

**REDUCE YOUR PATIENTS
POST-OPERATIVE
PAIN AND SWELLING WITH THE
*TENS 3900***

FROM

*MEDICAL FINANCE
RESOURCES*



TENS 3900

***For treatment of
Post-Operative Pain
and swelling***



How Does TENS Work?

TENS works through 2 different mechanisms:

- First, electrical stimulation of the nerves can block a pain signal as they travel from the site of injury to the spine and upwards to the brain. If these signals arrive at the brain we perceive pain - if they are blocked en-route to the brain we do not perceive pain - this is known as "Gate Control Theory." When using TENS to "close the gate" we use the Modulation mode. Continuous Modulation TENS mode produces a gentle and pleasant "tingling" under and between the electrodes. The "tingle" sensation helps to block the pain by closing the "pain gate" and slowing down the painful nerve signals - this produces analgesia (numbness) in the painful area.
- Secondly, the body has its own built in mechanism for suppressing pain. It does this by releasing natural chemicals called endorphins in the brain and spinal cord and these chemicals act as very powerful analgesics. The Continuous Modulation mode produces pulse, which should be strong enough to produce a "twitch" in the muscles underneath the electrodes. This muscle "twitch" helps to perform two benefits. First, the "twitch" releases endorphins and also helps the pain "switches" in the brain to be activated through muscular and reflex activity. Secondly, the "twitch" helps reduce post-operative edema.

What are the advantages of TENS?

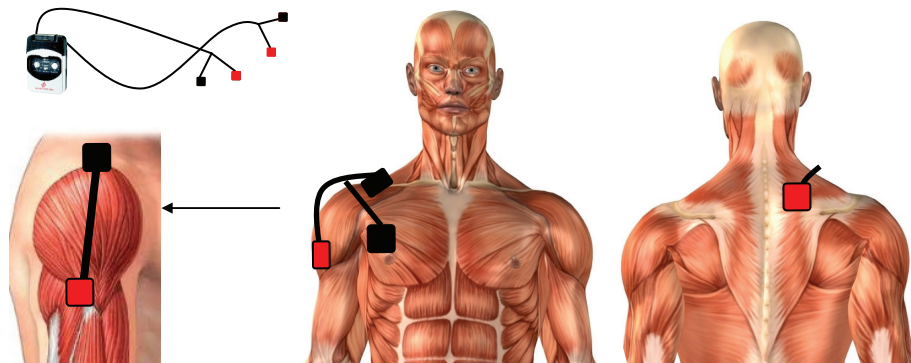
- Non-invasive
- Operation is entirely under the patient's control, as in a PCA pump.
- Easy to apply and use.
- Portable – Can be worn on a brace, belt or in a pocket allowing the patient to return to normal daily activities without restriction.
- Can be used for as long as required.
- No side effects – occasional, but minor, skin irritation after long-term use. We have special hypoallergenic available for sensitive or delicate skin patients.



Our representatives educate patients and staff for proper usage of TENS on a per case basis, ensuring that patients receive maximum results after surgical procedures.

ELECTRODE PLACEMENT CHARTS

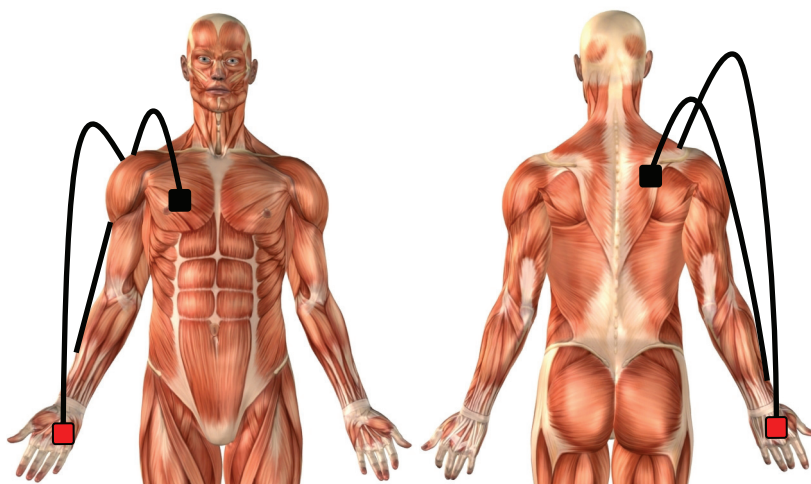
SHOULDER



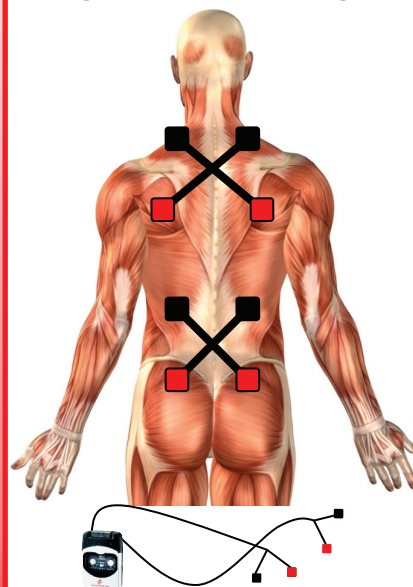
HIP PROCEDURE



WRIST, ARM, ELBOW & UPPER ARM



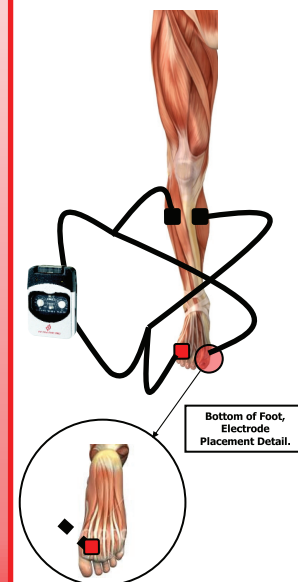
UPPER & LOWER BACK



KNEE



FOOT



Electrode Care

If you are receiving your TENS unit at the time of surgery, you will have sterile electrodes surrounding the surgical site. If they are underneath the dressings, do not attempt to remove them yourself until your physician has removed the dressings or has given you further instructions. Once the sterile electrodes have been removed or are no longer adhering to your skin, you may then use the reusable electrodes provided in the TENS case, following the instructions below:

Instructions for Reusable Electrodes Application (Pre or Post-Operation, Chronic I General Pain)

1. Clean skin thoroughly prior to each application of electrodes. Electrodes do not stick well if any lotion, oil, make-up, dirt, etc. is left on skin.
2. Remove the electrodes from the protective liner and apply firmly to skin. Adhesion improves when electrodes reach skin temperature.
3. Insert the pins of the lead wire from the device into the electrode wire connectors.

Removal

1. Lift at edge of electrode pad and peel. Do not pull on the lead wires when removing electrodes - you may damage the electrodes if you do so.
2. Place the electrodes on the protective liner and remove the lead wire by twisting and pulling at the same time.

Care and Storage

1. Between uses, store the electrodes in the resealable bag in a cool, dry place.
2. The life of the electrodes varies depending on skin conditions, storage, frequency of use, type of stimulation, and stimulation site. Electrode life may be extended by carefully following the application instructions above.

Important

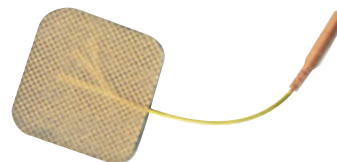
1. The electrodes are intended for single-patient use only.
2. Do not apply to broken skin. Should rash occur, discontinue use.

**TO RECEIVE ADDITIONAL ELECTRODES, CALL:
(TOLL FREE) 888.214.2455**

The TENS 3900 is not intended for use during pregnancy or for individuals with pacemakers. Please read Cautions and Warnings in your manual for further information.

Electrode Placement

Place the electrode pads so that they form a box around the painful area. When connecting the wires from the control unit to the electrodes, always form an "X" over the site by using a diagonal connection as illustrated on the diagrams. Always make sure the control unit is turned off before connecting, disconnecting, or reconnecting the wires to the unit or to electrodes, or before changing the battery.



Adjustment Control

Adjust the two control knobs on the top of the TENS to the level of highest intensity without causing discomfort. As the battery begins to lose power, the control setting may have to be increased accordingly.

The controls in the battery compartment have been preset for the recommended levels and should not be readjusted:

1. The Mode should be set to M.
2. The Timer should be set to C.
3. Pulse Width should be set to 150.
4. Pulse Rate should be set at 70.



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TENS 3900

3 Modes, Timer, Safety Amplitude Cap

Microprocessor Technology



HOW THE TENS 3900 WORKS

"TENS" stands for Transcutaneous (passing through the skin) Electrical Nerve Stimulator. Your body's large nerve fibers are also known as nociceptive fibers because they do not transmit pain. The TENS unit transmits electrical current along the large nerve fibers, stimulating them to produce counter signals which prevent the pain signals from reaching your brain. These large nerve fibers "close the gate" in the spinal cord, thus providing pain relief.

Matt Holowecky
Clinical Specialist
Phone (704) 975-4071
Fax (910) 339-3647



PATIENT INFORMATION							
Patient's last name:		First:	Middle:	<input type="checkbox"/> Mr. <input type="checkbox"/> Mrs.	<input type="checkbox"/> Miss <input type="checkbox"/> Ms.	Marital status (circle one) Single / Mar / Div / Sep / Wid	
Is this your legal name? <input type="checkbox"/> Yes <input type="checkbox"/> No	If not, what is your legal name?		(Former name):		Birth date: / /	Age:	Sex: <input type="checkbox"/> M <input type="checkbox"/> F
Street address:			Social Security no.:		Home phone no.: ()		
P.O. box:		City:		State:		ZIP Code:	
Occupation:		Employer:			Employer phone no.: ()		
INSURANCE INFORMATION							
Prescribing Physician		Clinic			Phone		
Person responsible for bill:		Birth date: / /	Address (if different):			Home phone no.: ()	
Occupation:	Employer:	Employer address:			Employer phone no.: ()		
Is this patient covered by insurance?		<input type="checkbox"/> Yes <input type="checkbox"/> No	Work injury	Auto Accident	Date of injury		
Insurance Company Name:							
Insurance Company Address:							
Policy#				Group#			
Insurance Company Phone:							
Policy Holder (Name):							
Patient's relationship to subscriber:		<input type="checkbox"/> Self	<input type="checkbox"/> Spouse	<input type="checkbox"/> Child	<input type="checkbox"/> Other		
Name of secondary insurance (if applicable):		Subscriber's name:			Policy#	Group#	
Patient's relationship to subscriber:		<input type="checkbox"/> Self	<input type="checkbox"/> Spouse	<input type="checkbox"/> Child	<input type="checkbox"/> Other		
PLEASE ENCLOSE COPY OF HEALTH INSURANCE CARD							

Documentation

Provided – Manufacturer Warranty Product w/ Supplier Standards Notice of Privacy Practices
Please Check: Documentation ☐ ☐ Serial # ☐ ☐ ☐

The above information is true to the best of my knowledge. I authorize my insurance benefits be paid directly to the Medical Finance Resources. I understand that I am financially responsible for any balance. I also authorize Medical Finance Resources or insurance company to release any information required to process my claims.

Patient/Guardian signature

Date



Matt Holowecky

119 Main Street
South River, NJ 08882
Phone 732-390-9751

RX – Prescription and Letter of Medical Necessity

Patient Name:	Date of Birth MM/DD/YYYY
Patient Address	Insurance Company
City, State, Zip	Insurance ID#
Patient Home phone	Insurance Phone#
SS#	Date of Incident

TENS 3900 EMS Unit Conductive Garment
LSO Brace
AFO Brace
Knee Brace
Wrist Brace
Cam Walker
Other _____

Primary Diagnosis(es) ICD-9

1: _____ 2: _____ 3: _____ 4: _____

Circle Length of Need: 2-3 months 4-6 months 6-8 months Long Term

Purchase: Yes No

I certify that the equipment and supplies I prescribed is Medically Necessary for this patient's well being. In my professional opinion, the equipment is both reasonable and necessary in reference to the accepted standards of medical practice and treatment for this patient's condition. Substitution is not allowed without my written approval.

Physician Signature _____ Date _____

Print Physician Name _____ NPI _____

Address _____ City _____ State _____ Zip _____

Phone _____ Fax _____

The Changing Role of Non-Opioid Analgesic Techniques in the Management of Postoperative Pain

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Given the expanding role of ambulatory surgery and the need to facilitate an earlier hospital discharge, improving postoperative pain control has become an increasingly important issue for all anesthesiologists. As a result of the shift from inpatient to outpatient surgery, the use of IV patient-controlled analgesia and continuous epidural infusions has steadily declined. To manage the pain associated with increasingly complex surgical procedures on an ambulatory or short-stay basis, anesthesiologists and surgeons should prescribe multimodal analgesic regimens that use non-opioid analge-

sics (e.g., local anesthetics, nonsteroidal antiinflammatory drugs, cyclooxygenase inhibitors, acetaminophen, ketamine, α 2-agonists) to supplement opioid analgesics. The opioid-sparing effects of these compounds may lead to reduced nausea, vomiting, constipation, urinary retention, respiratory depression and sedation. Therefore, use of non-opioid analgesic techniques can lead to an improved quality of recovery for surgical patients.

(Anesth Analg 2005;101:S5–S22)

The current armamentarium of analgesic drugs and techniques for the management of postoperative pain continues to grow at a rapid rate. However, effective treatment of acute postsurgical pain still poses unique challenges for practitioners (1). An increasing number of complex operations are being performed on an outpatient basis for which the use of conventional opioid-based IV patient-controlled analgesia (PCA) and central neuraxial (spinal and epidural) analgesia are not practical techniques for pain management. This expanding patient population requires a perioperative analgesic regimen that is highly effective, has minimal side effects, is intrinsically safe, and can be easily managed away from the hospital or surgical center (2).

Adequacy of postoperative pain control is one of the most important factors in determining when a patient can be safely discharged from a surgical facility and

has a major influence on the patient's ability to resume their normal activities of daily living (3). Perioperative analgesia has traditionally been provided by opioid analgesics. However, extensive use of opioids is associated with a variety of perioperative side effects, such as ventilatory depression, drowsiness and sedation, postoperative nausea and vomiting (PONV), pruritus, urinary retention, ileus, and constipation, that can delay hospital discharge (4). Intraoperative use of large bolus doses or continuous infusions of potent opioid analgesics may actually increase postoperative pain as a result of their rapid elimination and/or the development of acute tolerance (5). In addition, it has been suggested by the Joint Commission on Accreditation of Healthcare Organizations that excessive use of postoperative opioid analgesics leads to decreased patient satisfaction. Partial opioid agonists (e.g., tramadol) are also associated with increased side effects (e.g., nausea, vomiting, ileus) and patient dissatisfaction compared with both opioid (6) and non-opioid (7,8) analgesics.

Therefore, anesthesiologists and surgeons are increasingly turning to non-opioid analgesic techniques as adjuvants for managing pain during the perioperative period to minimize the adverse effects of analgesic medications. Multimodal or "balanced" analgesic techniques involving the use of smaller doses of opioids in combination with non-opioid analgesic

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Table 1. Non-opioid Drugs and Nonpharmacologic Techniques Used for Minimizing Pain After Surgery

Local anesthetics
• lidocaine, 0.5%–2% SQ/IV
• bupivacaine, 0.125%–0.5% SQ
• levobupivacaine, 0.125%–0.5% SQ
• ropivacaine, 0.25%–0.75% SQ
Nonsteroidal antiinflammatory drugs
• ketorolac, 15–30 mg PO/IM/IV
• diclofenac, 50–100 mg PO/IM/IV
• ibuprofen, 300–800 mg PO
• indomethacin, 25–50 mg PO/PR/IM
• naproxen, 250–500 mg PO
• celecoxib, 200–400 mg PO
• rofecoxib, 25–50 mg PO
• valdecoxib, 20–40 mg PO
• parecoxib 20–40 mg IV
Miscellaneous analgesic compounds
• acetaminophen, 0.5–2 g PO/PR/IV
• propacetamol, 0.5–2 g IV
• ketamine, 10–20 mg PO/IM/IV
• dextromethorphan, 40–120 mg PO/IM/IV
• amantadine, 200–400 mg PO/IV
• clonidine, 0.15–0.3 mg PO/TC/IM/IV
• dexmedetomidine, 0.5–1 µg/kg, followed by 0.4–0.8 µg/kg/h IV
• gabapentin, 600–1200 mg PO
• magnesium, 30–50 mg/kg, followed by 7–15 mg/kg/h IV
• neostigmine, 1–10 µg/kg EPI/IT
Nonpharmacologic therapies
• transcutaneous electrical nerve stimulation (TENS)
• transcutaneous acupoint electrical stimulation (TAES)
• acupuncture-like transcutaneous electrical nerve stimulation (ALTENS)

PO = oral; PR = per rectum; SQ = subcutaneous/tissue; IM = intramuscular; IV = intravenous; TC = transcutaneous; EPI = epidural; IT = intrathecal.

Adapted from White (4).

drugs, such as local anesthetics, ketamine, acetaminophen and nonsteroidal antiinflammatory drugs (NSAIDs), are becoming increasingly popular approaches to preventing pain after surgery (Table 1) (9–11). This review will discuss recent evidence supporting the use of non-opioid analgesic drugs and techniques during the perioperative period for facilitating the recovery process.

