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.

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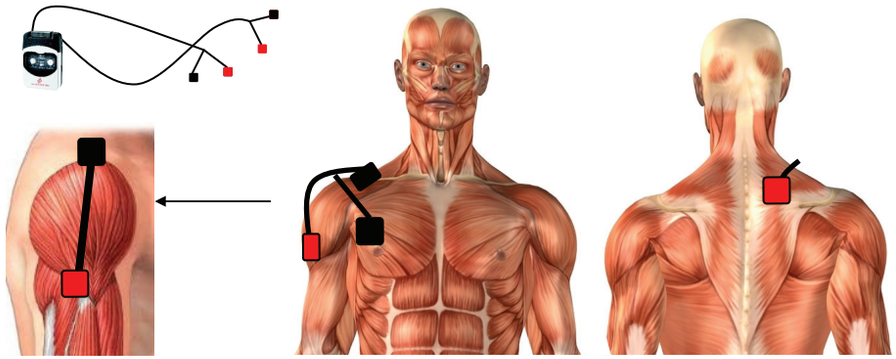
ELECTRODE PLACEMENT CHARTS

SHOULDER



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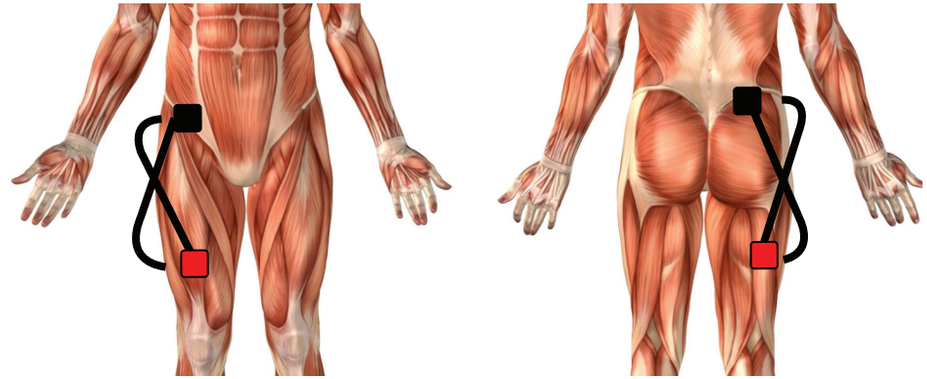
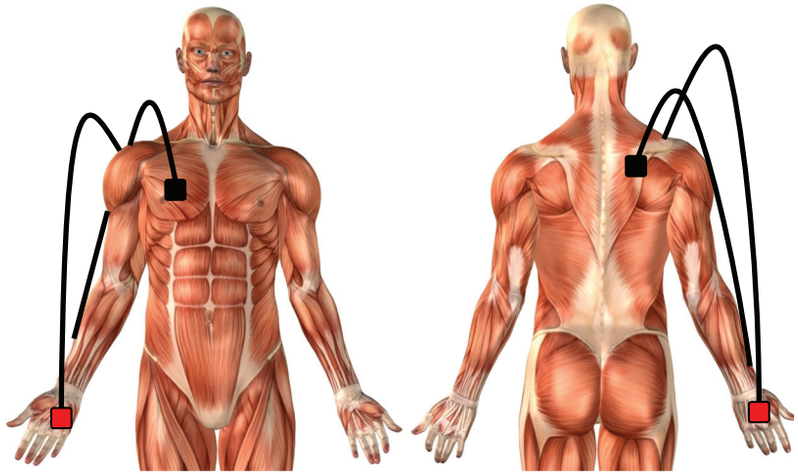
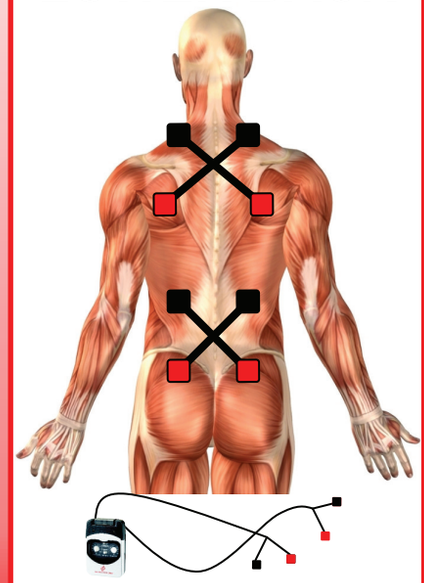


