Short-term Effect of Transcutaneous Electrical Nerve Stimulation (TENS) on Pain in Patients with Bone Metastasis: An Uncontrolled Pretest-Posttest Study

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ABSTRACT

Objective: To evaluate the short-term effect of TENS on pain for patients with bone metastasis.

Methods: An experimental descriptive study of 25 eligible advanced cancer patients with bone metastasis. Patients were enrolled in the study from June 1, 2018 to December 31, 2019. Pain intensity measurements were recorded at baseline prior to TENS application, then after 30 minutes and 60 minutes of TENS while the device was switched on. TENS was applied prior to radiotherapy at the same time every day for 5 days. Pain score was evaluated with the Visual Analogue Scale (VAS). Symptom assessment was measured by a Thai version of the Edmonton symptom assessment system (ESAS-Thai) on the first day prior to and five days after TENS application began. The paired t-test and Generalized Estimating Equations (GEE) were used analysis.

Results: Mean VAS scores decreased by 1.08 (-1.08; 95% CI; -1.66 to 0.50, $p < 0.001$) and 1.82 (-1.82; 95 CI; -2.40 to 1.24, $p < 0.001$) after 30 and 60 minutes, respectively, compared to the baseline. Lower VAS scores were also correlated to the number of TENS visits. Mean ESAS scores showed a statistically significant difference before and after TENS application (before: 4.32 (95% CI: 3.60–5.03); after: 3.08 (95% CI: 2.61–3.54), $p = 0.004$). During TENS application there was a reduction in VAS pain scores over time.

Conclusion: TENS is non-invasive, inexpensive and safe. It may be a useful adjunct to the multimodality treatment of pain and may reduce the need for morphine.

Keywords: TENS; cancer with bone metastasis (Siriraj Med J 2020; 72: 470-475)

INTRODUCTION

Bone is the fourth most common site for metastasis.[1] Bone pain is commonly reported among patients with metastatic bone disease.[2,3] Bone pain in most cancer patients initially occurs as intermittent dull aches and then becomes constant and more severe, especially at night.[4] Another characteristic of bone pain is breakthrough (episodic) pain, defined as recurrent episodes of severe pain breaking through the regimen administered to treat background pain.[5] It can be spontaneous or precipitated by some factors especially by movement.

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Bone cancer pain, which has both a nociceptive and neuropathic component,[6] is difficult to control with only one modality, typically requiring the use of multiple interventions including radiotherapy, surgery, chemotherapy, bisphosphonate, calcitonin, and analgesics.[7] Patients with pain have decreased quality of life in all domains, including physical functioning, social relationship and mental health.[8]

Standard analgesic approaches and radiotherapy can both be used to treat bone cancer pain.[9] Radiotherapy is estimated to produce complete pain relief at one month in approximately a quarter of patients.[10] Opioid-based therapy is the most common analgesic used to treat cancer bone pain and does not have a ceiling dose until unmanageable adverse effects occur.[11] However, adverse effects of sedation, constipation, nausea, and vomiting are common.[11] Others are confusion, hallucination, nightmares, urinary retention, myoclonus, dizziness, and dysphoria. Other adjunctive medications, such as NSAIDs and bisphosphonates are also associated with undesired side effects.[12,13]

Transcutaneous electrical nerve stimulation (TENS) is a non-invasive intervention used to relieve chronic pain, mostly commonly in non-cancer diseases. Systematic reviews have shown benefits for musculoskeletal and osteoarthritic pain.[14,15] TENS reduces pain through both peripheral and central mechanisms.[16] Its purpose is to selectively activate large diameter non-noxious afferents, which reduces nociceptor cell activity and sensitization in the central nervous system.[17] The afferent input is sent to the central nervous system to activate descending inhibitory systems to reduce hyperalgesia.[18] The peripheral blockade of TENS results in the reduction of substance P in dorsal root ganglia neurons in animals.[18] TENS may also alter the excitability of peripheral nociceptors to reduce afferent input to the central nervous system.[18]

A few studies have examined the effect of TENS on bone pain among cancer patients.[18,19] However, the evidence whether TENS is an effective tool for pain management among cancer patients is inconclusive.[20] Therefore, the objective of this study is to evaluate the short-term effect of TENS on pain for patients with bone metastasis.