Local Anesthetic Techniques

The routine use of peripheral nerve blocks and wound infiltration with long-acting local anesthetics as an adjuvant to local, regional, and general anesthetic techniques can improve postoperative pain management after a wide variety of surgical procedures (Table 2) (4). When administered before surgery, these simple techniques can also decrease anesthetic and

Table 2. Techniques for Administering Local Anesthesia During the Perioperative Period

Peripheral nerve blocks
• ilioinguinal/hypogastric (e.g., herniorrhaphy)
• paracervical (e.g., dilation/curettage, cone biopsy)
• dorsal penile (e.g., circumcision)
• peroneal/femoral/saphenous/tibial/sural (e.g., podiatric)
• femoral/obturator/lateral femoral cutaneous/sciatic (e.g., leg)
• brachial plexus/axillary/ulnar/median/radial (e.g., arm/hand)
• peribulbar/retrobulbar (e.g., ophthalmologic procedures)
• mandibular/maxillary (e.g., oral surgery)
• intravenous regional (Bier block) (e.g., arms, legs)
• intercostal/paravertebral (e.g., breast surgery)
Tissue infiltration and wound instillation
• cosmetic procedures (e.g., blepharoplasty, nasal, septum, endosinus)
• excision of masses and biopsies (e.g., breast, axilla, lipomas)
• field blocks or instillation technique (e.g., hernia repair, vasovasotomy)
• laparoscopic procedures (e.g., cholecystectomy, tubal ligation)
• arthroscopic procedures (e.g., knee, shoulder, wrist, ankle)
Topical analgesia
• eutectic mixture of local anesthetics (EMLA®) (e.g., skin lesions)
• lidocaine spray (e.g., bronchoscopy, endoscopy, hernia repair)
• lidocaine gel or cream (e.g., circumcision, urologic, oral surgery)
• cocaine paste (e.g., nasal, endosinus surgery)

Adapted from White (4).

analgesic requirements during surgery, as well as reduce the need for opioid-containing analgesics postoperatively. More effective pain relief in the early postoperative period, as a result of the residual sensory block produced by local anesthetics, facilitates recovery by enabling earlier ambulation and discharge home (i.e., “fast-track” recovery) (12–14). In addition, use of local anesthetic-based techniques for preventing pain can decrease the incidence of PONV because of their opioid-sparing effects. However, these techniques are most effective for superficial procedures and the duration of analgesia lasts for only 6–8 h.

Blockade of the ilioinguinal and iliohypogastric nerves significantly decreases opioid analgesic requirements in both children and adults undergoing inguinal herniorrhaphy by providing 6–8 h of postoperative pain relief (15,16). Similarly, a subcutaneous ring block of the penis provides effective perioperative analgesia for circumcision (17). Local anesthetic infiltration of the mesosalpinx significantly decreases pain and cramping after laparoscopic tubal ligation (18).

Simple instillation of local anesthetic after removal of the gallbladder also reduced right upper quadrant and shoulder pain (10,19). Pain after arthroscopic shoulder surgery was decreased significantly by a suprascapular nerve block (20) and pain after knee surgery was minimized with a femoral nerve block (21). However, more complete perioperative analgesia for painful shoulder and knee procedures requires use of interscalene brachial plexus (22) and combined femoral, obturator, lateral femoral cutaneous, and sciatic nerve (23) blocks, respectively. Although additional preparation time may be required when major peripheral nerve blocks are performed before surgery, these techniques can offer significant advantages compared with general and spinal anesthesia with respect to pain control in the postoperative period (12,13,22,23).

It has been suggested that performing neural blockade with local anesthetics before surgical incision prevents the nociceptive input from altering excitability of the central nervous system by preemptively blocking the *N*-methyl-D-aspartate- (NMDA) induced “wind up” phenomena and subsequent release of inflammatory mediators (24). The concept of preemptive analgesia, or treating postoperative pain by preventing establishment of central sensitization, seems intuitively logical. However, the clinical relevance of preemptive analgesia has been questioned. Only a small number of well controlled clinical studies have demonstrated any benefit of preincisional versus postincisional analgesic administration (25,26). A quantitative systematic review by Moiniche et al. (27) stated that evidence is still lacking to support the claim that the timing of single-dose or continuous postoperative pain treatment is critically important in the management of postsurgical pain. These investigators concluded that there was no convincing evidence that preemptive treatment with centrally or peripherally administered local anesthetics, NSAIDs, opioid analgesics, or ketamine offers any advantage with respect to postoperative pain relief when compared with a similar analgesic regimen administered after the surgical incision (27). Nevertheless, preincisional local anesthetic administration offers an obvious advantage over infiltration at the end of surgery because it can provide supplemental intraoperative analgesia as well as effective analgesia in the early postoperative period after emergence from anesthesia.

Preincisional infiltration of the surgical wound site with local anesthetics, combined with general anesthesia, is clearly superior to general or spinal anesthesia alone in reducing postoperative pain (28,29). For example, preincisional infiltration of the tonsillar bed with bupivacaine decreased the intensity of both constant pain and pain on swallowing fluids for up to 5 days after tonsillectomy procedures (29). Paracervical block with 0.5% bupivacaine also reduced pain and

the need for opioid analgesics after vaginal hysterectomy under general anesthesia (30). Preincisional ilioinguinal-iliohypogastric nerve block not only improves perioperative pain control for inguinal hernia repair but also reduces the need for oral opioid-containing analgesics in the postdischarge period (16). Although local infiltration can reduce incisional pain after laparoscopic cholecystectomy (31–34), some investigators have actually reported that infiltration of the trocar sites at the end of surgery provided better pain relief than when the local anesthetic was given before incision (32). The overall analgesic efficacy of trocar wound infiltration after laparoscopic surgery remains controversial (35).

Although preincisional infiltration of the operative site with local anesthetics remains popular for reducing the perioperative opioid analgesic requirement, other simpler local anesthetic delivery systems (e.g., topical applications) have been described (36–40). Topical analgesia with a lidocaine aerosol was effective in decreasing pain, as well as the opioid analgesic requirement, after inguinal herniorrhaphy in adults (36), and instillation of 0.25% bupivacaine before surgical closure compared favorably to an ilioinguinal-iliohypogastric nerve block in children undergoing hernia repair (37). Furthermore, the simple application of topical lidocaine jelly or ointment, as well as eutectic mixture of local anesthesia (EMLA) cream, have been shown to be as effective as peripheral nerve blocks or parenteral opioids in providing pain relief after outpatient circumcision (38–40). Use of a 5% lidocaine patch has also been reported to be effective in providing peripheral analgesia (41). However, further studies are needed to define the role (if any) of this analgesic device in the postoperative period.

Intracavitary instillation of local anesthetics is another simple, yet effective, technique for providing pain relief during the early postoperative period after laparoscopic and arthroscopic procedures. For example, when 80 mL of lidocaine 0.5% or bupivacaine 0.125% was administered intraperitoneally at the start of the laparoscopic procedure, postoperative scapular pain and the need for opioid analgesic during the first 48 h after surgery were significantly reduced (42). Compared with a control group receiving saline, use of intraperitoneal bupivacaine 0.5% (15–30 mL) also led to a larger percentage of patients going home on the day of surgery (79% versus 43%) (43). However, other studies involving intraperitoneal administration of local anesthetics during laparoscopy report inconsistent effects on postoperative pain and the need for opioid analgesics (44–54). Some investigators have suggested that the beneficial effects of intraperitoneal bupivacaine are transient and have little impact on patient recovery (49). Furthermore, when bupivacaine was injected at the preperitoneal fascial plane during extraperitoneal laparoscopic hernia repair, it also

failed to reduce postoperative pain (55). Subfacial infiltration with bupivacaine 0.5% at the trochar and incision sites reduced pain and the length of stay after laparoscopic nephrectomy procedures (56). Yndgaard et al. (57) demonstrated that subfascially administered lidocaine was significantly more effective than subcutaneous injection in reducing pain after inguinal herniotomy. It is obvious that the location, volume, and timing of the local anesthetic administration are key factors in determining efficacy of intraperitoneal instillation in preventing pain after both superficial and laparoscopic surgery (19,43,53).

Analogous to intraperitoneal administration, intrapleural instillation of local anesthetic solutions has been reported to improve pain control after laparoscopic surgery (58–66). Some investigators report that interpleural bupivacaine produced more effective analgesia than intraperitoneal bupivacaine (66) and compared favorably with epidural bupivacaine (58) after laparoscopic cholecystectomy. Compared with standard opioid analgesics, intrapleural bupivacaine achieved better pain relief and greater improvement in postoperative pulmonary function (59,64). In contrast, Oxorn and Whatley (65) reported that postoperative pulmonary mechanics were worsened after intrapleural bupivacaine. Adverse effects on pulmonary function (resulting from muscle weakness) and the risk of systemic local anesthetic toxicity (resulting from rapid systemic absorption) are the major concerns with this technique (66,67). Although intercostal nerve blocks can also improve pain relief after cholecystectomy procedures, this does not necessarily lead to improved pulmonary function (68).

Local anesthetics are also commonly injected into joint spaces to provide analgesia during and after arthroscopic procedures (69,70). In a placebo-controlled study, intraarticular instillation of 30 mL of 0.5% bupivacaine reduced opioid requirements and facilitated early mobilization and discharge after knee arthroscopy (70). In a follow-up study, a combination of intraarticular bupivacaine and systemic ketorolac (60 mg) further decreased pain in the early postoperative recovery period (71). In addition to the local anesthetics, a wide variety of other adjuvants (e.g., morphine, ketorolac, triamcinolone, and clonidine) have also been injected into the intraarticular space to decrease postarthroscopic pain (72–77). Small-dose intraarticular morphine, 0.5–1 mg, combined with bupivacaine, appears to provide the longest-lasting and most cost-effective analgesia after knee arthroscopy (76,77). Although administering intraarticular morphine before knee surgery was reported to provide a longer duration of analgesia and greater opioid-sparing effects than when it was given at the end of surgery (77), the clinical advantage of preemptive intraarticular local anesthetic administration remains controversial (27).

Although local anesthetic supplementation decreases the severity of incisional pain in the early postoperative period, many patients still experience significant pain when the local anesthetic effect wears off. Therefore, continuous (78,79) and/or intermittent perfusion (80,81) of the surgical wound (or peripheral nerve) with local anesthetic solutions has been reintroduced as a way of extending local anesthetic-induced incisional pain relief into the postoperative period. In a study by White et al. (82), infusion of 0.5% bupivacaine (4 mL/h) at the median sternotomy site reduced postoperative pain and opioid analgesic requirement after cardiac surgery. As a result of the opioid-sparing effect, these patients recovered bowel and bladder function more rapidly. Similarly, wound instillation with 0.2% ropivacaine (5 mL/h) improved pain control after spine fusion surgery (83). These continuous local anesthetic infusion techniques can be modified to allow for patient-controlled local anesthetic administration after surgery (84,85).

Investigators have failed to find consistent improvement in pain scores or opioid-sparing effects when the local anesthetic was infused at the incision site after abdominal surgery (57,86–88). Efficacy of local anesthetic infusion systems is enhanced when the catheter is placed at the subfacial level or near a peripheral nerve. For example, a continuous popliteal-sciatic nerve block provides improved postoperative analgesia, decreased opioid use, and enhanced patient satisfaction after painful foot and ankle surgery (89,90). Similarly, a continuous infraclavicular brachial plexus block provides highly effective pain control after discharge in patients undergoing shoulder surgery (91). Although continuous local anesthetic infusions with concomitant PCA capability appears to be superior to a continuous infusion alone for prolonging nerve blocks (92,93), many patients elect not to use the PCA function on their electronic pumps (91).

When using a continuous local anesthetic infusion, analgesic efficacy is influenced by a wide variety of factors in addition to location of the catheter system, including the concentration and volume of the local anesthetic solution (82), as well as the accuracy and consistency of the pumps (94). The use of a disposable, nonelectronic infusion system may offer advantages over the electronic pump because its simplicity minimizes the need for troubleshooting (95). However, accuracy of the infusion rate of the nonelectronic pumps can change over time (94). Temperature changes also influence the infusion rate of elastomeric pumps, and battery life is a limiting factor for the electronic pumps (94). With these catheter delivery systems, the risk of infection appears to be small. However, bacterial colonization of the catheter is a common occurrence (96). Patient satisfaction and comfort when using these delivery systems outside the hospital is high, and more than 90% of the patients are

comfortable removing the catheter at home (97). Finally, combining local anesthetic infusion techniques with other analgesic modalities as part of multimodal analgesic therapy further improves pain control throughout the perioperative period (98).

Peripheral nerve block techniques are simple, safe, and highly effective approaches to providing perioperative analgesia. Use of long-acting local anesthetics for neural blockade techniques involving the upper (e.g., interscalene brachial plexus block) and lower (e.g., femoral-sciatic nerve block) extremities can facilitate an earlier discharge after major shoulder and knee reconstructive procedures, respectively (99,100). Availability of long-acting local anesthetics that claim less toxicity and greater selectivity with respect to sensory and motor blockade (e.g., ropivacaine) may further enhance the benefits of local anesthetic supplementation after both major and minor surgery.

Although ropivacaine 0.2% provides better pain relief with less motor impairment than lidocaine 1% for continuous interscalene brachial plexus block (101), its clinical advantages relative to equipotent concentrations of bupivacaine are less well established. Addition of adjuvants (e.g., epinephrine, clonidine) that can prolong postoperative analgesia and facilitate recovery when using central and peripheral nerve blocks may be of greater clinical importance (102,103). Interestingly, a more recent study (104) found that clonidine's use as an adjunct to ropivacaine as part of a continuous perineural infusion technique failed to reduce postoperative pain and oral analgesic usage or improve the patient's quality of sleep after upper extremity surgery when compared with the local anesthetic alone. Although pain control can be improved after orthopedic procedures by continuously infusing local anesthetic solutions (89,90,105–107), availability of longer-acting local anesthetic suspensions and "delayed release" formulations containing liposomes or polymer microspheres may minimize the need for continuous infusion catheter delivery systems in the future.

NSAIDs

Oral NSAIDs have long been used for treating non-surgical pain syndromes because of their well known antiinflammatory, antipyretic, and analgesic properties. When parenteral preparations of NSAIDs (e.g., ketorolac, ketoprofen, diclofenac) became available, these drugs were more widely used in the management of acute perioperative pain. NSAIDs block the synthesis of prostaglandins by inhibiting cyclooxygenase (COX) types I and II, thereby reducing production of mediators of the acute inflammatory response. By decreasing the inflammatory response to surgical trauma, NSAIDs have been alleged to reduce peripheral nociception. Studies also suggest that the central

response to painful stimuli is modulated by NSAID-induced inhibition of prostaglandin synthesis in the spinal cord (27).

Early reports suggested that parenteral NSAIDs possessed analgesic properties comparable to the traditional opioid analgesics (108–110) without opioid-related side effects (111,112). Compared with the partial opioid agonist tramadol, diclofenac produced better postoperative pain relief with fewer side effects after cardiac surgery (8). When administered as an adjuvant during outpatient anesthesia, ketorolac was associated with improved postoperative analgesia and patient comfort compared with fentanyl and the partial opioid agonist, dezocine (112,113). Other investigators reported that ketorolac provided postoperative pain relief similar to that of fentanyl but was associated with less nausea and somnolence, as well as an earlier return of bowel function (114). In most studies, use of ketorolac has been associated with a less frequent incidence of PONV than the opioid analgesics. As a result, patients tolerate oral fluids and are fit for discharge earlier than those receiving only opioid analgesics during the perioperative period. Of interest, ketorolac (30 mg q 6 h) was superior to a dilute local anesthetic infusion (bupivacaine 0.125%) in supplementing epidural PCA hydromorphone in patients undergoing thoracotomy procedures (115). Furthermore, it has been found that the injection of ketorolac (30 mg) at the incision site in combination with local anesthesia resulted in significantly less postoperative pain, a better quality of recovery, and earlier discharge compared with local anesthesia alone (116). In fact, there is evidence for both a peripheral and central analgesic action of NSAIDs (117). However, when ketorolac was substituted for or combined with fentanyl during minor gynecologic and laparoscopic procedures, the beneficial effects of the NSAID were reduced (118,119).

Using shock wave lithotripsy to evaluate the effect of NSAIDs on visceral pain, diclofenac produced only a marginal opioid-sparing effect (120). However, when diclofenac (1 mg/kg IV) was administered before arthroscopic surgery, it was associated with similar pain scores to fentanyl (1 μ g/kg IV) (121). Preoperative diclofenac (50 mg) also decreased pain and the opioid analgesic requirements for 24 h after laparoscopic surgery (122). Similarly, preoperative administration of ketorolac to patients undergoing laparoscopic cholecystectomy (119) decreased postoperative opioid requirements and improved some ventilatory variables during the early postoperative period. A perioperative ketorolac infusion (2 mg/h) also improved the quality of postoperative pain relief after abdominal surgery (123). Compared to tramadol (100 mg IV), ketorolac (30 mg IV) produced comparable analgesia with a 68% decreased incidence of PONV after maxillofacial surgery (124). Of interest,

Table 3. Dosage Recommendations for Acute Pain and Duration of Action of COX-2 Inhibitors

Drug (dosage range)	Route of administration	Onset (min)	Duration (h)	Ratio COX-1/2 activity	Key issues
Celecoxib (200–400 mg)	PO	30–50	4–8	8	Sulfonamide allergy
Rofecoxib (25–50 mg)*	PO	30–50	12–24	35	Leg edema, hypertension
Paracoxib (20–40 mg)†	IM/IV	10–15	6–12	30	Wound infections
Valdecocix (20–40 mg)	PO	30–40	6–12	30	Steven's-Johnson syndrome
Etoricoxib (60–90 mg)	PO	20–30	≥24	106	Not known

COX-1/2 = Cyclooxygenase-1/2 receptor binding ratio.

* Withdrawn from the market because of cardiovascular complications associated with long-term use; † Intravenous prodrug of valdecocix (the active “analgesic” compound).

Adapted from White (4).

diclofenac (1 mg/kg) is alleged to be a more cost-effective alternative to ketorolac (0.5 mg/kg) (125,126).

