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AN OVERVIEW OF ELECTRICAL NERVE STIMULATION VIA TRANSDERMAL APPLICATION

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Abstract

The risk of dying from cardiovascular and cerebrovascular diseases is significantly increased by hypertension. The primary issues affecting public health at the moment are hypertension and its consequences. Some persons with hypertension, even under intensive therapeutic supervision, do not achieve the specified blood pressure (BP) treatment targets. Patients with resistant hypertension (RH) may be defined as those who need to take three or more different kinds of antihypertensive medications in order to reach their blood pressure target. Utilizing the body's natural bioelectric system, bioelectric technology is a relatively new approach. In auxiliary evaluation, pain management, and organ function rehabilitation, it is commonly used. Renal sympathetic denervation, carotid baroreflex activation therapy, electroacupuncture in traditional Chinese medicine, and transcutaneous electrical nerve stimulation are the primary forms of bioelectrical technology, which has advanced quickly in recent years as an effective treatment for RH.

Introduction

Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological intervention used in the treatment of acute and chronic pain conditions. TENS units are safe, inexpensive, over-the counter devices that deliver pulsed alternating current applied through electrodes placed on the skin. The parameters of pulse frequency and pulse intensity are adjustable and linked to TENS efficacy. TENS can be applied with low frequencies, 100 Hz, or mixed frequencies. Frequencies of stimulation result in unique mechanisms of action for TENS, as outlined below(1).

Electrical stimulation therapies are therapeutic adjuncts used in the management of chronic pain conditions such as osteoarthritis, fibromyalgia, and chronic primary low back pain (CPLBP). They include a range of non-invasive peripheral stimulation techniques to relieve pain. Among these therapies, transcutaneous electrical nerve stimulation TENS and interferential therapy are the most used low volatage electrical stimulation therapies. Both arereported to have similar mechanisms of action, namely acting through segmental inhibition or
activation of descending pain-inhibitory systems. TENS units are widely available and accessible globally.(2) A TENS unit is a battery-powered device that can be self-administered and delivers electrical impulses through electrodes placed on the intact skin surface near the source of maximal pain.

Interferential therapy involves a different form of electrical stimulation than TENS, and treatment is administered using two pairs of electrodes usually in a clinical setting. Compared to interferential therapy, TENS is used more frequently as a self-delivered intervention given that it is in expensive and easily accessible.

The purpose of TENS is to selectively activate nerve fibers. Maximal pain relief is achieved when TENS generates a strong non-painful electrical sensation beneath the electrodes. Pain relief is usually rapid in onset and stops shortly after TENS is turned off. For this reason patientsare encouraged to deliver TENS for as long as needed, which may be for hours at a time and throughout the day.(5) The main contraindication is patients with implanted stimulators such as pacemakers. In the UK, TENS devices can be purchased without prescription, although this isnot the case in some European countries. TENS devices,

including electrode leads, pads and battery, retail for approximately GBP although bulk buying can markedly reduce cost. Interestingly, TENS does not appear to be widely available for patient use in developing countries.

1. Physiological Principle of TENS Induced Pain Relief

The ancient Egyptians are usually acknowledged as the first people who used electrogenic fish to apply electricity for pain relief. Yet, the first documented use of this kind of pain relief is of a Roman Physician in 46 AD.(7) In 1786, Luigi Galvani, an Italian doctor, demonstrated that the leg of a frog contained electricity. This observation and other advancements in generating electricity lead to a resurgence in the use of electricity to treat different illnesses and relieve pain. However, increased use of pharmacological agents to manage pain resulted in the decline of the electrotherapy at the end of the 19th century. In 1965, Ronald Melzack from McGill University in Montreal Canada and Patrick Wall from University College London UK, published their seminal paper which proposed a gating mechanism in the central nervous system to regulate the flow of nerve signals from peripheral nerves en-route to the brain.

TENS is a technique to stimulate different categories of nerve fibers. The most commonly used TENS technique is termed conventional TENS. During conventional TENS, low-intensity pulsed currents are administered at high frequencies between 10-200 pulses per second, at the site of pain. Another technique, which is used less often is acupuncture-like TENS (AL-TENS) using high-intensity and low-frequency administered over muscles, cupuncture and trigger points. The purpose of AL-TENS is to activate small diameter afferents which has been shown to close the pain gate using extra segmental mechanisms. TENS can also be used as a counter-irritant, termed intense TENS, using high-intensity and high- frequency currents(10).

2. Mechanisms of TENS Underlying Analgesic Effects

TENS activates inhibitory mechanisms to reduce central excitability primarily in the central nervous system and to consequently reduce pain. TENS activates large afferent fibers in the periphery that send input to the central nervous system. This is turn activates descending inhibitory systems that reduce hyperalgesia(12). Specifically, prior studies show that blockade of neuron activity in the spinal cord, rostral ventromedial medulla and the periaqueductal gray inhibit analgesic effects of TENS. In parallel, studies in people with fibromyalgia show that TENS can restore central pain modulation, an indicator of central inhibition. In healthy human volunteers, brain responses measured with electroencephalography (EEG), demonstrate reduced cortical activity with both LF and HF TENS. Reductions in activity of the primary somatosensory (S1) and motor (M1) cortices occurred with both frequencies; however, reduced connectivity between SI or M1 and the prefrontal cortex were found only with LF TENS.