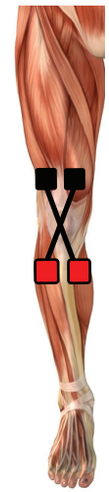
WRIST, ARM, ELBOW & UPPER ARM



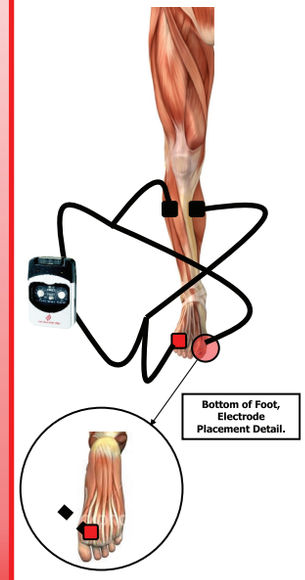
UPPER & LOWER BACK



KNEE



FOOT



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Medical Finance Resources

PATIENT INFORMATION

Patient's last name: First: Middle:			❑ Mr. ❑ Mrs.	❑ Miss ❑ Ms.	Marital status (circle one) Single / Mar / Div / Sep / Wid	
Is this your legal name? ❑ Yes ❑ No	If not, what is your legal name?	(Former name):	Birth date: / /	Age:	Sex: ❑ M ❑ 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? ❑ Yes ❑ 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:	❑ Self	❑ Spouse	❑ Child	❑ Other		
Name of secondary insurance (if applicable):	Subscriber's name:		Policy#	Group#		
Patient's relationship to subscriber:	❑ Self	❑ Spouse	❑ Child	❑ Other		

PLEASE ENCLOSE COPY OF HEALTH INSURANCE CARD

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

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*

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Phone 732-390-9751
Fax 732-390-4722

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 6.0
IF Stimulator
Precision Combo TENS/EMS
Other DME _____

Primary Diagnosis(es) ICD-9

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

Circle Length of Need: 2-3 months 4-6 months 6-8 months 9+ months

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 _____

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Hypoalgesic Effect of the Transcutaneous Electrical Nerve Stimulation Following Inguinal Herniorrhaphy: A Randomized, Controlled Trial

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§University Tiradentes, Aracaju, Sergipe, Brazil and
‖Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.

Abstract: **We investigated the effect of transcutaneous electrical nerve stimulation (TENS) for inguinal herniorrhaphy postoperative pain control in a prospective, randomized, double-blinded, placebo-controlled study. Forty patients undergoing unilateral inguinal herniorrhaphy with an epidural anesthetic technique were randomly allocated to receive either active TENS or placebo TENS. Postoperative pain was evaluated using a standard 10-point numeric rating scale (NRS). Analgesic requirements were also recorded. TENS (100 Hz, strong but comfortable sensory intensity) was applied for 30 minutes through 4 electrodes placed around the incision twice, 2 and 4 hours after surgery. Pain was assessed before and after each application of TENS and 8 and 24 hours after surgery. In the group treated with active TENS, pain intensity was significantly lower 2 hours ($P = .028$), 4 hours ($P = .022$), 8 hours ($P = .006$), and 24 hours ($P = .001$) after the surgery when compared with the group that received placebo TENS. Active TENS also decreased analgesic requirements in the postoperative period when compared with placebo TENS ($P = .001$). TENS is thus beneficial for postoperative pain relief after inguinal herniorrhaphy; it has no observable side effects, and the pain-reducing effect continued for at least 24 hours. Consequently, the routine use of TENS after inguinal herniorrhaphy is recommended.**

Perspective: ***This study presents the hypoalgesic effect of high-frequency TENS for postoperative pain after inguinal herniorrhaphy. This may reinforce findings from basic science showing an opioid-like effect provided by TENS, given that high-frequency TENS has been shown to activate δ-opioid receptors.***

