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Research Article

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Transcutaneous electrical nerve stimulation improved the nociceptive component of low back pain, while presenting no effect on its neuropathic component

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ABSTRACT

The objective of this study was to evaluate the efficacy of transcutaneous electrical neurostimulation portable device in patients with chronic nociceptive and neuropathic low back pain. Twenty-four patients with nociceptive and neuropathic lumbar pain were prospectively assigned to apply the active device at the lower back twice daily for 30-min, during 14 days in the morning and at night. Efficacy was evaluated by: 1) pretreatment and post treatment VAS pain scores, 2) type of pain (nociceptive or neuropathic), 3) capacity of performing routine physical activities, 4) quality of sleep, and 5) daily analgesic rescue medication consumption. Nociceptive pain improved ($p<0.05$) whilst neuropathic pain was maintained ($p>0.05$). The device decreased pain VAS by day-5th ($p<0.05$) up to day-14th ($p<0.02$). Rescue analgesics decreased ($p<0.05$) and quality of sleep improved ($p<0.05$). Prior to device, patients referred 2(1-2) (mean (25%-75%)) arousals during night compared to none on day-5th forward ($p<0.05$). 17 patients classified as improved capacity during the first 3-hours in the morning ($p<0.05$). There were no adverse effects. The device did not improve neuropathic pain while improved nociceptive pain, decreased the number of rescue analgesics, resulted in better sleep pattern, and enriched physical function in the morning.

Keywords: transcutaneous electrical neurostimulation, lumbar neuropathic pain, nociceptive pain.

INTRODUCTION

The data in the literature about transcutaneous electrical nerve stimulation (TENS) utility in Low Back Pain (LBP) is conflicting [1-2]. Most studies did not differentiate between the types of pain in a suffering patient. Either facet related pain (nociceptive somatic pain) or referred neuropathic pain may contribute to LBP [3]. The most common symptom for degenerative articular facet pain includes localized pain at the back, generally without radiation to the calf and foot, often more intense at bedtime; while conversely, neuropathic pain will frequently radiate in one or more lumbar or sacral dermatomes and improve with rest. Not uncommonly, patients may refer both types of pain, presenting nociceptive articular pain, more evident at night-time, whilst neuropathic pain will increase its intensity during the day-time [3]. The objective of the study was to compare the effectiveness of TENS device for management of both nociceptive and neuropathic components of LBP.

EXPERIMENTAL SECTION

The local Ethics Committee approved the study protocol, and informed consent was obtained. This prospective study evaluated the clinical utility of a new, very small and light, high frequency TENS device in 24 patients suffering from LBP with both neuropathic and nociceptive somatic pain components.

Patients aged between 20 and 45-year-old, with no other pathology apart from LBP for more than three months, with both characteristics of nociceptive somatic articular facetary pain and chronic neuropathic radicular pain were included to participate in this prospective study. For the final inclusion of 24 patients, the total of 31 consecutive patients were interviewed always by the same author to clarify whether they could clearly differentiate between their nociceptive and neuropathic pain. During the interview, it was demonstrated to the patient how to use the TENS device. The capacity to recognize both types of pain and to self-apply the TENS was double-checked by a second author who was not present during the first interview.

Patients included presented only nociceptive and neuropathic pain for more than 3 months, and did not present any acute radiculopathy, which by definition is accompanied of sensory or motor loss. All patients graded pain on average $\geq$ 4 cm on a visual analog scale (VAS), taking no other drugs apart analgesics such as metamizol or paracetamol, recruited at the Center for Pain Treatment- Teaching Hospital were potentially eligible for inclusion. Diagnosis of both neuropathic and nociceptive somatic pain was confirmed based on the clinical history and examination combined with lumbar magnetic resonance to exclude any pathologies. Patients were ineligible for the study if they had undergone surgery for radiculopathy within the last 3 months; if they had been previously treated with TENS, if they used non-steroidal anti-inflammatory drugs for the last 14-day prior to entrance into the study protocol; if any surgery was planned within the next 6 months; if they had a pacemaker; if they were naive of non-pharmacological treatments including physiotherapy, acupuncture, mesotherapy, manipulations, wearing a corset, or psychological support; if they had copper intrauterine dispositive device [4}, if their LBP was symptomatic of another condition (i.e., compression fractures or progressive inflammatory, neoplastic or infectious conditions); if the physician had estimated their life expectancy to be less than 3 months; and finally if articular, median branches, epidural, foraminal and facetary articular median branch blocks were planned during the study period, or if the patient was involved in an ongoing medico-legal dispute.

