Use of TENS In Pain Management

Recent advances in transcutaneous electrical nerve stimulation (TENS) have shed new light on the efficacy as well as the mechanism of action and provide a solid foundation for clinical utilization and subsequent research.

TENS has been around 40 or perhaps over 140 years, depending on which technology should be credited with bringing electrotherapy to the forefront of pain management. Recent meta-analysis indicates pain reduction from TENS averages 46%, which compares well to the 32% reduction achieved with opioids. The best therapy might be a combination, or electrochemical, approach as there are no known negative interactions between TENS and pharmaceuticals. TENS works best when the pain etiology is considered, and various protocols are attempted. This article does a fine job of reviewing historical and contemporary applications of TENS, mechanism of action, and effectiveness. The authors conclude that, when used properly, TENS has proven to be a safe and effective tool in pain management.

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The use of electricity in medicine has been in practice for literally thousands of years, with Aristotle cited as providing the earliest written documentation of this practice for pain relief.[1] Initial electrotherapy devices were not devices at all but rather fish, such as the Torpedo electric ray fish, capable of producing 8-220 volts of electricity. Placing the fish near the feet in a wet tub or shore was purported to cure arthritis, while placing it around the head was said to cure headache. In the eighteenth century, clinical electrotherapy began to make advances with the advent of electrical storage devices such as Leyden jars and batteries, but skepticism won out, and electrotherapy for pain management did not re-emerge until the 1960s.[2] Modern researchers have continued to refine these procedures and ultimately developed several modalities. Perhaps the most common of these, transcutaneous electrical nerve stimulation (TENS), has been used for approximately 40 years. In spite of, or even perhaps due to this long history of clinical utility, there has been a surprising lack of large randomized trials investigating the efficacy of TENS for pain relief. Instead, the publication history pertaining to the efficacy of TENS has been populated with smaller trials and case studies. This diversity in trial size and quality has led to two consequences for the field of electromedicine: a minor debate regarding the efficacy of TENS, and a relatively poor understanding of its mechanism of action. However, recent publications have begun to rectify the situation and will be discussed in this article.

Clinical Applications and Usage of TENS

TENS is the delivery of electrical current to peripheral nerves through intact skin using cutaneously-applied electrodes. TENS devices are designed for use either in the clinic or, in portable form, for patient self-administration. They typically consist of an electrical stimulator/power source equipped with controls to modulate frequency, current and, in some cases, waveform characteristics. Lead wires attach patient-connect electrodes to the device. In most cases, one or two sets of lead wires can be attached to a single device, allowing for the placement of two or four electrodes, respectively. Construction of the electrodes varies between and within various manufacturers, but most electrodes are self-adhesive and use a carbon- or silver ink-based conductive material. Electrode shapes and sizes vary to conform to various body parts and desired current density. In order to use the device, patients attach the lead wires to the electrodes, apply the electrodes to the specified area of the body, and connect the lead wires to the TENS device. Once this set up is complete, the patient turns on the device, selects a preset program (if available), and increases the current to a level typically described as "strong but comfortable" or "maximal tolerable."

The applied current can vary in terms of waveform, frequency, and current level. Application of TENS at frequencies above 50Hz is referred to as high-frequency or conventional TENS, while application at frequencies below 10Hz is termed low frequency TENS. Bursts of high frequency TENS applied during a low frequency session is known as acupuncture-like or burst TENS. Different frequencies have been shown to differentially affect physiological responses to stimulation and will be discussed later in this article.

This versatility in treatment parameters can allow the patient to play an active role in the therapy regimen, as he or she may be directed to modulate these parameters to achieve optimal comfort. However, the versatility at times has also created the perception that patient instruction and education is difficult and impracticable in the current healthcare setting. These perceptions may be changing as it is becoming clear that optimal treatment parameters do exist for such variables as current and duration of therapy.[3,4]

Just as manipulating variables such as frequency and current allows for a broad range of settings, there is also a broad range

