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PULSED ELECTROMAGNETIC FIELD THERAPY OF PERSISTENT ROTATOR CUFF TENDINITIS

A Double-blind Controlled Assessment

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Summary The value of pulsed electromagnetic fields (PEMF) for the treatment of persistent rotator cuff tendinitis was tested in a double-blind controlled study in 29 patients whose symptoms were refractory to steroid injection and other conventional conservative measures. The treated group (15 patients) had a significant benefit compared with the control group (14 patients) during the first 4 weeks of the study, when the control group received a placebo. In the second 4 weeks, when all patients were on active coils, no significant differences were noted between the groups. This lack of difference persisted over the third phase, when neither group received any treatment for 8 weeks. At the end of the study 19 (65%) of the 29 patients were symptomless and 5 others much improved. PEMF therapy may thus be useful in the treatment of severe and persistent rotator cuff and possibly other chronic tendon lesions.

Introduction

ROTATOR cuff tendinitis, a common cause of shoulder pain in the adult population, can be very disabling in those who do not respond satisfactorily to local corticosteroid injections.[1] All other forms of conventional conservative therapy are of limited or unproven benefit.[2,3] Of 328 patients referred to a shoulder clinic in our department over a period of 2 years, 138 (42%) were diagnosed as having rotator cuff tendinitis. 23% of this group did not respond or derived only temporary benefit from local corticosteroid injections.

Partial interruption of the blood supply to the rotator cuff tendons by compression of vessels between the humeral head and the acromion[4,5] is believed to be important in initiating tendon degeneration. This renders the rotator cuff liable to damage by trivial, often unrecognised, trauma. Since the vascular supply to adult tendon is normally poor, healing of these lesions is slow. Pulsed electromagnetic fields (PEMF) have been reported to accelerate bone repair,[6–10] nerve regeneration,[11,12] skin ulcer healing,[13] and recovery from both soft tissue injuries of the ankle[14] and avascular necrosis of the femoral head.[15] In addition, they have promoted the formation of collagen in various model systems.[16–18] These findings prompted us to study their use in the treatment of rotator cuff tendinitis lesions that had persisted for over 3 months despite therapy. In a pilot study (unpublished) PEMF produced marked improvement in 10 (67%) out of 15 patients. The maximum improvement in these 10 patients occurred within 4 weeks of start of therapy. The study described here included a control group.

Patients and Methods

Patients

Patients with rotator cuff tendinitis which had persisted for at least 3 months with no more than transient benefit from previous conservative therapy were considered for inclusion in the trial. The diagnosis of rotator cuff tendinitis was based on the criteria of Cyriax[19]—that is, shoulder pain being exacerbated by movement against resistance in one or more of the following: abduction (supraspinatus tendinitis); external rotation (infraspinatus tendinitis); internal rotation (subscapularis tendinitis). Although the active range of shoulder movement was usually limited by the pain, the passive range remained approximately normal. A "painful arc" on abduction was often but not invariably present. Patients were accepted if their lesions had arisen spontaneously or had been precipitated by minor trauma, but not if they had severe neck pain, neurological changes in the upper limbs, clinical or radiological evidence of glenohumeral, acromioclavicular, or generalised arthritis, radiological calcification of the soft tissues, a clinical diagnosis of rupture of the rotator cuff, or a painful and restricted (frozen) shoulder. Subjects also had to have normal erythrocyte sedimentation rates (Westergren) and latex tests for rheumatoid factor.

Shoulder Assessment

At each visit the following clinical variables were recorded:

(1) *Pain score.*—This consisted of the sum of the severity of pain at night, on movement, and at rest, as estimated (to the nearest 0·5 cm) by the patient on 10 cm horizontal visual analogue scales.

(2) *Pain on resisted movement.*—The pain induced by resisted abduction and external and internal rotation was assessed on a

4-point scale and the results were summated (0 = no pain; 1 = slight pain but full power; 2 = moderate pain and reduced power; 3 = severe pain with absent power against even minimum resistance).