The TENS device was applied by the patient at the lower back (perpendicular to the vertebrae canal, at the level of the 5th lumbar vertebrae). In each patient it was applied twice daily, during 14 days: 1) in the morning, during 30-min before getting out the bed, and 2) at night, for 30-min just after going to bed. The TENS device (Tanyx®) produced a conventional TENS characterized by continuous stimulation at high frequency (85 Hz), wave duration of 75 µs and intensity of up to 30 mA, potentially achieving painless paresthesia in the lumbar region or tingling sensation. Oral metamizol (500 mg) up to three times daily, minimal of 6-hour interval, but with the last intake no more than 6 pm, was used as rescue analgesic if necessary for pain control, in order to keep pain VAS less than 4 cm. If necessary, 500 mg oral paracetamol was also available at a minimum of 6-hour interval. Efficacy was evaluated by: 1) pretreatment and post treatment VAS pain scores, 2) type of pain (nociceptive or neuropathic) that changed characteristic for maintained, improved or worsened, 3) capacity of performing routine physical activities, defined as maintained, improved, or worsened, 4) quality of sleep also defined as maintained, improved or worsened, as well as number of night arousals; and 5) analgesic rescue medication daily consumption.

Each patient was given a personal diary which contained detailed instructions on self-administering the TENS treatment twice daily, including a silhouette showing the correct placement of the electrodes, as well as space for making notes of daily metamizol intake, daily lumbar VAS assessments before and after each TENS application, impression related routine physical activity and quality of sleep, and any adverse event experienced during the period of study. All patients had clearly the concept about the two types of pain they were supposed to evaluate. The articular somatic pain was defined as well localized at the lumbar back, with no reflection to limbs, and that occurred mainly after rest such as standing up after a time being seated and at arousal in the morning. The neuropathic type of pain was defined as the pain radiated to the lower limb that improved with rest but increased intensity with the time, being worst at the end of the day. Follow-up visits at the pain clinic were scheduled at 7th- and 14th-day.

Statistics

Each patient acted as his/her own control related to the types of pain. The sample size of the study was based on preliminary data conducted with 4 patients based on general VAS pain reduction. It was hypothesized that the TENS device would result in expected mean 3 cm and expected standard deviation 1.5 cm at 14th-day evaluation. The single tailored unpaired t-test was used with the level of significance 2.5% and the power of 80%. These assumptions would require at least 14 patients. Data was compared between the same group by Wilcoxon test or

Friedman test when evaluating more than one data, and chi-squared test or Fisher's exact test for qualitative variables. Tukey honest significance was used after Friedman if necessary. P<0.05 was considered significant.

RESULTS AND DISCUSSION

Twenty one patients with LBP with both neuropathic and nociceptive somatic pain components completed the study and could clearly differentiate their nociceptive and neuropathic pain. Exclusion were due to incomplete data (2 patients), while the third patient felt sleep while using TENS at bed-time, and had no idea about how much time it was kept on, although there were no complains of adverse effects. Demographics of patients are represented in Table 1. The 21 patients classified the nociceptive pain as "improved" when comparing day-1st to days-5th-10th ($p<0.05$); or day-1st to days-11th-14th ($p<0.02$) , whilst 19 patient classified neuropathic pain as "maintained" and 2 patients classified as "worsened" ($p>0.05$).

