The Analgesic Effect of Transcutaneous Electrical Nerve Stimulation (TENS) on the Opposite Side for Phantom Limb Pain


*Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, **Clinical Epidemiology Unit, Office for Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, ***Department of Anesthesiology, Dr. Wahidin Sudirohusodo-Hasanuddin University General Hospital, Makassar-Indonesia.

ABSTRACT

Objective: To observe the effects of TENS on the contralateral limb and PLP reduction.

Materials and Methods: This was a single center retrospective study of 20 amputee participants with phantom limb pain. The inclusion criteria were participants aged above 18, average pain of at least 4/10 on the numerical rating scale (NRS), duration of pain longer than one week and treatment with TENS on the opposite side. We recorded pain intensity before and after TENS application, response time to treatment, satisfaction, and adverse effects.

Results: Of the 20 amputee participants, all patients suffered from PLP and three also suffered from residual limb pain. The average pain score before use of TENS was 4.85/10 and after was 1.15/10. The mean pain intensity score was reduced by 3.7/10 (95% CI 2.95-4.45/10) or 76.28% (95% confidence interval 63.61-89.47%). The average overall satisfaction was 81.65%, and no adverse effects from application of TENS was reported.

Conclusion: The study shows that the application of TENS on the opposite side is a safe and effective treatment method for intractable pain from PLP.

Keywords: Transcutaneous electrical nerve stimulation; amputee; phantom limb pain; contralateral; neuromodulation; neuropathic pain (Siriraj Med J 2022; 74: 239-244)

INTRODUCTION

Up to 80% of amputees experience pain sensation to a limb after amputation (phantom limb pain: PLP) and/or pain at the stump (residual limb pain; RLP) that negatively impacts their quality of life.1-5 Although chronic PLP is common, evidence evaluating the efficacy of treatments remains scarce, and there is still no consensus for a standard treatment in standard guidelines.5,6 The most common treatments are pharmacological. However, strong evidence supporting the short and long-term efficacy of pharmacological treatments for PLP is still lacking.5,7

In an effort to identify additional effective treatment options for PLP, clinicians and investigators have examined a variety of non-pharmacological treatments such as application of mirror visual feedback8,9 and transcutaneous electrical nerve stimulation (TENS)10-13, especially for the patients who had limited success from pharmacological treatment. TENS delivers pulsed electrical currents across the intact surface of the skin to stimulate the peripheral
nerves and spinal cord, resulting in segmental and extrasegmental analgesia. Research indicates that the application of TENS at the site of residual limb pain or projected site of phantom pain is associated with decreases in pain intensity, both at rest and during movement. However, residual limb application of TENS can be challenging in certain situations because it may aggravate discomfort in patients with pre-existing pain or cause skin irritation that reduces stump integrity in recent amputees.

Contralateral TENS, by inhibiting the contralateral segmental in the dorsal horn from another side, potentially alleviates PLP and can address the problems associated with the stump. A number of reports and small case series have reported successful outcomes of contralateral TENS for PLP, and we already apply this treatment in our daily practice. As there is no data collection of large series for such treatment, we conducted this study to examine the effects in the Thai population.

We hypothesized that patients with PLP who received TENS on the contralateral limb would report significant pain reduction after treatment. The primary objective of this study was to observe the effects of TENS on the contralateral limb and PLP reduction. The secondary objectives included observing for adverse effects, satisfaction, and the duration of contralateral TENS treatment for PLP.

MATERIALS AND METHODS

In this retrospective observational study, in order to compare the analgesic effect before and after treatment, we performed sample size calculations with the aim to detect a 30% reduction in pain scores after treatment, which is a meaningful change. Using data from a pilot study, the mean pain score of patient suffering from phantom limb pain in our center was 5.2/10 (SD=2). By using PASW Statistics version 18 (Chicago, IL, USA), a sample size of 16 patients was enough to detect a difference, with an alpha error of 0.05 and power of 90%. As the estimate of incomplete data was 20%, the final number of patients needed for this study was adjusted to 20 patients.

