TENS improved the nociceptive component of Low Back Pain, while presenting no effect on its neuropathic component

Introduction: Most studies did not differentiate between the types of pain in a suffering patient**.** The objective of this study was to evaluate the efficacy of transcutaneous electrical neurostimulation (TENS) in patients with chronic low back pain (LBP) with both nociceptive and neuropathic pain.

Methods: Prospective, randomized, cross-over study. Twenty-four consecutive adult patients with both somatic and radicular LBP were interviewed. Patients were randomly assigned to receive active TENS at the lower back twice daily, for 14 days: 1) in the morning, during 30-min in the morning, and 2) at night, for 30-min just after going to bed. 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 also, as well as number of night arousals, and 5) daily analgesic rescue medication consumption.

Results: Nociceptive pain improved ($p<0.05$) whilst neuropathic pain was maintained ($p>0.05$). TENS decreased pain VAS by day-5^{th} ($p<0.05$) maintained up to day-14^{th} ($p<0.02$). Rescue analgesics decreased ($p<0.05$) quality of sleep improved ($p<0.05$). Prior to TENS, patients referred 2(1-2) (mean(25%-75%)) arousals during night compared to none on day-5^{th} 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.

Conclusions: TENS application did not improve neuropathic radicular pain while improved nociceptive pain, decreased the number of rescue analgesics, resulted in better sleep pattern, and improved physical function in the morning.

Key-words: TENS, lumbar pain, neuropathic pain, nociceptive pain.

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

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 pain) or sciatica (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 radicular 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 radicular 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.

Methods

The local Ethics Committee approved the study, 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 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 neuropathic radicular pain were included. For the final inclusion of 24 patients, the total of 31 consecutive patients was 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 radicular pain, and did not present any 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 radicular 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 they had experienced LBP for less than 3 months; if LBP was associated

with radiculopathy; 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 or foraminal 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 5^{th} 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 paraesthesia 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. Efficacy was evaluated by: 1) pretreatment and post treatment VAS pain scores, 2) type of pain (nociceptive or neuropathic) that changed characteristic for improved, maintained 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.

To each patient it 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 radicular type of pain was defined as the pain radiated to the lower limb that improved with rest but increased intensity with the time, being worse 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. We hypothesized that 100% of the patients receiving TENS twice daily would achieve a decrease of at least 50% on the pain VAS at 2-week compared with baseline for either type of pain. On this basis, with an alpha of 5%, it was calculated that at least 18 evaluable patients would be needed to achieve an 80% power to detect any effect of TENS in each type of pain (nociceptive or neuropathic). 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. $P<0.05$ was considered significant.

Results

Twenty one patients with LBP with both neuropathic radicular 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 other 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 I. The 21 patients classified the nociceptive pain as "improved" when comparing day-1st to day-14th ($p<0.05$), whilst 19 patient classified neuropathic pain as "maintained" and 2 patients classified as "worsened" ($p>0.05$). The neuropathic radicular pain 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). Pre- and post-treatment rescue metamizol consumption during day-time were also similar during the 14 days of the study, i.e., mainly 2 to 3 tablets daily (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). No patients took tablets at night time after TENS use, and took only daily oral metamizol ($p>0.05$). Nineteen of the patients took 500 mg oral metamizol at lunch time, while 2 patients took 500 mg metamizol at lunch time and 500 mg metamizol at 6 pm ($p<0.05$). No adverse effects were observed.

The TENS device decreased the pain VAS intensity of LBP for nociceptive pain decreased 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-1st to day-5th, and maintained up 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 3 patients defined as maintained. There were no complains of adverse effects.

Discussion

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 radicular pain. The results demonstrated that neuropathic radicular pain did not alter with high-frequency TENS use twice daily, in accordance to others (1-3), and patients kept intake of the same amount of metamizol tablets varying from 1 to 2 tablets during the day. 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.

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 (8), 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 (9). 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 (10). 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 (11), what could justify the analgesic effect upon nociceptive pain.

However, neuropathic pain 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 (12). Recent studies indicate that direct stimulation of the spinal cord releases substance P, serotonin, noradrenaline and 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 (13). In fact, only intracutaneos electrical stimulation (but not transcutaneous) attenuated both neuropathic and inflammatory-induced pain behaviors (12). While eletroacupuncture stimulation was demonstrated to effectively down-regulate serum inflammatory factors IL-1β and TNF-α levels, to upregulate anti-inflammatory factor IL-2 level in rats (14) and to attenuate systemic inflammatory responses through activation of muscarinic receptors in the central nervous system (15); high frequency TENS had no effect on serotonin induced inflammation (16).

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 (10,12), it was decided to use metamizol as rescue analgesic, a drug established as central and peripheral analgesic with no clinical anti-inflammatory action (17). In addition, it is free of charge for all patients as it is donated by the government for pain control, under prescription. 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 (18), nevertheless in a different population.