(3) *Painful arc on active abduction.*—This was also assessed on a 4-point scale (0 = no pain; 1 = catching only at 1 point; 2 = painful arc; 3 = unable actively to overcome the painful arc).

(4) *The total range of active movement.*—This was calculated as the sum of the range of total abduction, forward flexion, and rotation. Measurements were made with a spirit goniometer[20] attached by 'Velcro' straps to the upper arm with the patient sitting upright for total abduction and flexion. Total rotation was assessed with the patient lying supine with the shoulder in 90° of abduction and the goniometer attached to the dorsal aspect of the forearm.

Patients were reviewed fortnightly while undergoing therapy and monthly thereafter. Paracetamol was permitted if required but anti-inflammatory agents were stopped. The time at which the patient and the observer considered the shoulder much improved was recorded.

Study Design

Patients fulfilling the criteria were randomly allocated to the treatment group (A), or the control group (B). In the first 4 weeks (phase I), group A received active coils and group B received dummy coils. Neither patient not medical assessor was aware of the treatment group. At the end of 4 weeks and without breaking the code, both groups were given active coils and therapy was continued for another 4 weeks (phase II). Treatment was then stopped but patients continued to be reviewed for another 8 weeks (phase III), at the end of which the grouping was revealed to patient, medical assessor, and others involved in the study. After the code was broken patients were either discharged or offered alternative therapy.

PEMF Regimen

A single ovoid coil ($12 \cdot 2 \pm 1 \cdot 2 \times 13 \cdot 2 \pm 0 \cdot 7$ cm^2) consisting of 50 turns of copper wire (1·4 mm dia) covered by insulating tape was fitted over padding to the outer aspect of the affected shoulder so that the coil protruded from the centre of the pad. Two velcro straps held it in place. Patients were instructed to use the coil for 5–9 h each day, with each treatment session lasting at least 1 h. The coils were supplied with pulse generators set at 73±2Hz; waveform parameters (fig 1) for each active coil did not vary by more than 7%.

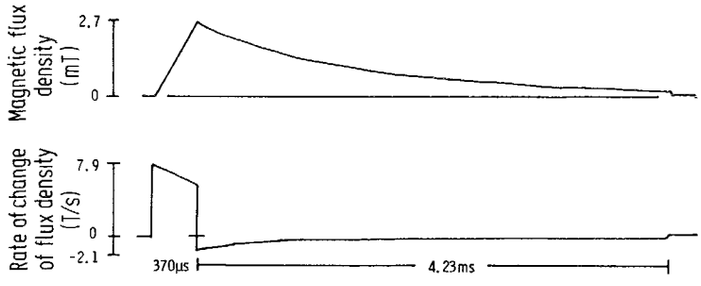

Fig 1—Waveforms showing the magnetic flux density (top) and rate of change of magnetic flux density (bottom) as measured by a Hall probe and search coil (7 mm diameter), respectively.

Statistical Analysis

The rate of recovery of each clinical variable in the two groups from time 0 to each follow-up visit was compared by the use of the Wilcoxon rank sum tests.

Results

Patients

29 patients fulfilled the criteria for the study. 15 entered the treatment group (A) and 14 the control group (B). There were no significant differences between the groups (table I). The supraspinatus tendon was most commonly affected, although this was often in association with infraspinatus tendon involvement.

TABLE I—PATIENT DETAILS

—	Treated group	Control group
Number of patients	15	14
Mean age (years)	54·4	53·2
Sex (male:female)	10:5	11:3
Duration of symptoms at presentation (months)		
Mean	9·2	9·5
Range	3–24	3–24
Tendon(s) affected		
Supraspinatus	8	6
Supraspinatus and infraspinatus	5	5
Infraspinatus	2	1
Subscapularis	—	2

28 of the 29 patients had received non-steroidal anti-inflammatory agents before inclusion in the study but only 3 patients (12%) found them beneficial. Analgesics on the other hand were considered to be of some value by 8 of the 18 patients (44%) who had received them. A particular benefit was reduction of night pain, facilitating sleep. 27 of the 29 patients had also received local corticosteroid injection therapy (mean 2·2 injections), but not within 1 month of inclusion in the study. 2 patients (1 in each group) had refused injections for the shoulder being investigated because of the severe pain they experienced when the opposite shoulder had been injected with corticosteroids.

