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ORIGINAL RESEARCH

Does electrode placement influence tens-induced antihyperalgesia in experimental inflammatory pain model?

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Abstract
Background: Transcutaneous electrical nerve stimulation (TENS) is a treatment commonly used for managing pain; however, the ideal placement of the electrodes is not fully understood.
Objective: To investigate the best way to apply TENS electrodes in an experimental inflammatory pain model.
Method: Knee joint inflammation was induced in rats, followed by administration of low-frequency TENS (4 Hz) under anesthesia for five days. Animals were randomly allocated to five groups according to electrode placement ($n = 6$, each): dermatome, contralateral, paraspinal, acupoint, and control. Interventions: Low-frequency TENS at sensory intensity and 100 μs pulse duration. Withdrawal thresholds to mechanical (von Frey) and thermal stimuli and joint edema were assessed before induction of inflammation and immediately before and after application of TENS.
Results: Reduced paw withdrawal threshold and thermal latency that occur 24 h after the induction of inflammation were significantly reversed by the administration of TENS in all groups when compared with sham treatment or with the condition before TENS treatment. No difference was observed in the edema measurement.
Conclusion: These results offer more options for practitioners to choose the area of the body most commodious for electrode placement, depending on the clinical condition of the patient, because the effect was similar at all sites. In addition, there was a loss of the

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effectiveness of TENS in reversing mechanical and thermal hyperalgesia on the fifth day, suggesting the development of the tolerance phenomenon.

Introduction

The American Physical Therapy Association defines Transcutaneous Electric Nerve Stimulation (TENS) as the application of electrical stimulation to the skin to control pain. TENS is a clinical treatment that is non-invasive, inexpensive, and easy to use. It is also safe and has few adverse side effects.[1] These side effects were seen only in the burst TENS, which inhibited collagen I and III production and impaired its alignment during partial rupture of the Achilles tendon in rats.[2]

TENS stimulates large diameter peripheral nerves through electrodes placed on the skin to achieve therapeutic effects.[3] The overall goal of TENS therapy is to relieve pain, thus allowing increased activity with less discomfort.[4,5] However, despite the large number of clinical trials showing the efficacy of TENS for pain management, it is still unclear which clinical conditions should be treated with TENS and which parameters of stimulation should be used.[6]

The clinical literature on TENS is controversial and difficult to interpret, mainly due to study limitations and poor design. TENS-related factors (i.e., frequency, intensity, pulse duration, number of weekly or even daily sessions, interval between administrations, duration of stimulation and shape of the electrode, number of channels, as well as form and area of electrode placement) are not always specified, appropriate, or consistent among patients. Further appropriate stimulation parameters may not always be used.

A recent meta-analysis investigating the effect of TENS on postoperative pain, measured as analgesic consumption, showed a 35% reduction for TENS applied at adequate stimulation parameters (frequency: 1–8 Hz for acupuncture-like TENS or 25–150 Hz for conventional TENS; intensity: strong subnoxious, maximal tolerable, or >15 mA). Without adequate frequency and intensity of stimulation, there was only a 4% reduction in analgesic consumption.[7] Similarly, Rakel and Frantz[8] found that TENS intensities >9 mA resulted in greater reduction in pain during gait and vital capacity activities postoperatively compared to TENS <9 mA. Thus, adequate dosing is essential to obtain a positive effect.

Electrode size, as presented by Cheing and Hui-Chan[9] and Resende et al.,[10] can intervene in the density of the electrical current transmitted to tissues under the electrode. With uniform electrode conductivity, the current density is inversely proportional to the electrode contact area. Therefore, as electrode contact area decreases, current density increases, meaning that if the same electrical voltage is applied first across a pair of small electrodes and then across a pair of large electrodes, the amplitude of stimulation will feel greater beneath the smaller pair. If one small and one large electrode are used in a single application, the stimulation will generally be perceived as greater beneath the small electrode.[11] Thus, larger electrodes will be able to deliver more current to the tissue. Moreover, application of electrodes in a linear, parallel, crossed, or alternating design and the distance between the electrodes are often detailed in studies.[8]

Thus, we aimed to compare the TENS effect in different body areas in an experimental model of inflammatory pain in rats. Moreover, we intended to determine whether electrode placement influences the development of tolerance to TENS and edema reduction.

Method

Animals

All experiments were approved by the Animal Care and Use Committee at Universidade Federal de Sergipe (UFS), Aracaju, SE, Brazil (approval number 88/10) and are in accordance with the guidelines of the Brazilian College of Animal Experimentation and the International Association for the Study of Pain for the use of laboratory animals. Thirty adult male Wistar rats, 6 in each group as suggested for animal research (weight range, 250–300 g), were kept at the Laboratory of Neuroscience Research at a temperature of 22–24 °C, in a light-controlled room (12 h/12 h light/dark cycle, lights on at 6:00 a.m.). The rats were housed with a maximum of five per cage, with water and food ad libitum.

Induction of inflammation

Immediately after baseline behavioral measurements, rats were anesthetized with 5% isoflurane, maintained with 1–2%. Knee joint inflammation was then induced by intra-articular injection of a mixture of 3% carrageenan and kaolin (0.1 mL in sterile saline; pH, 7.4) into the left knee joint.[12] The inflammation is considered acute for the first 24 h, when there is neutrophil infiltration. This model is used to mimic arthritic conditions and shows good predictability for drug effects.[13]

After induction of knee inflammation, the rats were returned to their cages and allowed to recover for 24 h. Within 24 h, the animals exhibited signs of inflammation such as edematous and warm knee joints and also behavioral signs such as guarding and decreased weight bearing on the inflamed limb.[14] Within 5 days of treatment, the animals were assessed for both mechanical and thermal hyperalgesia, as well as edema volume, before and after application of TENS.

Mechanical sensitivity

Paw withdrawal thresholds were tested for all groups of rats. Measurements were performed before the induction of

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