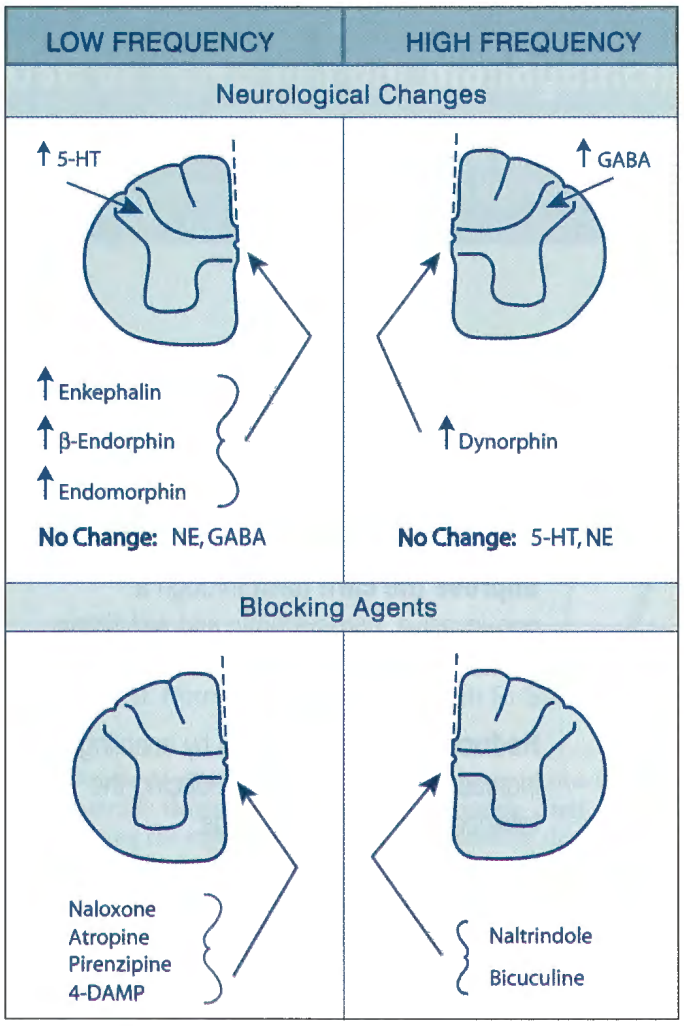

FIGURE 1. *Neurotransmitter system responses to low- or high-frequency TENS.*

of chronic pain states in which the efficacy of TENS has been demonstrated. These conditions have been reviewed in greater detail elsewhere[5] but include chronic low back pain, osteoarthritis, general chronic musculoskeletal pain, postoperative pain, shoulder pain following stroke, pain associated with dysmenorrhea, and labor pain. TENS is covered by many insurance providers, including Medicare. Still, reimbursement is not universal, and some managed care organizations have declared TENS to be an investigational or experimental therapy, with inconclusive or conflicting evidence regarding its efficacy most commonly cited as the rationale for this classification. However, this opinion is not the norm in the managed care industry and, for most patients, reimbursement is not an issue.

Is TENS Effective?

During the 1980s, the electrotherapy industry was enjoying rapid growth with relatively wide acceptance across multiple clinical settings. However, the landscape was significantly altered with the publication of a study by Deyo et al[6] in the *New England Journal of Medicine* that found TENS was no better than placebo for the treatment of chronic low back pain. Despite its flawed protocol, this high profile article led to changes in clinician attitudes and unfavorable managed care coverage. However, an apparent benefit of the Deyo study is that it spurred a general increase in the quality of clinical research regarding the efficacy and utility of TENS including higher quality studies with more relevant outcomes. Studies such as those by Moore and Shurman[7] began to demonstrate that—when used correctly for the appropriate conditions and patient populations—TENS can be a highly effective tool for the treatment of chronic pain.

Perhaps the most important change in the research landscape was the demonstration and realization that adequate placebo controls can be used in studies involving electrotherapy. Another study conducted by Deyo and colleagues demonstrated the level of blinding that can be achieved in electrotherapy studies. While 100% of subjects in the active TENS group felt their units were working properly, 84% of subjects in the sham TENS group also believed their units were working properly.[8] The effective blinding also extends to investigators. In the same study, clinicians correctly guessed the treatment allocation (active TENS versus sham TENS) for subjects 61% of the time, relatively close to the 50% that would be expected by chance. The authors concluded that the keys to successful blinding in studies involving TENS were to ensure that: 1) sham TENS devices appeared and sounded exactly like the active devices, 2) patients with previous TENS experience were eliminated from placebo-controlled studies, 3) cross-over designs should be avoided, and 4) steps should be taken to ensure that subjects in both groups receive identical instructions and modifications relating to electrode placement.