When diclofenac was administered preoperatively to pediatric patients, the incidence of restlessness and the incidence of crying, as well as the postoperative opioid requirements, were less than in acetaminophen-treated patients (127). Similarly, oral ketorolac (1 mg/kg) was superior to small-dose acetaminophen (10 mg/kg) in children undergoing bilateral myringotomy procedures (128). In children undergoing inguinal hernia repair (129), ketorolac (1 mg/kg IV) compared favorably with caudal bupivacaine 0.2% with respect to pain control and postoperative side effects. In addition, ketorolac-treated children had an improved recovery profile, including less vomiting, shorter times to voiding and ambulation, and earlier discharge home. Intraoperative administration of ketorolac as an adjuvant to general anesthesia in pediatric patients provided postoperative analgesia comparable to morphine with less PONV (130). When ketorolac or morphine is administered for pain control in pediatric patients, ketorolac-induced analgesia developed more slowly but lasted longer (131).

Oral or rectal administration of NSAIDs is also effective and less costly in the prophylactic management of surgical pain (132). For example, when oral naproxen was administered before laparoscopic surgery, postoperative pain scores, opioid requirements, and time to discharge were significantly reduced (133). Furthermore, premedication with oral ibuprofen (800 mg) was associated with superior postoperative analgesia and less nausea compared with fentanyl (75 µg IV) after laparoscopic surgery (134). However, the more important role for oral NSAIDs may be in the postdischarge period. Ibuprofen liquogel (400 mg po) was significantly more effective than celecoxib (200 mg po) in treating pain after oral surgery (135). Ibuprofen (5 mg/kg po) compared favorably to rofecoxib (0.625 mg/kg po) for minimizing postoperative pain when used in combination with acetaminophen (20 mg/kg) before tonsillectomy procedures (136). When used as part of a multimodal analgesic technique consisting of alfentanil, lidocaine, and ketorolac (137), oral ibuprofen (800 mg q 8h) was equianalgesic

to paracetamol 800 mg in combination with codeine 60 mg (q 8h) during the first 72 h after discharge, and resulted in better global patient satisfaction and less constipation than opioid-containing oral analgesics. Ibuprofen (400 or 600 mg po) appears to produce comparable analgesia to the combination of tramadol (75–112.5 mg) and acetaminophen (650 or 975 mg) for acute postoperative pain relief (138). To achieve the optimal benefit of using NSAIDs in the perioperative period, these compounds should be continued during the postdischarge period as part of a preventative pain management strategy (98).

Despite the obvious benefits of using NSAIDs in the perioperative period, controversy still exists regarding their use because of the potential for gastrointestinal mucosal damage and renal tubular and platelet dysfunction (139). Although some studies have found increased blood loss and risk of reoperation when ketorolac was administered to children undergoing tonsillectomy procedures (140,141), a recent systematic review of the literature suggested that the evidence supporting an increase of bleeding was equivocal at best (142).

COX-2 Inhibitors

In an effort to minimize the potential for operative site bleeding complications, as well as gastrointestinal damage, associated with the classic nonselective NSAIDs such as ketorolac and diclofenac, the more highly selective COX-2 inhibitors are increasingly being used as non-opioid adjuvants for minimizing pain during the perioperative period (Table 3) (143). Early clinical studies in surgical patients evaluated the use of celecoxib, rofecoxib, and valdecocix as preventative analgesics when administered for oral premedication (144–148). Rofecoxib (50 mg po) produced more effective and sustained analgesia compared with celecoxib (200 mg po) after spinal surgery (144). Celecoxib (200 mg po) was equivalent to acetaminophen (2 g po) when administered before otolaryngologic operations (145). However, the analgesic efficacy of celecoxib is

dose-related and 400 mg is the currently recommended dose for prevention of acute pain (146). Rofecoxib (50 mg po) produced significantly more effective analgesia than acetaminophen (2 g po) and the pain relief was more sustained in the postdischarge period (147). Premedication with rofecoxib also facilitated recovery by reducing postoperative pain and improving the quality of recovery from the patient's perspective (148). It has also been suggested that the long-acting rofecoxib is more cost-effective than celecoxib in the perioperative period (149). In one study (143), a single preoperative dose of rofecoxib, 25–50 mg po, produced a 44%–59% reduction in the PCA morphine requirement after major abdominal surgery (150). However, clinical studies suggest a more sustained benefit can be achieved when the drug is administered both before and after surgery (148,151). The recent withdrawal of rofecoxib from the market by its manufacturer because of an increased risk of cardiovascular side effects after prolonged use (>16 mo) has led investigators to begin re-evaluating other COX-2 inhibitors in the perioperative period.

Valdecoxib has been introduced recently for the prevention of postoperative pain, with doses of 20–40 mg reducing the opioid requirement by 25%–50% after elective surgery (152,153). In patients undergoing oral surgery and bunionectomy, premedication with valdecoxib 40 mg appears to produce the optimal analgesic effect in the postoperative period (152). Valdecoxib is as rapidly acting and effective as oxycodone in combination with acetaminophen but has a longer duration of action and fewer side effects when used for the management of pain after oral surgery. Valdecoxib (40 mg po) was alleged to be even more effective than rofecoxib, 50 mg po, in treating pain after oral surgery (154).

A parenterally active COX-2 inhibitor, parecoxib (a prodrug which is rapidly converted to valdecoxib), has been investigated as an alternative to the parenteral NSAIDs (155–157). However, to achieve equianalgesia with the IV prodrug, a larger dose may be required compared with the orally active drug valdecoxib. Parecoxib is similar pharmacokinetically to both celecoxib and valdecoxib. Preliminary studies suggested that parecoxib (40–80 mg IV), was as effective and longer-acting than ketorolac (30 mg IV) in reducing pain after oral (158) and laparotomy surgery (159). Both preoperative and postoperative administration of this COX-2 inhibitor resulted in significant opioid-sparing effects, reduced adverse effects, and improved quality of recovery and patient satisfaction with postoperative pain management (152,160). Unfortunately, one study in patients undergoing cardiac surgery suggested that perioperative use of parecoxib and valdecoxib as part of a 14-day analgesic treatment regimen

increased adverse events, including sternal wound infections (161). Another recent study found that although parecoxib, 40 mg IV, was given at induction of anesthesia, it was less effective than ketorolac, 30 mg IV, after tonsillectomy procedures (141). A new more highly-selective COX-2 inhibitor, etoricoxib (120 mg po), provided rapid and long-lasting pain relief after dental surgery (162). A recent study also suggested that etoricoxib was associated with fewer side effects than a standard opioid-containing oral analgesic. Current evidence suggests that the newer COX-2 inhibitors appear to offer minimal advantages over the first-generation COX-2 inhibitors and the nonselective NSAIDs (163,164).

In addition to the growing controversy regarding the potential adverse cardiovascular risks of the COX-2 inhibitors, many orthopedic surgeons are also concerned about the negative influence of these compounds (as well as the traditional NSAIDs) on bone growth (165,166). As COX-2 activity appears to play an important role in bone healing (167–169), some orthopedic surgeons have recommended that these drugs be avoided in the early postoperative period (164,165). Because the effect on bone growth is dose-dependent and reversible (166), COX-2 inhibitors should only be used for 3–5 d in the early postoperative period. Although several review articles on the COX-2 inhibitors have recently been published (163,170–172), the question remains as to whether these compounds truly overcome the perceived *limitations* of the nonselective NSAIDs (173).

Acetaminophen (Paracetamol)

Of the non-opioid analgesics, acetaminophen (also known as paracetamol) is perhaps the safest and most cost-effective non-opioid analgesic when it is administered in analgesic dosages. Although both parenteral and rectal acetaminophen produce analgesic effects in the postoperative period, concurrent use with a NSAID is superior to acetaminophen alone (145,147). The addition of acetaminophen, 1 g every 4 h, to PCA morphine improved the quality of pain relief and patient satisfaction after major orthopedic procedures (174). Although Watcha et al. (128) reported minimal analgesic-sparing effects after a 10 mg/kg oral dose of acetaminophen, Rusy et al. (140) found that a larger dose (35 mg/kg pr) was as effective as ketorolac (1 mg/kg IV) in reducing pain after tonsillectomy procedures and was associated with less postoperative bleeding. Subsequently, Korpela et al. (175) demonstrated that the opioid-sparing effect of rectal acetaminophen was dose-related up to 60 mg/kg. The optimal dosing regimen for acetaminophen in children appears to consist of a preoperative initial dose of

30–40 mg/kg followed by a maintenance dose of 15–20 mg/kg every 6–8 h during the early postoperative period (176). In adults, acetaminophen 2 g orally was equivalent to celecoxib 200 mg but less effective than celecoxib 400 mg, rofecoxib 50 mg, or ketoprofen 150 mg in preventing pain after ambulatory surgery (145–147).

An IV formulation of a prodrug of acetaminophen, propacetamol, has been administered to adults as an alternative to ketorolac in the perioperative period (177,178). Propacetamol reduced PCA morphine consumption by 22%–46% in patients undergoing major orthopedic surgery (179,180). However, in patients undergoing cardiac surgery, propacetamol (2 g IV every 6 h for 3 d) failed to enhance analgesia, decrease opioid usage, or reduce adverse side effects in the postoperative period (181). Propacetamol has become a popular adjuvant to opioid analgesics for postoperative pain control in Europe; however, this drug may soon be replaced when an investigational IV formulation of acetaminophen becomes available for clinical use (182). Rectal acetaminophen (1.3 g) has also been successfully used as an adjuvant to NSAIDs and local anesthetics as part of a multimodal fast-tracking surgery recovery protocol (183). Given the adverse effects associated with both NSAIDs and COX-2 inhibitors in patients with preexisting cardiovascular disease, acetaminophen may assume a greater role in postoperative pain management in the future (184).

NMDA Antagonists

Ketamine is a unique IV anesthetic with analgesic-like properties that has been used for both induction and maintenance of anesthesia (185), as well as an analgesic adjuvant during local anesthesia (186,187). As a result of its well known side-effect profile (Table 4), ketamine fell into disfavor in the late 1980s. However, adjunctive use of small doses of ketamine (0.1–0.2 mg/kg IV) appear to be associated with a opioid-sparing effects and a less frequent incidence of adverse events and greater patient and physician acceptance (188). Several studies have described the use of small-dose ketamine in combination with local anesthetics and/or opioid analgesics (189–199). However, when ketamine (1 mg/mL) was combined with morphine (1 mg/mL) for PCA after major abdominal surgery, it did not significantly improve pain relief and was associated with increased side effects (e.g., vivid dreaming) compared with the opioid alone (191). One study (192) supports use of a PCA morphine-ketamine combination in a 1:1 ratio with a lockout interval of 8 min for pain control after major orthopedic procedures. Further studies are obviously needed to clarify ketamine's role as a supplemental analgesic.

Table 4. Potential Side Effects of Opioid and Non-Opioid Analgesic Drugs

Opioid analgesics
• respiratory and cardiovascular depression
• nausea, vomiting, retching and ileus
• urinary hesitancy and retention
• pruritus and skin rash
• sedation and dizziness
• tolerance and dependence
Local anesthetics
• residual motor weakness
• peripheral nerve irritation
• cardiac arrhythmias
• allergic reactions
• sympathomimetic effects (due to vasoconstrictors)
Nonsteroidal antiinflammatory drugs and COX-2 inhibitors
• operative-site bleeding
• gastrointestinal bleeding
• renal tubular dysfunction
• allergic reactions (e.g., Steven's-Johnson syndrome)
• bronchospasm
• hypertension
• pedal edema
Acetaminophen
• gastrointestinal upset
• sweating
• hepatotoxicity
• agranulocytosis
Ketamine and NMDA antagonists
• hypertension
• diplopia and nystagmus
• dizziness and confusion
• cardiac arrhythmias
• nausea and vomiting
• psychomimetic reactions
Alpha-2 adrenergic agonists
• sedation
• dizziness
• hypotension
• bradycardia
Miscellaneous drugs
• somnolence, dizziness and peripheral edema (gabapentin)
• nausea and vomiting (neostigmine)
• muscle weakness and sedation (magnesium)
Nonpharmacologic techniques
• skin irritation and erythema
• cutaneous discomfort

NMDA = *N*-methyl-D-aspartate; COX-2 = cyclooxygenase-2.
Adapted from White (4).

Administration of ketamine, $4\text{--}18\ \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, in combination with propofol, $30\text{--}90\ \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, obviated the respiratory depression produced by commonly used sedative-opioid combinations while producing positive mood effects after surgery, and it may even provide for an earlier recovery of cognitive function (186,187). In addition, a single bolus dose of ketamine, 0.1–0.15 mg/kg IV, during surgery has been reported to produce significant opioid-sparing effects after painful

orthopedic and intraabdominal procedures without increasing the incidence of side effects (194–200). Ketamine (0.1 mg/kg IM) reduced swallowing-evoked pain after tonsillectomy procedures in children receiving a multimodal analgesic regimen (198). Small doses of epidural ketamine (20–30 mg) enhanced epidural morphine-induced analgesia after major upper abdominal surgery (199). Although it was alleged that ketamine possesses preemptive analgesic effects as a result of its ability to inhibit central NMDA receptors (200), well controlled clinical studies have failed to demonstrate significant preemptive analgesic effects (201,202). Interestingly, a modest dose of ketamine (250 μ g/kg) after surgery was alleged to improve analgesia in the presence of opioid-resistant pain (203). Acute tolerance to opioid-induced analgesia leading to long-lasting hyperalgesia may be prevented by repeat doses of this NMDA antagonist (204).

Small-doses of the S(+) and R(-) isomers of ketamine have been administered both IV and epidurally in an effort to decrease injury-induced hyperalgesia. Although S(+) ketamine (0.5 mg/kg IV followed by 0.125–1 μ g/kg/min) failed to improve pain control after arthroscopic knee surgery (205), epidural S(+) ketamine (0.25 mg/kg) enhanced ropivacaine-induced analgesia after total knee arthroplasty (206). Interestingly, transdermal nitroglycerin (5 mg) has been alleged to enhance the spinal analgesia produced by epidural S(+) ketamine (0.1–0.2 mg/kg) (207). Consistent with an early comparative clinical study involving the ketamine isomers (208). R(-) ketamine (1 mg/kg IV) produced only a short-lasting analgesic effect in the postoperative period (209).

Dextromethorphan, another NMDA receptor antagonist that inhibits wind-up and NMDA-mediated nociceptive responses in dorsal horn neurons, has been alleged to enhance opioid, local anesthetic and NSAID-induced analgesia. Premedication with dextromethorphan (150 mg po) reduced the PCA morphine requirement in the early postoperative period after abdominal hysterectomy procedures but failed to produce prolonged beneficial effects on wound hyperalgesia (210). In patients undergoing laparoscopic cholecystectomy or inguinal herniorrhaphy procedures, dextromethorphan (90 mg po) improved well-being and reduced analgesic consumption, pain intensity and sedation, as well as thermal-induced hyperalgesia (211). Preincisional administration of dextromethorphan, 40–120 mg IM, provided some evidence of preemptive analgesia in patients undergoing laparoscopic cholecystectomy and upper abdominal surgery (212,213). Perioperative dextromethorphan (40–90 mg IM) reduced the opioid requirement and/or improved pain control after modified radical mastectomy (214). Interestingly, in patients undergoing knee surgery, dextromethorphan (200 mg q 8 h) failed to significantly improve pain management (215). Compared

with ibuprofen (400 mg po), dextromethorphan (120 mg po) was significantly less effective in providing postoperative analgesia and was associated with increased nausea in the preoperative period (216). In patients undergoing knee replacement surgery with epidural anesthesia, dextromethorphan (40 mg IM) also failed to produce any preemptive analgesic effect but did enhance pain control in the postoperative period (217).

Other NMDA antagonists are being actively investigated in the perioperative setting. Preoperative amantadine, 200 mg IV, failed to enhance postoperative analgesia in patients undergoing abdominal hysterectomy procedures (218). However, a more recent study reports that perioperative amantadine reduced PCA morphine requirement after radical prostatectomy surgery (219). Further clinical studies are clearly needed to better define the role of noncompetitive NMDA receptor antagonists in the perioperative setting.

Alpha-2 Adrenergic Agonists

The α_2 -adrenergic agonists, clonidine and dexmedetomidine, produce significant anesthetic and analgesic-sparing effects. Premedication with oral and transdermal clonidine decreased the PCA-morphine requirement 50% after radical prostatectomy surgery (220). Clonidine also improved and prolonged central neuraxis (221,222) and peripheral nerve blocks (223) when administered as part of multimodal analgesic regimens. For example, epidural infusion of clonidine in combination with ropivacaine improved analgesia after major abdominal surgery in children (224). Adding intrathecal clonidine (0.075 mg) to local anesthesia provided excellent analgesia for up to 8 h after urologic surgery (225). Although clonidine, 4 μ g/kg IV over 20 min, failed to reduce PCA morphine requirement after lower abdominal surgery in adults, it did reduce pain, nausea, and vomiting while improving patient satisfaction with their pain relief (226). However, when used to treat postoperative pain, clonidine (0.3 mg IV) was apparently ineffective (227).

Dexmedetomidine is a pure α_2 -agonist that also reduces postoperative pain and opioid analgesic requirement (228). However, its use was associated with increased postoperative sedation and bradycardia. When used for premedication before IV regional anesthesia (229), dexmedetomidine (1 μ g/kg IV) reduced patient anxiety, sympathoadrenal responses, and intraoperative opioid analgesic requirement. Compared with propofol (75 μ g \cdot kg⁻¹ \cdot min⁻¹), dexmedetomidine (1 μ g/kg followed by 0.4–0.7 μ g \cdot kg⁻¹ \cdot h⁻¹) had a slower onset and offset of sedation but was associated with improved analgesia and reduced morphine use in the postoperative period

(230). Administration of dexmedetomidine, $1 \mu\text{g}/\text{kg}$ followed by $0.4 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, was also associated with a 66% reduction in PCA morphine use in the early postoperative period after major inpatient surgery (231).