Key words: *Transcutaneous electric nerve stimulation, postoperative pain, analgesia, inguinal hernia.*

Inguinal herniorrhaphy results in significant postoperative pain that is traditionally treated with opioid analgesics.[7,16] Appropriate doses of opioid medicines, administered sufficiently to control pain, usually result simultaneously in significant side effects that include nausea, dizziness, pruritus, sedation, vomiting, and respiratory complications.[35] Postoperative pain treatment not only can be treated pharmacologically but also with nonpharmacological approaches.[47] Transcutaneous electrical nerve stimulation (TENS) is one of the several nonpharmacological, noninvasive alternatives to drug treatment for painful conditions.[35,42] Moreover, TENS is simple and inexpensive and without side effects.[48]

High-frequency TENS reduces pain by interfering with transmission of the nociceptive input at the level of the spinal cord through activation of δ-opioid and $GABA_A$ receptors, subsequently reducing input through the as-

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1526-5900/$34.00

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cending spinothalamic tract.[1,6,13,20,25,26,39] Several previous studies show TENS applied near the surgical incision reduces postoperative opioid analgesic consumption and reduces pain.[3,9,45] However, no study has presented benefits in using TENS to treat postoperative pain after inguinal herniorrhaphy. The objective of this prospective, controlled, randomized, double-blinded study was to analyze the postoperative pain intensity and the analgesic requirement for patients undergoing unilateral inguinal herniorrhaphy.

Methods

Participants

This study was a prospective, randomized, double-blinded, placebo-controlled trial. The study protocol was approved by Tiradentes University Committee on Human Experimentation (Brazil). After obtaining written informed consent in the preoperative visit, 40 male subjects with ASA (American Society of Anesthesiology) physical status I-II undergoing elective inguinal herniorrhaphy were included in this study. The subjects were randomly assigned to either an active TENS (n = 20) or placebo TENS group (n = 20), using a computer-generated randomization sequence. Randomization occurred in the order in which patients were enrolled in the study according to the computer-generated randomization schedule prepared before the start of the study. A blocking randomization was performed to generate a sequence of allocation to ensure that there was a close balance of the numbers in each group at any time during the study. After every block, the number of participants in each group would be equal, in a 1:1 ratio.

An estimation of desired sample size for dependent groups was determined by using pain intensity scores of the first 15 subjects enrolled in the study. An $\alpha = 0.05$ and power = 70% required a sample size of 20 subjects per group.

The inclusion criteria were (1) use of Lichtenstein surgical technique; (2) no recidivating inguinal hernia (3) surgeries performed in the morning to avoid influences of the circadian cycle[26]; (4) male adults ages between 21 and 45 years; (5) ASA I or II physical status, according to American Society of Anesthesiology[3,18,36,44]; (6) no hearing, visual, or speaking impairments; (7) no cognitive disturbances.[15,23,32]

Exclusion criteria included (1) nonPortuguese speaking; (2) diagnoses of malignant cancer[23,33]; (3) liver (serum bilirubin >2.0 mg/dL), kidney (serum creatinine >1.5 mg/dL),[11] or cardiovascular insufficiency (ejection fraction <35%)[41]; (4) neurological (eg, prior stroke, Parkinson's or Alzheimer's disease, cerebral tumor traumatic brain injury, dementia, multiple sclerosis, or substance abuse) or pulmonary diseases, such as oxygen-dependent chronic obstruction, that would seriously affect the results of the tests[5,9,14,17,22,32]; (5) cardiac illness such as cardiac arrhythmia, angina pectoris, congestive heart failure, uncontrolled hypertension[11,32]; (6) contraindication for TENS application, such as placing electrodes directly over open wounds; (7) chronic use of opioids[11,14,17] or antidepressives[9,43]; (8) preoperative use of opioids (for more than 2 weeks during the 6-month period before surgery as determined by patient interview)[32]; (8) prior TENS use[9,18,23,32]; (9) use of psychoactive drugs or glucocorticosteroid 24 hours before the surgery[49]; (10) conditions precluding use of TENS, such as a pacemaker, because of the unknown effects of TENS on the electrical conduction system of the heart[5,11,23,32,34,46]; and (11) morbid obesity (weight more than 100 pounds of ideal weight).[5] Persons with alcohol intake exceeding 2 drinks per day were also excluded based on the National Institute on Alcohol Abuse and Alcoholism criteria of 60 drinks per month as heavy drinking and the recent findings that heavy social drinking is associated with mild and moderate cognitive deficits.[29,46]