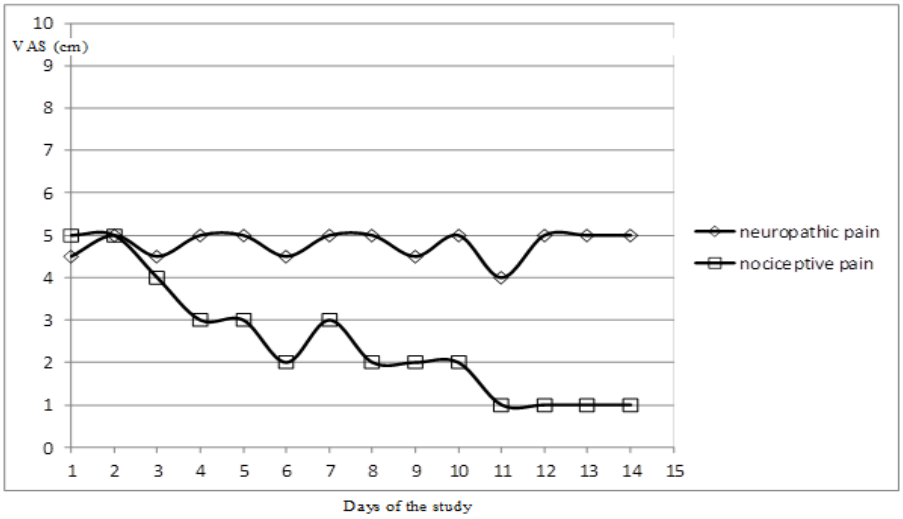

Figure 1. Visual analog pain scores (0-10 cm) during the 14-days study for description of neuropathic type of pain and somatic type of pain. Pain VAS intensity for nociceptive pain decreased in a strictly segmental manner for all 21 patients by the 5th-day ($p<0.05$), improving up to the 12th-day of evaluation and maintained up to the 14-day evaluation ($p<0.02$)

Table 1. Patients demographics

Age (years)	32±8
Gender (M/F)	15/6
Weight (kg)	81±14
Height (cm)	170±8
ASA status (I/II)	17- ASA I 4- ASA II (allergy to pollen, dusty)
No. of patients taking daily metamizol (prior to treatment)	17 patients- 1000 mg 4 patients- 1500 mg
No. of patients waking up at least once during night due to pain (prior to treatment)	21
No. of patients taking daily 500 mg paracetamol (prior to treatment)	4
No. of patients taking daily metamizol (during 14^{th} -day treatment)	16 patients- 500 mg 5 patients- 1000 mg
No. of patients taking daily 500 mg paracetamol (during treatment)	0

ASA- American society of Anesthesiology physical status

Regarding the VAS pain score for the neuropathic type of pain, it did not improve after TENS use, as pre- and post-treatment pain scores were similar for all days of the study compared to previous pain score values before treatment ($p>0.05$; Fig. 1). However, concerning VAS pain score for the nociceptive type of pain, it decreased when comparing day-1st to days-5th-10th ($p<0.05$); or day 1st to days 11th-14th ($p<0.02$; Figure 1).

Pre- and post-treatment daily rescue metamizol consumption decreased when comparing day-1st to day-14th ($p<0.05$, Table 1) (mean (25%-75%): 1(1-2) and mean 2 (2-3) to day-1st and day-14thm, respectively (Table I; $p>0.05$). Prior to TENS treatment, 17 patients were taking 1000 mg metamizol while 4 of the patients were taking 1500 mg metamizol plus oral 500 mg paracetamol (500 mg). Sixteen patients took daily 500 mg oral metamizol, while 5 patients took 1000 mg daily metamizol ($p<0.05$; Table 1). No adverse effects were observed.

The TENS device decreased the pain VAS intensity of LBP for nociceptive pain in a strictly segmental manner for all 21 patients by the day-5th ($p<0.05$), improving up to the day-12th of evaluation and maintained up to the 14-day evaluation ($p<0.02$) (Fig. 1). There was a statistically significant drop in mean pain score (VAS) from pretreatment to post-treatment for the nociceptive facetary articular pain (day-1st compared to day-14th, $p<0.05$). Consequently, the quality of sleep improved for all 21 patients, and the number of arousals due to pain secondary to change of position in bed steadily decreased from day-5th to day-14th, when compared to the sleep time previous to the TENS application. Prior to TENS application, all patients referred 2(1-2) (mean (25%-75%)) arousals during night time compared to none on day-5th forward ($p<0.05$).

Related to capacity of performing routine physical activity, it was considered improved during the first 3 hours in the morning just after arousal from the bed by 17 of 21 patients from day-4th, resulting in facility of getting off the bed, and for routine activities ($p<0.05$), while 4 patients defined as maintained. There were no other complains of adverse effects.

TENS was introduced more than 35 years ago as an adjunct to pharmacologic pain management for LBP. However, despite its widespread use, evidence for its efficacy as an isolated intervention in the management of chronic LBP is limited and inconsistent [5,6]. The results of the actual study demonstrated that the two types of pain could be clearly differentiated by each patient, named nociceptive somatic pain and neuropathic pain. The results demonstrated that neuropathic radicular pain did not alter with high-frequency TENS use twice daily, in accordance to otherS [1-3],. However, the nociceptive somatic pain was clearly improved by the use of the TENS device twice daily, in accordance to otherS [7}, who also applied 30-min TENS, and patients decreased the amount of daily rescue analgesics. Recently, a group of LBP patients who used TENS compared with a matched group without TENS at 1-year follow-up had significantly fewer hospital and clinic visits, used less diagnostic imaging, had fewer physical therapy visits, and required less back surgery, associated to a lower total annual costs[8].