Miscellaneous Non-Opioid Compounds

A diverse array of non-opioid pharmacologic compounds used during the perioperative period, such as adenosine (232,233), droperidol (234), magnesium (235), neostigmine (236), and gabapentin (237,238), have been alleged to possess analgesic-sparing properties. Although the analgesic-sparing effects of these compounds have not been extensively evaluated and their use for acute postoperative pain management is considered investigational, the preliminary findings are nonetheless intriguing. For example, use of an adenosine infusion as an alternative to an opioid analgesic (remifentanyl) for controlling acute autonomic responses during lower abdominal surgery resulted in a significant reduction in both postoperative pain scores and the requirement for opioid analgesics (232).

Gabapentin (a structural analog of gamma-aminobutyric acid) is an anticonvulsant that has proven useful in the treatment of chronic neuropathic pain and may also be a useful adjuvant in the management of acute postoperative pain (237–242). For example, premedication with gabapentin (1.2 g po) reduced postoperative analgesic requirement significantly without increasing side effects (237). When gabapentin (1.2 g) was continued for 10 d after breast surgery (238), it reduced the postoperative opioid analgesic requirement and movement-related pain; however, the overall incidence of chronic pain was unaffected. Recent studies by Dierking et al. (239), Turan et al. (240), and Rorarius et al. (241) suggested that the improvement in postoperative pain control with gabapentin was not necessarily associated with a decrease in opioid-related side effects. Pregabalin, a related compound, has also been reported to possess analgesic potential comparable to that of ibuprofen in treating acute dental pain (242). This review article discussed the potential role of gabapentin and pregabalin in “protective premedication.”

Magnesium, a divalent cation, is also alleged to possess antinociceptive effects. For example, Kara et al. (235) reported that perioperative magnesium ($30 \text{ mg}/\text{kg}$ IV followed by an infusion of $0.5 \text{ g}/\text{h}$) yielded a significant reduction in the postoperative analgesic requirement after abdominal hysterectomy. A bolus dose of magnesium ($50 \text{ mg}/\text{kg}$ IV) at induction of anesthesia also led to improved pain control and better patient satisfaction with less opioid medication after major orthopedic surgery (243).

However, magnesium $50 \text{ mg}/\text{kg}$ IV failed to produce opioid-sparing effects after open cholecystectomy procedures (244). In addition, a non-opioid multimodal analgesic regimen that included magnesium produced comparable postoperative pain relief with fewer side effects than fentanyl in obese patients undergoing gastric bypass surgery (245). However, other investigators have failed to demonstrate a beneficial effect of magnesium (30 – $50 \text{ mg}/\text{kg}$ followed by 10 – $15 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) with respect to reducing postoperative pain or the need for opioid analgesics (246). Of interest, intrathecal magnesium was reported to prolong fentanyl analgesia (247).

Neostigmine, a cholinesterase inhibitor, has been reported to possess analgesic properties when doses of 10 – $200 \mu\text{g}$ were administered in the subarachnoid or epidural spaces (236,248). Although peripherally administered neostigmine failed to produce postoperative analgesia, epidurally administered neostigmine ($1 \mu\text{g}/\text{kg}$) produced more than 5 h of pain relief after knee surgery (249). Neostigmine ($10 \mu\text{g}/\text{kg}$) also enhanced epidural local analgesia (250). Both epidural ($60 \mu\text{g}$) and spinal (1 – $5 \mu\text{g}$) neostigmine enhanced morphine-induced neuraxial analgesia (251–254). In patients undergoing knee replacement surgery with intrathecal bupivacaine, adjunctive use of neostigmine ($50 \mu\text{g}$) was alleged to produce better postoperative analgesia than morphine ($300 \mu\text{g}$) (255). In addition, transdermal nitroglycerin enhanced spinal neostigmine-induced postoperative analgesia without increasing perioperative side effects (256). However, epidural neostigmine (75 – $300 \mu\text{g}$) alone produced only modest analgesia after cesarean delivery (257). The primary adverse effects associated with neuraxial neostigmine appear to be mild sedation (257) and PONV (15% – 30%) (237,253).

Cannabinoids have been reported to reduce hyperalgesia and drug-induced allodynia. However, clinical studies have failed to demonstrate any evidence of postoperative analgesia (258,259). A new antiinflammatory drug, inositol triphosphate, reduced postoperative pain and the need for opioid analgesics after cholecystectomy surgery (260). However, additional well controlled clinical trials are needed with all of these novel adjunctive drugs.

Nonpharmacologic Techniques

Nonpharmacologic “electroanalgesic” techniques such as transcutaneous electrical nerve stimulation (TENS), acupuncture-like transcutaneous electrical nerve stimulation, and percutaneous neuromodulation therapy can also be useful adjuvants to pharmacologic compounds in the management of acute postoperative pain (261). Given the inherent side effects

produced by both opioid and non-opioid analgesics (Table 4), it is possible that the use of nonpharmacologic approaches will assume a more prominent role in the future management of acute postoperative pain (262).

Clinical studies suggest that electroanalgesia can reduce opioid analgesic requirements up to 60% after surgery (263,264). In addition to reducing pain and the need for oral analgesics, Jensen et al. (265) reported a more rapid recovery of joint mobility after arthroscopic knee surgery. When used as an adjuvant to pharmacologic analgesia, TENS reduced the intensity of exercise-induced pain and facilitated ambulation after abdominal surgery (266). In reviewing the medical literature, Carroll et al. (267) found conflicting results regarding the effect of TENS on the requirement for opioid analgesic medication and the quality of postoperative pain relief. Studies suggest that the location, intensity, timing, and frequency of electrical stimulation are all important variables influencing the efficacy of electroanalgesics therapies (263,264,268). More recent studies have confirmed the importance of these variables in achieving improved pain relief with TENS therapy (269).

Of interest, simple (mechanical) intradermal needles placed in the paravertebral region before abdominal surgery reduced postoperative pain and the opioid analgesic requirement as well as PONV (270). However, a "minute sphere"-induced acupressure technique (in which 1-mm stainless steel spheres are applied at known analgesic acupoints) failed to relieve pain after major abdominal surgery (271). Other non-pharmacologic approaches that have been used as analgesic adjuvants in the perioperative period include cryoanalgesia (272), ultrasound (273), and laser stimulation (274), as well as hypnotherapy. However, well controlled clinical studies are needed to establish benefits of these nonpharmacologic modalities on postoperative pain and patient outcomes after surgery.

Summary

As more extensive and painful operations (e.g., laparoscopic cholecystectomy, adrenalectomy, and nephrectomy procedures, as well as prostatectomy, laminectomy, shoulder and knee reconstructions, hysterectomy) are performed on an outpatient or short-stay basis, the use of multimodal perioperative analgesic regimens involving non-opioid analgesic therapies will likely assume an increasingly important role in facilitating the recovery process and improving patient satisfaction (4). Pavlin et al. (275) confirmed the importance of postoperative pain on recovery after ambulatory surgery. Moderate-to-severe pain prolonged recovery room stay by 40–80 min. Use of local

anesthetics and NSAIDs decreased pain scores and facilitated an earlier discharge home. Additional outcome studies are needed to validate the beneficial effect of these non-opioid therapeutic approaches with respect to important recovery variables (e.g., resumption of normal activities, dietary intake, bowel function, return to work). Although many factors other than pain *per se* must be controlled to minimize postoperative morbidity and facilitate the recovery process (1), pain remains a major concern of all patients undergoing elective surgical procedures (276).

Opioid analgesics continue to play an important role in the management of moderate-to-severe pain after surgical procedures. However, adjunctive use of non-opioid analgesics will likely assume a greater role as minimally invasive ("key hole") surgery continues to expand (2,4). In addition to the local anesthetics, NSAIDs, COX-2 inhibitors, acetaminophen, ketamine, dextromethorphan, α -2 agonists, gabapentin, magnesium, and neostigmine may all prove to be useful adjuncts in the management of postoperative pain in the future. Adjunctive use of droperidol (234) and glucocorticoid steroids (277,278) also appear to provide beneficial effects in the postoperative period. Use of analgesic drug combinations with differing mechanisms of action as part of a multimodal regimen will provide additive (or even synergistic) effects with respect to improving pain control, reducing the need for opioid analgesics, and facilitating the recovery process (279). Safer, simpler, and less costly analgesic drug delivery systems are needed to provide cost-effective pain relief in the postdischarge period as more major surgery is performed on an ambulatory (or short-stay) basis in the future. In introducing new therapeutic modalities for pain management, it is important to carefully consider the risk:benefit ratio (280).

In conclusion, the optimal non-opioid analgesic technique for postoperative pain management would not only reduce pain scores and enhance patient satisfaction but also facilitate earlier mobilization and rehabilitation by reducing pain-related complications after surgery. Recent evidence suggests that this goal can be best achieved by using a combination of pre-emptive techniques involving both central and peripheral-acting analgesic drugs and devices.

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Evaluation of Transcutaneous Electrical Nerve Stimulation (TENS) in Podiatric Surgery

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Transcutaneous Electrical Nerve Stimulation (TENS) transmits an electrical signal through the skin to the appropriate underlying nerves to alter the message of pain traveling to the brain. This study evaluates the usefulness of TENS in the treatment of acute postoperative pain following podiatric surgery. Three patient categories, 1) actual TENS, 2) placebo TENS and 3) random controls are reported. The findings illustrate subjective relief of pain and decreased use of analgesic medications, utilizing TENS.

It would be ideal if one could relieve a patient's pain without the use of powerful analgesics, which often have many side effects of their own. Electrical neural stimulation may be an answer to this perplexing problem.

In 46 A.D., electricity's analgesic properties were discovered when Scribonius Largus, a Roman physician, used the electric ray of a torpedo fish to treat headache and gout.¹ In 1745, Galvani experimented with the effects of direct current; Faraday discovered alternating current in the 1830's.¹ In 1918, a device called Electreat was introduced by a naturopath. The medical community began to show a skeptical interest in electrical neural stimulation. However, with new advances in biomedical engineering and pain theory, this device was later replaced with more sophisticated models.

In 1965, Melzack and Wall published the "Gate Theory of Pain."² They offered the first explanation on the theory of electrical nerve stimulation, postulating that stimulation of large non-pain impulse fibers will inhibit the smaller pain-carrying fibers in

the spinal cord. Because the large myelinated fibers have a lower threshold to stimulation, they are more readily activated electrically. Although there is now doubt as to the accuracy of this theory, it opened a new field in medicine.

One practical utilization of this new concept was with the dorsal column stimulator. These devices were electrical nerve stimulators employing electrodes implanted endodurally proximal to the dorsal column of the spinal cord. Transcutaneous nerve stimulation was initially used as a screening procedure before dorsal column stimulators were implanted. It was subsequently shown, however, that certain patients could obtain pain relief with TENS alone and thus avoid the risk of surgical intervention.

Much of the preliminary work with TENS has been performed by three investigators.¹ Dr. Norman Shealy, director of the pain Rehabilitation Center at St. Francis Hospital in La Crosse, Wisconsin; Dr. Charles V. Burton, then associate professor of neurosurgery at Temple University, Pennsylvania; and Dr. Donlun M. Long, chairman of neurosurgery at Johns Hopkins Hospital. Shealy found that TENS produced excellent results in 80% of his patients suffering from acute pain. In treating chronic pain, only 25% of his patients received

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complete relief and 60% were able to decrease their analgesics. Long experimented with chronic pain and achieved a 39% relief of pain in his series. According to Burton, TENS has its greatest application in low grade constant pain. Hymes et al.³ have conducted studies using TENS for acute postoperative pain. Their study dealt with thoracic and abdominal surgery and the postoperative complications. Results showed that 31% of the controls, who had abdominal surgery, developed postoperative atelectasis as compared to 6% of those treated with TENS. Most of the patients reported 60 to 80% relief of postoperative pain.

In 1973, work was begun at Northlake Hospital utilizing TENS to control postoperative pain; results at that time were not published. This paper presents our experience utilizing TENS over the last 1½ years.

Materials and Methods

One hundred and twenty-five patients between the ages of 17 and 79 undergoing podiatric surgery at Northlake Hospital were selected for the study. Bunion surgery and minor rearfoot surgery were used as minimal criteria for participation in the study. The routine practice of intraoperative use of bupivacaine hydrochloride (Marcaine^{®1}) and dexamethasone phosphate (Hexedrol^{®2}) was continued for all patients in the study. The average hospital stay per patient was 4 days. There were three categories of patient involvement. Group 1 had 50 patients receiving TENS. Group 2 was comprised of 25 patients receiving placebo TENS. Group 3 consisted of 50 patients whose medication records were selected and reviewed on a random basis.

The TENS units used were NEUROMOD PULSE GENERATORS (Medtronic, Inc.). The Model 3701 system (single channel) was used for unilateral cases and the Model 3702 system (dual channel) was used for bilateral cases (Fig. 1). Specifications of the stimulators can be found in Table 1. The electrical stimulation perceived by the patient is altered by the following controls: A (amplitude), PW (pulse width) and R (rate). The individual settings range from 0 to 10. A placebo TENS effect was obtained by reversing the batteries for our group 2 patients.

Groups 1 and 2 were randomly selected and participation within the study was voluntary. Informed consent was obtained after briefly discussing the theory of TENS and the operation of the unit.

^{®1} Winthrop Laboratories, New York, New York.

^{®2} Organon Pharmaceuticals, West Orange, New Jersey.

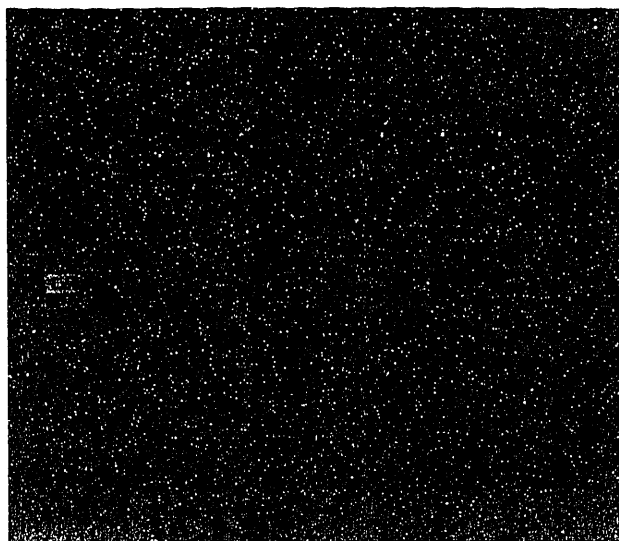


Figure 1. Nueromod Pulse Generators (Medtronic, Inc.); Model 3701 (left) single channel system and Model 3702 (right) dual channel system. Approximate size of each unit is 2.75 x 4.25 x 1 inch.

Table 1. Generator Specifications

Characteristic	Model 3701, Pulse Generator-3721	Model 3702, Pulse Generator-3722
Pulse amplitude	0-50 mA. (constant current), adjustable	0-112 mA. peak per channel (constant current)
Pulse rate	12-100 pulses/sec.	3.5-100 pulses/sec.
Pulse width	50-400 μ sec. adjustable	150 μ sec measured at ½ amplitude with max. output
Type of wave	Biphasic square wave	Biphasic spike wave

Rubber carbon electrodes were then placed proximal to the bandage and patients were instructed not to remove the electrodes during their hospital stay. Patients were permitted to utilize any combination of settings to achieve maximal pain relief and were advised to use TENS as often as needed with no time limit per stimulation. Group 1 patients were told to expect a tingling sensation at the electrode sites. Group 2 patients were told not to expect to feel any sensation; the unit would work by means of a deep nerve interference.

Patients were assured that pain medications prescribed by their podiatrist would be available if TENS did not relieve their pain, and also that they could withdraw from the study at any time. All study participants were supplied with daily log sheets to document time and duration of each stimulation, settings used and percentage relief of pain.

Patients were consulted daily to evaluate their progress.

Application

Subsequent to informed consent TENS was applied to patients in groups 1 and 2 in the following manner. Skin surfaces and rubber electrode pads were cleansed with alcohol prior to application. After experimentation with various electrode sites, the pretibial area was selected for electrode placement (Fig. 2). The pretibial area provides greater electrode contact than more distal locations on the feet. This placement site also seemed to be more comfortable to the patient. Electrode gel was applied to the rubber carbon electrodes to provide optimal contact. Standard adhesive tape was utilized to affix the electrodes to the skin. Patients with either a history of tape allergy or use of cardiac pacemakers were eliminated from this study since they are contraindicated.

In our group of 75 patients receiving TENS, we observed no significant skin reactions. Patients were instructed to walk freely, within the limits of their podiatrists' orders, during the period of TENS application. In those patients requiring below the knee cast application, the placement of the electrodes was above the knee. This electrode site appeared to yield satisfactory results.

Stimulation, Dosage and Duration

Patients were advised to use any combination of TENS control settings, for a duration as long as necessary, and at intervals as frequent as needed for pain control. We found the average duration of stimulation to be approximately 20 to 40 min. The interval between stimulations was too variable to correlate. TENS control settings in group 1 were unique to each patient and were dependent on each patient's perception and tolerance of the tingling sensation. Average settings fell into the realm of 3 to 4 amplitude, 3 pulse width, and 3 to 4 rate. It was found in group 2 patients receiving placebo TENS that average settings were much higher. It was not uncommon to have a patient utilize a setting of 10 on all controls to achieve a psychologic relief of pain.

