# THE EFFICIENCY OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN ASSOCIATION WITH GABAPENTIN IN THE TREATMENT OF NEUROPATHIC PAIN IN PATIENTS WITH SPINAL CORD INJURY

**Cozac Vitalii[1], Pascal Oleg[2]**

*[1]Institute of Neurology and Neurosurgery, Chisinau, Republic of Moldova*
*[2]Department of Neurorehabilitation, Institute of Neurology and Neurosurgery, Chisinau, Republic of Moldova*

## ABSTRACT

**Objectives.** The aim of the study was to investigate the effect of low-frequency transcutaneous electrical nerve stimulation (LF-TENS) in the treatment of neuropathic pain in patients with spinal cord injury (SCI).
**Methods.** A total of 25 SCI patients with neuropathic pain were included in the study during October 2013 and April 2014. History, duration, localization and characteristics of pain were recorded. Visual analog scale (VAS) was used to investigate the effect of LF-TENS two times during the day. Patients were randomly assigned to study and control groups. The study group was treated with 30 min of LF-TENS daily for 10 days while the control group with 30 min of placebo TENS.
**Results.** The mean age of the patients was 30.38 ± 6.91 years. Out of 21 patients, 3 were tetraplegic and 18 were paraplegic. Four patients had complete SCI while 17 patients had incomplete injuries. Two groups were similar with respect to age, gender, duration, level and severity of injury. All patients were assigned to therapy with gabapentin for 10 days. In the LF-TENS treatment group, a more statistically significant reduction of the VAS values was observed than in the control group.
**Conclusion.** This study revealed that in treatment of neuropathic pain of SCI patients, LF-TENS may be effective in combination with gabapentin. This article presents LF-TENS may effectively complement pharmacological treatment in patients with SCI andneuropathic pain.

**Keywords:** transcutaneous electrical nerve stimulation, neuropathic pain, spinal cord injury

## INTRODUCTION

Neuropathic pain is a frequent complication of spinal cord injuries (SCI) making approximately 30% of all pain syndromes in SCI (1). Neuropathic pain severely decreases patients' quality of life (2). These complications of SCI are hard to treat, with an unsatisfying level of theoretical and practical experience in this field (3). Different treatment options have been proposed (4), mainly pharmacological. The clinical guidelines (National Clinic Protocol) in Republic of Moldova refer to gabapentin as drug of the first choice in case of neuropathic pain.

There are numerous non-pharmacological options, proposed for neuropathic pain: acupuncture, relaxation and massage, physical therapy, psychological coping and others. Treatment with transcutaneous electrical nerve stimulation (TENS) has been reported as effective in different pain syndromes (5) including peripheral neuropathic pain (6), but is less studied in central neuropathic pain, the results are often controversial (5). The variation in results may be a consequence of insufficient

Author for correspondence:
Cozac Vitalii, Institute of Neurology and Neurosurgery, 2038, str. Zelinski 28/2-1, Chisinau, Republic of Moldova
E-mail: vitaliicozac@gmail.com

knowledge of stimulation parameters of choice – frequency, intensity, duration, electrode sites, also low number of patients studied as well as different outcome measures used to evaluate improvement (7).

Our aim is to investigate the effect of low frequency TENS (LF-TENS) for the treatment of neuropathic pain in SCI patients in a case-control, single blind, prospective study.

## MATERIALS AND METHODS

This study included 25 SCI in-patients with neuropathic pain at or below the level of cord injury. Inclusion criteria: patients older than 18 years with traumatic SCI; the presence of neuropathic pain was confirmed with Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) score of 12 and above. Exclusion criteria: possibility of pain other than neuropathic: having diabetes mellitus, renal dysfunction, alcoholism, human immune deficiency virus positive, varicella zoster positive, and severe spasticity (Modified Ashworth Scale score MAS > 3). Patients signed a written informed consent on their first examination.

All 25 patients were assigned to therapy with gabapentin, which started with the dose of 300 mg (this day counting as day 1). The duration of the treatment was ten days. The dosage was increased in three days with the pace of 300 mg daily, thus on day 3 the dosage was 900 mg, which was considered as basic dose. If the patient still reported no change in the severity of pain, the basic dose was increased with the same pace.

All 25 patients were randomly assigned as study and control groups. Enrolled patients from control group were assigned to sham TENS-therapy, which started on day 1. The patients from study group were assigned LF-TENS stimulation according to the protocol, which started on day 1.

All TENS applications were performed by the same specialist between 8:00 and 12:00 hours. In both groups two electrodes were placed to the proximal and two to the distal parts of the region with neuropathic pain. We used two channels with four round electrodes, which had 40 mm in diameter. Electrodes were located separately. Patients in the study group were treated daily with LF-TENS (pulse frequency 4 Hz, pulse duration 200 ms and pulse amplitude 50 mA) for a duration of 30 min for 10 days, whereas patients in the control group were treated with sham placebo TENS (applying electrodes without stimulation). Both TENS appliances were turned on and counting down from 30 min.

