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Original Article

Comparison of the effective intensity of transcutaneous electrical nerve stimulation contralateral to a pain site for analgesia

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Abstract. [Purpose] This study aimed to compare the effectiveness of transcutaneous electrical nerve stimulation contralateral to the pain site for analgesia to identify the effective stimulation intensity. [Participants and Methods] Ten healthy adult females were recruited for the study. The same heat stimulation was applied to the left wrist joint of each participant to induce pain, serving as the control. Transcutaneous electrical nerve stimulation was then randomly administered to the right wrist, corresponding to the same dermatome contralateral to the painful site, at the intensities of comfortable stimulation, pain threshold, and maximum pain. The effect of transcutaneous electrical nerve stimulation was assessed using a Visual Analogue Scale and by analysis of heart rate variability. [Results] The Visual Analogue Scale score was significantly lower after stimulation with the maximum pain intensity than that for control, and there were no significant differences among the intensities of comfortable stimulation, pain threshold, and maximum pain. No significant differences were found among the groups in terms of high and low-to-high frequency components. [Conclusion] Transcutaneous electrical nerve stimulation at the maximum pain intensity to the dermatome area contralateral to that of the dorsal pain site of the left wrist was considered effective.
Key words: Transcutaneous electrical nerve stimulation (TENS), Intensity of TENS, Autonomic nervous system

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INTRODUCTION

Conventional transcutaneous electrical nerve stimulation (TENS) for the contralateral limb or cutaneous node of the contralateral limb is becoming increasingly widespread[1)], which is different from the traditional use of TENS with comfortable intensity for analgesia. To improve the current situation in which TENS[2)] cannot be performed on the painful area for analgesia in cases of phantom limb pain, severe allodynia, bleeding, or open wounds, treatment using the side contralateral to the painful area, the contralateral dermatome, or other sites is useful, as reported in basic animal studies[3–9)] and in human clinical studies[10–19)].

In a disease such as Complex Regional Pain Syndrome (CRPS), which is associated with pain, hyperalgesia, and allodynia, there have been reports[9, 20)] in rats regarding analgesia by TENS to the side contralateral to the symptoms. These disorders can also cause imbalances between the sympathetic and parasympathetic nervous systems, thereby disrupting the autonomic nervous system, and they have been difficult to manage. Treatment to provide analgesia and regulate the autonomic nervous system is essential in these cases. TENS can be one of the methods for this purpose, but it is important to systematize the evaluation and treatment by TENS.

There have been reports of the use of various stimulus intensities for TENS, including comfortable stimulus intensities based on gate control theory[21)] and strongest possible intensities[22–24)] that induce diffuse noxious inhibitory controls

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(DNIC)[25]. Furthermore, TENS has the potential to exert analgesic effects on central sensitization, expanding the therapeutic area[26–28]. On the contrary, there are only scattered reports comparing the analgesic effects of contralateral intensity of the stimulus and focusing on changes in sympathetic and parasympathetic nerves in the autonomic nervous system[29–31].

The purpose of this study was to identify the stimulation intensity that provides effective analgesia by comparing the effective intensity of the stimulus of TENS to the side contralateral to the pain site for the purpose of analgesia and to understand the effects on the autonomic nervous system.

PARTICIPANTS AND METHODS

The participants in this study were 10 healthy adult females [mean age of 21.8 ± 0.4 (range, 21–22) years] without neurological or orthopedic diseases of the limbs or trunk.

The Research Ethics Committee of Konan Women's University approved this study (2014205), and all participants gave their written, informed consent to participate after receiving a full explanation of the purpose of study and methods. The study complied with the ethical standards of the Declaration of Helsinki 1964 and subsequent revisions.

The design of this study was set as a single session of heat stimulation during measurement based on the single-epoch design of Koyama et al.[32] (Fig. 1). The study protocol involved 60 seconds of a resting sitting position at baseline, followed by a control (Cont) of 60 seconds of heat stimulation with conductive heat at 47°C from a Peltier device using a pain thermometer (UDH-201; Unique Medical Co., Ltd., Tokyo, Japan) to produce quantitative pain in advance in the left dorsal wrist joint[13].

Next, to achieve pain-relief, a total of three different types of TENS were applied randomly. These three TENS interventions involved TENS applied to the contralateral right dorsal wrist joint at the same dermatome level as the site of pain in the left dorsal wrist joint (CW). Five minutes of rest was scheduled before each TENS intervention, and 90 seconds of rest was scheduled at the end after completion of all TENS interventions. CW was performed on a rectangular site measuring 10 cm horizontally and 5 cm vertically, established on the skin on the dorsum of the right wrist joint at the same dermatome level as the site of pain in the left dorsal wrist joint. The myelomere levels of this dermatome were C6, C7, C8, and T1 (Fig. 2).

