ZUSAMMENSTELLUNG VON WISSENSCHAFTLICHEN PUBLIKATIONEN ZUR WIRKUNG DER PULSIERENDER MAGNETFELDTHERAPIE AUF KNOCHEN- UND KNORPELZELLEN

1982

Effects of a pulsed electromagnetic field on a mixed chondroplastic tissue culture

Abstract

A mixed tissue culture predominantly composed of chondroblastic tissue was perturbed by a pulsed electromagnetic field (PEMF). Some cultures were nonconfluent, and purposely retarded in growth to resemble an atrophic nonunion, while others were grown to confluence in about one-half the time as a model for a hypertrophic nonunion. These two groups tested the effect of growth rate upon the products of cell proliferation and differentiation. The slowly growing cultures were stimulated to synthesize hydroxyproline. The rapidly growing cultures showed a large increase in lysozyme activity, and increase in hyaluronate and DNA, and a decrease in glycosaminoglycan. Exogenous lysozyme further decreased the glycosaminoglycan synthesis in the presence of PEMF. Chitotriose, a specific lysozyme inhibitor abolished this effect. Cycloheximide, a protein synthesis inhibitor, did not abolish the activation of lysozyme found in the matrix. Thus lysozyme appears to be activated by PEMF. These observations of the rapidly growing confluent cultures are consistent with events described in the normal healing of a bone fracture or endochrondral growth. Thus, PEMF appears to promote normal healing, probably by altering cartilaginous lysozyme activity in the matrix, and possibly the sequence of events leading to calcification.

1990

c-fos Expression Precedes Osteogenic Differentiation of Cartilage Cells in Vitro

Abstract

We have investigated the temporal pattern of expression of c-fos in cartilage cells in mouse mandibular condyles. During in vitro cultivation, the progenitor cells in this organ differentiate to osteoblasts, and hypertrophic chondrocytes start to show features indicative of osteogenic differentiation. Prior to these processes we observed two distinct patterns of c-fos expression. High, transient c-fos expression was found in the entire tissue within 30 min of culture. This type of c-fos expression appeared to result from mechanical forces applied during dissection. The second type of c-fos expression appeared in individual cells in the zone of hypertrophic chondrocytes. A varying number

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of formerly quiescent chondrocytes expressed high levels of c-fos mRNA after between 30 min and 10 d in culture, with a peak in the number of cells between days 1 and 3. c-fos expression in these cartilage cells was followed by DNA replication and expression of genes typifying osteoblastic differentiation. After 7 d in culture, groups of cells with the typical ultrastructural features of osteoblasts, and surrounded by an osteoid-like matrix, were observed in single chondrocyte-type lacunae, suggesting division of chondrocytes and differentiation to osteoblasts. The data suggest that c-fos may play a crucial role in the perturbation of determined pathways of skeletoblast differentiation and in the regulation of endochondral bone formation.

1991

Effects of pulsing electromagnetic fields on cultured cartilage cells

Abstract

In order to evaluate the effects of pulsing electromagnetic fields (PEMFs) on cell proliferation and glycosaminoglycan (GAG) synthesis and to study the action site of PEMF stimulation in the cells, we performed a series of experiments on rabbit costal growth cartilage cells and human articular cartilage cells in culture. A PEMF stimulator was made using a Helmholz coil. Repetitive pulse burst electric currents with a burst width of 76 ms, a pulse width of 230 microseconds and 6.4 Hz were passed through this coil. The magnetic field strength reached 0.4 mT (tesla) on the average. The syntheses of DNA and GAG were measured by 3H-thymidine and 35S-sulfuric acid incorporations. The effects on the cells treated with lidocaine, adriamycin and irradiation were also measured using a colony forming assay. The PEMF stimulation for the duration of 5 days promoted both cell proliferation and GAG synthesis in growth cartilage cells and intermittent stimulation on and off alternatively every 12 h increased them most significantly, while, in articular cartilage cells, the stimulation promoted cell proliferation, but did not enhance GAG synthesis. PEMF stimulation promoted cells treated with lidocaine more significantly than with other agents. These results present evidence that intermittent PEMF stimulation is more effective on both cell proliferation and GAG synthesis of cartilage cells than continuous stimulation, and that the stimulation could exert effects not by nucleus directly, but by the cellular membrane-dependent mechanism. This study provides further basic data to encourage the clinical application of PEMF stimulation on bone and cartilage disorders.