Despite high-quality studies that have been done recently, there is still not a consensus as to how effective TENS is for treating chronic pain. Searching databases such as Medline or EMBASE using "TENS" and "pain" as keywords highlights two significant characteristics of the clinical research performed in this arena: the wide variety of acute and chronic pain conditions treated with TENS and the low number of patients enrolled in a typical study. Given these factors, it should not be surprising that there has been debate regarding the efficacy of TENS. A number of potential causes for this controversy are likely, but foremost are: 1) insufficient statistical power due to too few patients enrolled in most studies, 2) large variation in the types or etiologies of the disease states/chronic pain conditions studied, and 3) significant variability in key treatment parameters such as stimulation frequency, current level, duration, number of sessions per day, electrode placement, etc. As such, the versatility and variability of TENS that has made it attractive to clinicians may have somewhat hindered its advancement through rigorous clinical research.

The debate regarding the efficacy of TENS for the management of chronic pain spurred meta-analyses of existing TENS studies.[9-17] However, these analyses did little to rectify the situation as they have generally taken the standard approach of restricting inclusion criteria to specific chronic pain states (e.g., low back pain, osteoarthritis of the knee, rheumatoid arthritis of the hand). This ultimately led to many of the same issues encountered by the individual studies — there typically was not sufficient statistical power to reliably detect meaningful treatment differences. Recently, Johnson and Martinson[15] approached the issue of the efficacy of electrical nerve stimulation by expanding their inclusion criteria and modifying their statistical approach to accommodate the increased variability associated with the expanded inclusion criteria. The result of these modifications was that the analysis included 38 studies from 29

Table 1. Meta-Analysis of TENS Efficacy, modified from Johnson and Martinson[13]

Title	Author	Year	Trials	N	Conclusions
Transcutaneous electrical nerve stimulation (TENS) for chronic low back pain	Khadikar	2005	2	175	Evidence to support TENS as a stand-alone therapy is sparse and conflicting
Transcutaneous electrical nerve stimulation (TENS) for chronic pain	Carroll	2004	19	763	Insufficient data extracted to perform meta-analysis
Transcutaneous electrical nerve stimulation (TENS) for the treatment of rheumatoid arthritis of the hand					Acupuncture-like TENS reduces joint pain and tenderness, but had no effect on grip strength
Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea	Proctor	2002	9	213	High frequency TENS found to be effective for the treatment of primary dysmenorrhoea
Transcutaneous electrical nerve stimulation for knee osteoarthritis	Osiri	2002	7	294	Active and acupuncture-like TENS over at least 4 weeks provide significant pain relief and reduce stiffness
Efficacy of the transcutaneous electrical nerve stimulation (TENS) for the treatment of chronic low back pain	Brosseau		5	170	No evidence to support the use or non-use of TENS for the treatment of chronic low back pain
Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain	Bjordal	2003	21	1350	TENS significantly reduces analgesic consumption for postoperative pain
Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: a meta-analysis of randomized controlled trials	Johnson	2007	38	1227	Electrical nerve stimulation significantly reduces chronic musculoskeletal pain
Transcutaneous electrical nerve stimulation (TENS) for chronic low back pain	Milne	2002	5	421	No significant effect of TENS versus placebo in any outcome measure

manuscripts, with a total of 1,227 patients. These numbers were significantly higher than those obtained in previous meta-analyses on the efficacy of TENS (see Table 1).

Overall, the results of the meta-analysis by Johnson and Martinson[13] showed a highly significant ($P < 0.0005$) and clinically relevant reduction in pain with electrical nerve stimulation, as the average pain reduction was 46%, nearly three-fold greater than that seen with placebo treatment. The magnitude of this effect validates the claims that inconsistencies in earlier published results were indeed due to a lack of statistical power and, more importantly, the benefit of electrotherapy can produce very meaningful clinical results.