We wanted the patient to measure their pain severity with visual analog scale (VAS) two times a day (morning and evening) on day 0 and the tenth day of the study. The specialist who managed patients measuring VAS scores, did not know whether patients were in the TENS or sham TENS group. At the beginning VAS, values were used as a baseline measurement of pain. Finally, second set of VAS values were recorded.

## RESULTS

Twenty five patients were enrolled in the study. Two refused to continue the study on the day 3, two others were found with high levels of blood glucose, dysmetabolic axonopathy on electromyography examination, and were excluded. Twenty-one patients (19 men and 2 women) participated in thestudy. Patients' demographic characteristics are summarized in Table 1.

***TABLE 1.*** *Patient demographics*

| Patient demographics | All patients (n = 21) | Study group (n = 11) | Control group (n = 10) |
|---|---|---|---|
| Age (mean±s.d.) | 30.38 ± 6.91 | 31.72 ± 7.70 | 28.90 ± 6.10 |
| Female | 2 | 1 | 1 |
| Male | 19 | 10 | 9 |

Mean age was 30.38 ± 6.91 years. There was no statistical difference between groups in terms of age and gender. Three patients were tetraplegic and 19 patients were paraplegic (Table 2).

***TABLE 2.*** *Characteristics of spinal cord injury*

| Level of injury | All patients (n = 21) | Study group (n = 11) | Control group (n = 10) |
|---|---|---|---|
| Tetraplegia (n, %) | 3; 14.3% | 2; 18.2% | 1; 10.0% |
| Paraplegia (n, %) | 18; 85.7% | 9; 81.8% | 9; 90.0% |
| Type of injury | | | |
| Complete injury (n, %) | 4; 19.0% | 2; 18.2% | 2; 18.2% |
| Incomplete injury (n, %) | 18; 81.0% | 9; 81.8% | 9; 81.8% |

Average period after injury was 16.04 months (1-35 months) forthe patients studied. Average time lapse between the injury and the development of pain was 5.24 months (0.5-14 months), and average pain duration was 12.70 months (0.5-23 months). Locations of neuropathic pain are seen in Table 3. When locations and duration of pain, average time lapse between the injury and pain were compared, no statistically significant differences were observed between the groups.

Mean LANSS score was 15.95 (s.d. ± 1.85) with range 13-20. On the day 0, neuropathic pain mean

***TABLE 3.*** *Location of pain*

| | Foot | Knee and caudal | Femur and caudal | Back and caudal | Cervical and caudal |
|---|---|---|---|---|---|
| Study group (n = 11) | 2 | 3 | 5 | 1 | 1 |
| Control group (n = 10) | 1 | 4 | 3 | 1 | 0 |
| All patients (n = 21) | 3 | 7 | 8 | 2 | 1 |

VAS value was 8.09 ± 0.97 in the study group and 8.05 ± 1.05 in the control group. Nosignificant difference was observed when the first-day VAS meanvalues of the two groups were compared (P=0.448). On the tenth day (after 10 days of treatment), neuropathic pain mean VAS value was 3.95±1.70 in the study group and 5.25 ± 1.86 in the control group. After 10 days of treatment, a statistically significant difference was observed in mean VAS values (P = 0.023; Fig. 1).

In the study group, morning mean VAS value was 7.81 ± 0.98 on day 0 while 3.18 ± 1.60 on the tenth day; evening mean VAS value was 8.36 ± 0.92 on the day 0 while 4.72 ± 1.48 on the tenthday. In the control group, morning mean VAS value was 7.80 ± 0.91 on day 0 while 4.80 ± 2.04 on the tenth day; evening mean VAS value was 8.30 ± 1.15 on the day 0 while 5.70 ± 1.63 on the tenth day.

A statistically significant reduction was observed between the first evaluation and tenth-day values. No side effects of LF-TENS were seen.

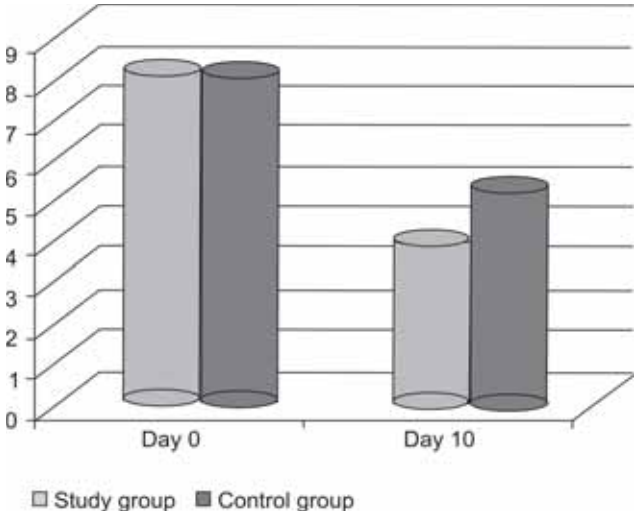


***FIGURE 1.*** *First – and tenth – day mean VAS scores of study and control groups.*

Mean gabapentin dose was 1036.36 mg in the study group and 1560 mg in the control group, thus the basic dose was increased by 136.36 mg of gabapentin in the study group and by 560 mg in the control group (P=0.004; Fig. 2).Three patients from the control group reported drowsiness and dizziness on the ninth day of treatment (doses of gabapentin increased to 2700, 2400 and 1800 mg) and one patient reported blurred vision (dose of gabapentin increased to 2700 mg). No side effects of gabapentin were reported in the study group.