In addition, 17 of the patients referred improvement in matinal 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 (19). 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 (20).

As conclusions, TENS application twice daily did not improve neuropathic radicular pain, and in accordance to others, TENS was not considered useful for neuropathic radicular pain (1-3). Nevertheless, TENS application improved 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.

References

1. Khadilkar A, Odebiyi DO, Brosseau L, Wells GA. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. Cochrane Database Syst Rev 2008;4:CD003008.
2. Dubinsky RM, Miyasaki J. Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2010;12:173-176.
3. Buchmuller A, Navez M, Milletre-Bernardin MP, et al. Value of TENS for relief of chronic low back pain with or without radicular pain. Eur J Pain 2012; 16:656-665.
4. Zhou HH, Lu F, Chen SD, et al. Effect of electroacupuncture on serum copper, zinc, calcium and magnesium levels in the depression rats. J Tradit Chin Med 2011;31:112-114.
5. Khadilkar A, Milne S, Brosseau L, et al. Transcutaneous electrical nerve stimulation for the treatment of chronic low back pain: a systematic review. Spine (Phila Pa 1976) 2005;30:2657-2666.
6. van Middelkoop M, Rubinstein SM, Kuijpers T, et al. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. Eur Spine J 2011; 20:9-39.
7. Itoh K, Itoh S, Katsumi Y, Kitakoji H. A pilot study on using acupuncture and transcutaneous electrical nerve stimulation to treat chronic non-specific low back pain. Complement Ther Clin Pract 2009;15,22-25.

8. Radhakrishnan R, Sluka KA. Deep tissue afferents, but not cutaneous afferents, mediate transcutaneous electrical nerve stimulation-Induced antihyperalgesia. J Pain 2005;6:673-680.
9. DeSantana JM, Da Silva LF, De Resende MA, Sluka KA. Transcutaneous electrical nerve stimulation at both high and low frequencies activates ventrolateral periaqueductal grey to decrease mechanical hyperalgesia in arthritic rats. Neuroscience 2009;163:1233-1241.
10. Sabino GS, Santos CM, Francischi JN, de Resende MA. Release of endogenous opioids following transcutaneous electric nerve stimulation in an experimental model of acute inflammatory pain. J Pain 2008;9:157-163.
11. Santuzzi CH, Neto HD, Pires JG, et al. High-frequency transcutaneous electrical nerve stimulation reduces pain and cardio-respiratory parameters in an animal model of acute pain: Participation of peripheral serotonin. Physiother Theory Pract 2013;(Epub ahead of print)
12. Vera-Portocarrero LP, Cordero T, Billstrom T, et al. Differential Effects of Subcutaneous Electrical Stimulation (SQS) and Transcutaneous Electrical Nerve Stimulation (TENS) in Rodent Models of Chronic Neuropathic or Inflammatory Pain. Neuromodulation 2013; [Epub ahead of print]
13. Fukazawa K, Hosokawa T. Spinal cord stimulation. Masui 2009;58:1393-1400.
14. Li WX, Huang YR, Lei LD, Li N. Effects of electroacupuncture and manual acupuncture interventions on contents of serum inflammatory cytokines in rats with chronic adjuvant arthritis]. Zhen Ci Yan Jiu 2012; 37:271-276.

15. Song JG, Li HH, Cao YF, et al. Electroacupuncture improves survival in rats with lethal endotoxemia via the autonomic nervous system. Anesthesiology 116;406-414.
16. Santos CM, Francischi JN, Lima-Paiva P, et al. Effect of transcutaneous electrical stimulation on nociception and edema induced by peripheral serotonin. Int J Neurosci 2013; [Epub ahead of print]
17. Serdiuk SE, Gmiro VE. Peripheral acting mediators pain and analgesia potentiate the central analgesic action of fentanyl and dipyrone. Ross Fiziol Zh Im I M Sechenova 2012;98:325-330.
18. Lauretti GR, Chubaci EF, Mattos AL. Efficacy of the use of two simultaneously TENS devices for fibromyalgia pain. Rheumatol Int 2013; [Epub ahead of print]
19. Carbonario F, Matsutani LA, Yuan SL, Marques AP. Effectiveness of high-frequency transcutaneous electrical nerve stimulation at tender points as adjuvant therapy for patients with fibromyalgia. Eur J Phys Rehabil Med 2013; [Epub ahead of print]
20. Zaniewska R, Okurowska-Zawada B, Kułak W, Domian K. Analysis of quality of life in patiens with low back pain after receiving transcutaneous electrical nerve stimulation (TENS). Med Pr 2012;63:295-302.

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 5^{th}-day ($p<0.05$), improving up to the 12^{th}-day of evaluation and maintained up to the 14-day evaluation ($p<0.02$).