TENS was performed using an electrostimulator (ES-520; Ito Co., Ltd., Tokyo, Japan) for 60 seconds at a frequency of approximately 15 Hz[33] and a wavelength of 200 μs, which can trigger the release of large quantities of hormones, including endorphins, enkephalins, β-endorphin, and dynorphins, which are opioid peptides. The intensity of TENS was set at a comfortable intensity of the stimulus (CF) based on gate control theory, the intensity at pain threshold (PT), and the intensity inducing maximum pain (MP) at the threshold of pain for CW based on DNIC[25] at CW, at the same dermatome contralateral to the painful site on the left hand joint.

CF, PT, and MP were set to be of intensities that could be easily explained to and understood by patients in clinical practice.

To determine the therapeutic effect, a visual analogue scale (VAS) was used for pain evaluation during 60 seconds for each of Cont, CF, PT, and MP. The VAS is a pain rating scale (from 0 to 100), with 0 defined as no pain and 100 as the worst imaginable pain.

To evaluate the autonomic nervous system, electrocardiograms (ECG) were measured using myBeat WHS-1/RRD-1 (UNION TOOL CO. Tokyo, Japan). Skin electrodes were applied to the fourth intercostal space at the center of the left anterior chest, and the RR interval (sampling frequency 1 kHz) was recorded.

The power (ms^2) in the high frequency (0.15 to 0.4 Hz) components (HF), which reflects parasympathetic nervous system activity, and the power in the low frequency (0.05 to 0.15 Hz) components (LF)/HF components (LF/HF), which reflects sympathetic nervous system activity, were analyzed as an index of frequency components of heart rate variability. HF (ms^2) and LF/HF were measured for 60 seconds during each of Cont, CF, PT, and MP, and the numeric values obtained were tallied and calculated as means.

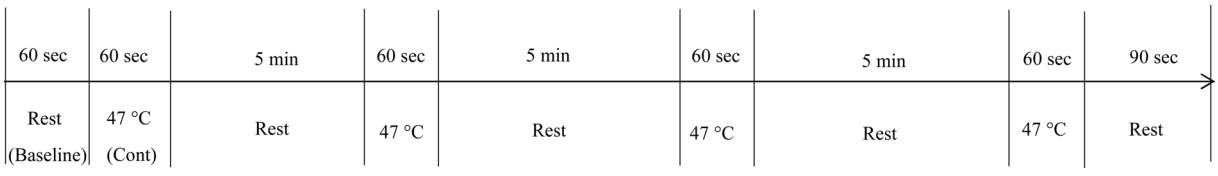

Fig. 1. Experimental protocol (single-epoch design).
After a baseline session of 60 seconds, Cont is performed followed by three 60-second interventions (TENS to CF, PT, and MP). The rest between the control and the three interventions is 5 minutes. TENS is applied to CF, PT, and MP using heat stimulation at 47°C. Rest: Baseline session of 60 seconds, 60 sec: Control and three interventions performed for 60 seconds, 5 min: Rest between control and three interventions, 90 sec: Rest at the end of all TENS interventions, 47°C: heat stimulation at 47°C, Cont: Control; Heat stimulation at 47°C applied to the left wrist joint to produce pain, CF: TENS of a comfortable stimulation intensity, PT: TENS of the intensity at pain threshold, MP: TENS of the intensity inducing maximum pain, TENS: transcutaneous electrical nerve stimulation.