Factors That Directly Affect TENS Efficacy

TENS management emphasized the importance of factors influencing TENS efficacy including dosing parameters, timing of the outcome measure, interactions with medications, and repeated use. In the current review of the literature common problems in determining if an effective dose or appropriate outcome measure was utilized are still evident(13). Overall, systematic reviews commonly describe that there is limited reporting on TENS parameters, adverse events, high risk of bias, low number of participants, inadequate blinding, and limited reporting of methodology. This has led to a number of systematic reviews showing inconclusive or weak evidence.

Pathophysiology by which mechanism promote RH

The pathogenesis of RH is the persistence of multiple factors that influence the abnormal activation of the central integration system(15). Studies have indicated that continuously activated sympathetic as well as renin-angiotensin-aldosterone system (RAAS) activity are among the important pathogenic mechanisms of RH. RH tends to have sustained stimulation by longer-term risk factors. These co-stimulations cause vascular remodeling and volume expansion, leading to the development of RH.

According to the latest 2018 European Society of Cardiology/European Society of Hypertension guidelines for the management of arterial hypertension, the diagnosis of RH requires detailed information regarding the following items (16).

- ✓ The patient's history, including lifestyle characteristics, alcohol and dietary sodium intake, interfering drugs or substances and sleep history.
- ✓ the nature and dosing of the antihypertensive treatment.
- ✓ a physical examination, with a particular focus on determining the presence of hypertension-mediated organ damage (HMOD) and signs of secondary hypertension.
- ✓ confirmation of treatment resistance by out-of-office BP measurements.
- ✓ laboratory tests to detect electrolyte abnormalities hypokalaemia, associated risk factors diabetes, organ damage advanced renal dysfunction and secondary hypertension.
- ✓ confirmation of adherence to BP-lowering therapy.

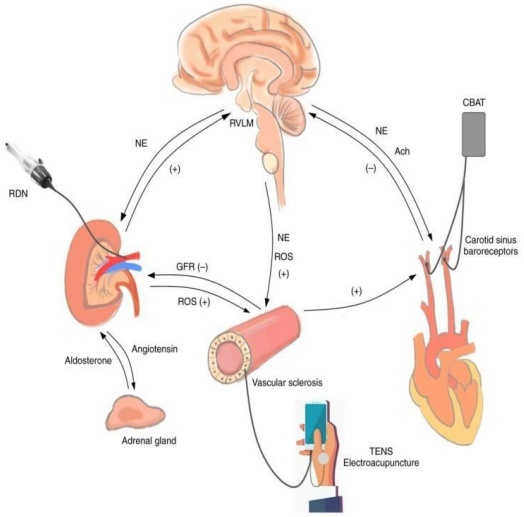


Figure:1

3. Peripheral Mechanisms of TENS

A few studies have shown peripheral effects of TENS. HF TENS reduces tissue-injury increases in substance P in dorsal root ganglia neurons, blockade of peripheral opioid receptors prevents the analgesia produced by LF and HF TENS, and blockade of CB1 receptors prevents production of analgesia by HF and LF TENS. Thus, TENS may also alter excitability of peripheral nociceptors to reduce afferent input to the central nervous system. Interestingly, in α-2a adrenergic knockout mice, LF and HF TENS analgesia does not occur; this effect is mediated peripherally since the blockade of peripheral, but not spinal or supraspinal, α-2 receptors prevents the analgesia produced by TENS(17). In humans, there are increases in blood flow with TENS at intensities greater than 25% above motor threshold that produce motor contractions. Thus, some of the analgesic effects of automatic function.

4. Evidence of tens for pain management

Acute Pain

For TENS used in individuals with acute pain, systematic reviews in the last nine years have focused on four areas with respect to acute pain: acute pain in general, the pre-hospital setting, paramedic pain management of femur fracture, and acute low back pain. A Cochrane review of TENS use for acute pain, last updated in 2015, included a total of 19 clinical trials with pooled analysis of 1346 individuals(18). Importantly, this systematic review only included trials where TENS was delivered as a stand-alone treatment at an adequate dose emphasizing a strong but comfortable patient sensation. The types of acute pain were varied and categorized as procedural pain or non-procedural pain. Six trials were added to the data from the previous systematic review in 2011.The success of the TENS depended on the application of active TENS and varied between theclinical trials. For TENS use with femur fracture, 72 participants received either active TENS. Pain in the active

