A Descriptive Study Investigating the Feasibility and Selectivity of Current Perception Threshold in the Objective Assessment of Post-operative Sub-acute Knee Pain

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Abstract. [Purpose] The aim of this study was to investigate the feasibility of using the current perception threshold (CPT), in a comparison with the visual analog scale (VAS), to assess its selectivity in assessing the excitability of Aβ, Aδ and C fibers in subjects with sub-acute post-operative pain who were being treated with conventional transcutaneous electrical nerve stimulation (TENS). [Subjects and Methods] A total of 17 subjects (mean age of 29.2 ±10.8 years) participated in this study. For all subjects, the study commenced on the fifth post-operative day and continued for the next five consecutive days following a descriptive time-series design. Both CPT and VAS were measured for all subjects on all five days following 15 minutes rest with the TENS output intensity set at zero on the baseline days (Days 1, 3, 5), and after 15 minutes TENS stimulation on the intervention days (Days 2 and 4). [Results] The results demonstrate that CPT was able to selectively assess the excitability of the Aβ and Aδ fibers. However, the selectivity of CPT in assessing the C fibers could not be verified in this study. [Conclusion] The various limitations of the time series design used in this study suggest the need to verify some of these results in a different experimental design in future studies.

Key words: Current Perception Threshold, Pain assessment, Transcutaneous Electrical Nerve Stimulation (TENS)

INTRODUCTION

Transcutaneous electrical nerve stimulation (or TENS) is a non-invasive, low-risk treatment method which is commonly used for the management of pain, using electrical energy applied over the skin to stimulate the sensory nerve fibers1). TENS has been reported to be effective at controlling pain associated with various types of medical condition such as cancer, rheumatoid arthritis, knee and back injuries, labor and menstrual pains, and post-operative pain, among others2). The neurophysiological mechanisms of pain relief attributed to TENS include an increase in the sensory threshold with a concomitant decrease in the excitability of peripheral nociceptors, activation of the gate control mechanisms via increased non-noxious input from the large myelinated Aβ fibers, activation of inhibitory cortical descending pathways via the pain matrix, as well as an increase in the release of endogenous opiates1, 3). These neurophysiological mechanisms of pain relief are achieved through different stimulation conditions such as frequency and output intensity of alternating current (AC) and pulse current (PC), as well as pulse duration of PC1, 3). Seven different combinations of stimulation conditions (or modes) have been described1) and each of these modes is supposed to target different neurophysiological mechanisms of pain relief1). The two most common modes used in clinical practice are conventional TENS (high frequency > 50 Hz; low output intensity below the motor threshold) and acupuncture-like TENS (low frequency < 10 Hz; high output intensity below the pain threshold)1–3). The onset of pain relief following conventional TENS, which targets the gate control mechanism, is very quick (within minutes) but the carry-over effect after cessation of stimulation is very short (up to 30 to 60 minutes). In contrast, the onset of pain relief following acupuncture-like TENS, which targets the endogenous opiate system, is slow (within hours) but the carry-over effects are longer (up to 24 hours)1–3). Compared with acupuncture-like TENS, conventional TENS is usually more comfortable for patients since the stimulation intensity is below the motor threshold and without accompanying muscle contractions. This is particularly useful for treating patients with acute or sub-acute pain where unwanted muscle contractions can aggravate muscle spasms associated with the body’s protective mechanisms1). Depending on the aim of the treatment and the desired target mechanism, the clinician usually chooses between these two commonly
used TENS modes. For example, for patients with acute or sub-acute post-operative pain, conventional TENS, which is more easily tolerated than acupuncture-like TENS, is often used to target the gate control mechanism as an adjunct to pharmaceutical pain management4.