MATERIALS AND METHODS

Research design

This study was designed as a pre-experimental pretest-posttest study design without a control group. The study protocol was reviewed and approved by Udonthani Cancer Hospital Ethics Committees for Human Research (reference number UCH–CT 13/2561). Pre-experimental studies are important for informing future decisions about sample size and feasibility when information is limited.[21]

Eligibility

The study population comprised patients aged 15 and older receiving palliative radiotherapy treatment at Udonthani Cancer Hospital for bone metastasis formed the study population. Participating patients were required to have advanced cancer with radiologically confirmed bone metastasis (by plain film, CT, MRI, or bone scan), pain rated at least 3 out of 10 on a numerical pain-intensity scale at rest or on movement, a life expectancy of more than 4 weeks, and a prescription of regular analgesic medication. Patients with a pacemaker, history of seizure, skin infection or abnormal sensation over the area of bone pain were excluded from the study. Each patient's analgesic drug and also non-pharmacological treatment prior to the intervention were maintained over the duration of the study. Patients were enrolled in the study from June 1, 2018 to December 31, 2019.

TENS application protocol

TENS was applied to the site of bone pain by a physical therapist using a dual channel TENS device. TENS pads were 61 x 27 x 96 mm in size and were placed between 5-10 cm apart on the site of skin with a pulse width of 200 microseconds, and pulse frequency of 80 Hz. The intensity was increased over 60 minutes until patients indicated maximum tolerance while still feeling comfortable.

Outcome measures

Pain intensity was assessed by the VAS. Scores were recorded by marking on a horizontal line (100 mm in length) that represented a continuum between "no pain" and "worst pain".

Pain intensity measurements were recorded at baseline prior to TENS application, then after 30 minutes and 60 minutes of TENS while the device was switched on. TENS was switched off and electrode pads were removed immediately after 60 minutes. TENS was applied prior to radiotherapy at the same time every day for 5 days. Participants were observed at the end of each TENS application for adverse reaction.

Symptom assessment was measured by a Thai version of the Edmonton symptom assessment system (ESAS-Thai)[22] on the first day prior to and five days after TENS application began.

Medical records of all patients were reviewed and demographic data were recorded including age, histologic

types of malignancy, sites of metastasis, performance status, prescribed treatments and analgesic drugs.

Statistical analysis

Paired t-test and Generalized Estimating Equations (GEE) were employed to calculate the intensity change which estimated with ESAS and the correlation between active TENS and VAS change respectively. Statistical analysis was carried out in STATA version 15.0 Copyright by Faculty of Public Health, Khon Kaen University. (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

RESULTS

Patient characteristics

In total, 25 patients were recruited in this study. Sixteen of them (64%) were female and 9 (36%) were male. The average age was 50.7 years old (range 22-78) Table 1. The most common site of the primary malignancy was breast (32%), followed by head and neck (12%), colorectal (12%), lung (12%), bile duct (12%), prostate (8%), cervix (8%), and ovaries (4%). ECOG performance status of 1-4 were 13 (52%), 8 (32%), 2 (8%) and 2 (8%), respectively.

Treatment outcome

The mean VAS score at baseline was 5.90 and gradually decreased during the first treatment Table 2. After 30 minutes of TENS treatment the mean VAS was 3.82, and after 60 minutes the mean VAS was 2.68 on the first visit. Similar decreases during treatment were observed in the second through fifth treatments. Additionally, the pre-treatment VAS decreased throughout the treatment series, decreasing from 5.90 at baseline to 2.31 prior to the fifth treatment.

Effect analysis

The duration of TENS treatment was related to VAS pain intensity scores which exhibited statistically significant reduction at 30 and 60 minutes Table 3. Mean VAS pain score decreased by 1.08 at 30 minutes (difference -1.08; 95%CI -1.66, -0.50; $p<0.001$) and decreased by 1.82 at 60 minutes (difference -1.82; 95%CI -2.40, -1.24; $p < 0.001$) compared to baseline at 0 minutes when TENS was initiated. Similarly, the number of applied TENS visit was correlated to VAS. The mean scores reduced by 1.63 (-1.63; 95% CI; -2.07 to -1.19, $p < 0.001$), 2.04 (-2.04; 95% CI; -2.48 to -1.60, $p < 0.001$), 2.39 (-2.39; 95% CI; -2.82 to -1.95, $p < 0.001$), and 2.49 (-2.49; 95% CI; -2.92 to -2.05, $p < 0.001$) at the second, third, fourth and fifth visit respectively compared to the first visit.

The mean ESAS score before TENS application was 4.32, compare to a score of 3.08 post TENS application ($p = 0.004$) Table 4. There were no reports of adverse events related to TENS application.

