to determine the efficacy of pulsed electromagnetic field treatment on physical fitness in children with JRA. PEMF therapy has been found to be effective in reducing pain and improving physical fitness in children with JRA.

Juvenile rheumatoid arthritis is the most common chronic rheumatic disease in childhood and one of the leading causes of pediatric acquired disability [20]. JRA persists into adulthood in up to 55% of patients, and may have a major impact on physical or psychosocial function. Children with JRA have reduced vigorous physical activity levels, sports participation and decreased fitness. Muscle atrophy,

Character	Study group (A)	Placebo control group (B)	F-Value	P-Value
Right Knee joint Pain	48.191 + 8.27	34.13 + 9.77	18.114	*0.00
Left Knee joint Pain	47.56 + 7.97	36.79 + 5.26	19.036	*0.00
Functional Capacity (6MWT) (m)	47.84 + 0.704	13.73 + 0.401	265.98	*0.00

Table 3: Comparison between the percentages of change in each variable of both groups

Level of significance at P<0.05. \*= significant \*\*= non-significant

weakness and anemia contribute to reduced fitness, but deconditioning from reduced physical activity is likely the greatest cause. Reduced participation because of disease symptom severity, treatment-related side effects or worries that exercise may aggravate disease is problematic [21]. So it was the cause to conduct our study on those children with JRA.

The 6MWT is an inexpensive instrument for measuring functional exercise capacity in pediatric populations. The 6-min walk test is easier to administer, a better reflection of daily activities and better tolerated than other walk tests. Reproducibility testing has shown good reliability (ICC 0.96 in 0.98) for children with or without chronic disease [22].

The results of our study revealed a reduction in pain at the end of the treatment program. The results of this study come in agreement with Jacobson et al. [23] and Hinman [24]; they revealed that there was a significant pain relief due to the application of magnetic field for patients with RA. Magnetic field-related pain relief may be contributed to the analgesic effect of low frequency and low intensity pulsed magnetic field therapy that could be attributed to one of the following mechanisms:

**First**, the physiological mechanism for pain relief due to the application of magnetic field may be due to presynaptic inhibition or decreased excitability of pain fibers [24]. Others postulated that magnetic field influences the small C fibers [25]. Also, Holcomb et al. [26], found that exposure to magnetic field produces a reversible blockade of sodium-dependent action potential firing and calcium-dependent responses to the irritant.

**Second,** the molecular mechanism of the effect of magnetic field may involve conformational changes in the ion channels or neuronal membrane. Considering the time required for the effect on action potentials, multiple mechanisms must be acting simultaneously, possible including indirect effects, such as reduction in activity of channel phosphorylating enzymes [27].

**Third,** evidence exists that pulsed magnetic fields can modulate the actions of hormones, anti-bodies and neurotransmitters at surface receptor sites of a variety of cell types [28].

The PEMF has been shown to increase upregulation of gene expression for aggrecan, type II collagen synthesis [29] and TGF $\beta$  [30]. TGF $\beta$  stimulates the aggrecan and collagen synthesis, suppresses the pro-enzyme forms of collagenase and interleukin-1 [31], which may result with pain reduction. The optimal frequency, intensity and duration required for the completion of these biological effects and for total recovery in human tissues, are unknown.

In the present study, the improvements in functional level in the PEMF group have been found superior to those of the placebo group. Improvement in the stiffness level of the PEMF group can be due to enhanced blood circulation in the periarticular compartment. PEMF has been shown to activate the synthesis of nitric oxide which may enhance blood flow [32].

Scientific data on the mechanism of the effect of pulsed magnetic field therapy on fatigue are still unknown but some studies showed that short term exposure to pulsed electromagnetic fields can influence a variety of cellular and neurological processes, such as patterns of cortical activation and inhibition [33] and activity of various neurotransmitters [34-36]. However, most of these studies are based on small sample groups and used extreme different treatment protocols which could lead to different results between studies.