Two investigators were involved in data collection in this study and were trained to standardize treatment and measurements. Investigator 1 was responsible for the patient evaluation and pain assessment in all subjects. Investigator 2 applied TENS treatment in all patients. Only investigator 2 knew if the subject received active or placebo TENS therapy. Both investigator 1 and the subject were blinded to the TENS therapy. Further, to minimize investigator bias, the investigator who applied TENS therapy instructed patients to say nothing about their stimulation-related perception to the investigator who was assessing pain intensity. The patients were told that 2 types of TENS treatment were being tested, one in which a strong but comfortable tingling sensation would be perceived and one in which little or no sensation would be perceived, a silent stimulation. The placebo TENS group received no electrical stimulation, but the unit displayed an active indicator light, suggesting to the patient that the unit was active.

Apparatus and TENS Treatment

TENS treatment was provided with the use of a Tensys ET 871, KLD Biossistemas unit (São Paulo, Brazil), whose generator emits asymmetrical, balanced, biphasic square waveform and has control buttons for variation for frequency and amplitude. Four autoadhesive electrodes (12 cm^2) were placed on the skin at the inguinal region parallel to the surgical incision (Fig 1). In the active TENS group, TENS was delivered for 30 minutes at a frequency of 100 Hz and a pulse duration of 100 μs. TENS therapy was applied twice, 2 and 4 hours after surgery. Sensory intensity (strong tingling sensation but no muscle contraction) was obtained at a range between 9 and 18 mA on the TENS unit for the active TENS group. The intensity (amplitude) on each channel was increased until the patient was able to feel a comfortable tingling sensation. The placebo group was identical to the treatment unit but did not provide current. It is important to emphasize that the TENS unit was calibrated before the start of data collection using a digital oscilloscope TEKTRONIX TDS210 (Tektronix Inc., Beaverton, OR).

Procedures

Surgical as well as anesthetic procedures were standardized and performed by a single surgical team. Be-

sides epidural anesthesia (20 mL of 2% plain lidocaine), no additional anti-inflammatory or analgesic opioid drugs were administered during the intraoperative period. A standard herniorrhaphy was performed through a straight incision parallel to the inguinal ligament and placement of mesh protheses of polypropylene according to Lichtenstein et al.[24] No local infiltration of the incisional area was used and preoperative analgesia was recorded.

The patients then were transferred to the Post Anesthesia Care Unit (PACU) and after pain measurements, electrodes were placed in the dermatome corresponding to the surgical incision. Two applications of TENS were performed at intervals of 2 hours each (2 and 4 hours after surgery), both with a duration of 30 minutes. Subjects received dipyrone (1 g IV) every 6 hours as requested for control of pain after surgery. Subjects also received metochlopramide (10 mg IV) every 4 hours as requested for nausea. Nursing staff delivered all postoperative medications.

Pain Measurements

All subjects (treated and control) received equal baseline assessments. An 11-point numeric rating scale (NRS) was used to assess self-report of pain intensity at rest. Subjects were required to state a number that indicated their postoperative pain intensity between 0 and 10, where 0 was no pain and 10 was the most intense pain imaginable. This tool has established validity and reliability for measuring acute[10,12,19,22,28] and postoperative pain.[37] The NRS was also used to measure satisfaction of the patients with the treatment (from 0, no satisfaction, to 10, major satisfaction with the treatment). These evaluations were done before and after each active or placebo TENS application (2 and 4 hours after surgery) as well as 8 and 24 hours after the surgery. Postoperative analgesic requirements as well as request for nausea medication were recorded.

TENS-Related Questions

After discharge from the PACU, the patients were transferred to a hospital room where they stayed until discharge from the hospital. A short follow-up was performed before discharge 24 hours after the surgery. The subjects, both active and placebo, were asked: (1) Was TENS therapy comfortable for you? (2) Would you like to use TENS again if you have to undergo another surgery in the future?