Clinically, post-operative pain can interfere with patient recovery by limiting patients’ voluntary movements and their ability to participate in exercise therapy. Pharmaceutical management of post-operative pain with analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) are useful, but are not without various side-effects. These pain medications also require supervision and administration by skilled personnel. TENS, on the other hand, can be self-administered by the patient with minimal supervision, and has been reported to be effective not only at controlling post-operative pain directly, but also at reducing patients’ reliance on pain medication5. In most studies investigating the effects of treatment of pain, the visual analogue scale (VAS) is used to assess subjects’ pain perception. Bjordal et al., in their meta-analysis of studies investigating the use of TENS for management of post-operative pain, criticized the use of VAS, a subjective measure, as inadequate4. They argued that in most of the trials, analgesics were provided to the patients as a co-intervention and this could have influenced the VAS scores. Bjordal et al. suggested that measuring the amount of analgesic consumption may serve as an objective measure of the effectiveness of TENS in post-operative patients. However, they failed to recognize that even this has several limitations and is influenced by confounding variables such as gender (males may have higher pain tolerance than females), ratios of sleep to wakefulness (patients who are asleep more often than awake are less likely to request medication), and ward medication rounds (medications may be prescribed and administered at regular intervals regardless of patient’s request), among others. An alternative objective measurement of pain intensity that has been proposed is the current perception threshold (CPT)5, 6. However, the feasibility of using this tool in clinical trials has not been clearly established. In addition, it is not clearly understood how CPT measurements are different from, or similar to, the present standard measurement of pain using the VAS.

CPT is a double blind objective method for assessing the sensory threshold of sensory nerves which uses electrical stimulation of the skin with surface electrodes at different frequencies5. A commonly used CPT device is the Neurometer NS3000 (Neurotron Inc., Baltimore, Maryland, USA) which employs a constant alternating sinusoidal current to deliver electrical stimulus at frequencies of 2000, 250 and 5 Hz5. It has been reported that these 3 frequencies can selectively stimulate, and therefore assess, the large myelinated Aβ fibers, the small myelinated Aδ fibers, and the unmyelinated C fibers, respectively5, 9. Since CPT devices are usually constant current stimulators, skin impedance is not a limiting factor and the results are unaffected by skin temperature, skin thickness or elasticity7. Kudoh et al. reported the use of such a device to assess the post-operative pain tolerance of patients with chronic schizophrenia in a comparison with normal controls10. Their results show that patients with chronic schizophrenia had higher post-operative pain tolerance than normal controls as shown by their increased CPT values and lower VAS pain scores10. In other words, when CPT values are high, pain perception is decreased as reflected by low VAS scores. Conversely, when CPT values are low, pain perception is increased as reflected by high VAS scores.

The aim of this study was to investigate the feasibility of using CPT in a comparison with VAS, to assess its selectivity in assessing the excitability of Aβ, Aδ and C fibers in subjects with sub-acute post-operative pain who were being treated with conventional TENS. The clinical relevance of this study is twofold: the results will determine the feasibility of using objective outcome measures such as CPT to evaluate changes in pain perception following treatments such as TENS; and this study can clarify the use of conventional TENS for pain management in post-operative patients in order to facilitate voluntary movement and the early implementation of exercise therapy, both of which are usually inhibited by pain.

SUBJECTS AND METHODS

The subjects of this study were recruited from an affiliated university hospital. They were scheduled for elective reconstructive surgery of the anterior cruciate ligament of the knee. Informed consent was received from the subjects prior to their inclusion in the study. Subjects were excluded from the study if they had sensory disturbance of the skin surrounding the knee joint, or any other contraindications to percutaneous electrical stimulation such as wound infection. A total of 17 subjects (11 males, 6 females) with a mean age (+standard deviation) of 29.2 (+10.8) years old participated in this study which was approved by the Faculty of Medicine Ethical Review Board of Shinshu University.