A possible -and may be the most reasonable- explanation for the improved mobility of the PEMF -treated joints that were reflected by the increased covered distances during the 6 minutes' walk could be an enhanced blood flow. Support for this idea could be found in the observation that PEMF activates synthesis of nitric oxide (NO) [37] and synthesis of NO in endothelial cells could be involved in enhancing blood flow. Furthermore, it was recently shown that PEMF increases in vivo and in vitro angiogenesis through the endothelial release of fibroblast growth factor-2, an important angiogenic factor [38]. Thus, there are data indicating that improved blood circulation in the periarticular compartment could occur following treatment. Recent data from several laboratories have suggested that PEMF activates cellular signaling processes rapidly within5-10 min [39-42] and signaling is largely blunted after 30 min. Thus, future studies could benefit from applying a shorter duration of PEMF-stimulation, that is, less than one hour but several times a day.

#### CONCLUSION

The results of the current study confirm past findings in humans exposed to chronic pain that exposure to a specific PEMF has a modest pain reducing effect in children with JRA. For these patients, exposure to a low frequency PEMF produced decreases in pain and an increase in physical fitness beyond those found in a placebo treatment control group. Future research using possibly more optimal PEMF parameters should be conducted to better understand how and when PEMF produce improvement in physical fitness.

#### REFERENCES

- Berkow RB, Fletcher AJ. The merck manual of diagnosis and therapy, 1992, (16thed.). Rahway, NJ: Merck Research Laboratories. 1340.
- McCarty DJ, Koopman WJ. Arthritis and Allied Conditions, 1993, 12th ed. vol 1, PhiladelphiaLea & Febiger.
- Labyak SE, Bourguignon C, Docherty S. Sleep quality in children with juvenile rheumatoid arthritis. Holistic Nursing Practices, 2003; 17(4), 193-200.
- Simmons BP, Nutting JT, Bernstein RA. Juvenile rheumatoid arthritis. Hand Clin 1996; 12:573-589.
- Wessely S, Hotopf M, Sharpe M. Chronic Fatigue and Its Syndromes,1998; Oxford University Press: Oxford.
- Rangel LA, Garralda ME, Levin M, Roberts H. The course of chronic fatigue syndrome. Journal of the Royal Society of Medicine, 2000; 93: 129–134.

- Guseo A. Pulsing electromagnetic field therapy of multiple sclerosis by the Gyuling-Bordacs device: 88 Multiple Sclerosis Journal 18(1) Double-blind, crossover and open studies. J Bioelectr 1987; 6: 23–25.
- Carnethon MR, Gidding SS, Nehgme R, Sidney S, Jacobs DR Jr, Liu K. Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. JAMA 2003, 290:3092–100.
- Bassett CA, Schink-Ascani M. Long-term pulsed electromagnetic field (PEMF) results in congenital pseudarthrosis. Calcif Tissue Int. 1991;49:216–220.
- Ganguly KS, Sarkar AK, Datta AK, et al. A study of the effects of pulsed electromagnetic field therapy with respect toserological grouping in rheumatoid arthritis. J Indian MedAssoc. 1998, 96:272–275.
- Pipitone N, Scott DL. Magnetic pulse treatment for kneeosteoarthritis: a randomized, double-blind, placebocontrolledstudy. Curr Med Res Opin. 2001, 17:190–196.
- Trock DH. Electromagnetic fields and magnets. Investigational treatment for musculoskeletal disorders. Rheum Dis Clin North Am. 2000, 26:51–62.
- Thumm S, Loschinger M, Glock S, et al. Induction of camp-dependent protein kinase A activity in human skin fibroblasts and rat osteoblasts by extremely lowfrequency electromagnetic fields. Radiat Environ Biophys.1999, 38:195–199.
- Pezzeti F, De-Mattei M, Caruso A, et al. Effects of pulsed electromagnetic fields on human chondrocytes: an in vitro study. Calcif Tissue Int. 1999, 65:396–401.
- Kim SS, Shin HJ, Eom DW, et al. Enhanced expression of neuronal nitric oxide synthase and phospholipase C-II in regenerating murine neuronal cells by pulsed electromagnetic field. Exp Mol Med. 2002, 34:53–59.