Phase I (Week 0–4)

The improvement in the mean pain score (fig 2) was greater in the treated than in the control group both at 2 ($p<0 \cdot 05$) and 4 ($p<0 \cdot 02$) weeks. The reduction in scores for the painful arc on abduction (fig 3) and for pain on resisted movement (fig 4) and the improvement in active range (fig 5) showed an even greater advantage ($p<0 \cdot 005$) for group A at both 2 and 4 weeks.

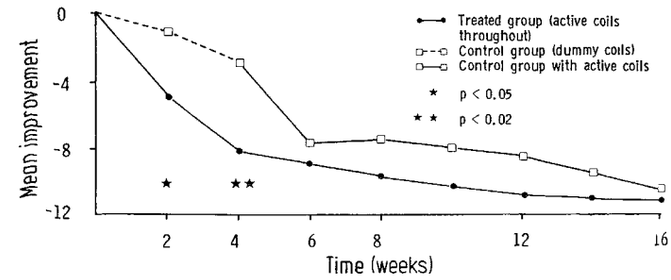

Fig 2—Improvement in pain score versus time.

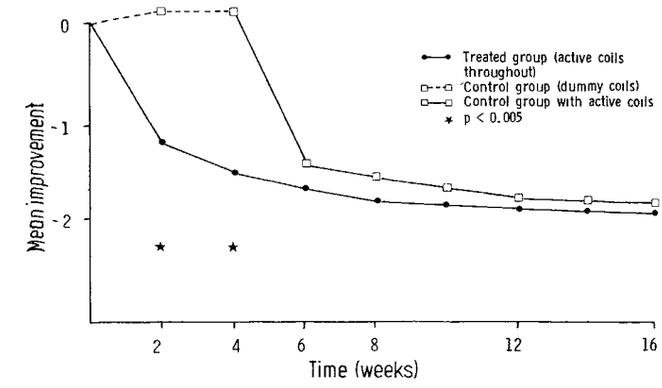

Fig 3—Improvement in painful arc versus time.

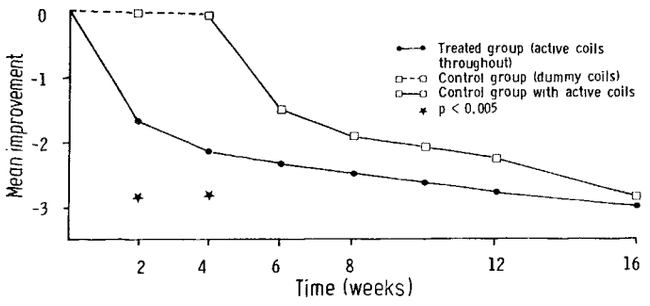

Fig 4—Improvement in pain on resisted movement versus time.

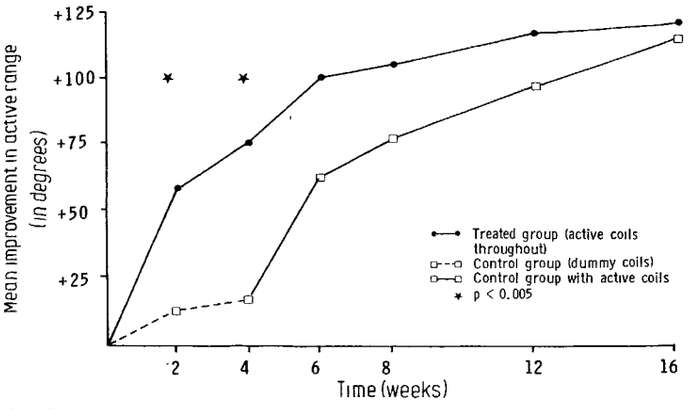

Fig 5—Improvement in active range versus time.