Results

To evaluate the patient response to TENS we chose to use the following parameters: 1) percentage of incidence of meperidine hydrochloride (Demerol®) and codeine preparations usage at four levels: none,

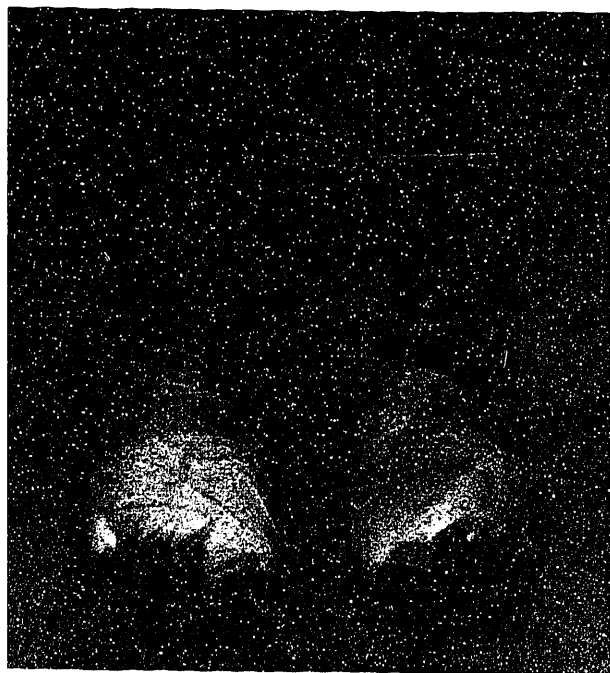


Figure 2. Dual channel system with electrodes in place over pretibial area.

light, moderate and heavy for each group; 2) subjective assessment by the patient of TENS pain relief; 3) average milligrams of Demerol and codeine preparations taken per individual for each group. The subjective assessment was accomplished by categorizing the patient response as excellent (75 to 100% relief of pain), fair (50 to 75% relief of pain) and poor (under 50% relief of pain).

Analysis of the three groups revealed significant differences in the incidence of Demerol ($P < .025$) and codeine preparations ($P < 0.005$) usage among the three groups. Upon examination of our random group of 50 patients without TENS we found that 30% of these patients (Fig. 3) utilized Demerol at some time during their postoperative hospital stay and that 80% (Fig. 4) needed codeine preparations during this same period. Average Demerol usage was computed at 45 mg. per hospital stay, while average intake for codeine preparations was 102 mg. (Table 2).

In comparison to our random group, it was found that fewer patients in group 1 (utilizing actual TENS) required analgesics. Incidence of usage of Demerol and codeine preparations in group 1 during the postoperative hospital stay was 12% (Fig. 3) and 32% (Fig. 4), respectively. These patients took an average of 12 mg. of Demerol and 20.4 mg. of codeine preparations (Table 2).

In evaluating the 25 patients in group 2 (those receiving placebo TENS treatment), the percentage

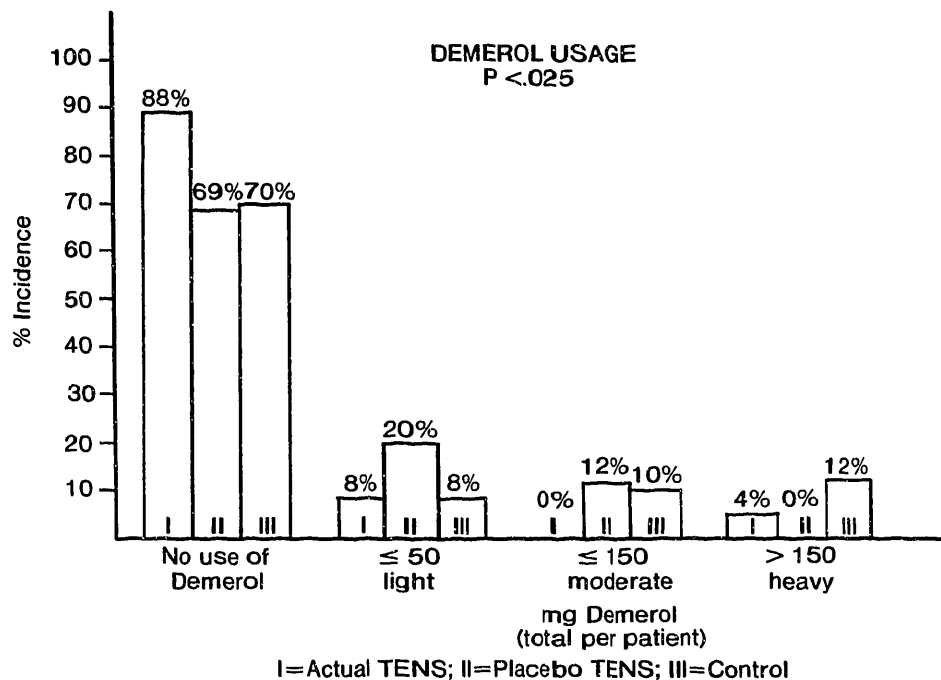


Figure 3.

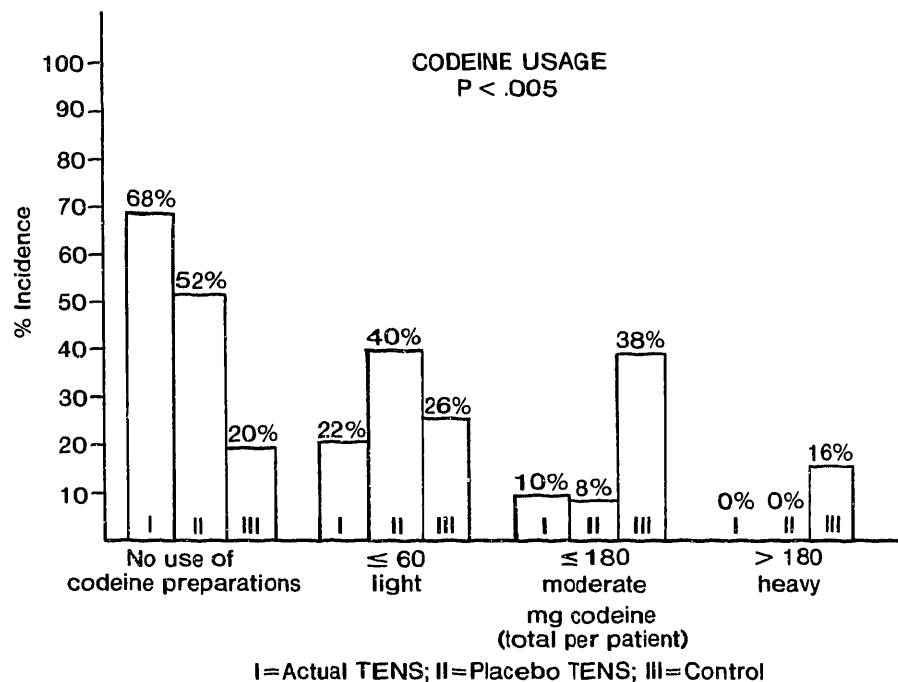


Figure 4.

need for analgesics within this group was 32% requiring Demerol (Fig. 3) and 48% needing codeine preparations (Fig. 4). The average usage of Demerol was 26.0 mg. and 27.6 mg. of codeine preparations (Table 2).

Significant differences were also seen among the three groups in the subjective patient response to pain relief ($P < 0.005$) (Fig. 5); 32 or 74% of the

group 1 patients, relating symptoms of pain, had excellent pain relief as compared to 4 or 17% of the group 2 patients. Fair pain relief was achieved by 9 or 20% of the patients in group 1 and 5 or 21% of the patients in group 2. Two patients or 4% in group 1 were judged to have poor relief of pain using TENS as compared to 14 patients or 60% claiming poor response in group 2. Seven patients in group

Table 2. Comparison of Demerol and Codeine Usage

	Group I	Group II	Randoms
<i>Demerol Usage</i>			
Total milligrams	600 mg.	650 mg.	2,250 mg.
Group average	600/50 = 12.0 mg.	650/25 = 26.0 mg.	2,250/50 = 45 mg.
Group percentage	6/50 = 12.0%	8/25 = 32.0%	15/50 = 30.0%
<i>Codeine Usage</i>			
Total milligrams	1,020 mg.	690 mg.	5,120 mg.
Group average	1,020/50 = 20.4 mg.	690/25 = 27.6 mg.	5,120/50 = 102 mg.
Group percentage	16/50 = 32.0%	12/25 = 48.0%	40/50 = 80.0%

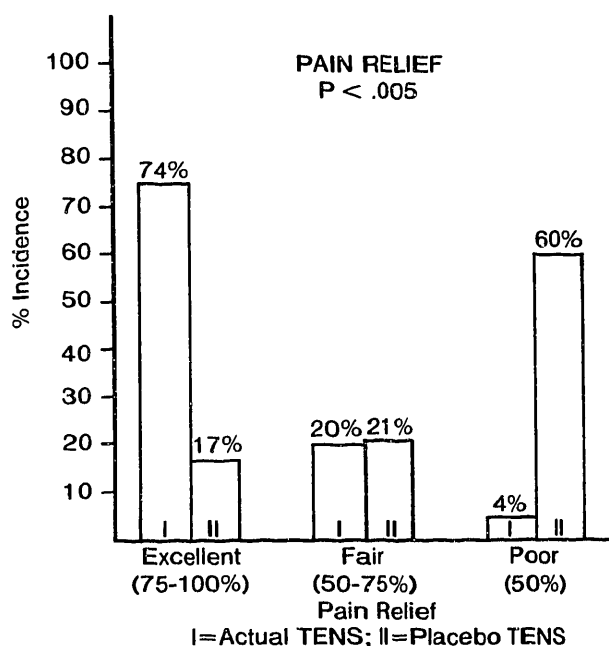


Figure 5.

1 and 2 patients in group 2 related no subjective complaint of pain during their postoperative course significant enough to require a TENS treatment or analgesic medication. Nine of our 50 random group patients also related no complaint of pain significant enough to warrant postoperative analgesic medications. Incidence levels of patients reporting no subjective level of pain for the three groups did not vary significantly ($P < 0.5$) (Fig. 6).

Discussion

Patient Response. We have successfully demonstrated a significant analgesic effect with the use of TENS. We have also shown a significant placebo effect. Thornsteinsson et al.⁴ demonstrated a 48% analgesic effect with actual TENS, and a 32% analgesic effect with placebo TENS. Their study, however, was conducted in patients with chronic pain. Our study has shown a higher success rate with the actual TENS and a lower success rate with the placebo device.

In a number of studies dealing with the relief of

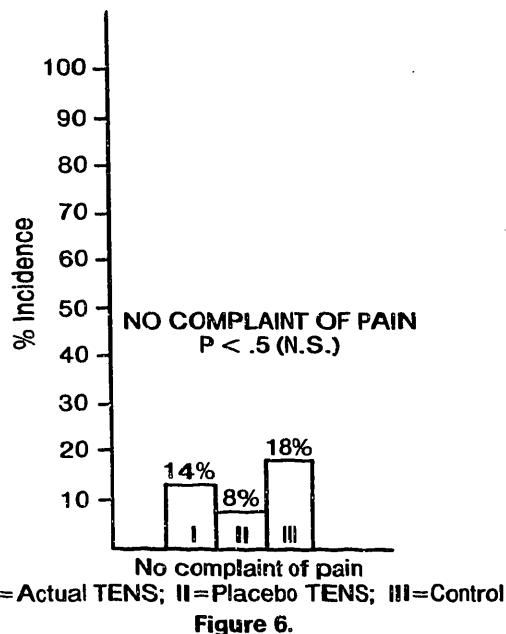


Figure 6.

chronic pain the placebo effect of TENS lasted up to 2 weeks. In our study, the placebo effect was most effective during the first postoperative day and decreased with subsequent trials.

Theory. Since 1965, Melzack and Wall's Gate-Control hypothesis² has been used to explain the mechanism of such pain relief. The effectiveness for TENS to relieve pain has been demonstrated in clinical trials by Wall and Sweet.⁵ Their basic premise was that pain relief was from central spinal cord suppression. In recent years, however, several authors have disputed this theory. Ignelzi and Nyquist^{6, 7} have conducted experiments with isolated peripheral nerves and have found that peripheral changes in the nerves occur before the first spinal cord synapse. Their results have shown that repetitive stimulations of the isolated peripheral nerve causes changes in both the A-alpha and beta and the A-delta waves of the compound action potential. Their experiments successfully correlated A-delta wave suppression and pain relief.

Similar findings have been reported by Taub and Campbell.⁸ There have also been varying studies

relating the analgesic effect of electrical stimulation to the release of endogenous morphine-like substances, termed endorphins.^{9, 10} Reversal of electrically induced analgesia has been achieved with naloxone hydrochloride (a narcotic antagonist).¹¹ This adds credence to the fact that an endogenous, morphine-like substance is secreted centrally.

Other uses. We have also utilized TENS successfully in treating athletes' pain conditions associated with overuse syndromes. The scope of TENS is unlimited and we are just now beginning to utilize it to its fullest capacity. TENS should especially be considered in the patient allergic to analgesic medication and in the patient with respiratory disease, where respiratory depression from narcotic analgesics may be a factor.

Summary

1. TENS has been shown to be an effective modality for the control of acute postoperative pain. In our study, 74% of the patients demonstrated 75 to 100% relief of pain utilizing TENS and 20% of the patients achieved a 50 to 75% relief of pain.
2. A definite placebo effect has been illustrated in this study. Utilizing placebo TENS, 17% of the patients received a 75 to 100% relief of pain, 21% received a 50 to 75% relief of pain and 60% of the patients utilizing placebo TENS stated less than 50% relief of pain.
3. The frequency of patients requiring postoperative analgesics was less for patients using TENS than those receiving placebo TENS and a random group of patients using no TENS.
4. The computed average Demerol and codeine preparations intake levels were less for patients using TENS than those with placebo TENS and a group of 50 random patients without TENS.

Acknowledgment. The authors wish to thank Medtronic, Incorporated for its cooperation with this project.

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Evaluation of Transcutaneous Electrical Nerve Stimulation for Pain Relief in Peripheral Neuropathy

A Clinical Documentation

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Key Words: *Electric stimulation, Pain, Peripheral nerve disease, Physical therapy.*

Transcutaneous electrical nerve stimulation (TENS) is currently being used in the management of a variety of acute and chronic pain syndromes.¹⁻⁴ To date, little information on specific methods of patient evaluation and TENS application has been documented. Although continuous assessment of a patient's response to treatment and subsequent modification of the treatment plan have been an important part of most physical therapy regimens, these issues have not been clearly defined for treatment protocols for TENS. In addition, patients' long-term responses to TENS treatment have not been evaluated. Therefore, accurate assessment of the long-term effectiveness of this modality for control of chronic pain is difficult.

This case history describes specific evaluation and treatment data for a patient who received TENS as part of a pain-management program. The patient's response to treatment during a six-month follow-up period is presented and appropriate modification of TENS application is suggested.

HISTORY

A 53-year-old Caucasian man initially complained of severe burning pain along the dorsal aspects of

both feet following coronary artery bypass surgery in October 1977. The discomfort was accompanied by edema and muscle cramps, primarily of the toe flexors. His medical history included four myocardial infarctions. He also experienced a brief period of depression accompanied by alcohol abuse in 1972. He underwent psychiatric treatment for six weeks, after which time these problems were considered resolved.

The patient was evaluated by a neurologist in August 1978. Upon physical examination, dorsalis pedis pulses were absent bilaterally, the patellar tendon reflex was slightly diminished, and the Achilles tendon reflex was markedly diminished bilaterally. Sensitivity to touch, pain, and temperature was reduced, but joint position sense was preserved in the lower leg. The possibility of ischemic peripheral neuropathy was ruled out during evaluation by a vascular surgeon. The neurologist described the patient's diagnosis as a peripheral neuropathy of unknown cause, and pharmacological treatment was initiated (Section A in Tab. 1).

The patient reported no relief from the drug therapy and was referred to the Emory University Pain Control Center for further evaluation in November 1978. An anesthesiologist concurred with the neurologist's diagnosis and added a course of fluphenazine hydrochloride (Prolixin®) and amitriptyline hydrochloride (Elavil®) to the medications previously prescribed (Section B in Tab. 1). However, the onset of bradykinesia and drooling, which are early symptoms of parkinsonism associated with fluphenazine hydrochloride toxicity, necessitated the discontinuation of this therapy.

In February 1979, the patient complained of increased burning pain in the feet and subsequent diminished mobility. His ability to ambulate independently deteriorated rapidly, and retaining part-time

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TABLE 1
Pain Medication Intake

Date	Medication	Daily Dosage
A		
8-78	chlordiazepoxide hydrochloride (Librium®)	25 mg × 5
	aspirin	325 mg
	flurazepam hydrochloride (Dalmane®)	30 mg × 1
	carbamazepine (Tegretol®)	800 mg
	phenytoin sodium (Dilantin®)	30 mg
	thiamine	200 mg
	prednisone	50 mg
B		
11-9-78	fluphenazine hydrochloride (Prolixin®)	2.5 mg × 3 (discontinued)
	amitriptyline (Elavil®)	25 mg × 3
C		
2-15-79	amitriptyline	50 mg × 3
	quinine sulfate	600 mg × 4

employment became impossible. Additional medications were introduced (Section C in Tab. 1), and the patient was referred to the Department of Physical Medicine for evaluation and treatment with TENS.

EVALUATION FOR TENS

A physiatrist and physical therapist examined the patient. The patient reported a constant burning pain along the dorsum of both feet, of 17-months' duration. The plantar surfaces of the feet felt cold to the patient. Pain increased during standing and walking, and was aggravated by wearing socks and shoes. Sitting or supine positioning with both feet elevated resulted in a slight diminution of pain.