- Price DD, McGrath PA, Rafi A, Buckingham
  B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983, 17:45-56.
- Ruperto N, Murray K, Gerloni V, Wulffraat N, De Oliveira S, Falcini F, et al. A randomized trial of parenteral method text in intermediate versus higher doses in children with juvenile idiopathic arthritis who failed standard dose. Arthritis Rheum, 2004, 50 (7): 2191–2201.
- ATS statement: guidelines for the sixminute walk test. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. Am J Respir Crit Care Med 2002, 166: 111–117.
- Trock DH, Bollet AJ, Dyer PH, Fielding LP, Minger WK. Markoll R. A. Double blind trial of the clinical effects of pulsed electromagnetic fields in osteoarthritis. J Rheumatol 1993, 20: 456-60.
- Ruperto N, Levinson JE, Ravelli A, Shear ES, Tague BL, Murray K, et al. Long term health outcomes and quality of life in America and Italian inception cohorts of patients with juvenile rheumatoid arthritis.
   I. Outcome status. J Rheumatol 1997, 24:945–51.
- 20. Klepper SE. Exercise and fitness in children with arthritis: Evidence of benefits for exercise and physical activity. Arthritis Rheum 2003, 49:435-43.
- Solway S, Brooks D, Lacasse Y, Thomas S. A qualitative systemic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. Chest 2001, 119: 256–270.
- 22. Jacobson J ,Gorman R, Yamanashi W, Saxena B and Clayton L. Low amplitude, extremely low frequency magnetic field for the treatment of osteoarthritic knee: a double blind clinical study. Altern Ther Health Med 2001, 7 (5): 54-64, 66-69.
- 23. Hinman MR, Ford J and Heyl H. Effects of Static magnets on chronic Knee Pain and Physical Function: a double-blind study. Altern-Ther-Health-Med. 2002, 8(4): 50-5.

- 24. Weintraub MI. Magnetic biostimulation in painful diabetic peripheral neuropathy: a novel intervention- a randomized, double-placebo crossover study. Am J Pain manage1999, 9 (q1): 8-17.
- 25. Holcomb RR, Parker RA, Harrison MS. Biomagentics in the treatment of human pain-past, present, future. Environ Med. 1991, 8:24-30.
- Segal N, Huston J, Fuchs H, Holcomb R. McLean M. The efficacy of a static magnetic device against knee pain associated with inflammatory arthritis. J Clin Rheumatol 1999, 5: 302-4.
- 27. Adey WR. Physiological signaling across cell membranes and cooperative influences of extremely low frequency electromagnetic fields. In: Frohlich H, ed. Biological Coherence and Response to External Stimuli. 1989 New York, NY: Springer-Verlag.
- 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.
- 29. Aaron RK, Wang S, Ciombor DM. Up regulation of basal TGF beta1 levels by EMF coincident with chondrogenesisimplications for skeletal repair and tissue engineering. J
- 30. Orthop Res 2002, 20: 233-40.
- Chandrasekhar S, Harvey AK. Transforming growth factor beta is a potent inhibitor of IL-1 induced protease activity and cartilage proteoglycan degradation. Biochem Biophys Res Commun 1988, 157: 1352-9.
- 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.
- Richards TL, Lappin MS, Acosta-Urquidi J, et al. Double-blind study of pulsing magnetic field effects on multiple sclerosis. J Altern Complement Med 1997, 3:21–29.

- Sandyk R. Treatment with weak electromagnetic fields improves fatigue associated with multiple sclerosis. Int J Neurosci 1996, 84: 177–186.
- 35. Sandyk R. Weak electromagnetic fields potentiate the effects of 4-aminopyridine in multiple sclerosis. Int J Neurosci 1996, 85: 125–129.
- Sandyk R. Application of weak electromagnetic fields facilitates sensorymotor integration in patients with multiple sclerosis. Int J Neurosci 1996, 85: 101– 110.
- 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 (1): 18-23.
- Tepper OM, Callaghan MJ, Chang EI, Galiano RD, Bhatt KA, Baharestani S, et al. Electromagnetic fields increase in vitro and in vivo angiogenesis through endothelial release of FGF-2. FASEB J 2004, 18(11): 1231-3
- 39. Rahbek UL, Tritsaris K, Dissing S. Interactions of low frequency, pulsed electromagnetic fields with living tissue: biochemical responses and clinical results. Oral Biosci Med 2005, 2(1).
- Uckun FM, Kurosaki T, Jin J, Jun X, Morgan A, Takata M, et al. Exposure of B-lineage lymphoid cells to low energy electromagnetic fields stimulates Lyn kinase. J BiolChem 1995, 270:27666-70.
- 41. 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.
- 42. 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 kinase-dependent phospholipase CI2 activation in lymphoma B cells exposed to low energy electromagnetic fields. J BiolChem 1998, 273:4035-9.