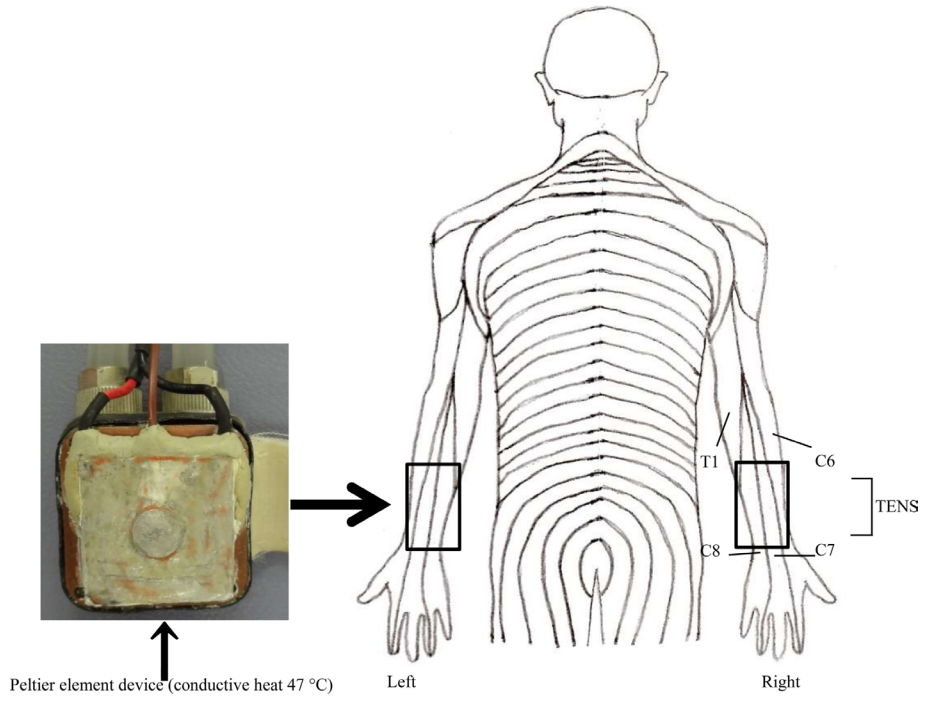

Fig. 2. Placement of right TENS electrodes for the site of pain in the left dorsal wrist joint. Right TENS electrodes are placed on the contralateral right dorsal wrist joint (C6-T1) at the same dermatome level as the site of pain in the left dorsal wrist joint. TENS: transcutaneous electrical nerve stimulation.

The VAS and the HF and LF/HF value obtained from ECG were used in statistical processing. One-way analysis of variance was used for comparisons by condition, and Tukey's post hoc test was used for multiple comparisons. The level of significance was set at $p<0.05$ for all tests. All statistical analyses were performed using IBM SPSS Statistics 20 (Tokyo, Japan).

RESULTS

The mean intensity of TENS at CF at a gate control theory-based comfortable intensity was 3.3 ± 1.0 mA (2–5 mA), PT at the threshold of pain was 5.4 ± 1.5 mA (3–8.5 mA), and MP at the DNIC-based threshold of pain, the intensity inducing maximum pain, was 8.0 ± 2.3 mA (4–12 mA). Significant differences in the intensity of TENS were observed among CF, PT, and MP in all combination comparisons.

The levels of pain measured by VAS of Cont, CF, PT, and MP were 29.8 ± 14.4, 26.7 ± 16.3, 23.7 ± 14.4, and 17.3 ± 12.4, respectively; the VAS of MP was significantly lower than that of Cont. Multiple comparisons of post-intervention levels of pain measured by VAS among the three interventions (CF, PT and MP) showed no significant difference between any of the combinations.

No significant differences in HF and LF/HF were observed among Cont, CF, PT, and MP in all combination comparisons (Table 1).

DISCUSSION

Electrical stimulation for analgesia was first applied against the background of the gate control theory of Melzack and Wall[21], and later, based on the principles of DNIC, etc., the stimulation site was changed from the pain site to other sites[25], and the intensity of the stimulus and other stimulus have been improved. TENS was performed at the site of pain, the same dermatome as the site of pain, the same dermatome contralateral to the site of pain, and a different site from the site of pain.

In the present study of TENS, the degree of pain as measured by the VAS was significantly lower in MP than in Cont. In contrast, since there was no significant difference between MP and CF or PT, we believe that MP can be used as a better intensity, since there was no clear difference between MP and CF or PT stimulus intensities. However, previous studies[22–24] have shown the same tendency. The reasons may include analgesia to central sensitization[26–28], the descending pain modulatory system[24, 34, 35], DNIC[25], and release of endogenous opioid peptides[35, 36].