Upon physical examination the physical therapist noted the absence of dorsalis pedis pulses, trophic skin changes including the loss of hair along the distal

one-third of both legs, and diminished cutaneous sensation as described earlier. Motor deficit was not noted in any muscles of the lower leg.

The patient's own perception of his pain was assessed by two written evaluations. A pain-intensity rating was obtained by asking the patient to place an "X" anywhere along a 100-mm line to describe the intensity of his pain immediately before, during, and after each TENS treatment (Figure). The patient rated his pain for each leg separately, and the percent change in pain was calculated by comparing the difference between the pretreatment and posttreatment ratings on that day (see below).

The patient also completed the McGill Pain Questionnaire Word List, a compilation of pain descriptors developed by Melzack.⁵ He was asked to select one word in each of 20 categories that best described his pain. If no word in a particular category fit his pain description, he was to ignore that category. Two scores were derived from this evaluation: the number of words chosen (range = 0-20) and the average intensity value of the words (range = 1, lowest; 5, highest). The patient completed this evaluation immediately before and after each TENS treatment.

TREATMENT #1

TENS was administered with the Stimtech Dual Channel EPC Clinical Stimulator* during outpatient treatment sessions. Pulse widths ranged from 0.050-0.500 msec, pulse rate ranged from 20-200 pps, and intensity ranged from 0-50 mA. The area of burning pain and the peripheral nerve innervating the plantar surface of the foot were selected as initial electrode placement sites. A pair of carbon-impregnated silicone electrodes (5 by 5 cm²) from Channel 1 were placed on the right foot: one electrode on the dorsal aspect just distal to the ankle joint, the second electrode immediately posterior to the medial malleolus, over the medial plantar nerve. The two electrodes

* Stimtech Inc, 9440 Science Center Dr, Minneapolis, MN 55428.

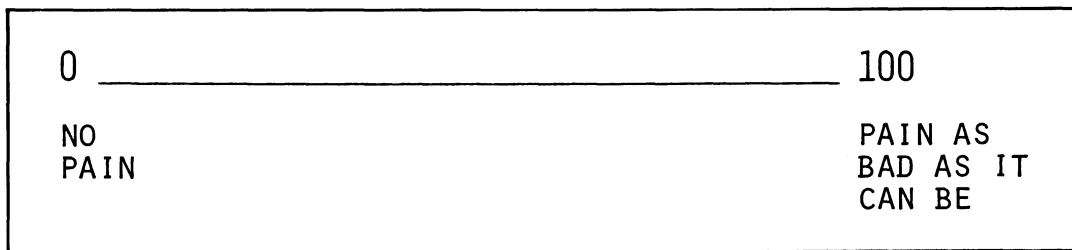


Figure. Pain Intensity Rating Scale.

TABLE 2
Pain Intensity Rating Scores

Treatment #	Pretreatment Rating (Range: 0–100)		Posttreatment Rating (Range: 0–100)		% Reduction of Pain	
	<i>Right</i>	<i>Left</i>	<i>Right</i>	<i>Left</i>	<i>Right</i>	<i>Left</i>
1	40	40	0	40	100	0
2	60	70	0	0	100	100

from Channel 2 were placed on the left foot in an identical configuration. Stimulation settings were chosen empirically to evoke a strong, nonnoxious sensation as described by the patient. The pulse width for Channel 1 was set initially at 0.200 msec, and intensity was increased slowly to 28 mA. Several pulse rates between 20 and 200 pps were tested; the patient described 110 pps as the most comfortable setting. On Channel 2, pulse width remained at 0.200 msec, and the intensity was increased to 26 mA. A pulse rate of 110 pps was again selected by the patient. The patient reported a 60 percent reduction of the burning pain in the right foot with 15 minutes of TENS treatment. No change in pain intensity was noted in the left foot. Therefore, a third electrode pair, attached to a second Stimtech Dual Channel EPC Clinical Stimulator was applied to the left lower leg. One electrode from this additional pair was placed at the apex of the popliteal fossa to stimulate the common peroneal nerve, and the second electrode was applied just posterior to the fibular head, activating the deep peroneal nerve. Stimulation settings were selected in the manner previously described: pulse width, 0.200 msec; pulse rate, 110 pps; intensity, 25 mA. The patient was treated for one hour while sitting in a chair with his feet resting on the floor. He was encouraged to stand and walk several steps every 15 minutes. This one-hour session constituted Treatment #1.

The patient's evaluation of his pain state before and after the first treatment is described by the results of the Pain-Intensity Rating Scale (Tab. 2, Treatment #1) and the McGill Word List (Tabs. 3 and 4, Treatment #1). Both measures indicated complete relief of the burning pain in the right foot after one hour of TENS treatment. No change in pain was reported in

the left foot. The patient also described a sensation of numbness in the right foot after treatment.

The patient was instructed to note the duration of his pain relief in the right foot at home following the first treatment. Because the patient lived 100 miles from the hospital, a second treatment session was scheduled three weeks later.

TREATMENT #2

At the second treatment, the patient reported that the burning pain in the right foot returned three hours after the first TENS treatment session. The patient completed the written pain evaluations again, and the second treatment was begun. During this session, electrode placement was revised. Only one electrode pair was used for treatment. One electrode was placed immediately posterior to the medial malleolus of the right ankle, and the other was placed in an identical position at the left ankle. Pulse width was set at 0.100 msec, and intensity was increased to 30 mA. For this electrode configuration, the patient selected a pulse rate of 75 pps as the most comfortable frequency.

The patient reported complete relief of the burning pain in both feet 20 minutes after TENS was initiated. This relief persisted throughout the treatment session (one hour) and was noted in the patient's posttreatment pain evaluations for treatment #2 (Tabs. 2, 3, and 4).

HOME PROGRAM

Usually three to five outpatient treatment sessions are desirable to assess the effectiveness of using TENS

TABLE 3
*McGill Pain Questionnaire Word List:
Number of Words Chosen*

Treatment #	Pretreatment Score (Range: 0–20)		Posttreatment Score (Range: 0–20)		% Reduction of Pain	
	<i>Right</i>	<i>Left</i>	<i>Right</i>	<i>Left</i>	<i>Right</i>	<i>Left</i>
1	7	7	0	7	100	0
2	9	9	0	0	100	100

TABLE 4
McGill Pain Questionnaire Word List:
Average Intensity Value

Treatment	Pretreatment Score (Range: 0–5)		Posttreatment Score (Range: 0–5)		% Reduction of Pain	
	<i>Right</i>	<i>Left</i>	<i>Right</i>	<i>Left</i>	<i>Right</i>	<i>Left</i>
1	2.43	2.43	0	2.43	100	0
2	2.50	2.50	0	0	100	100

in managing a particular pain problem. However, because the patient had difficulty in obtaining transportation to the hospital, and considering the favorable outcome of the second treatment session, the physical therapist and physiatrist decided to initiate a home TENS program after only two outpatient treatment sessions. The patient rented a portable, single-channel Neuromod† TENS unit for one month (ranges: pulse width, 0.050–0.400 msec; pulse rate, 12–100 pps; intensity, 0–50 mA). Electrode placements duplicated those of the second treatment session. Stimulation settings were adjusted to approximate the stimulation received during this treatment. The patient was instructed in TENS application procedures, skin care, and safety considerations. He was to apply the TENS for one hour, four times daily, and to note his pain status in a daily diary.

The patient returned for a follow-up visit one month later. He reported 100 percent reduction in the burning pain while wearing the TENS unit. A mild burning sensation began to return one half-hour following treatment, and the pain returned three to four hours after treatment, especially if he walked extensively during that time. The treatment schedule was revised. The patient now activated the TENS unit eight hours a day, particularly when he was standing, walking, or gardening. He decided to purchase the portable TENS unit at this time.

When the patient returned six weeks later for reevaluation, he was using the TENS unit ten hours a day and was on his feet and active most of this time. He described a recurrence of the burning pain two to three hours after treatment if he remained active in the evening. Mild edema was noted above the ankles in the evening, possibly associated with his increased mobility and activity. Revision of the treatment plan was not recommended at this time.

The patient was reevaluated after an additional six weeks. He was using the TENS during his waking hours (16 hours a day) and was pain free during this time. He did report an intermittent burning sensation in the feet, which was not bothersome to him. He

noted that the burning pain returned six to eight hours after treatment was completed.

Upon physical examination, signs of improved circulation in the feet were observed. Patellar and Achilles tendon reflexes did not change from the time of the neurologist's evaluation. The skin at the electrode placement sites was in good condition. The patient will continue to use the TENS unit during waking hours and will return in three months for reevaluation.

DISCUSSION

The need for developing objective evaluation criteria and scientifically applicable protocols for TENS is apparent in this case study. Careful evaluation of the patient's perception of his pain during the first treatment indicated that the patient was not obtaining noticeable pain relief in the left foot. This finding resulted in application of an additional electrode pair during the first treatment, placed over the proximal portion of the common peroneal and deep peroneal nerves. Stimulation of the major peripheral nerve trunks innervating the painful site in addition to stimulation applied directly over a painful region or dermatome was selected as an alternative method to achieve optimal pain relief. In his evaluation of the first treatment, the patient reported excellent relief of pain in the right foot and no change in pain in the left foot. Apparently, further revision of electrode placements and stimulation settings was necessary to achieve maximum pain reduction.

During the second treatment, only one electrode pair was used. One electrode was placed over each medial plantar nerve, immediately posterior to the medial malleolus, to activate the distal portion of the major nerve innervating the painful region. This revision of electrode placement necessitated reevaluation of stimulation settings.

In this case, the pulse width, pulse rate, and intensity all required revision to maintain a strong, comfortable sensation for the patient. According to the patient's evaluation of his pain following the second treatment, 100 percent pain relief was achieved in both feet with these revised electrode placements and stimulation settings.

† Medtronic, Inc, 3055 Old Highway Eight, PO Box 1453, Minneapolis, MN 55418.

To implement a home treatment program, the physical therapist and patient should review application techniques used in previous treatment sessions and select the procedure that affords optimal pain control. The patient should be instructed in these specific application techniques as well as in safety procedures. A flexible treatment schedule, including the number and duration of daily TENS treatments, should be prescribed for the patient.

Interestingly, this patient chose to increase his treatment time as the duration of treatment effectiveness diminished in the months after the initial evaluation. This phenomenon has been observed in several of our patients. Endogenous opioid substances have been implicated in analgesic effects of TENS.⁶ A postulation worthy of systematic study is that prolonged use of TENS may lead to development of a physiological tolerance to the modality, similar to that seen with opiate-containing substances. Perhaps the development of this tolerance could be delayed by limiting long-term use of TENS to several hours a day. The decision to limit the use of TENS, however, must be weighed against the benefits of increased mobility and function as described in this case history.

Regularly scheduled reevaluations for patients using TENS at home are necessary to afford the clinician the opportunity to monitor the patient's progress

and revise or discontinue treatment as indicated. This consideration is particularly important because the long-term benefits of TENS have not been clearly established in the literature.^{1,7} The efficacy of TENS for management of chronic pain over a prolonged period of time may be established only through conscientious, regular reevaluation of the patient and revision of treatment protocols as indicated. Objective evaluation techniques, scientific application of TENS, consistent reevaluation of the patient's progress, and perseverance on the part of the clinician and patient are paramount to the achievement of optimal pain control with TENS.

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Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain

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Abstract

Aim. We investigated the literature of randomised placebo-controlled trials to find out if transcutaneous electrical nerve stimulation (TENS) or acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) can reduce analgesic consumption after surgery.

Results. Subgroup analysis for adequate treatment (pulse frequency: 1–8 Hz [ALTENS] or 25–150 Hz [TENS], current intensity: “strong, definite, subnoxious, maximal tolerable” or above 15 mA, and electrode placement in the incision area) were performed. Twenty-one randomised, placebo-controlled trials with a total of 1350 patients were identified. For all trials, the mean reduction in analgesic consumption after TENS/ALTENS was 26.5% (range –6 to +51%) better than placebo. Eleven of the trials comprising 964 patients, had reports which stated that a strong, subnoxious electrical stimulation with adequate frequency was administered. They reported a mean weighted reduction in analgesic consumption of 35.5% (range 14–51%) better than placebo. In nine trials without explicit confirmation of sufficient current intensity and adequate frequency, the mean weighted analgesic consumption was 4.1% (range –10 to +29%) in favour of active treatment. The difference in analgesic consumption was significantly ($p = 0.0002$) in favour of adequate stimulation. The median frequencies used in trials with optimal treatment was 85 Hz for TENS and 2 Hz in the only trial that investigated ALTENS.

Conclusion. TENS, administered with a strong, subnoxious intensity at an adequate frequency in the wound area, can significantly reduce analgesic consumption for postoperative pain.

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Keywords: Transcutaneous electrical nerve stimulation; Postoperative pain; Analgesic consumption

1. Introduction

Transcutaneous electrical nerve stimulation (TENS) is a modality that in experimental settings has been able to reduce pain (Walsh and Baxter, 1996). However, the gap from promising laboratory research to clinical effectiveness is difficult to bridge and the clinical literature on TENS seems equivocal and inconclusive in several areas (Carroll et al., 1997; Milne et al., 2001).

Systematic reviews for the treatment of postoperative pain, have concluded that there is little—if any—evidence in favour of TENS (Carroll et al., 1996; Reeve et al., 1996). The Bandolier evidence-based health care web site relies on one of these review conclusions as the best available evidence and states: “*Clinical bottom line: TENS is not effective in the relief of postoperative pain. Patients should be offered effective methods of pain relief*” (Bandolier, 2000). However, this advice may be based on an evaluation model that is volatile, because trials with possible ineffective treatment dose were not excluded (Bjordal and Greve, 1998). Information from the reports of trials included in these reviews suggests that

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low, and possibly ineffective, current intensities of 0–15 mA (Cuschieri et al., 1985) or sensory threshold intensity were used (Smedley et al., 1988).

We have previously used a model for evaluating the scientific evidence for therapies with unknown optimal treatment procedure. The model allows for testing the hypothesis that an assumed optimal dose exists, and for other electrophysical agents, this model has aided identification of specific treatment doses and procedures that were significantly more effective than others in tendinopathies (Bjordal et al., 2001).

Another problem with previous systematic reviews on TENS and postoperative pain is that, although outcome measures have not been standardised, dichotomised interpretation (positive or negative) of pain scores seem to be the source of conclusions about ineffectiveness. Systematic reviews on TENS and postoperative pain also dichotomise complex trial data as positive or negative, which may overlook clinically relevant effects. This has led to inconsistency in the interpretation of trial outcome by reviewers. For example, Conn et al. (1986) reported that there were no differences between active and sham TENS in postappendicectomy pain relief. The review by Carroll et al. (1996) judged this finding as negative outcome based on the lack of differences in pain relief scores between the groups. However, the review by Reeve et al. (1996) judged Conn et al.'s study as positive outcome, possibly based on the finding that TENS significantly reduced the need for additional analgesics when compared to sham.

Drug administration by patient-controlled analgesia (PCA) is common (Cook & Riley, 1997), and all available postoperative trials on TENS use analgesic drugs as co-interventions. It is possible that pain scores in these trials may be compromised because patients were given free access to analgesics either by PCA or analgesic request. Truly, significant differences in pain scores can be expected in cases where drugs of variable effectiveness are compared. But trials comparing equally effective analgesic drugs, seldom find significant differences in VAS-scores (Kostamovaara et al., 1998; Ilkjaer et al., 1998; Forst et al., 1999), as most patients titrate their analgesic consumption to a similar and tolerable level of pain intensity. It is important to emphasise that experimental studies of TENS effectiveness only provides support for partial pain relief, whereas analgesic drugs have the potential to produce complete pain relief. One problem with high doses of analgesic drugs however, is that undesirable side effects such as depressed respiration, nausea, and sedation reduces patient satisfaction (Pang et al., 1999). A clinically meaningful perspective is if TENS can reduce analgesic consumption by PCA or analgesic request without significant increase in pain scores. Our hypothesis is that TENS can reduce PCA doses *without* increasing pain scores when compared to PCA combined with placebo TENS.

Surgery leads to a fairly standardised sequence of early recovery from oedema and postincision pain. The first 3-day postoperative sequence seems particularly suitable for assessing the size of effect from TENS. Statistical pooling of trial results can give a valid quantification of treatment effects in such cases (Thompson, 1991; Moore et al., 1998).

This meta-analysis of randomised placebo-controlled trials examines the reduction of analgesic consumption using TENS after surgery using assumed optimal TENS parameters. Thus, trials were included if TENS was administered at a subjective intensity that was described as “strong and/or definite subnoxious, and/or maximal non-painful, and/or maximal tolerable” or a current amplitude above 15 mA. There exists scattered evidence that pulse frequencies of 1–8 Hz for acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) (Sjolund, 1988; Tulgar et al., 1991) or 25–150 Hz for conventional TENS (Sjolund, 1985; Johnson et al., 1989; Tulgar et al., 1991) provide better pain relief than other frequencies. For this reason these frequency ranges were assumed optimal in this meta-analysis.

2. Materials and methods

2.1. Literature search

A literature search for randomised controlled trials from 1966–2001 was performed on Medline, Embase, Cinahl, PedRo, and the Cochrane Controlled Trial Register as advised by Dickersin et al. (1994). Key words were: transcutaneous electrical nerve stimulation, transcutaneous electrical, acupuncture-like electrical, postoperative pain, TENS, ALTENS. Handsearching was also performed in National Physiotherapy and Medical Journals from Norway, Denmark, Sweden, Holland, England, Canada, and Australia. Additional information was gathered from researchers in the field.

3. Methods

3.1. Inclusion criteria

The trials were subjected to the following inclusion criteria:

- (1) Surgical in-patients were included.
- (2) Electrical stimulation performed with electrode placement on intact sensory innervated area around incision.
- (3) Randomisation reported.
- (4) Attempts of blinding reported.
- (5) Amount of analgesic consumption reported.
- (6) Endpoints within 3 days after inclusion.

