ORIGINAL ARTICLE

Alternating Frequencies of Transcutaneous Electric Nerve Stimulation: Does it Produce Greater Analgesic Effects on Mechanical and Thermal Pain Thresholds?

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ABSTRACT. Tong KC, Lo SK, Cheing GL. Alternating frequencies of transcutaneous electric nerve stimulation: does it produce greater analgesic effects on mechanical and thermal pain thresholds? Arch Phys Med Rehabil 2007;88:1344-9.

Objective: To determine whether alternating frequency transcutaneous electric nerve stimulation (TENS) at 2 and 100Hz (2/100Hz) has a more potent hypoalgesic effect than a fixed frequency at 2 or 100Hz in healthy participants.

Design: A single-blind randomized controlled trial with a convenience sample.

Setting: University physiotherapy department.

Participants: Sixty-four healthy volunteers (32 men [mean age, 28.1±5.9y], 32 women [mean age, 27.7±5.6y]) were recruited and randomly divided into 4 groups.

Interventions: The 4 groups received TENS delivered at (1) 2Hz; (2) 100Hz; (3) 2/100Hz alternating frequency; and (4) no treatment (control group), respectively. Electric stimulation was applied over the anterior aspect of the dominant forearm for 30 minutes.

Main Outcome Measures: Mechanical pain thresholds (MPTs) and heat pain thresholds (HPTs) were recorded before, during, and after TENS stimulation. The data were analyzed using linear mixed models, with *group* treated as a between-subject factor and *time* a within-subject factor.

Results: During and shortly after electric stimulation, HPT increased significantly in the alternating frequency stimulation group ($P=.024$). MPT increased significantly in both the 100Hz ($P=.008$) and the alternating frequency groups ($P=.012$), but the increase was substantially larger in the 100Hz group.

Conclusions: Alternating frequency stimulation produced a greater elevation in the HPT, but a greater increase in the MPT was achieved using 100Hz stimulation.

Key Words: Pain; Rehabilitation; Transcutaneous electric nerve stimulation.

THE INVOLVEMENT OF ENDOGENOUS opioids is believed to be among the mechanisms of transcutaneous electric nerve stimulation (TENS) analgesia. In the 1970s, Sjolund[1,2] and colleagues demonstrated that low-frequency electroacupuncture increases the level of endorphins in cerebrospinal fluid (CSF) in patients with chronic pain. Later studies[3-6] found that different frequencies of electroacupuncture or TENS[7,8] activate the release of different endogenous opioids at both the supraspinal and spinal levels. Han et al[7] examined the effects of low- (2Hz) and high- (100Hz) frequency TENS by measuring the CSF before and after stimulation in patients with neurologic disorders. There was a 367% increase in Met-enkephalin-Arg-Phe after 30 minutes of 2Hz stimulation, whereas 30 minutes of 100Hz stimulation produced a 49% increase in immunoreactive dynorphin A. It is believed that low-frequency (2–4Hz) stimulation mostly causes an increase in the release of enkephalin, β-endorphins, and endomorphins[9-11] acting on the μ- and δ-opioid receptors.[12] High-frequency (100Hz) stimulation mainly enhances the release of dynorphin, which acts on the κ-opioid receptors.[7] Therefore, high- and low-frequency electric stimulation analgesia trigger the release of different opioid peptides.[13,14] Different stimulation frequencies therefore tend to involve slightly different analgesic mechanisms.[15]

Chen et al[16] proposed that the delivery of TENS at an alternating frequency stimulation of 2 and 100Hz would produce an optimal release of both enkephalin and dynorphin simultaneously, thus achieving a more potent analgesic effect. The idea of using alternating frequency stimulation was mainly based on reports of the synergistic interaction between different opioid peptides. Studies[17-19] have found that synergistic effects occur between the μ-opioid agonists and δ-opioid agonists, and interactions between the δ-opioid agonists and κ-opioid agonists.[20,21] The relative contribution of each opioid was unknown, however, and the mechanism for the synergistic action produced by different combinations of opioid was not well understood. There is limited evidence or research showing that this synergistic effect of different endogenous opioids triggered by alternating frequency stimulation will lead to a more potent analgesic effect in human beings.

Chen[16] applied a 2 and 15Hz alternating frequency stimulation of TENS to 12 orthopedic patients. The levels of Met-enkephalin-Arg-Phe and dynorphin A in CSF were measured before and after electric stimulation. There was an increase in opioids level in the CSF in all patients. No comparison was made with other fixed frequency stimulations or with a control group. Recent studies have compared alternating and fixed frequency stimulations. Hamza et al[22] examined the effects of different stimulation frequencies of TENS on the postoperative opioid analgesic requirements and recovery profiles of patients. One hundred women who had undergone major gynecologic procedures were randomly assigned into 4 groups: (1) patient control analgesia plus sham TENS; (2) patient control analgesia plus 2Hz TENS; (3) patient control analgesia plus 100Hz TENS; and (4) patient control analgesia plus an alternating

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0003-9993/07/8810-11706$32.00/0
doi:10.1016/j.apmr.2007.07.017

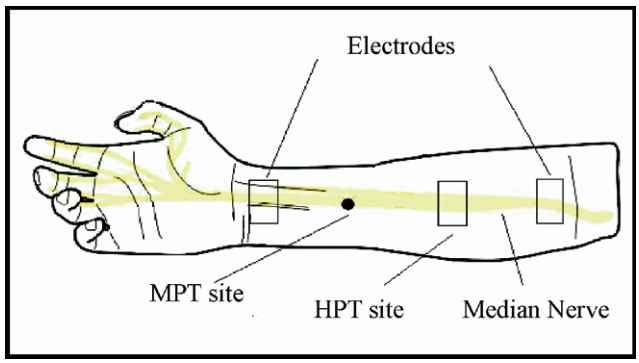

Fig 1. Placement of TENS electrodes recording sites for the MPT and HPT.

frequency TENS at 2 and 100Hz (2/100Hz). TENS was given for 30 minutes every 2 hours during the day. Visual analog scale scores (VASs) for pain and analgesic drug requirements were recorded as outcome measurements. There were no differences in VAS scores between the groups, but the use of alternating frequencies had a slightly greater effect in decreasing morphine requirements than did just the 2 or 100Hz frequencies.