In this actual study a high frequency TENS device was used. It is generally believed that high frequency TENS analgesia is caused mainly by differentially blocking the activation of large diameter primary afferents from deep somatic tissues, but not superficial cutaneous afferents [9], and also to mediated analgesia through the periaqueductal gray that sends projections through the rostroventralmedial medulla to the spinal cord to produce an opioid-mediated analgesia through δ-receptors [10]. Hyperalgesia through central sensitization was also demonstrated to be ameliorated in rats, as the application of high frequency TENS to the contralateral paw reversed the hyperalgesia of the inflamed paw [11]. High frequency TENS was also capable of inducing analgesia, most likely related to increased serum serotonin release, apart from blockade of the adverse cardiovascular and respiratory changes induced by pain [12], what could justify the analgesic effect upon the nociceptive type of pain.

However, neuropathic pain in the model used in this actual study (chronic neuropathic) was not affected by high frequency TENS. In accordance, TENS was demonstrated to be effective in the inflammation model, while it did not reveal significant analgesic effects in the neuropathic pain rodent model [13]. Recent results in mice suggested that the application of early TENS (it means on the first day of neural injury) relieved hyperalgesia in a model of neuropathic pain and inhibited: a) glial activation, b) mitogen-activated kinase activation, protein kinase C-γ, c) phosphorylated anti-phospho-cyclic AMP response element-binding protein expression; d) the proinflammatory cytokines expression; as well as kept maintenance of spinal opioid receptors [13]. However, the same study demonstrated that the analgesic effects were only present if the TENS was started on day one after the nerve injury, but had no results when starting on 7th-day or 14th-day after the injury [14], what is also in accordance to our results.

Other studies indicate that direct stimulation of the spinal cord releases substance P, serotonin, noradrenaline and gamma aminobutyric acid (GABA) in the dorsal horns, and activation of the GABA-B receptor may be linked to a decrease in the release of glutamate and other excitatory amino acids, resulting in a decrease of neuropathic pain [15]. In fact, only intracutaneos electrical stimulation (but not transcutaneous) attenuated both neuropathic and inflammatory-induced pain behaviors [13]. While eletroacupuncture stimulation was demonstrated to effectively down-regulate serum inflammatory factors interleukin-1β and tumoral necrosis factor-α levels; to upregulate anti-inflammatory factor interleukin-2 level in rats [16]; and to attenuate systemic inflammatory responses through activation of muscarinic receptors in the central nervous system [17], high frequency TENS had no effect on serotonin induced inflammation [18].

Anti-inflammatory drugs were not included as part of the protocol, as they could interfere with the course of the disease, and not only masking the pain sensation, what could lead to misinterpretation of the data. Because high frequency TENS was previously described to be related to anti-inflammatory mechanism of action [11,13], it was decided to use metamizol as rescue analgesic, a drug established as central and peripheral analgesic with no clinical

anti-inflammatory action [19]. In addition, it is free of charge for all patients as it is donated by the government for pain control, under prescription, as much as paracetamol. Indeed, the action of TENS on inflammation remains to be clarified.

Related to sleep comfort, all patients noticed improvement in sleep pattern, decreased arousals at night time achieving complete night of sleep from day-5th, and no patients took metamizol as rescue analgesic at night time, compared to previous data before starting the study protocol, in accordance to our previous study [20], nevertheless in a different population.

In addition, 17 of the patients referred improvement in morning physical activities during the first 3-hours. Others have likewise demonstrated improvement in fibromyalgic patients after high frequency TENS, with relevant improvement of pain, work performance, fatigue, stiffness, anxiety and depression compared to those not receiving TENS [21]. The utility of TENS was correspondingly described in computer workers. Apart from pain relief, patients also reported improved social relationships, social support, sexual activity and mental health. After treatment a significant increase in the flexion of lower back was observed in the majority of patients. No significant correlations between the quality of life and the intensity of pain and the flexion of lower back before and after treatment were found [22].

CONCLUSION

As conclusions, TENS application twice daily did not improve chronic neuropathic pain, and in accordance to others, TENS was not considered useful for neuropathic radicular pain [1-3]. Nevertheless, TENS application improved the nociceptive somatic type of pain, decreased the number of arousals at night time, resulted in better sleep pattern, and improved physical function in the morning, suggesting its applicability for LBP when the nociceptive somatic component such as degenerative articular facet is present.

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