After approval by the Mahidol University-IRB, the research team identified the medical records of patients who suffered from phantom limb pain at the Siriraj Pain Clinic and received contralateral TENS treatment for pain relief at Siriraj Hospital from January 1, 2018 to December 31, 2018. The research team collected the following data points:

1. General demographic and medical history, including age, sex, and cause of amputation
2. Pain history, including pain diagnosis, past medications and previous treatment(s) for PLP, and pain-related interference assessed by a validated Thai version of a brief pain inventory questionnaire
3. NRS before and after treatment
4. Side effects and patient satisfaction of treatment

In routine practice, we offer the treatment to adult patients who have moderate to severe pain (average pain intensity from numeric rating scale more than 3 out of 10) despite appropriate pharmacological treatment (the patients had taken at least two analgesics). TENS was not offered in contraindicated conditions such as pregnancy, epilepsy, active malignancy, deep vein thrombosis, frail or damaged skin or to patients with cardiac pacemakers or implantable cardioverter defibrillators.

We used commercially available TENS units in our daily practice (Fig 1) due to their low cost and ease of use. First, we applied TENS’ electrodes on the contralateral limb, mimicking the pain area on the opposite side. As the commercial TENS units were obtained from a variety of brands and did not have measurable parameter settings (frequency, pulse width, amplitude), we used clinical response as our end point. We turned on the stimulation and increased the intensity until the patient felt pain-free paresthesia.

We recorded an initial pain score, then applied the stimulation for at least 30 minutes and recorded their subsequent pain score. If the patient did not report any change, the session was extended to 45 minutes or 60 minutes. At the end of the session, we assessed the patient satisfaction scale (0-100) and the presence of any adverse effects. There was no long-term follow-up after the session.

Fig 1. Commercially available TENS unit.
RESULTS

We collected data from a total of 21 patients who received treatment. However, one patient was excluded because of amputation on both legs. There is no exclusion due to unreliable reporting of pain score because of psychological or physical morbidities. Finally, the data of 20 patients were included in this analysis. All patients had been suffering from PLP, and three of them also suffered from residual limb pain (RLP). The demographic data of all patients is shown in Table 1. The average pain score was 4.85 out of 10 despite the use of at least two analgesics such as gabapentin, tricyclic antidepressant, or opioids (Table 2). The pain-related interferences were evaluated by a brief pain inventory questionnaire. The average total score of pain-related interference (impact of pain on general activity, mood, work, relationships, sleep, and enjoyment of life) was 16.35 out of 60. The average time elapsed since amputation before this treatment was 1.9 years.

Pain intensity

Pain intensity was rated by the average numeric rating pain score (NRS). The average NRS before application of TENS was 4.85/10 ±1.18, and it decreased to 1.15/10±1.38 after the treatment. The difference in average pain intensity was 3.7±1.59 with a p-value of <0.001 for the paired T-test (95% confidence interval was 2.95-4.45). The NRS ranged from 3-8 out of 10 before application of TENS and decreased to 0-5 post-treatment.

Nineteen out of 20 patients reported clinically significant pain relief (pain score decreased by more than 30%). The mean percentage of pain reduction was 76.54 ± 6.18% (95% confidence interval was 63.61-89.47%).

The individual responses to treatment are shown in Fig 2. Only one patient who had PLP after a right elbow amputation due to recurrent fibrosarcoma (number 12) did not respond to treatment. This patient also did not respond well to other treatments, including gabapentin and tricyclic antidepressants.

Duration of treatment

In this study, we applied TENS on the contralateral limb until the pain score decreased or for 60 minutes, if pain did not improve. Sixteen participants responded to treatment in the first 30 minutes, and another three responded after it was extended to 45 minutes. Only one participant (patient 12) reported no significant change in NRS after 60 minutes. The median time required for TENS to decrease pain was 30 minutes. The cumulative number of responders over time is shown in Fig 3.

### Table 1. Patient’s demographic data. PLP (phantom limb pain), RLP (residual limb pain).

| Demographic data (n=20) |     |
|------------------------|--|---|
| Sex                    | Male | 10 (50%) |
|                        | Female | 10 (50%) |
| Age: mean ( SD) years | 57.1 (15.63) |
| Pain                   | PLP | 20 (100%) |
|                        | PLP+RLP | 3 (15%) |
| Level of amputation    | Transhumeral | 5 (25%) |
|                        | Transfemoral | 9 (45%) |
|                        | Transtibial | 6 (30%) |
| Cause                  | Vascular | 8 (40%) |
|                        | Trauma | 5 (25%) |
|                        | Tumor | 7 (35%) |

### Table 2. Medication used for treatment of phantom limb pain.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Number of patients (Percentage)</th>
<th>Dose range (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>20 (100%)</td>
<td>600-3000</td>
</tr>
<tr>
<td>Tricyclic antidepressants (amitriptyline, nortriptyline)</td>
<td>15 (75%)</td>
<td>10-25</td>
</tr>
<tr>
<td>Weak opioids (tramadol, codeine)</td>
<td>11 (55%)</td>
<td>Tramadol 50-400 mg/day</td>
</tr>
<tr>
<td>Strong opioids (morphine)</td>
<td>1 (5%)</td>
<td>20 mg/day</td>
</tr>
</tbody>
</table>
Adverse effect and satisfaction

The application of transcutaneous electrical nerve stimulation on the contralateral side was tolerated by all participants without any adverse events during the session. Participants reported no difficulty in using TENS and titrating the amplitude. The average overall satisfaction was 81.65% (0-100% and 0% for patient 12).