1994

Combined magnetic fields increased net calcium flux in bone cells

Abstract

Low energy electromagnetic fields (EMF) exhibit a large number of biological effects. A major issue to be determined is “What is the lowest threshold of detection in which cells can respond to an EMF?” In these studies we demonstrate that a low-amplitude

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combined magnetic field (CMF) which induces a maximum potential gradient of 10-5 V/m is capable of increasing net calcium flux in human osteoblast-like cells. The increase in net calcium flux was frequency dependent, with a peak in the 15.3 – 16.3 Hz range with an apparent bandwidth of approximately 1 Hz. A model that characterizes the thermal noise limit indicates that non-spherical cell shape, resonant type dynamics, and signal averaging may all play a role in the transduction of low-amplitude EMF effects in biological systems.

1999

Correlation between pulsed electromagnetic fields exposure time and cell proliferation increase in human osteosarcoma cell lines and human normal osteoblast cells in vitro

Abstract

We have exposed cultured bone cells to a pulsed electromagnetic field (PEMF) for different times to find the minimal exposure time necessary to stimulate an increase of DNA synthesis. We used two different human osteosarcoma cell lines, TE-85 and MG-63, and human normal osteoblast cell (NHOC) obtained from surgical bone specimens. The cells were placed in multiwell plates and set in a tissue culture incubator between a pair of Helmoltz coils powered by a pulse generator (1.3-ms pulse, repeated at 75 Hz) for different periods of time. [3H]Thymidine incorporation was used to evaluate cell proliferation. The two osteosarcoma cell lines increase their thymidine incorporation when exposed to a PEMF for at least 30 min, both in a medium containing 10% fetal calf serum and in a serum-free medium. NHOC are known to increase their cell proliferation when exposed to PEMF but only if cultured in the presence of 10% fetal calf serum. In this experimental condition, three of the four cell lineages studied required at least 9 h of PEMF exposure to increase their DNA synthesis, whereas one cell lineage increased its cell proliferation after 6 h of PEMF exposure. Our observations confirm the hypothesis that the proliferative responses of NHOC and human osteosarcoma cell lines to PEMF exposure are quite different. Moreover, NHOC required minimal exposure times to PEMF to increase their cell proliferation, similar to that needed to stimulate bone formation in vivo.

1999

Effects of pulsed electromagnetic fields on human chondrocytes: an in vitro study

Abstract

A 1984 study determined the effect of a 72 Hz pulsating electromagnetic field (PEMF) on bone density of the radii of post-menopausal (osteoporosis-prone) women, during and after treatment of 10 h daily for 12 weeks. Bone mineral densities of the treated radii increased significantly in the immediate area of the field during the exposure period and

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decreased during the following 36 weeks. Bone density determination of the radii of these women, remeasured after eight years, suggests no long-term changes. The bone density- enhancing effect of PEMFs should be further studied, alone and in combination with exercise and pharmacologic agents such as the bisphosphonates and hormones, as prophylaxis in the osteoporosis- prone postmenopausal woman and as a possible block to the demineralization effect of microgravity.

2002

Low frequency EMF regulates chondrocyte differentiation and expression of matrix proteins