The research design of this study employed a time series reversal design, commonly known as the A-B-A-B design11. This quasi-experimental design begins with a baseline measurement (the first A), followed by a post-intervention measurement (the first B), the withdrawal of the intervention to establish a second baseline (the second A), followed by the re-introduction of the same treatment (the second B). Variations to this design include repeating the A-B cycle more than twice, or ending the cycle with an A rather than a B. Compared with other experimental designs such as a randomized controlled trial (RCT), the A-B-A-B design has the advantage of avoiding the ethical dilemma of withholding treatment from subjects in the control group. In this design, the subjects serve as their own “control” during the “reversal” stage of the study. Another advantage to the A-B-A-B design is that fewer subjects are needed, compared to a RCT design, since there is only one group. However, since the A-B-A-B design is a descriptive study by nature, it was not the intention of this study to investigate the effectiveness of TENS treatment.

Based on the abovementioned considerations, this study followed an A-B-A-B-A design (Fig. 1). For all subjects, the study commenced on the fifth post-operative day and continued for the next five consecutive days. The first, third, and fifth days were the non-intervention days (“A” or baseline days). On the second and fourth days, subjects were treated with TENS (“B” or intervention days). Both
CPT and VAS were measured for all subjects on all five days following 15 minutes rest with the TENS output intensity set at zero on the baseline days, and after 15 minutes TENS stimulation on the intervention days (Fig. 1).

The TENS device used was the Trio300 (ITO Co. Ltd., Tokyo, Japan) and the stimulation conditions were: 100 Hz frequency, 200 μsec pulse duration, 15 minutes treatment duration, and a current intensity of between 6 and 22 mA (sensory stimulation). The bipolar electrodes were placed approximately 15 cm apart at just below the patella and medial to the tibial tuberosity, and above at the superior lateral border of the patella.

CPT was measured using the Neurometer NS3000 (Neurotron Inc., Baltimore, Maryland, USA). The Neurometer electrodes were placed about 5 cm apart along the superior and medial border of the patella. The test procedure was dictated by the device’s software, based on a double-blind protocol, and the CPT values for 2000 Hz, 250 Hz and 5 Hz were recorded for each subject in this manner.

VAS was recorded using a sliding ruler on a 10-cm scale (Pfizer Japan, Tokyo). Subjects were instructed to rate their perceived pain level on the 10-cm line, by sliding the knob on the ruler. Measurements were recorded in millimeters.

For the analysis, the dependent variables were VAS and CPT (CPT2000 Hz, CPT250 Hz, CPT5 Hz), and the independent variable was days (Day 1 to 5). Descriptive statistics (mean ± SD) of the dependent variables were calculated and tabulated over the five days. All statistical analyses were carried out using the SPSS 11.0 J for Windows software (SPSS Inc., Chicago, IL, USA).

RESULTS

The means and standard deviations of VAS and CPT2000 Hz, CPT250 Hz and CPT5 Hz are summarized in Table 1.

The results for VAS show a sharp decrease between Day 1 (baseline) and Day 2 (post-TENS), and between Day 3 (baseline) and Day 4 (post-TENS). However, between post-TENS days and the next baseline days, there was only a slight decrease (between Day 2 and 3) and even an increase (between Day 4 and 5) in the VAS scores. Overall, there was a general decrease in VAS scores between the first and the final days.

The results for CPT2000 Hz show a very slight increase between Day 1 (baseline) and Day 2 (post-TENS), and between Day 4 (post-TENS) and 5 (baseline). However, from Day 2 to 4, there was an almost linear decrease in CPT2000 Hz. Overall, the CPT2000 Hz decreased between the first and final days.

The results for CPT250 Hz show an increase between both baseline and post-intervention days (between Day 1 and 2, and between Day 3 and 4). Between post-intervention and baseline days, however, there was a decrease in CPT250 Hz. Overall, the CPT250 Hz decreased between the first and final days.

The results for CPT5 Hz show a decrease from Day 1 to 3, and thereafter remained relatively unchanged until Day 5. Overall the CPT5 Hz decreased between the first and the final days.