Phase II and III (Weeks 4–16+)

With the rapid improvement in group B after the change to active coils (figs 2–5) there was no significant difference between the groups in any of the clinical variables at week 6. Altogether 7 patients (25%) had a minor flare-up of symptoms after stopping therapy (phase III) but this resolved without further treatment.

Outcome

19 of 29 patients (66%) were symptomless at week 16 (table II) and were discharged. Of the 10 who remained under follow-up, 2 became symptomless; 3 were discharged with only minor residual disability; 2 had pain and tenderness at the acromioclavicular joint and received local steroid injections; and 3 had no improvement despite further steroid injections into the subacromial bursa.

TABLE II—STATUS OF PATIENTS 4 MONTHS AFTER ENTRY TO THE STUDY

Status at 4 months	Treated group (n = 15)	Control group (n = 14)
Symptomless	9	10
Minor residual symptoms	5	2
Severe disability	1	2

Timing of Maximum Improvement

If the 4 weeks of placebo therapy in group B were disregarded, maximum subjective pain relief occurred at a mean of 5·7 weeks (range 2 weeks–6 months). Full recovery on examination was, however, delayed until 13·2 weeks (4 weeks to >6 months) from initiating therapy.

Side-effects

Although many patients found the coils cumbersome, especially at night, no untoward reactions were reported during the controlled study; but during the pilot study 1 patient with known cervical spondylosis treated with cervical laminectomy had recurrence of neck pain and neurological deficit in both upper limbs following successful treatment of shoulder pain.

Factors of Possible Relevance to Outcome

19 patients were able to sleep with the coils in situ and achieved treatment times of 6–10 (mean 8·2) h per day. The other 10 achieved treatment times of only 3–8 (mean 4·7) h per day during waking hours. 4 patients (all group A) refused therapy after 4 weeks since symptoms had resolved. Thus 11 patients had active therapy over 8 weeks and 18 patients over only 4 weeks. However, the duration of therapy did not affect the outcome. The duration of symptoms before start of active therapy was also not important; but outcome was influenced by severity of lesion, in particular, involvement of more than one tendon, which was present in 8 of the 10 patients who still had symptoms at 4 months. The development of acromioclavicular tenderness (2 patients) was also associated with a poor result. 3 of the 5 patients with recurrence of severe pain during the extended follow-up period were manual labourers and their work was judged to be responsible for several of the minor and temporary flare-ups after cessation of therapy.

Discussion

Rotator cuff tendinitis is extremely common and usually responsive to local corticosteroid injections, but 23% of our patients at our shoulder clinic with this lesion respond poorly or only transiently to this treatment. The response to non-steroidal anti-inflammatory agents is usually unsatisfactory, but analgesics may be of some value, especially in patients in whom night pain is a prominent symptom.

The design of our controlled study was chosen because many patients in our pilot study improved rapidly with PEMF therapy. In the first phase the treated group had a significant advantage over the placebo group, but the latter group soon improved once they were put on active therapy, and no significant differences were noted thereafter. Patient and observer bias was minimised by maintaining the code relating to treatment groups until all the patients had completed 4 months of follow-up.

Rotator cuff tendinitis, like many soft tissue lesions, offers few objective clinical variables for use in serial follow-up. All four variables chosen for this study reflect pain and therefore presumably severity of the underlying condition. All improved more with treatment than with placebo. The pain score, based on visual analogue scales, was the most subjective variable and showed more placebo effect and less (but still significant) advantage for the treated than did the other three variables, which were based on observer assessment. Subjective improvement was noted by many of our patients before objective evidence of healing was recorded by the medical assessor; this difference suggests that there may be other local effects which induce pain relief.

Treatment was generally well tolerated although many patients found the treatment coils cumbersome and uncomfortable. The duration of therapy varied from 3–10 h per day over 4–8 weeks, but there was no evidence that either longer daily treatment sessions or longer overall treatment times conveyed an advantage. The stimulation signal pulse used was empirically based on other clinical[6] and experimental[18] data.