Law and Cheing[23] examined the optimal stimulation frequency of TENS in people with knee osteoarthritis. Thirty-four participants were randomly allocated into 4 groups: TENS at either a (1) 2Hz, (2) 100Hz, or (3) 2/100Hz alternating frequency stimulation, or (4) a placebo TENS. Treatment was given 5 days a week for 2 weeks. VASs, knee range of motion, and the results of a Timed Up & Go test were recorded. The results seem to suggest that 2, 100, and 2/100Hz alternating frequencies produced similar treatment effects.

The above studies focused on clinical pain. A patient's medical history and severity of pain, as well as the course of the disease, however, can influence the effect of electric stimulation on clinical pain. The degree of confounding and variability might be lower if experimental pain was used. To date, there has been no study on the effectiveness of alternating frequency stimulation on experimental pain in healthy people. Our purpose in this study was to investigate whether an alternating frequency stimulation of TENS (2/100Hz) would produce greater analgesic effects than a fixed frequency delivered at 2 or 100Hz in healthy subjects.

METHODS

Participants

We recruited a convenience sample of 32 male and 32 female physiotherapy students and staff, aged 20 to 45. Excluded from the study were people with cardiac pacemakers, or with arrhythmia, tumors, diabetes mellitus, peripheral vascular disease, local skin infections, or pain conditions in the upper limbs. Participants also needed to pass both the hot and cold test and the pin-prick test before being randomly allocated to 1 of 4 groups. The Hong Kong Polytechnic University approved the study.

The 4 groups received TENS at: (1) 2Hz; (2) 100Hz; (3) 2/100Hz alternating frequency; or (4) were given no treatment (control group), respectively. In this study, we used a closed envelope method to randomize the participants and we randomized men and women separately because the 2 sexes may react differently to pain stimulation. Participants knew only that they would receive different protocols of TENS or placebo, but did not know the detailed implications of the stimulation protocols.

Experimental Procedures

Before the experiment, its purpose and procedures were explained to the participants and their written consent was obtained. We collected demographic data about age, sex, body weight, height, and body mass index (BMI) to compare the homogeneity between groups. The TENS machine[a] was located in a quiet and isolated room, with the temperature maintained at 21° to 23°C and relative humidity at 55%. The participants were seated in a comfortable and upright position with their dominant forearm resting on a table. The pulse width was set at 1000μs for the stimulation frequency of 2Hz and at 700μs for the stimulation frequency of 100Hz. For the alternating frequencies of 2 and 100Hz, 3.5 seconds of 2Hz stimulation with a 1000μs pulse width were followed by 2.5 seconds of 100Hz stimulation with a 700μs pulse width.

Demonstrations on the recording of the heat pain threshold (HPT) and mechanical pain threshold (MPT) were performed on the nondominant forearm. Each stimulation site was cleaned with alcohol. A pair of $3.5\times5cm^2$ rubber electrodes was prepared with gel and fixed over the anterior aspect of the dominant forearm with micropore tape. The electrodes were located over the distribution of the median nerve. The anode electrode was placed just proximal to the middle of the wrist crease and the cathode electrode was placed just distal to the middle of the elbow crease. HPT and MPT measurements were performed along the same dermatome (fig 1). For the 3 active TENS groups, the intensity of the current was increased to "strong but comfortable." The current was adjusted if the participants accommodated themselves to the current 5 minutes into the stimulation. Participants in the control group did not receive any electric stimulation, and no electrodes were placed on their forearms.

The testing procedures were based on those used in a previous study.[24] HPTs and MPTs were measured at 15-minute intervals before, during, and after the intervention (fig 2). There were a total of 6 recording periods, with 3 trials of HPT and 1 trial of MPT. Two baseline measurements were performed at −15 minutes (t1) and 0 minutes (t2) before the TENS intervention. Two measurements were obtained at 15 minutes (t3) and 30 minutes (t4) during the application. Two postintervention measurements were collected at 45 minutes (t5) and 60 minutes (t6) (see fig 2).

Outcome Measures

We measured the HPT with a thermal sensory analyzer,[b] which is a computer-controlled device with a 30×30mm con-

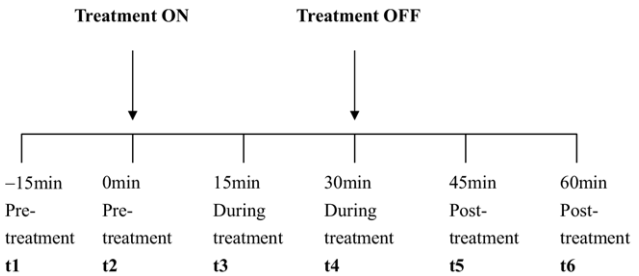

Fig 2. HPT and MPT were recorded at various time intervals; baseline measurements were recorded at t1 and t2; t3 and t4 were time periods when intervention took place; postintervention measurements were recorded at t5 and t6.