DISCUSSION

Our study found the benefit of TENS for bone cancer pain and quality of life. VAS scores in patients decreased relative to the duration and number of visit of the TENS application. Symptom assessment scores according to the ESAS decreased after the TENS application. The findings showed a similar efficacy to some previous studies. Loh and colleagues reported reduction in VAS scores by 9.8 on a 0-100 mm scale and NRP scores by 0.8 on a 1-10 scale following TENS application.[23] A smaller study.[24] and case report[18] using TENS for pain reduction among cancer patients have shown that nearly all patients reported reductions in perceived pain, which is consistent with our findings. Furthermore, a multicenter phase III trial of TENS in patients with cancer bone pain showed that TENS relieved pain intensity, particularly during movement as compared to at rest.[19] However, no large randomized controlled trials (RCTs) have been conducted to test improvement in bone pain in cancer patients. A Cochrane systematic review and meta-analysis found only three studies which met the eligible criteria as of 2011. The results were inconclusive due to a lack of suitable RCTs.[20]

The limitations of this study included the small sample size and lack of comparison arm. Therefore, the results may not be generalizable to broader populations, and the independent effect on pain reduction attributable to TENS could not be assessed. Another limitation was that the doctor and patient were not blinded to the treatment. Finally, the follow-up was short-term. Therefore, we could not assess the long-term effect on pain from TENS.

There are two potential confounding factors in this study. First, the intervention of being part of the trial and the attentions of the physiotherapist could have a significant placebo effect each day, and from day-to-day. Second, radiotherapy would be expected to reduce pain (although maybe not immediately) and thus influence the ESAS and final intensity rating.

Bone metastasis is a common cause of pain in cancer patients. The therapeutic goal is not only optimal pain control but also improvement of quality of life. Therefore, multimodality treatment including pharmacological and non-pharmacological treatments is important for patient care.

TABLE 1. Patient demographics and baseline characteristics.

Patient characteristics	No. (N=25)	(%)
Gender		
Female	16	64
Male	9	36
Age (years)		
Mean	50.68 (range 22-78)	
Malignancy		
Breast cancer	8	32
Head and neck cancer	3	12
Colorectal cancer	3	12
Lung cancer	3	12
Cholangiocarcinoma	3	12
Prostate cancer	2	8
Cervix cancer	2	8
Ovarian cancer	1	4
Site of TENS application*		
C spine	1	4
T spine	15	60
L spine	9	36
Pelvis	7	28
Scapula	2	8
Femur	2	8
Performance status**		
ECOG 1	13	52
ECOG 2	8	32
ECOG 3	2	8
ECOG 4	2	8
Metastasis site		
Bone	18	72
Bone, liver	4	16
Bone, lung	2	8
Bone, liver, lung	1	4
Previous treatment		
Chemotherapy and radiotherapy	10	40
Radiotherapy	9	36
Chemotherapy	6	24
Analgesics		
Weak opioid	15	60
Strong opioid	10	40
NSAIDs	5	20
Gabapentin	2	8
TCA	3	12
Acetaminophen	7	28

*One person was able to have TENS applied to more than 1 site.

**Eastern Cooperative Oncology Group performance status.

TABLE 2. Visual analogue scale (VAS); Mean and SD.

Visit	Baseline		30 minutes Active TENS		60 minutes Active TENS	
	Mean	SD	Mean	SD	Mean	SD
1	5.90	2.36	3.82	2.00	2.68	2.07
2	3.36	1.76	2.48	1.78	1.65	1.65
3	2.74	1.45	1.90	1.12	1.63	1.47
4	2.63	1.69	1.72	1.04	0.87	0.78
5	2.31	1.83	1.54	1.35	1.00	0.87

TABLE 3. Correlation between active TENS and VAS change.

Correlation structure	Parameter	Coefficient	Standard error	Z	95% CI Upper	Lower	*P*-value
Exchange correlation	Baseline	Reference					
	30 minutes	-1.08	0.29	-3.65	-1.66	- 0.50	< 0.001
	60 minutes	-1.82	0.29	-6.16	-2.40	- 1.24	< 0.001
	Visit 1	Reference					
	Visit 2	-1.63	0.22	-7.33	-2.07	-1.19	< 0.001
	Visit 3	-2.04	0.22	-9.16	-2.48	-1.60	< 0.001
	Visit 4	-2.39	0.22	-10.74	-2.83	-1.95	< 0.001
	Visit 5	-2.49	0.22	-11.16	-2.92	-2.05	< 0.001

TABLE 4. ESAS difference.

Variable	Mean	95% Confidence interval of the difference		t	*P*-value
		Lower	Upper		
ESAS (baseline)	4.32	3.60	5.03	3.19	0.004
ESAS (after TENS)	3.08	2.61	3.54		

CONCLUSION

This uncontrolled pre-experimental pretest-posttest study found reductions in pain among cancer patients, as reported by visual analog scale. The reductions were reported immediately following TENS treatment, as well as proportional to the number of TENS treatments given. Long-term improvements on pain were not assessed. As a non-invasive, inexpensive, and safe treatment, TENS may be a beneficial component of multimodal pain treatment and may reduce the need for morphine. The results of this study may inform the design of future RCTs, which are needed to measure the efficacy of TENS relative to controls or other treatments.

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