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The Effect of a Pulsed Electromagnetic Field with Time on Pain in Muscle Crushed Rat Model

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Acute injuries to skeletal muscles can lead to significant pain and disability. Muscle pain results in muscle weakness and range of motion (ROM) decreases. Pulsed electromagnetic fields (PEMF) promote tissue repair, healing rates and reduce musculoskeletal pain. The results of many previous studies suggest that PEMF can contribute to chronic pain reduction, particularly in musculoskeletal injurys. However, we do not have enough information of its effects compared to a placebo. The principal objective of this study was to investigate differences in acute pain induced by the direct destruction of muscle tissue (extensor digitorum) with varying times of the application of PEMF, measured through the expression of c-fos on the spinal cord. Significant reduction of pain was found in groups exposed to PEMF and the group exposed to PEMF immediately after muscle injury showed the most significant differences. In conclusion, PEMF may be a useful strategy in reducing acute pain in muscle injury.

Keywords : pulse electromagnetic fields, acute pain, muscle injury, c-fos

1. Introduction

Common acute injuries to skeletal muscles can lead to significant pain and disability. Traumatic muscle injuries including contusions, crushing, lacerations or freezing occur relatively infrequently but when they do occur they can have dramatic and prolonged effects on the muscles functional capacity [1].

The healing phases for an injured muscle include degeneration, inflammation, regeneration and remodeling; these stages are considered to be common among these injury types [2]. Muscle pain is induced by the activation of specific receptors, these receptors are specialized in the detection of stimuli that are objectively capable of damaging tissue and that are subjectively perceived as painful. They consist of free nerve endings and are connected to the central nervous system (CNS) by way of thinly myelinated or unmyelinated fibers. They can be sensitized and activated by mechanical stimuli, such as trauma or mechanical overloading, as well as by endogenous inflammatory mediators including bradykinin (BK), serotonin and prostaglandin E2 (PGE2) [3].

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In the pain signaling pathways, the immediate early gene c-fos is expressed in neurons as a response to painful stimulus [4]. Several reports have shown that the expression of c-fos mRNA or immunoreactivity is up-regulated in the spinal cord following harmful visceral stimulation. In contrast, the expression of c-fos in the spinal cord is weakened by pretreatment of analgesia [5]. Thus, the expression of c-fos mRNA can be used as a marker of neurons activated by painful sensations [6].

The application of pulsed electromagnetic field (PEMF) treatment to the area of injury produces changes in the cell environment and restores the integrity and function of tissues within the organism [7]. Besides this, PEMF was also found to be effective in reducing pain and edema after soft tissue injury [8]. However, research evidence to support such a treatment course is lacking.

Therefore, the objective of this study is to investigate differences in pain with varying times of the application of PEMF, measured through the expression of c-fos on the spinal cords of rats after skeletal muscle crush injuries.

2. Materials and Methods

2.1. Animals

45 male Sprague-Dawley rats weighing between 270 g

and 300 g were used and maintained in a 12-hour on/12-hour off light/dark cycle with *ad libitum* access to food and water. All the experiments were conducted in accordance with the protocols established by the University of Daegu Animal Experiment Committee, based on the NIH Guidelines for the Care and Use of Laboratory Animals (NIH publication, 1996). The animals were randomly divided into 3 groups: the control (n = 15), PULS1 (n = 15) and PULS2 (n = 15) groups.

2.2. Experimental procedure

After crush injuries were inflicted on the left extensor digitorums of all animals, the PULS1 group began being exposed to PEMF on day 1 while PULS2 group started treatment after 3 days.

A Diapulse machine (Diapulse Corp., USA) was used to deliver PEMF to the injury site. The PEMF was delivered at a frequency of 27.12 MHz with an intensity of 5 gauss and a pulse output of 450 W for 15 minutes per day.

The experimental animals were killed 1, 3, and 5 days after injury for the gene expression studies.

2.3. c-fos mRNA analysis by RT-PCR

The reverse transcription-polymerase chain reaction (RT-PCR) was used to evaluate the mRNA expression in the spinal cord tissue.

The animals were sacrificed via anesthesia with a mixture of 2 ml/kg-50% Zoletil and 50% Xylazine hydrochloride followed by perfusion through the heart with 200 ml of 0.9% NaCl solution. The spinal cords were removed, and all the RNA was acquired from the collected spinal cords using STAT-60, a monophasic solution of phenol and guanidine isothiocyanate (Tel-Test, Friendswood, TX, USA). Reverse transcription (RT) was conducted using 3 μg of RNA with a reverse transcription system kit (AccuPower RT PreMix, Bioneer, Daejeon, Korea) with oligo$(dT)_{18}$ primers. Five microliters of the RT products were then amplified using a polymerase chain reaction (PCR) kit (AccuPower PCR Premix) under the following conditions: denaturation at 94 °C for 5 min and 30 cycles at 94 °C for 45 sec, 55 °C for 30 sec and 72 °C for 30 sec followed by 5 min of extension at 72 °C. The primers used were: 5'-CCGACTCCTTCTCCAGCAT-3' (forward), 5'-TCACCGTGGGGATAAAGTTG-3 (reverse) for c-fos. PCR for β-actin was also conducted as RNA quantity control.