Abstract

STUDY DESIGN: The clinical study conducted was a prospective, randomized, double-blind, placebo-controlled trial.
OBJECTIVES: The purpose of this study was to evaluate the effect of combined magnetic fields on the healing of primary noninstrumented posterolateral lumbar spine fusion.
SUMMARY OF BACKGROUND DATA: Combined magnetic fields, a new type of biophysical stimulus, have been shown to act by stimulating endogenous production of growth factors that regulate the healing process. This is the first placebo-controlled study to assess the effect of an electromagnetic stimulus on primary noninstrumented posterolateral lumbar spine fusion surgery as well as the first evaluation of combined magnetic fields as an adjunctive stimulus to lumbar spine fusion.
METHODS: This multicenter investigational study was conducted at 10 clinical sites under an Investigational Device Exemption from the United States Food and Drug Administration. Eligible patients had one-level or two-level fusions (between L3 and S1) without instrumentation, either with autograft alone or in combination with allograft. The combined magnetic field device used a single posterior coil, centered over the fusion site, with one 30-minute treatment per day for 9 months. Randomization was stratified by site and number of levels fused. Evaluation was performed 3, 6, and 9 months after surgery and 3 months after the end of treatment. The primary endpoint was assessment of fusion at 9 months, based on radiographic evaluation by a blinded panel consisting of the treating physician, a musculoskeletal radiologist, and a spine surgeon.
RESULTS: Of 243 enrolled patients, 201 were available for evaluation. Among all patients with active devices, 64% healed at 9 months compared with 43% of patients with placebo devices: a significant difference (P = 0.003 by Fisher's exact test). Stratification by gender showed fusion in 67% of women with active devices, compared with 35% of those with placebo devices (P = 0.001 by Fisher's exact test). By contrast, there was not a statistically significant effect of the active device in this male study population. In the overall population of 201 patients, repeated measures analyses of fusion outcomes (by generalized estimating equations) showed a main effect of treatment, favoring the active treatment (P = 0.030). In a model with main effect and a time by treatment interaction, the latter was significant (P = 0.024), indicating acceleration of healing. Performed in the full sample of 243 patients, results of the

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intent-to-treat analysis were qualitatively the same as in the evaluable sample of 201 patients.
DISCUSSION: This investigational study demonstrates that combined magnetic field treatment of 30 min/d increases the probability of successful spine fusion, and statistical analysis using the generalized estimating equations model suggests an acceleration of the healing process. This is the first randomized clinical trial of noninstrumented primary posterolateral lumbar spine fusion, with evaluation by a blinded, unbiased panel. This is the first double-blind study performed to date assessing noninstrumented fusion outcome with extremely critical radiographic criteria. The lower overall fusion rates in this study are attributed to the high-risk patient group with an average age of 57 years, the use of noninstrumented technique with posterolateral fusion only, and the reliance on extremely critical radiographic and clinical criteria and blinded panel for fusion assessment without surgical confirmation.
CONCLUSIONS: In conclusion, the adjunctive use of the combined magnetic field device was statistically beneficial in the overall patient population, as has been shown in previous studies of adjunctive bone growth stimulation for spine fusion. For the first time, stratification of fusion success data by gender demonstrated that the female study population responded positively to the adjunctive combined magnetic field treatment, with no statistically significant effect observed in the male study population. Adjunctive use of the combined magnetic field device significantly increased the 9-month success of radiographic spinal fusion and showed an acceleration of the healing process.

2002

Effects of pulsed electromagnetic field (PEMF) stimulation on bone tissue like formation are dependent on the maturation stages of the osteoblasts

Abstract

The effects of pulsed electromagnetic field (PEMF, 15 Hz pulse burst, 7 mT peak) stimulation on bone tissue-like formation on osteoblasts (MC3T3-E1 cell line) in different stages of maturation were assessed to determine whether the PEMF stimulatory effect on bone tissue-like formation was associated with the increase in the number of cells and/or with the enhancement of the cellular differentiation. The cellular proliferation (DNA content), differentiation (alkaline phosphatase activity), and bone tissue-like formation (area of mineralized matrix) were determined at different time points. PEMF treatment of osteoblasts in the active proliferation stage accelerated cellular proliferation, enhanced cellular differentiation, and increased bone tissue-like formation. PEMF treatment of osteoblasts in the differentiation stage enhanced cellular differentiation and increased bone tissue-like formation. PEMF treatment of osteoblasts in the mineralization stage decreased bone tissue-like formation. In conclusion, PEMF had a stimulatory effect on the osteoblasts in the early stages of culture, which increased bone tissue-like formation. This stimulatory effect was most likely associated with enhancement of the cellular differentiation, but not with the increase in the number of cells. - CNOTE: Copyright 2002 Wiley-Liss, Inc.

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