TENS group decreased from 89 ± 9 mm to 59 ± 6 mm, whereas the sham group decreased from86 ± 12 mm to 79 ± 11 mm. In the pre-hospital setting, active TENS compared with sham Using the criterion of two points or greater decrease in pain on a 0–10 scale, active TENS decreased pain 53.8% of the time as compared with placebo TENS at 11.5%. For acute low back pain, a systematic review included three placebo-controlled studies with a pooled analysis of 192 participants. In one study, a 30 min TENS treatment while in transport to the hospital reduced pain by 28.0 mm when compared with the placebo(20). A clinical practice guideline CPG for older adults with hip fracture supports the use of TENS when pain is unmanaged with usual interventions

5. TENS reduces central excitability

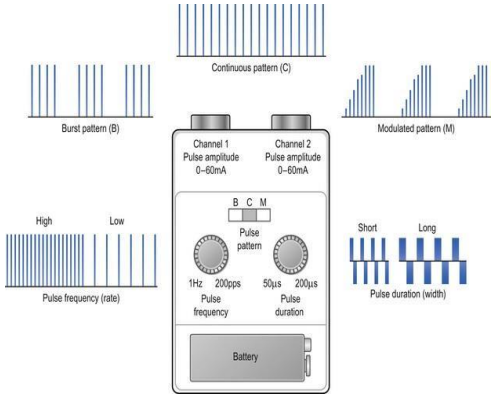
TENS directly reduces the activity of nociceptive dorsal horn neurons in uninjured animals and the sensitization of dorsal horn neuron in injured animals. In parallel, there is a reduction in both primary and secondary hyperalgesia by both LF and HF TENS and release of the excitatory neurotransmitters glutamate and substance in the spinal cord dorsal horn in animals with inflammation, neuropathic, or incisional pain(19). Furthermore, in people with FM and osteoarthritis, there is a reduction in pressure pain thresholds not only at the site of TENS stimulation but also at sites outside the area of application, implicating a reduction in central excitability. Both HF and LF TENS also reduces microglia and astrocyte activation in the spinal

Cord in both osteoarthritic and neuropathic pain animal models, and associated pro inflammatory cytokines, intracellular messengers, and transcription factors.

Pain management in developing countries:

The International Association for The Study of Pain IASP speculate that “the prevalence of most types of pain may be much higher in developing countries than in developed countries although epidemiological evidence is lacking. It is known that there is a higher incidence of pain conditions associated with epidemics such as HIV or aids in the developing world.

TENS has a rapid onset of action, unlike medication, and there is no potential for toxicity or overdose.(22) Clearly, there is a case to use TENS for pain management in the developing world. However, research is needed to determine the feasibility of TENS use in developing countries. Perhaps health promotion authorities should alert the public and heath care practitioners to the role of TENS as an important aid in the fight against pain.

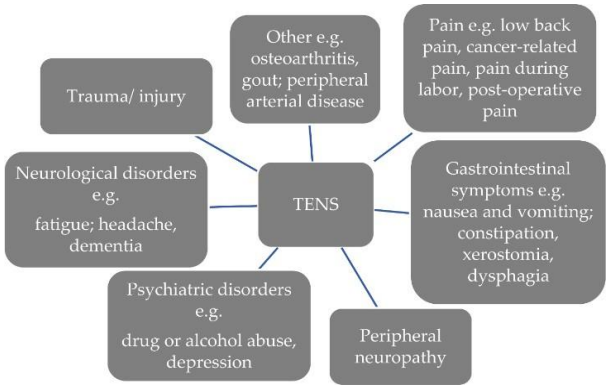


6. TENS Unit Instructions
   - Ensure the unit is turned OFF.
   - Re-position the electrodes to the relevant part of your body.
   - Turn the unit ON and up one setting.
   - Select your mode of choice.
   - Increase the intensity to a comfortable level.(23)
   - Leave for the desired time.
   - Turn the unit OFF

TENS used across an artificial cardiac pacemaker may cause interference and failure of the implanted device. Serious accidents have been recorded in cases when this principle was not observed. TENS should also be used with caution in people with epilepsy or pregnant women; do not use over area of the uterus as the effects of electrical stimulation over the developing fetus are not known.

7. Clinical effectiveness of TENS

In Western clinical practice TENS has been shown to have a role in pain management. There are many systematic reviews on TENS although evidence is often inconclusive because of shortcomings in RCT methodology(25). Early systematic reviews suggested that TENS was of limited benefit as a standalone pain therapy for acute pain. Carroll et al. judged there to be no benefit of TENS for postoperative pain because 15 of 17 RCTs found no differences in pain relief between active and placebo TENS.



Conclusion

In order to provide practitioners, researchers, and commissioners with a valuable reference resource, we have assessed all relevant systematic reviews and meta-analyses of RCTs assessing the impact of TENS on pain intensity. A long-standing ambiguity over clinical efficacy is resolved by our analysis of the study evidence. Examples of meta-analyses with "sufficient data" that show benefit are shown by our judgment. Meta-analyses with "sufficient data" that showed no advantage were not present in any instances. TENS should thus be taken into consideration as a therapeutic approach, per our recommendation.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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