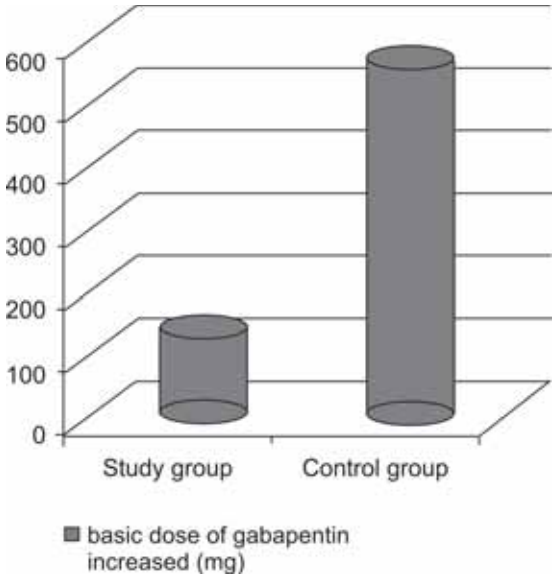


***FIGURE 2.*** *Mean values of gabapentin dose increasing*

## DISCUSSIONS

SCI-related neuropathic pain is often very difficult to treat (8). Treatment with TENS is rarely associated with negative side effects and has been reported to be effective in patients with neuropathic pain (6,8). We researched the effects of LF-TENS for the treatment of neuropathic pain in SCIpatients in a case-control, prospective study. The results of this study revealed that LF-TENS reduced neuropathicpain intensity both in the morning and evening times but predominantly in the morning, in SCI patients.

Combination of LF-TENS with pharmacological approach permitted to use lower doses of gabapentin, thus avoiding side effects of the drug.

When long-term effects of TENS were assessed in patients with chronic pain, positive results were found with respect to being able to resume work, home and social activities; increased activity level and pain management; and lower use of drugs and other treatments (7).

Unfortunately, we have not measured long-term effects of TENS, and we did not assess the effect of LF-TENS beyond 15 days.

Constraints of this study are low participant number and inability to study long-term effect of

LF-TENS. However, it is still important asa placebo-controlled study. Determination of the effect of giventreatment to pain severity in the different intervals of the day is another important aspect of this study. After this study, evaluation of day-time pain severity is an important issue in pain treatment. Further studies associated with different frequencies of TENS are needed.

## CONCLUSIONS

Until treatment options for SCI-related neuropathic pain become adequate, all interventions that might help a patient should be considered. LF-TENS may effectively complement pharmacological treatment with gabapentin in patients with SCI and neuropathic pain, avoiding dose increasing and the side effects of the drug.

## REFERENCES


1. **Putzke J.D., Richards J.S., Hicken B.L., Ness T.J., Kezar L., DeVivo M.** Pain classificationfollowing spinal cord injury: the utility of verbal descriptors. *Spinal Cord* 2002; 40:118-127
2. **Widerström-Noga E.G., Turk D.C.** Types and effectiveness of treatments used by people with chronic pain associated with spinal cord injuries: influences of pain and psychosocial characteristics. *Spinal Cord* 2003; 41: 600-609
3. **Calmels P., Mick G., Perrouin-Verbe B.** Neuropathic pain in spinal cord injury: identification,classification, evaluation. *Annals of Physical and Rehabilitation Medicine* 2009; 52: 83-102
4. **Norrbrink C.** Transcutaneous electrical nerve stimulation for treatment of spinal cordinjury neuropathic pain. *Journal of Rehabilitation Research & Development* 2009; 46: 85-94
5. **To T.P., Lim T.C., Hill S.T., Frauman A.G., Cooper N., Kirsa S.W. et al.** Gabapentin forneuropathic pain following spinal cord injury. *Spinal Cord* 2002; 40: 282-285
6. **Sun R., Kuo-Hsuan C.** Neuropathic pain: mechanisms and treatments. *Chang Gung Medical Journal* 2005; 28: 597-604
7. **Celik E.C., Erhan B., Gunduz B., Lakse E.** The effect of low-frequency TENS in the treatment of neuropathic pain in patients with spinal cord injury. *Spinal Cord* 2013; 51:334-337
8. **Siddall P.J.** Management of neuropathic pain following spinal cord injury: now and inthe future. *Spinal Cord* 2009; 47: 352-359