2.4. Statistical analysis

The results were expressed as means ± a standard error (S.E.). All experiments were analyzed via the analysis of variance, some experiments were analyzed via comparisons of the treatment mean with the controls via Bonferroni-Dunn's test. The difference was regarded as statistically significant at a p of < 0.05.

3. Results and Discussion

In this study similar patterns of in the control, PULS1 and PULS2 groups were observed. We found that the 3 day group demonstrated a significant reduction in c-fos expression compared to the 1 day groups while the 5 day groups showed an even greater reduction in c-fos expression compared to the 3 day groups (Fig. 1, 2, 3). However, significantly greater reductions were found in the PULS1 group than in the PULS2 group. All groups in PULS1 showed a significant reduction compared to the control groups and remarkable improvements over the PULS2 groups were found on day 3 and 5 (Fig. 4).

One such treatment modality is PEMF therapy, this uses electromagnetic fields with an on-off effect of pulsing to produce athermal effects that promote tissue healing and reduce pain and inflammation [9].

Different soft tissues may respond differently when exposed to PEMF [10]. McCarthy *et al.* (2006) studied the

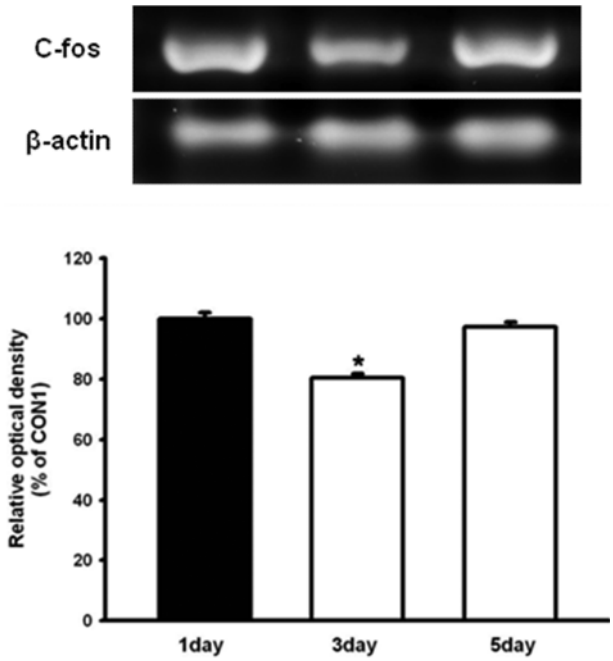

Fig. 1. Expression of c-fos mRNA in rat spinal cord in control groups. The amounts of c-fos mRNA were detected via RT-PCR, respectively, as described in the Materials and Methods section. Each example shown is representative of three experiments. The values represent the means ± SE of three independent experiments conducted in triplicate dishes. *p < .05 vs. day 1.

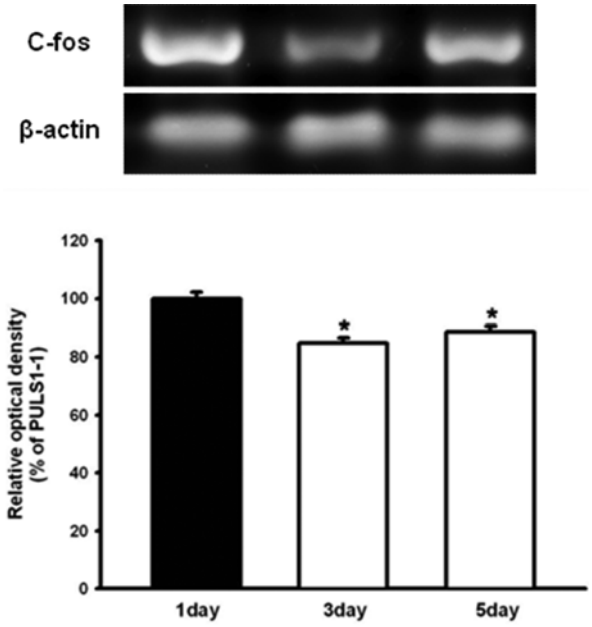

Fig. 2. Expression of c-fos mRNA in rat spinal cord in PULS1 groups. The amounts of c-fos mRNA were detected via RT-PCR, respectively, as described in the Materials and Methods section. Each example shown is representative of three experiments. The values represent the means±SE of three independent experiments conducted in triplicate dishes. *p < .05 vs. day 1.