3.2. Exclusion criteria

1. Trials listed as non-randomised in review by Carroll et al. (1996) (i.e., randomisation is not reported, a control group was included retrospectively, or group allocation was selected by authors).

3.3. Outcome measures

Main outcome measure is analgesic consumption. For each trial, analgesic consumption between active treatment group and placebo group was registered and differences between groups were calculated and presented as percentual differences. Secondary outcome measure was pain on a visual analogue scale.

3.4. Statistical pooling

In the statistical pooling, we used the mean percentual difference in analgesic consumption between groups in each trial and multiplied this value with the number of included patients in the trial. These products were added and divided by the total number of participating patients in all trials, which gives the mean weighted difference (MWD) in analgesic consumption between active treatment and placebo treatment from all the included trials:

$$\left(\sum [\text{Difference between groups for each trial (\%)} \times \text{number of patients in same trial}] \right) / \text{number of patients in all trials.}$$

3.5. Adverse events

The number of adverse events from TENS/ALTENS was registered.

3.6. Subgroup analysis

Analysis for trials, which described both of the following assumed optimal treatment parameters, was performed:

Pulse frequency: 1–8 Hz [ALTENS] or 25–150 Hz [TENS].

Current intensity: strong, definite, subnoxious, maximal tolerable [TENS] or above 15 mA.

A test for statistical significance of analgesic consumption differences, between the trials with assumed optimal treatment parameters, and the assumed non-optimal treatment parameters was performed with Students two-tailed *t* test ($p < 0.05$). If significant differences were found between assumed optimal and non-optimal treatment, an analysis of the median electrical

frequency and an analysis of side effects for the optimal treatment trials would be performed.

4. Results

4.1. Results of inclusion procedure

The literature search identified 128 reports with TENS, of which 51 were controlled trials. Nineteen of these had to be excluded as they met our exclusion criteria for non-randomisation as defined by Carroll et al. (1996). Another 11 trials (Rainov et al., 1994; Rosenberg et al., 1978; Pike, 1978; Stubbing and Jellicoe, 1988; Reuss et al., 1988; Hargreaves and Lander, 1989; Bayindir et al., 1991; Jones and Hutchinson, 1991; Laitinen and Nuutinen, 1991; Walker et al., 1991; Chiu et al., 1999) had to be excluded for various reasons (see Table 1).

The remaining 21 trials were randomised, placebo-controlled trials including 1350 patients fulfilling our inclusion criteria (Table 2).

4.2. Results for analgesic consumption regardless of stimulus parameters

The MWD in reduction of analgesic consumption was calculated to be statistically significant ($p = 0.005$) at 26.5% better than placebo for all 21 trials.

4.3. Results of subgroup analysis for assumed optimal treatment

Eleven trials, including 964 patients, (Lim et al., 1983; Jensen et al., 1985; Van der Ark and McGrath, 1975; Smith et al., 1986; Benedetti et al., 1997; Wang et al., 1997; Gilbert et al., 1986; Fodor-Sertl et al., 1990; Taylor et al., 1983; Hamza et al., 1999; Hershman et al., 1989), satisfied our criteria of assumed optimal treatment. They reported a MWD reduction in analgesic consumption that was 35.5% (range 14–51%) better in the TENS group than in the placebo TENS group (Fig. 1). The MWD between assumed optimal and assumed non-optimal TENS treatment was highly significant ($p = 0.0002$).

4.4. Results of subgroup analysis for assumed non-optimal treatment

In the 10 trials that used assumed non-optimal TENS treatment (Davies, 1983; Warfield et al., 1985; Galloway et al., 1984; Conn et al., 1986; Forster et al., 1994; Smedley et al., 1988; Navarathnam et al., 1984; Sim, 1991; Cuschieri et al., 1985; McCallum et al., 1988), the MWD in analgesic consumption between active TENS and placebo TENS was 4.1%, which was not statistically significant ($p = 0.56$).

Table 1

List of excluded trials given by first author, publication year, sample size, diagnosis, outcome and reason for exclusion

First author	Publication year	Number of patients	Type of surgery	Reduction (%) in analgesic consumption vs. control	Reason for exclusion	Assumed optimal treatment
Rosenberg	1978	12	Cholecystectomy	60	Lacks placebo treatment in control group	Yes (TENS)
Pike	1982	40	Hip prosthesis	73	Lacks placebo treatment in control group	Yes (TENS)
Hargreaves	1988	75	Abdominal	Missing (28% on VAS)	Lacks data on analgesic consumption	Yes (TENS)
Laitinen	1991	50	Cholecystectomy	–15 (data only for first 16 h)	Control group received Indomethacin	Yes (ALTENS/TENS)
Walker	1991	36 (48)	Total knee arthroplasty	11	Electrode placement not described	Yes (TENS)
Jones	1991	31	Abdominal	Missing (25% on VAS)	Lacks data on analgesic consumption	Yes (TENS)
Rainov	1994	234	Lumbar discectomy	39	Lacks placebo treatment in control group	Yes (TENS/ALTENS)
Stubbing	1988	40	Thoracotomy	–2	Lacks placebo treatment in control group	No (TENS, only slight tingling sensation)
Reuss	1988	64	Cholecystectomy	–5	Lacks placebo treatment in control group	No (TENS, “amplitude 0–50 A”)
Bayinder	1991	89	Median sternotomy	75	Lacks data on analgesic consumption	No (ALTENS, sensory threshold)
Chiu	1999	60	Hemorrhoidectomy	46	Electrodes not placed around incision	No (Distant acupoint ALTENS)

4.5. Results for secondary outcome measure (pain on VAS)

The MWD in pain measured on VAS was not significant as only two trials reported significant reduction for the active TENS (Gilbert et al., 1986; Smith et al., 1986), while the remaining nine trials reported no significant differences in VAS for active TENS.

4.6. Results of median frequency in trials with optimal treatment

The median frequency for TENS of 11 trials with optimal treatment parameters was 85 Hz, while 2 Hz was used in the only trial that had an ALTENS group (Hamza et al., 1999).

4.7. Side effects and adverse events

No negative side effects from TENS/ALTENS were reported. The effect from TENS/ALTENS on opioid-

related side effects was reported in two trials with optimal treatment (Wang et al., 1997; Hamza et al., 1999). In TENS/ALTENS groups, patients reported 20.6% (mean \pm 20 SD) less nausea and 29.4% (mean \pm 21 SD) scored better on various scores of alertness. No adverse events from TENS/ALTENS were reported.

5. Discussion

The results suggest a significant dose-dependent effect from TENS in postoperative pain. A possible limitation of this interpretation, is that our selected main outcome measure has been analgesic consumption. If TENS is effective in relieving postoperative pain, it would either reduce VAS-ratings, analgesic consumption or both. We have assumed that by having free access to analgesics, most patients would use this to achieve a comfortable pain level. This assumption is supported by one trial with postoperative PCA, which showed that most, but

Table 2

List of included trials by first author, publication year, sample size, diagnosis, stimulation type, outcome for analgesic consumption, optimal/non-optimal stimulation

First author	Year	Type of surgery	Number of patients	Type of treatment	Mean effect vs. placebo (%)	Intensity of stimulation described	Optimal treatment	Notes
Van der Ark	1975	Abdominal/thorax	100	TENS	51	Strong (20–35 mA)	Yes	
Lim	1983	Abdominal	30	TENS	25	Strong	Yes	
Taylor	1983	Abdominal	77	TENS	32	Subnoxious	Yes	
Jensen	1985	Meniscectomy	90	TENS	28	21 mCoulomb	Yes	
Smith	1986	Caesarean	18	TENS	22	30 mA	Yes	44% better than placebo on VAS
Gilbert	1986	Inguinal hernia	40	TENS	14	Max. tolerable	Yes	38% better than placebo on VAS
Hershman	1989	Cholecyst./colorect.	95	TENS	36	Definite tingling sensation	Yes	
Fodor-Sertl	1990	Thoracotomy	40	TENS	35	Strong < 40 mA	Yes	
Benedetti	1997	Thorax	324	TENS	35	Strong	Yes	
Wang	1997	Abdominal	50 (101)	TENS	42	Strong	Yes	
Hamza	1999	Gynaecological	100	TENS/ ALTENS	40	Strong	Yes	
Galloway	1984	Abdominal	40	TENS	29	Adjusted to each patients comfort	No (?)	10% better than placebo on VAS
Warfield	1985	Thoracotomy	24	TENS	10	Amplitude 7 (Tenzcare 6240)	No (?)	23% better than placebo on VAS
Davies	1983	Caesarean	32	TENS	17	Amplitude as wished	No	No effect of TENS after epidural analgesia
Navaratnam	1984	Thorax	31	TENS	14	Comfortable	No	29% better on expiratory lung flow
Cuschieri	1985	Abdominal surgery	106	TENS	–10	Comfortable max 15 mA	No	Time to analgesic request 24% better than placebo
Conn	1986	Appendicectomy	28 (42)	TENS	22	Tingling sensation, no discomfort	No	
Smedley	1988	Inguinal hernia	62	TENS	–6	Sensory threshold	No	
McCallum	1988	Lumbar laminect.	20	TENS	6	Comfortable	No	
Sim	1991	Cholecystectomy	30	TENS	5	0–5 mA	No	
Forster	1994	Coronary bypass	45	TENS	6	comfortable Strong, but comfortable	No	Frequency too high (258 Hz)

not all, titrated PCA consumption to achieve a tolerable level of pain intensity (Woodhouse and Mather, 2000). Consequently, the consumption of analgesics seems to be the most valid outcome measure, although one would also expect to find occasional significant results for VAS-scores, if the intervention was effective. It is interesting to note that the two trials (Gilbert et al., 1986; Smith et al., 1986) with the smallest reductions in analgesic consumption, recorded significantly better VAS-scores in the active treatment groups. We consider these

results to add further weight to a conclusion of TENS' effectiveness in postoperative pain.

Measuring interventional effects on mild pain remains a complicated issue, because several factors may have influence on the results. In addition, the inter-subject variance in registered pain scores is large, and does not necessarily reflect the physiological status of the patients (Tyler et al., 1996). Psychological factors like health locus of control, anxiety, and depression have been shown to significantly affect PCA consumption and pain

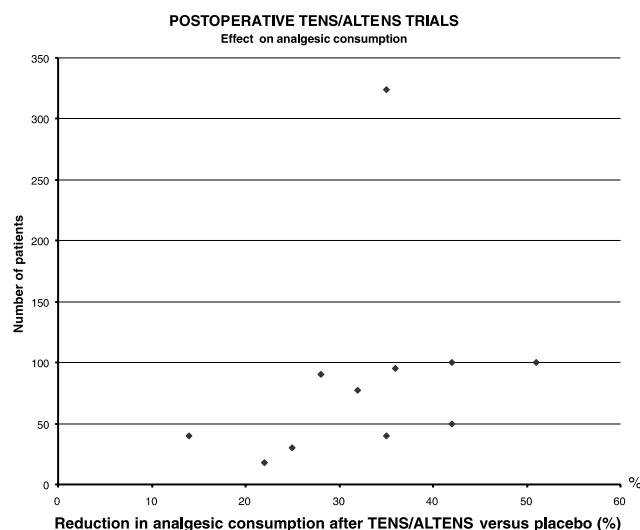


Fig. 1. Effect size plot for trials with optimal treatment procedure.

(Johnson et al., 1989; Gil et al., 1990; Thomas et al., 1995), while age seems to be of no significant importance (Gagliese et al., 2000). In one of the included trials, psychological factors were investigated separately, and no significant differences between groups were reported (Lim et al., 1983). We found no indication of uneven distribution of psychological factors between groups in the included trials. Interpretation of randomisation was performed rather strictly, in the sense that we excluded every trial that had been excluded by the randomisation criteria in previous reviews (Carroll et al., 1996; Reeve et al., 1996). We think that randomisation, combined with a rather large patient sample, most probably have secured an even distribution of possible psychological confounders in placebo and active treatment groups.

Apart from randomisation, adequate blinding has been considered to be an important trial quality factor that may affect outcome results. While earlier studies suggested that only a positive outcome was exaggerated by poor blinding (Schulz et al., 1995), more recent papers have reported that poor blinding causes the outcome variance in both directions to increase (Verhagen et al., 2000). Maybe some authors have used too low current intensities, in fear of compromising the blinding the respective treatment groups. However, in one placebo-controlled TENS-trial where a TENS-unit without batteries served as placebo, no significant difference between the groups was found when they were asked if their unit was active or sham (Deyo et al., 1990). In our material we have taken this further by showing that there was a significant difference in analgesic consumption between groups receiving an adequate strong, submaximal electrical stimulus, and groups given a non-optimal (but above sensory threshold) electrical stimulus. The latter group may be considered as a placebo group too. Because of the small differences in effect be-

tween groups receiving no electrical stimulus, and those receiving an inadequate electrical stimulus above sensory threshold, one possible implication is that future trials can use the latter as placebo treatment.

As all patients in hospital were under homogeneous environmental conditions during a period of 1–3 days, co-interventions were avoided, and withdrawals hardly occurred. In TENS-trials for chronic pain in out-patient settings, several extrinsic factors may be difficult to control. A postoperative hospital setting where patients have mild, postoperative pain, probably represents one of the “cleanest” possible clinical study situations, in which TENS effectiveness can be investigated.

Our findings are contrasting the negative conclusions on TENS effectiveness of previous reviews (Carroll et al., 1996; Reeve et al., 1996; McQuay & Moore, 1998). These reviews have dichotomised trial results into negative or positive outcome. The review by Carroll et al. has one clear punchline: the importance of randomisation. Although we agree on the importance of randomisation, dichotomisation is a potential source of bias. Inconsistency in the judgments between trial authors and different reviewers, has been described for TENS-trials (Johnson, 2000) and dichotomised interpretations of trial reports tend to be systematically biased towards the reviewers’ conclusion (Bjordal and Greve, 1998). Another important difference between our review and the others is that we have chosen a different and standardised main outcome measure (analgesic consumption).

Our literature search is more extensive, and includes several large, well-designed trials (Benedetti et al., 1997; Wang et al., 1997; Hamza et al., 1999) that have been missed out in earlier reviews. Consequently, the base for our conclusions should be broader and several aspects also suggest that the conclusions are robust to changes in exclusion criteria.

The non-randomised-controlled trials that were excluded from this review, have nearly all reported effects in favour of active TENS. In the heterogeneous sample of excluded randomised, controlled trials in Table 1, the same tendency of a significant pain-reducing effect from TENS is seen. Thus, any alteration of exclusion criteria for trial design, would not have altered our conclusion. In addition, the graphical distribution of results from optimal TENS treatment, resembles that of a “funnel-plot”. This is by some authors considered to strengthen the evidence of a positive effect from treatment (Egger et al., 1997).

The variation in effect size seems large across the TENS-trials, but it may be partly explained by differences in treatment procedures and patient samples. The two trials using analgesic medication by PCA (Wang et al., 1997; Hamza et al., 1999) provided larger reduction in analgesic consumption, than the trials where patients had to require rescue analgesics from the

nursing staff. Better pain relief has been reported for patients using PCA when compared to patients that had to require analgesics from the hospital staff (Passchier et al., 1993). Epidural analgesia may also influence the result by lessening the effect of TENS (Davies, 1983). There is also evidence that TENS is less effective after major surgical interventions like thoracotomy (Benedetti et al., 1997). TENS is a sensory modality which acts directly on the nervous system by activating A-beta peripheral fibres, and this leads to a reduction in central nociceptive cell activity (Garrison and Foreman, 1994). The physiological processes that generate the self-report of postoperative pain differ in their contribution for mild, moderate, and severe pain. Thus, the outcome of A-beta activity induced by TENS may also differ. The observation that TENS relieves rather than exacerbates A-beta touch evoked pain in patients with tactile allodynia highlights our lack of understanding of the effects of TENS induced A-beta afferent activity on different levels of pain and tissue damage (Devor, 2001).

TENS is no panacea that can substitute strong analgesics. Clinical use of TENS can be limited by the time required to educate patients on administration techniques. Evidence presented in this meta-analysis that TENS provides benefit over and above placebo, coupled with its ability to increase the self-efficacy of the patient with only minor adverse effects suggests a role for TENS in the management of postoperative pain.

6. Conclusion

There is credible evidence that TENS reduces postoperative pain through less analgesic demand during the first 3 days after surgery. In addition, there is some evidence that suggests a reduction of side effects, like nausea and sedation, from opioid analgesia. The effect of TENS is dose-dependent and requires a strong sensation of currents. The median stimulation frequency in trials with stimulation parameters within the assumed optimal dose range, was 85 Hz for conventional TENS.