DISCUSSION

The results of the VAS assessment of pain show a sharp drop immediately after TENS on both intervention days, which was expected. However, due to the limitations of the study design, it was not possible to attribute this to the TENS treatment alone. Descriptively, however, the results indicate that this decrease immediately after TENS treatment may be due to factors other than just time. This result is consistent with current evidence indicating that TENS is effective in the treatment of pain4. Interestingly, the VAS score increased from Day 4 to 5 and this coincided with the patients starting to ambulate from Day 4.

The CPT evaluation was performed at the 3 frequencies, 2000 Hz, 250 Hz and 5 Hz, corresponding to evaluation of the Aβ, Aδ and C fibers7, 8. In theory, the effect of TENS on each of these 3 types of fibers should be different since they represent three different neurophysiological mechanisms of pain2.

The results for CPT2000 Hz suggests that the nerve excitability of the Aβ fibers actually increased over the 5 days. The Aβ fibers have a direct input into the gate control mechanism, and an increase in Aβ fibers excitability would...

<table>
<thead>
<tr>
<th>DAY</th>
<th>VAS (mm)</th>
<th>CPT2000 Hz (X10μA)</th>
<th>CPT250 Hz (X10μA)</th>
<th>CPT5 Hz (X10μA)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>1</td>
<td>25.65</td>
<td>21.31</td>
<td>142.35</td>
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<td>143.76</td>
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<tr>
<td>5</td>
<td>14.24</td>
<td>12.05</td>
<td>115.29</td>
<td>57.85</td>
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Table 1. Descriptive statistics (mean±SDs) for VAS, CPT2000 Hz, CPT250 Hz, and CPT5 Hz

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suggest that activation of the gate control mechanism was facilitated, resulting in decreased pain perception. The decrease in VAS score evidentially supports this hypothesis. This suggests that the conventional mode TENS used in this study was quite effective at decreasing post-operative pain via activation of the gate control mechanism. However, it is not possible to attribute this solely to the effects of the TENS intervention because of the limitations of the time series design. Nevertheless, this result does seem to support the proposed mechanism of pain relief by conventional TENS through the gate control mechanism. It will be necessary to confirm this finding with a RCT design in future studies. More importantly, the result of this study seems to validate the use of CPT at 5 Hz for the assessment of the excitability of Aβ nerve fibers.

The result for CPT at 5 Hz may be the clearest indication that the conventional TENS used in the study was effective at decreasing pain perception via decrease of the excitability of the Aβ fibers. The sensory threshold of the Aβ fibers increased immediately following TENS intervention on Days 2 and 4. On the other hand, the results for the CPT at 5 Hz indicate that the conventional TENS used in this study had no effect whatsoever on altering the nerve excitability of the C fibers. Both the small myelinated Aδ fibers and the unmyelinated C fibers are nociceptors directly involved in transduction of noxious stimuli, transmitting them to the dorsal horn of the spinal cord. Aδ fibers are responsible for the transmission of fast sharp pain while the unmyelinated C fibers are responsible for the slower dull aching pain. If the sensory threshold increases, this suggests that transduction of the noxious stimuli would be less likely and therefore, pain transmission would also decrease. Conversely, if the sensory threshold decreases, this suggests that transduction of the noxious stimuli would be more likely, and therefore, pain transmission would increase. The results of this study demonstrated that immediately following conventional TENS, there was an increase in the sensory threshold of the Aδ fibers, but not the C fibers. This suggests that conventional TENS was more effective at decreasing the transduction of fast pain rather than slow pain, and therefore was more effective at treating sub-acute post-operative pain. However, it can be argued that this study did not measure the effects of conventional TENS on C fibers as CPT evaluation was carried out immediately after TENS treatment, and was not followed up a few hours after the treatment. Changes in the sensory threshold of C fibers may take longer to manifest and therefore, changes in the transduction of noxious stimuli would be less likely, and therefore, pain transmission would also decrease. Conversely, if the sensory threshold decreases, this suggests that transduction of the noxious stimuli would be more likely, and therefore, pain transmission would increase.

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