More than 70% of patients improved on PEMF therapy. All the patients were followed up for at least 4 months, with few showing evidence of recurrence during this time. This study suggests that PEMF therapy is safe and may be effective in the treatment of persistent soft tissue lesions such

as rotator cuff tendinitis which have been resistant to conventional conservative measures.

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REFERENCES

1. Fearnley ME, Vadasz I. Factors influencing the response of lesions of the rotator cuff of the shoulder to local steroid injections. *Ann Phys Med* 1969; **10:** 53–63.
2. Berry H, Fernandes L, Bloom B, Clark RJ, Hamilton EBD. Clinical study comparing acupuncture, physiotherapy, injection and oral anti-inflammatory therapy in shoulder cuff lesions. *Curr Med Res Opin* 1980; **7:** 121–26.
3. Kessel L, Watson M. The painful arc syndrome. *J Bone Jt Surg* 1977; **58B:** 166–72.
4. Olsson O. Degenerative changes in the shoulder joint and their connection with shoulder pain. *Acta Chir Scand* 1953: Suppl 181.
5. Macnab I. Rotator cuff tendinitis. *Ann Roy Coll Surg Engl* 1973; **53:** 271–87.
6. Bassett CAL, Pilla AA, Pawluk RJ. A non-operative salvage of surgically resistant pseudarthrosis and non-unions by pulsing electromagnetic fields. *Clin Orthop* 1977; **124:** 128–43.
7. Sharrard WJW, Sutcliffe ML, Robson MJ, MacEachern AG. The treatment of fibrous non-union of fractures by pulsing electromagnetic stimulation. *J Bone Jt Surg* 1982; **64B:** 189–93.
8. Mulier JC, Spaas F. Outpatient treatment of surgically resistant non-unions by induced pulsing current—clinical results. *Arch Orthop Traumat Surg* 1980; **97:** 293–97
9. Bassett CAL, Mitchell SN, Gaston SR. Pulsing electromagnetic field treatment in ununited fractures and failed arthrodeses. *JAMA* 1982; **247:** 623–28.
10. Sutcliffe ML, Goldberg AAJ. The treatment of congenital pseud-arthroses of the tibia with pulsing electromagnetic fields. *Clin Orthop* 1982; **166:** 44–57.
11. Wilson DH, Jagadeesh P, Newman P, Harrison D. The effects of pulsed electromagnetic energy on peripheral nerve regeneration. *Ann NY Acad Sci* 1974; **238:** 575–85.
12. Kort J, Ito H, Bassett CAL. Effects of pulsing electromagnetic fields on peripheral nerve regeneration. *J Bone Jt Surg Orthop Trans* 1980; **4:** 238.
13. Wolcott LE, Wheeler PC, Rowley BA. Accelerated healing of skin ulcers by electrotherapy. *Southern Med J* 1969; **62:** 715–801.
14. Wilson DH. Treatment of soft tissue injuries by pulsed electrical energy. *Br Med J* 1972; i: 269–70.
15. Bassett CAL, Schink MM, Mitchell SN. Treatment of osteonecrosis of the hip with specific pulsed electromagnetic fields (PEMFs); a preliminary report. In: Hungerford DS, ed. Proceedings of 3rd International Symposium on circulation in bone. Baltimore: Williams and Wilkins, 1983.
16. Braun KA, Lemons JE. Effects of electromagnetic fields on the recovery of circulation in mature rabbit femoral heads. *Trans Orthop Res Soc* 1982; **7:** 313.
17. Luben RA, Chin CD, Chen MCY, Rosen DM, Adey WR. Effects of electromagnetic stimuli on bone cells in vitro, inhibition of responses to parathyroid hormone by low energy low frequency. *Proc Natl Acad Sci USA* 1982; **79:** 4180–84.
18. Fitton-Jackson S, Bassett CAL. The response of skeletal tissues to pulsed magnetic fields. In: Richards RJ, Rajan KT, eds. Tissue culture in medical research (II). Oxford: Pergamon Press, 1980: 21–28.
19. Cyriax J. Diagnosis of soft tissue lesions. In: Textbook of Orthopaedic Medicine. London: Baillière Tindall, 1971.
20. Clarke GR, Willis LA, Fish WW, Nichols PJR. Assessment of movement at the glenohumeral joint. *Orthopaedics Oxford* 1974; **7:** 55–71.