DISCUSSION

This study aimed to determine if the application of TENS on the opposite limb could reduce pain intensity in patients suffering from PLP. Our findings suggest a significant reduction of NRS immediately after treatment. Additionally, the treatment led to high satisfaction rates and no report of adverse events.

Following amputation, up to 80% of patients reported pain, either in the part that was amputated (phantom pain) or at the site of amputation (residual limb pain), or both. This pain can affect their quality of life and prevent proper rehabilitation and prosthetic usage. PLP is poorly understood and one of the most difficult type of pain to treat. The underlying pathophysiology of PLP is unclear, although it is generally accepted that nociceptive and neuropathic processes are involved and that neuropathic changes include reorganization and adaptation within the peripheral and central nervous systems. Additionally, evidence evaluating the efficacy of treatments for chronic PLP remains scarce. Currently, multimodal treatment strategies are used, including pharmacological treatments (gabapentinoids, tricyclic antidepressants, and opioids), pain intervention (sympathetic blocks, sympathectomies), mirror box therapy, and TENS. However, there is no strong evidence that supports the long-term efficacy of each treatment for PLP.

TENS delivers pulsed electric currents across the intact surface of the skin to stimulate peripheral nerves and the spinal cord, resulting in segmental and extra-segmental analgesia. Additionally, physiological and clinical research suggest that TENS inhibits second-order nociceptive neurons, may increase blood flow, reduces muscle spasms, and selectively activates large diameter afferent fibers, which reduces nociceptor cell activity and sensitization in the central nervous system, all of which are potential analgesic mechanisms for phantom pain and/or residual limb pain. Mulvey et al, indicates that TENS application at the site of residual limb pain or on the site of phantom pain is associated with decreases in
pain intensity, both at rest and with movement (frequency 100 hertz, pulse width 80 microseconds and the current increased until the patient achieved strong non-painful sensations). However, residual limb application of TENS can be challenging in certain situations because this stimulation may aggravate pain in patients with preexisting pain or allodynia. The application of TENS on the residual limb can also cause skin irritation that reduces stump integrity in recent amputees.

Contralateral TENS can address problems associated with residual limb TENS. Moreover, a number of case reports and small case series have reported successful outcomes of contralateral TENS for PLP/RLP and phantom limb sensation. Additionally, Carabelli described a better response when TENS was applied to the contralateral limb compared to residual limb stimulation. The beneficial effects may be the result of stimulation on contralateral segmental inhibition in the dorsal horn.

The case series of contralateral TENS were done by Kawumara (10 cases), Katz (2 cases), and Carabelli (3 cases). The settings of TENS applications in these studies varied from frequency 4-80 hertz, pulse width 90-225 microseconds and range of amplitude 50-80 MA depending on patients’ tolerance. Compared to these previous studies, we use commercially available machines without standard settings, but adjusted the treatment by clinical response. Nevertheless, the results from our larger series still confirmed that contralateral TENS application successfully reduced pain significantly in 95% of patients. The NRS pain score decreased by an average of 3.7/10 (from 4.85 to 1.15/10) or 76.28%. Since almost all patients in this study experienced moderate to severe pain despite the use of at least two analgesics and suffered a negative impact on their quality of life, the population in this study were considered patients with difficult to treat or intractable PLP. To the best of our knowledge, this is the largest application of contralateral TENS for intractable PLP. Moreover, the treatment is associated with high satisfaction rates and no reported adverse events. The suggested duration of treatment is at least 30 minutes and may be extended up to 45 minutes.

CONCLUSION
This cohort study shows that the application of TENS in the contralateral limb can lead to meaningful reduction of pain in patients suffering from difficult to treat phantom limb pain. This treatment has a high success rate and is associated with high satisfaction rates and no reported adverse events. The suggested duration of treatment is at least 30 minutes and may be extended up to 45 minutes.

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