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ARTIGO ORIGINAL

Effect of transcutaneous electrical nerve stimulation (TENS) for the management of postoperative surgical pain after lower extremity amputation: a pilot study

Efeito da estimulação elétrica nervosa transcutânea (TENS) no tratamento de dor pós-cirúrgica após amputação de membro inferior: estudo piloto

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ABSTRACT

Introduction: Transcutaneous electrical nerve stimulation (TENS) is a noninvasive, nonmedical modality. There are a lot of dilemmas and opposing attitudes regarding the use of TENS in pain management after lower limb amputations. **Objective:** To establish the role of TENS for the management of postoperative surgical pain after lower limb amputations. **Material and methods:** Randomized controlled trial, which included forty-six subjects who had undergone lower limb amputations, randomly divided into control and treatment group. The control group received standard postoperative care, whereas the treatment group received standard postoperative care plus TENS. Forty subjects successfully completed the study according to the study protocol. The majority of the individuals had undergone transtibial amputation due to complication of diabetes. Five TENS XL-A1 portable devices with four self-adhesive electrodes were used. This was the conventional TENS mode, characterized by the delivery of electrical impulses with a duration of 200 microseconds, frequency of 110 Hz, and amplitude of 44V. Treatment was carried out for 2 hours a day, during 10 days. The evaluation of TENS efficacy was performed using the horizontal VAS (0-100 mm). Student T test was used in the statistical analysis. **Results:** Pain intensity was significantly diminished in both groups at the tenth in comparison with the first postoperative day. There were no significant differences between the control (VAS = 4.18 ± 1.48) and the treatment group (VAS = 3.59 ± 1.44) according to the daily mean pain intensity ($t = 1.25$; $df = 38$). Pain intensity on the tenth postoperative day was significantly lower in the treatment (VAS = 1.65 ± 0.80) when compared with the control group (VAS = 3.2 ± 1.15 ; $t = 5$; $df = 38$; $p < 0.01$). **Conclusion:** Conventional TENS (dose: 200 microseconds, 110 Hz, 44V), administered two hours a day during ten days, significantly reduced postoperative surgical pain in twenty subjects who had undergone lower limb amputations.

KEYWORDS

transcutaneous electric nerve stimulation, amputation, pain, postoperative

RESUMO

Introdução: A estimulação elétrica nervosa transcutânea (TENS) é uma modalidade não-médica e não-invasiva. Há muita controvérsia e atitudes contrárias em relação ao lugar que a TENS ocupa no tratamento da dor após amputação de membro inferior. **Objetivo:** Avaliar o papel da TENS no tratamento de dor cirúrgica pós-operatória após amputação de membro inferior. **Material e métodos:** Teste controlado randomizado, conduzido com 46 indivíduos submetidos à amputação de membro inferior, que foram aleatoriamente divididos em grupo controle e grupo tratado. O grupo controle recebeu cuidados-padrão no pós-operatório; o grupo tratado recebeu cuidados-padrão e aplicação de TENS. Quarenta indivíduos completaram efetivamente o estudo de acordo com o protocolo de estudo. A maior parte das amputações consistiu de amputação transtibial devido a complicações da diabetes. Foram utilizados cinco dispositivos portáteis Ultima TENS XL-A1 com eletrodos auto-adesivos. Esta é a aplicação convencional da TENS, caracterizada pela aplicação de impulsos elétricos com a duração de 200 microssegundos, frequência de 110 Hz e amplitude de 44 V. O tratamento foi administrado durante 10 dias, 2 horas por dia. A avaliação da eficácia da TENS foi feita utilizando-se a escala visual analógica (EVA) horizontal (0-100 mm). O teste

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t de Student foi usado na análise estatística. Resultados: A intensidade da dor estava significativamente diminuída em ambos os grupos no 10º dia em comparação ao 1º dia de pós-operatório. Não houve diferenças significantes entre o grupo controle ($EVA = 4,18 \pm 1,48$) e o grupo tratado ($EVA = 3,59 \pm 1,44$), de acordo com a intensidade média diária da dor ($t = 1,25$; $df = 38$). A intensidade da dor no 10º dia de pós-operatório foi significativamente menor no grupo tratado ($EVA = 1,65 \pm 0,80$) versus o grupo controle ($EVA = 3,2 \pm 1,15$; $t = 5$; $df = 38$; $p < 0,01$). Conclusão: A TENS convencional (dose: 200 microssegundos, 110 Hz, 44 V), administrada 2 horas por dia, durante 10 dias, significativamente reduziu a dor cirúrgica pós-operatória em 20 indivíduos com amputação de membro inferior.

PALAVRAS-CHAVE

estimulação elétrica transcutânea do nervo, amputação, dor pós-operatória

INTRODUCTION

Transcutaneous electrical nerve stimulation (TENS) is a noninvasive, nonmedical modality. It is the most frequently used electrotherapy for producing pain relief.¹ TENS mean the application of controlled low-voltage electrical pulses to the nervous system by passing electricity through the skin via electrodes placed on the skin. It is easy to administer and has few side-effects and no drug interactions. There is no potential for overdose or toxicity. Patients can administer TENS themselves and titrate the dosage of treatment. TENS is cheap when compared with long-term drug therapy. Its effects can be subdivided into analgesic and non-analgesic effects. It is using for relief acute as well as chronic pain. Acute postoperative pain is important indication for analgesic effects of TENS.^{1,2}

The incidence of major amputations, in the USA for example, is estimated to be at least 70 000 cases annually. Prevalence is estimated to be over 500 000 cases of major amputation.³ Approximately 70% of lower extremity amputations in adults are the results of complications of diabetes and peripheral vascular disease. Most of these amputations occur in people age 60 years and older.⁴ With the increasing trend in the incidence of limb loss, there is a growing interest for the better treatment and rehabilitation of amputees.⁵ The postoperative management after lower extremity amputations implies the rigid removal dressing, application of immediate postoperative prosthesis, soft or semi rigid postoperative dressing, pain management, treating of skin complications and other complications. The pain after lower extremity amputations can be subdivided into postoperative surgical pain, phantom limb pain (PLP), phantom sensation, and the pain caused by tumor or vascular disorders.⁶ Esquenazi divides this pain into post surgical pain, residual limb pain, prosthetic pain, and phantom pain.⁷

There are a lot of dilemmas and contrary attitudes in regard to place of TENS in the pain management after lower extremity amputations. Most of the authors emphasize a benefit of using TENS in treatment of post amputation pain: especially for treatment of PLP.^{3,6,8, 9,10} However, there are authors who do not suggest administration of TENS in this condition.^{4,11,12} Gnezdilov et al,¹³ for example, have found only 25% of 24 patients with PLP who had

completely relieved pain after TENS administration. Hanley et al¹⁴ have found that TENS was "not at all helpful" in 60,3% of 101 patient with PLP. Similarly, there are no overall acceptable attitudes in regard to TENS administration in the postoperative surgical pain. There is practical guideline for the management of post-operative pain.² TENS was suggested as an effective adjunct for providing postoperative pain control. Toward this guideline TENS can facilitate movement and exercise by decreasing pain perception and improved physical functioning. Thorsteinsson¹⁵ asserts that TENS can be important adjunct to the management of pain in elderly patients. Linchitz et al¹⁶ consider TENS as the important adjunct method for all types of musculoskeletal pain. Beside this, there are some rehabilitation authorities who do not mention TENS for the management of postoperative surgical pain.^{4,6,12}

Esquenazi, writing about management of acute post surgical pain after extremity amputation, suggests galvanic and electrical stimulation. But it was not specific. What kind of electrical stimulation? What mode of transcutaneous electrical nerve stimulation? What about of dose of this treatment? There are many reports in a literature about effect of TENS in the acute post surgical pain conditions.^{1,17,18} We found only one report of TENS administration in the acute post surgical pain after major amputation.¹⁹

AIM OF THE STUDY

The aim of this study was to ascertain the role of TENS for the management of postoperative surgical pain after lower extremity amputations.

MATERIALS AND METHODS

This was randomized controlled trial. Forty six inpatient subjects from The Military Medical Academy at Belgrade, Serbia, were recruited to participate in this study. Potential subjects were asked if they were willing to volunteer for a research study looking at a treatment for the management of postoperative surgical pain after lower extremity amputations. Inclusion criteria were as follows: male or female patients between the ages of 30 and 90 with lower extremity amputation; preserve mental capability measured by mini mental state exam; complains of pain that rated at least 3 of 10 on a visual analog scale (VAS), at first postoperative day. All amputation etiologies were included in this study. Exclusion criteria included a history of epilepsy and/or a pacemaker as well as a severe heart disease, because the use of TENS is not indicated in these patients population.¹

Subjects were randomly assigned into a control group or a treatment group. The control group received the standard of care treatment after lower extremity amputation. This involved soft dressing, positioning of the stump, early mobilization, exercise therapy and administration of nonsteroidal anti-inflammatory drugs (diclofenac sodium – Diklofenak, one or two amp. per day) as indicated. The treatment group continued to receive the standard of care in addition to their assigned TENS parameter for 2 hour a day, 10 days. TENS therapy started at first postoperative day. The

treatment group received conventional TENS using the high frequency, low intensity mode. This mode is characterized by delivery of electrical impulses having duration 200 microseconds, frequency 110 Hz and amplitude 44 V. This mode was selected towards the manufacturer's suggestions and in the direction of attitudes of some rehabilitation authorities.^{1,10}

Five TENS XL-A1 (Manufacturer "Tens Care", England) units were purchased for this study. This is the portable units with four self-adhesive electrodes. Subjects were educated regarding the proper use of TENS and the proper application of electrodes. The education entailed verbal instruction and demonstration by the therapist. Electrodes were applied on the healthy skin in the proximally parts of the stump, over the main nerve trunk arising from the site of pain.

The evaluation of efficacy of TENS for the management of postoperative surgical pain after lower extremity amputation was performed using horizontal VAS (0-100 mm). All study subjects were educated regarding the use of the VAS scale. Subjects were instructed to record their pain at the same time every day to control for the degree of pain. Subjects were asked to view the scale and state the number that best represents his or her present level of pain. The scale ranges from 0 to 10, with 0 being no pain and 10 the worst possible pain. All subject rated their pain once a day, starting from the first postoperative day. Student T test was used in statistical analysis. We accepted $p < 0,05$ for the level of significance.

RESULTS

Forty subjects successfully completed the study according to the study protocol. Six of the 46 subject who were recruited initially withdrew from the study, died, or did not complete the study according to protocol. Of these 6 subjects, three were in the control group, and three were in the treatment group. Of these 3 subjects in control group two died, and one was withdrawn because of lack of protocol compliance. Of these 3 subjects in treatment group one died, one had contra lateral leg ischemia and one was withdrawn because of lack of protocol compliance. Of the 40 subjects who completed the study, 20 were in control group and 20 were in the treatment group. Most of the subjects in both group had transtibial amputation caused by complication of diabetes. No subjects reported complications or issues associated with the study. Two subjects in the treatment group had mild erythema after the first and the second application of TENS.

Evaluating the initial comparability between groups, it was found that the two groups not differ significantly from each other (Table 1.)

There were no significantly differences between control group ($VAS=5,0 \pm 2,0$) and treatment group ($VAS=5,95 \pm 1,98$) according to the pain intensity ($t=1,39$; $df=38$) at the first postoperative day (Fig 1.).

Pain intensity was significantly diminished in both group at the tenth day versus the first postoperative day (Fig 1.)

There were no significantly differences between control group ($VAS=4,18 \pm 1,48$) and treatment group ($VAS=3,59 \pm 1,44$) according

Table 1
Clinical characteristics of subjects

Clinical characteristics	Control group (X \pm SD;%)	Treatment group (X \pm SD;%)	t	p
AGE	67,5 \pm 15,0	70,9 \pm 9,85	0,82	ns.
SEX				
– males	14 (70)	15 (75)	0,21	ns.
– females	6 (30)	5 (25)		
MINI MENTAL SCORE	26,0 \pm 2,73	25,8 \pm 3,18		
LEVELS OF AMPUTATIONS				
– partial foot	3 (15)	1 (5)		
– transtibial	13 (65)	12 (60)		
– transfemoral	5 (25)	7 (35)		
CAUSE OF AMPUTATION				
– complications of diabetes	15 (75)	14 (70)		
– other	5 (5)	6 (6)		
Student t-test				

to the daily mean pain intensity ($t=1,25$; $df=38$). (Fig 2.)

Pain intensity at the tenth postoperative day was significantly lower in treatment group ($VAS=1,65 \pm 0,80$) versus in control group ($VAS=3,2 \pm 1,15$; $t=5$; $df=38$; $p < 0,01$). (Fig 3.)

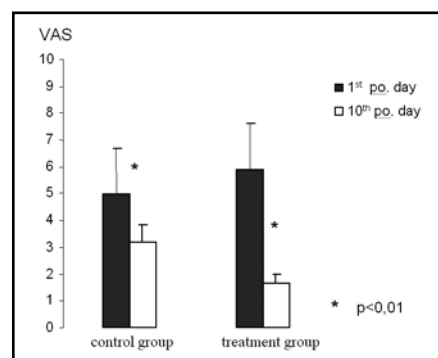


Figure 1
Pain intensity in both group at the first and the tenth postoperative day

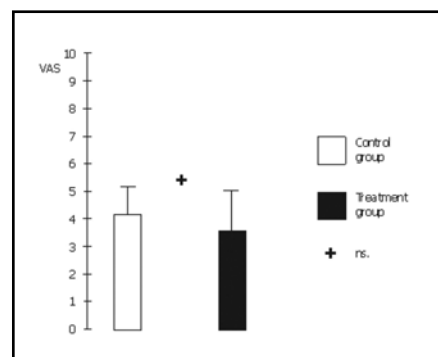


Figure 2
Daily mean VAS scores: control versus treatment group

DISCUSSION

The results of this study indicate that TENS significantly reduced postoperative surgical pain after lower extremity amputations in the patient population sampled. In the tenth postoperative day, pain intensity in treatment group was significantly lower in regard to control group. But, in the both group pain was significantly lower in the tenth day in regard to the first postoperative day. We can ascribe this to influence of postoperative care and administration of nonsteroidal anti-inflammatory drugs. Besides many dimensions of pain, average pain intensity is first component of the pain experience.²⁰ There were no significant differences between groups according to the daily mean pain intensity. Thus, TENS only contributed that postoperative pain would be significantly diminished after limited period of time. The question is: would be pain significantly lower in treatment group at the end of the third postoperative week for example? Post surgical pain is the sharp, localized pain experienced by the patient at the surgical site in the postoperative period, generally one to three weeks following the amputation.⁷ The subjects in both groups described pain as not only sharp, but pricking, aching and cramping pain. These are characteristics of cutaneous and muscle pain.²¹ This pain was moderate on the average, according to the VAS score. The post surgical pain is to be expected as part of surgical trauma to bone, nerve, and soft tissues and is usually self-limited. It will be gradually resolving as edema decreases and the amputation wound heals. According to our results, TENS significantly contributed to this self-limitation of pain after lower extremity amputations.

There are several theories of alternating the perception of pain by TENS. The gate control theory states that stimulation of non-nociceptors or their axons can interfere with the relay of sensation from nociceptors to higher centers in the brain where pain is perceived. TENS stimulates sensory A fibers with high-frequency stimulation. These impulses flood the pathway to the brain and close the "gate" to transmission of pain thus managing the pain threshold. TENS can produce neuromodulation by three routes: presynaptic inhibition of the spinal cord; direct inhibition of an excited, abnormally firing nerve or restoration of afferent input.^{22,23,24} Stimulation of sensory nerves with TENS causes release of the opiates, which minimize the perception of pain.^{25,26}

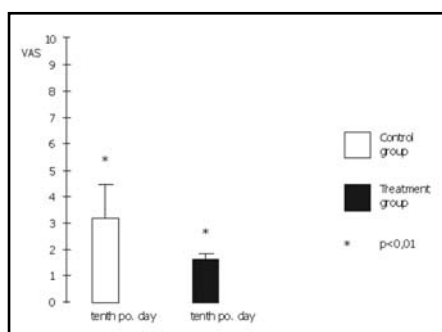


Figure 3

Pain intensity in the tenth postoperative day: control versus treatment group

Vasodilatation induced by TENS alters the ischemic area by enhancing blood flow, reducing the pain response.²⁷ There is theory relates to acupuncture, which is based on energy lines and entry points. Stimulating these points, TENS affects the flow of energy and altering the condition causing pain.²⁸ We think that the gate control theory best represents the affect of TENS on patients with postoperative surgical pain after lower extremity amputations. Additionally, TENS probably affected on the blood flow, improving of edema resorption, diminishing of inflammation and accelerating of wound healing.

We can not completely compare our results with results of other authors. They have treated different acute pain conditions by TENS or they have used different TENS modes or different research protocols in the same contrition.¹⁸ Finsen et al¹⁹ studied the effects of TENS on stump healing and postoperative and late phantom pain in the sample of 51 subjects with major amputation of the lower limb. They compared three different protocols: sham TENS and chlorpromazine medication, sham TENS only, and active low frequency TENS. They found no significant differences in the analgesic requirements or reported prevalence of phantom pain between groups during the first four weeks. In this randomized controlled trial the authors, contrary to us, did not establish any significant effects of TENS. Placebo controlled clinical trials should be used to determine absolute effectiveness of treatment so that the effects due to active ingredient (TENS) can be isolated from the effects associated with the act of giving the treatment. In this sense, Carroll et al. demonstrated the impact of using non-randomized trials in determining TENS effectiveness; 17 of 19 non-randomized controlled trials (non-RCTs) reported that TENS had a positive analgesic effect, whereas 15 of 17 randomized controlled trials (RCTs) reported that TENS had no effect for postoperative pain.¹ But, we agree with Johnson,²⁹ who says that we should be careful in accepting the findings of the systematic reviews on TENS and postoperative pain without further scrutiny.

Our results are in accordance with the attitudes of many authors.^{8,9,10,24,30} But these results must be accepted with some reserve. This was RCT but not placebo RCT. Pain is multidimensional phenomenon. There is the impact of patient motivation on the pain intensity.³¹ We can not exclude influence of self-suggestion on the rating of pain intensity in the treatment group. Besides the fact that VAS is good clinical tool for estimation of pain,^{23,26} it can not enclose all of its dimension.³¹

The results of this study relate specifically to the conventional TENS parameter; that is high- frequency, low-intensity mode. Additional studies looking at other TENS parameters for pain modulation could be explored.

CONCLUSION

Conventional TENS (dose: 200 microseconds, 110 Hz, 44 V), administered two hour a day in ten days, significantly reduced postoperative surgical pain in twenty subjects with lower extremity amputation.

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