Table 1. VAS, HF, and LF/HF comparison of TENS between Cont and each intensity (n=10)

	Cont	CF	PT	MP
Intensity (mA)		3.3 ± 1.0[*1]	5.4 ± 1.5[*1]	8.0 ± 2.3[*1]
VAS	29.8 ± 14.4	26.7 ± 16.3	23.7 ± 14.4	17.3 ± 12.4[*2]
HF (ms^2)	314.7 ± 204.4	336.3 ± 197.3	292.0 ± 215.5	460.8 ± 381.0
LF/HF	1.5 ± 1.2	2.1 ± 2.1	2.1 ± 1.6	1.7 ± 1.5

[*1] Significant difference in all comparisons, Tukey's post-hoc test ($p<0.05$), one-way analysis of variance ($F=19.403$, $df=2, 27$, $p<0.001$).
[*2] Significant difference compared with the control, Tukey's post-hoc test ($p<0.05$), one-way analysis of variance ($F=3.797$, $df=3, 36$, $p<0.05$).
No significant differences in HF and LF/HF were observed among Cont, CF, PT, and MP in all combination comparisons.
Cont: Control; Heat stimulation at 47°C applied to the left wrist joint to produce pain, CF: TENS of a comfortable stimulation intensity, PT: TENS of the intensity at pain threshold, MP: TENS of the intensity inducing maximum pain, VAS: Visual Analogue Scale. VAS is a pain rating scale (from 0 to 100), with 0 defined as no pain and 100 as the worst imaginable pain, HF: power in the high frequency (0.15 to 0.4 Hz) components reflecting parasympathetic nervous system activity, LF/HF: power in the low frequency (0.05 to 0.15 Hz) components (LF)/HF reflecting sympathetic nervous system activity, TENS: transcutaneous electrical nerve stimulation.

The duration of the stimulus in this study was 60 seconds, which was shorter than the 30 minutes in the previous study, and it is possible that the analgesic tolerance was not adequately considered. However, given that this strong TENS also has the issue of tolerance[37–39], it is necessary to prepare for tolerance by modulating the frequency and increasing the stimulation intensity during treatment.

TENS has been used as an analgesic treatment for central sensitization induced by pain stimulus, and the effects have been reported[26–28]. The analgesic effects of the treatment to central sensitization is based on TENS to the site of pain.

Contralateral stimulation has been reported in studies that recorded brain activity at the site of brain response to pain stimuli in both the contralateral and ipsilateral cerebral hemispheres using magnetoencephalography[40–42]. Because it is possible to record equivalent current dipoles that respond to unilateral electrical stimulation in the somatosensory cortices of both the contralateral and ipsilateral cerebral hemispheres, applying stimulation to a site contralateral to the site of pain could stimulate the ipsilateral hemisphere responding to the site of pain and, thereby, be a useful intervention, because the same stimulus may have ascended as the TENS at the ipsilateral site of pain.

The intensity of TENS to the dorsal right wrist at the same dermatome contralateral to the left pain site was significantly more effective with MP than with Cont. This suggests that TENS applied to the same dermatome contralateral to the site of pain could be effective in patients whose site of impairment cannot be treated directly due to wound, amputation, or other reason. The affected site cannot be directly treated in patients with phantom limb pain, symptoms of acute trauma, and CRPS including allodynia and post-herpetic neuralgia, so alternative locations for the application of TENS must be considered. Whether there are other effective analgesic treatment sites besides the affected site in conditions such as phantom limb pain and reflex sympathetic dystrophy has been investigated. Our accumulated studies indicate that it is important to make effective use of other sites, including contralateral dermatomes and trunk dermatomes[12, 13].

Although the stimulation site is different from the site of pain, the CW is at the level of the same dermatome on the contralateral side of the dorsal pain site of the left wrist joint, which is easy to visualize and to explain that it is the same dermatome symmetrical to the site of pain.

As for the effect on the autonomic nervous system, a previous comparative study[29–31] before and after TENS with a treatment time of 30 minutes at 4–10 Hz showed an increase in HF, which reflects parasympathetic nervous system activity. In the present study, the stimulation duration of TENS was 60 seconds, which was short, and this may be the reason why there was no effect on the autonomic nervous system.

By establishing the effective stimulation intensity of TENS to the contralateral side of the pain site, we expect to begin TENS to the contralateral side of the pain site at an early stage to reduce pain and to shorten the duration of analgesic treatment.

A possible limitation of this study was that the setting of the modulation of the frequency of tolerance suppression of TENS, the waveform of the stimulus, the duration of the stimulus, and the treatment time, which are important factors other than the intensity of the stimulus in implementing TENS on the contralateral side of the pain site, were not clear, and the comparison was only made by stimulus intensity based on the combination of the contralateral stimulus and stimulus intensity.

The anatomical and physiological basis of the stimulus input pathways and analgesic mechanisms may be unclear. Reported mechanisms are those based on analgesia to central sensitization, the descending pain modulatory system, DNIC, and release of endogenous opioid peptides. It is important to continue to elucidate the therapeutic effects of TENS in both basic and clinical research investigations and to establish appropriate treatment protocols.

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Conflict of interest

The authors declare no conflict of interest.

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