A central tenet to the Johans and Martinson's argument is that the broad inclusion criteria provided adequate statistical power for their study, a characteristic that had been missing from the vast majority of studies to date. While this assertion is clearly supported by the results of the paper, another important characteristic is the inclusion of studies involving musculoskeletal pain of any anatomical origin. The basis for this decision is supported by opinions that pain states can—and should—be classified based on mechanism as much as, if not more than, on anatomy, duration, or causative agent.[18]

Another demonstration of the efficacy of TENS as a pain relieving modality is the effect of TENS on the amount of medication required to achieve acceptable pain relief. Numerous studies have shown that when TENS is used along with conventional analgesics, analgesic consumption declines. A recent meta-analysis on this topic examined this property of TENS for post-surgical pain.[9] Across all studies, TENS reduced the analgesic requirement an average of 26.5% more than placebo TENS. Importantly, given that TENS was added to a standard PCA regimen, the degree of pain relief that was achieved with active TENS plus PCA with reduced analgesics was equivalent to placebo TENS plus PCA. That is, TENS decreased analgesic consumption while maintaining the same degree of pain relief. While the ability of TENS to decrease analgesic consumption has been shown most often for post-surgical pain, a similar effect has been seen in chronic pain conditions as well.[19-21] Although it has not been thoroughly investigated, it seems likely that a reduction in medication consumption (while maintaining the same or greater level of pain relief) would lead to a reduction in side effects and/or adverse events. This area is clearly worthy of further investigation as it may serve to expand the therapeutic index as well as the safety profile of a number of analgesic drugs. Another important consideration regarding these results is that TENS is free of any known negative drug interactions and, as such, provides clinicians with another powerful tool for their armamentariums.

How Does TENS Work?

Similar to most other analgesic therapies, TENS was used clinically before its mechanism of action was understood. At present, two mechanistic theories are generally used to explain its efficacy. The first is the gate control theory initially described by Melzack and Wall.[22] The proposal of the gate control theory of pain—and the subsequent publication of clinical support for this hypothesis[23]—led to this as the first proposed mechanism of action for TENS. According to this theory, the stimulation of large, myelinated afferent fibers leads to disruption of nociceptive signaling in the dorsal horn of the spinal cord. Nerve conduction velocity studies in humans have shown that TENS does preferentially stimulate Aß fibers,[24] an important requirement for the gate control theory to apply to TENS.

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Animal studies have permitted more invasive investigations into the mechanism of action of TENS. It has been shown that application of TENS leads to the suppression of neuronal activity in the spinal cord that is normally seen in response to painful stimuli. Garrison and Foreman[25] recorded wide dynamic range neurons in the spinal cord of cats and found that the normally robust neuronal activity shown by these cells in response to a noxious mechanical stimulus (pinch) applied to the limb is significantly reduced during the time of TENS application to the receptive field of the neuron. Similar results were also found in monkeys, and those results were further supplemented by data showing that TENS does not affect the firing of peripheral nerves, but only responses in the spinal cord.[26] It was later shown that this inhibition of responses in the spinal cord is not dependent upon descending inhibitory mechanisms since TENS-induced alterations in spinal cord physiology were not different in intact or decerebrate animals.[27] Leem and colleagues[28] also found similar results using a rat model of neuropathic pain. In those studies, the authors reported that the increased stimulus-evoked firing of wide dynamic range neurons in the spinal cord common to neuropathy is significantly diminished with TENS application.