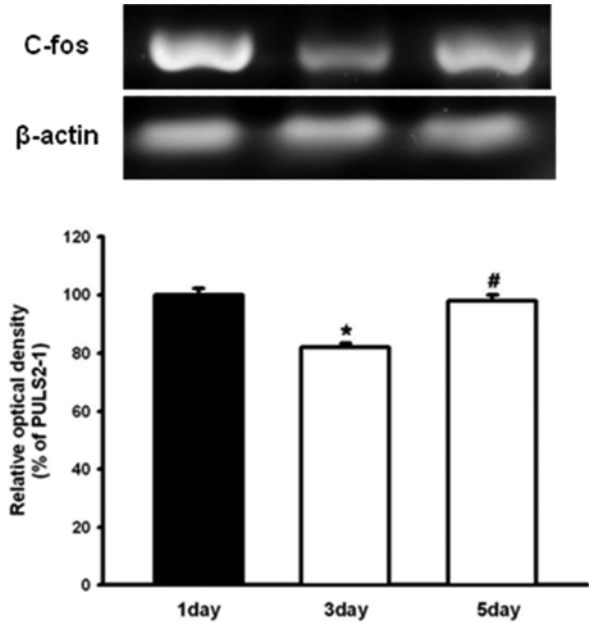

Fig. 3. Expression of c-fos mRNA in rat spinal cord in PULS2 groups. The amounts of c-fos mRNA were detected via RT-PCR, respectively, as described in the Materials and Methods section. Each example shown is representative of three experiments. The values represent the m eans±SE of three independent experiments conducted in triplicate dishes. *p < .05 vs. day 1. #p < .05 vs. day 3.

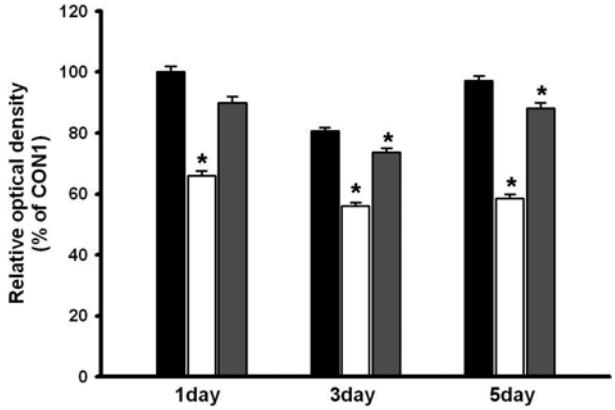

Fig. 4. Comparison between groups. *p < .05 vs. control group on 1, 3, and 5 day.

effects of PEMF on the pain from knee osteoarthritis. They found that PEMF has no clinically significant benefit beyond that achieved by the placebo treatment in terms of the pain experienced by the patients [9].

However, considerable prior work has demonstrated the beneficial effects of PEMF in humans. Thomas *et al.* (2007) reported that PEMF may be a novel, safe and effective therapeutic tool for use in, at least, a certain subsets of patients with chronic, nonmalignant pain from fibromyalgia (FM), musculoskeletal injury or inflammation [11].

Moreover, there is evidence that PEMF actually changes brain wave activity, suggesting that the symptom-altering effects of the electromagnetic waves are the result of a direct effect on central nervous function [12].

Expression of the c-fos mRNA in spinal cords is a valuable tool in pain research. Following peripheral noxious stimuli, it was found that spinal neurons that express c-fos are located in laminae I, II and laminae V, VI of the dorsal horn [6].

In our study, c-fos expression was observed primarily in lamina I, II and V. In particular, the expression patterns in the spinal lamina I and II were stronger.

In this study, we investigated the expression of c-fos in spinal cord after muscle crush injury. Expression of c-fos mRNA in PULS1 groups was consistently down-regulated compared to the control and PULS2 groups. This evidence suggests that PEMF may have significant analgesic effects on acute pain in muscles.

Cheing *et al.* (2005) examined the effects of ice therapy and PEMF in reducing pain and swelling on days 1, 3, 5 after the immobilization period following a distal radius fracture. Results after 5 days show a significant reduction in the visual analogue scores (VAS) [13]. Although PEMF was applied as an adjunct treatment, it is clear that PEMF is effective in reducing musculoskeletal pain.

Therefore, the results of this study show that PEMF

may constitute a useful strategy in reducing acute pain in muscle injuries.

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