HUMAN RECOMBINANT INTERLEUKIN-2 PARTLY RECONSTITUTES DEFICIENT IN-VITRO IMMUNE RESPONSES OF LYMPHOCYTES FROM PATIENTS WITH AIDS

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Summary The lymphokine interleukin-2 is required for the development of various cell-mediated immune functions that are known to be deficient in patients with acquired immunodeficiency syndrome (AIDS). The effects of pure human recombinant interleukin-2 (rIL-2), produced by *Escherichia coli* containing the cloned human gene, on in-vitro immune responses were studied in 16 patients with AIDS and 10 age-matched healthy heterosexual men. Exposure of lymphocytes from most AIDS patients to 1–100 U/ml rIL-2, increased mitogen and alloantigen induced proliferation and augmented natural killer (NK) cell function in a dose-dependent manner. NK activity was the function most consistently improved, with deficient patient responses uniformly restored to normal after incubation of effector cells with rIL-2. Patient responsiveness to rIL-2 did not appear to depend upon the primary manifestation of disease (opportunistic infection, Kaposi's sarcoma, or both) or other clinical variables. rIL-2 also augmented the responses of lymphocytes from healthy subjects, but to a lesser degree. Pure rIL-2 seems capable of at least partly reconstituting some in-vitro immunological defects characteristic of AIDS. The availability of highly purified rIL-2 makes in-vivo testing feasible.

Introduction

THE acquired immunodeficiency syndrome (AIDS) is a disorder characterised by deficient cellular immunity occurring predominantly within certain epidemiologically defined high risk groups. No currently available therapy appears capable of restoring normal immune function in patients with AIDS. The clinical manifestations of the syndrome include opportunistic infections caused by viral, fungal, protozoal, and intracellular bacterial agents, as well as malignant neoplasms, most notably Kaposi's sarcoma and malignant lymphomas.[1–6] Cutaneous anergy is common, and peripheral-blood T lymphocyte subsets are almost invariably markedly depleted of helper/inducer (Leu-3$^+$, OKT-4$^+$) cells, with relative sparing of the suppressor/cytotoxic (Leu-2$^+$, OKT-8$^+$) subset.[7] In-vitro assays of cellular immune function have demonstrated markedly decreased natural killer (NK) cell activity and diminished proliferative responses to mitogens and alloantigens in AIDS.[1–3,6,8]

Preparations enriched for the lymphokine interleukin-2 (IL-2) can obviate the requirement for T-cell help in several in-vitro systems,[9,10] and have been shown to augment significantly in-vivo immune responses in animals.[11] Moreover, IL-2 preparations derived from the supernatants of mitogen-stimulated lymphocytes enhanced some deficient immune responses in patients with AIDS,[12] but whether the effects were due to IL-2 or to other substances present in the supernatants is not known. Cloning of the gene for human IL-2[13,14] has increased the purity and potency of available preparations. We have tested the ability of this recombinant-DNA-derived IL-2 (rIL-2), purified to apparent homogeneity, to enhance in-vitro immune responses of AIDS patients.

Methods

Subjects

We studied 16 homosexual men aged 28–57, with AIDS[15] who had biopsy-documented Kaposi's sarcoma, and/or *Pneumocystis carinii* pneumonia. Not all the assays were performed on every subject because in some the number of lymphocytes available was limited (see accompanying table). 10 age-matched healthy heterosexual men served as controls.

Lymphocyte Subset Studies

Whole blood was stained with fluorescein-isothiocyanate-conjugated monoclonal antibodies to Leu-2, Leu-3, Leu-4, Leu-7, Leu-11, Leu-12, and HLA-DR determinants (Becton-Dickinson, Mountain View, CA). Erythrocytes were eliminated by hypotonic lysis and stained samples were analysed on an Ortho System 50H cytofluorograph. Leu-2 and Leu-3 are antigens expressed on