As the physiological responses that occur in the spinal cord in response to TENS application have been elucidated, advances in our understanding of the neurochemical changes from TENS have also been made. Interestingly, evidence from studies using rats indicates that the neurotransmitter systems responsive to low- or high-frequency TENS are unique in many ways (see Figure 1). High-frequency TENS induces the release of the inhibitory neurotransmitter GABA in the dorsal horn of the spinal cord and the opioid peptide dynorphin, but has no effect on the levels of norepinephrine, serotonin, or other opioid peptides. High-frequency TENS also reduces the levels of the excitatory neurotransmitters glutamate and aspartate in the spinal cord. Conversely, low-frequency TENS induces the release of serotonin, as well as the opioid peptides beta-endorphin, enkephalin, and endomorphin, while leaving the levels of norepinephrine and GABA unchanged.[5,29,30] Likewise, the efficacy of TENS in rat models of arthritis can be blocked by administration of various drugs: muscarinic antagonists block the analgesic effects of either low- or high-frequency TENS[31] and serotonergic antagonists only inhibit the effects of low-frequency TENS.[32] Selective opioid receptor antagonists also show differential effects against either low- or high-frequency TENS: the mu-opioid receptor antagonist naloxone blocks analgesia produced by low-frequency TENS, whereas the delta-opioid receptor antagonist naltrindole inhibits high-frequency induced analgesia.[33,34]

While some of the neurochemical mechanisms suggested by the research cited above indicate gate control as a mechanism of action for TENS, a number of these studies indicate a second, complimentary mechanism as well. It is clear from studies in both animals and humans that TENS application results in the release of endogenous opioids. This was first shown in the 1970s by Sjolund and Erikson[35] who measured the levels of beta-endorphin in the cerebrospinal fluid of chronic pain patients and found increases in CSF beta-endorphin levels in approximately half of these subjects after application of TENS. In a similar study, endorphin levels in the cerebrospinal fluid of chronic pain patients were measured before and after one week of daily treatment with high-frequency TENS. There was a significant increase in endorphin levels after TENS treatment and, more importantly, the relative increase in endorphin levels showed a positive correlation with the degree of pain relief.[36] Further evidence for an opioid-mediated effect of TENS was provided by the same group who showed that TENS-induced analgesia can be blocked by administration of the opioid antagonist, naloxone.[37] These findings have been confirmed by other authors who have shown increases in levels of opioid peptides in the CSF or the blood following TENS.[38-40] These results have been further investigated in animal studies in which it has been demonstrated that the frequency of stimulation affects the specific family of opioid peptides released. Low frequency stimulation (< 4Hz) has been shown to be dependent upon intact mu opioid receptors, whereas high frequency stimulation (> 100Hz) is dependent upon intact delta opioid receptors.[33,34] These data, combined with the data showing that high frequency stimulation is more efficacious than low frequency stimulation in morphine-tolerant rats,[41] suggests that the frequency of stimulation may be of critical importance to the clinician using TENS to treat patients currently receiving opioid therapy. As virtually all opioids act via the mu opioid receptors, the use of high frequency stimulation or stimulation that alternates between low and high frequency may provide greater pain relief.

How Effective is TENS?

While the debate regarding whether TENS is effective appears to be resolved, the question regarding the relative efficacy of TENS is not yet fully answered. The meta-analysis by Johnson and Martinson[13] found a 46% reduction in pain after electrical nerve stimulation therapy of any sort, indicating comparable, if not superior, efficacy relative to conventional therapeutics. However, in order to firmly establish comparative efficacy, head to head trials are required. Although relatively few such trials have been conducted, such trials have provided evidence for equivalent

or superior efficacy of TENS. Two studies compared the efficacy of TENS with either naproxen or diclofenac in patients with osteoarthritis of the knee. Lewis and colleagues[42] found no difference between TENS and naproxen, but Lone et al found greater efficacy of TENS versus diclofenac in terms of ratings of mean pain intensity and scoring of walking distance.[43] More recently, TENS was shown to have significant efficacy reducing pain and stiffness, at a level that was equivalent, if not slightly superior to, that of intra-articular injection of hyaluronic acid.[44]

Conclusions

The entirety of the body of evidence indicates that TENS can be used as an effective pain management option through activation of spinal gate control mechanisms and the release of endogenous opioids. Further, TENS can be used as a stand alone therapy, or in conjunction with other standard therapies. As the population over the age of 65 increases, and the incidence of age-related diseases such as osteoarthritis concurrently increases as well, the need for an expanded number of options for pain management will be critical. As TENS is free from polypharmacy interactions and is relatively free of side effects, it should be considered as a staple in the practicing physician's armamentarium. ■

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