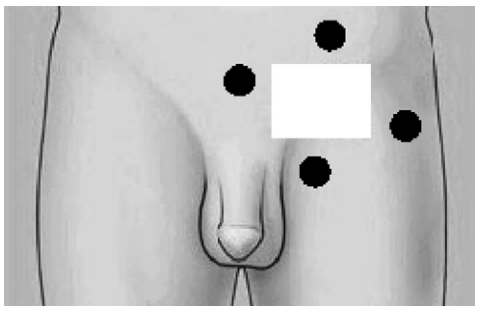

Figure 1. Schematic representation for the placement of electrodes. White rectangle represents dressing covering the incision on the inguinal region; black circles represent electrodes.

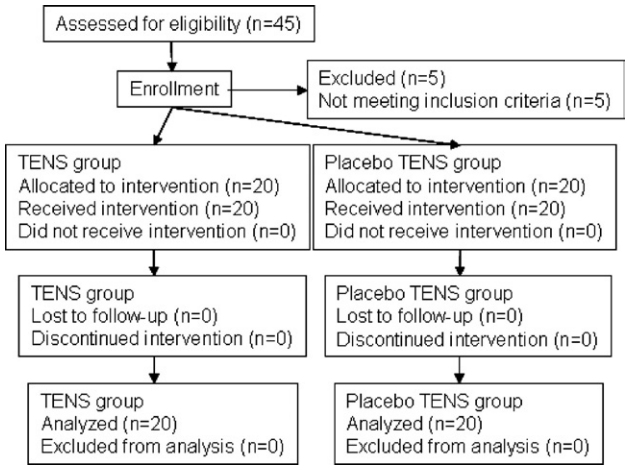

Figure 2. Eligibility and enrollment of subjects. TENS, transcutaneous electrical nerve stimulation.

Statistical Analysis

Data for the active TENS and placebo TENS groups were compared by using the Mann-Whitney test, and intragroup differences were analyzed by using the Wilcoxon matched-pairs signed-ranks test. Basic characteristics of the population and differences for analgesic requirement were compared by using Student's *t* test, and time between arrival at PACU and beginning of stimulation was compared by ANOVA. Data are represented as mean ± standard error mean (SEM). P values $< .05$ were considered statistically significant.

Results

Subject Characteristics and Trial Profile

Forty-five men who underwent inguinal herniorrhaphy were enrolled in this clinical trial. Five patients were not included in the sample due to recidivating hernia (n = 2) and advanced age (n = 3). Twenty men were randomly assigned to the active TENS group, and the other 20 men to the placebo TENS group. The randomization process was computer-generated in blocks (20 patients per group). Fig 2 depicts the trial profile according to the CONSORT flowchart diagram. There was no significant statistical difference in the mean age, weight, height, body mass index, and ASA physical status at enrollment between the groups. Anesthetic and surgical

Table 1. Basic Patient Characteristics

Characteristics	TENS (Average ± SEM)	Placebo TENS (Average ± SEM)
Age (y)	48.5 ± 10.8	42.2 ± 17.5
Weight (kg)	76.0 ± 4.3	77.8 ± 3.3
Height (cm)	172 ± 3	168 ± 5
Body mass index (kg/m^2)	25.7 ± 0.8	27.5 ± 0.3

Table 2. Mean Pain Scores for TENS and Placebo TENS Groups

Postoperative Period	TENS (Average ± SEM)	Placebo TENS (Average ± SEM)	P Value
2 h before TENS	5.2 ± 1.8	5.3 ± 2.5	.654
2 h after TENS	1.4 ± 1.2	5.0 ± 3.4	.028*
4 h before TENS	3.7 ± 1.3	5.0 ± 3.1	.304
4 h after TENS	0.9 ± 0.8	4.8 ± 3.6	.022*
8 h	1.7 ± 1.2	5.9 ± 3.3	.006*
24 h	0	3.4 ± 2.2	.001*

Mann-Whitney test, *$P < .05$. TENS, transcutaneous electrical nerve stimulation.

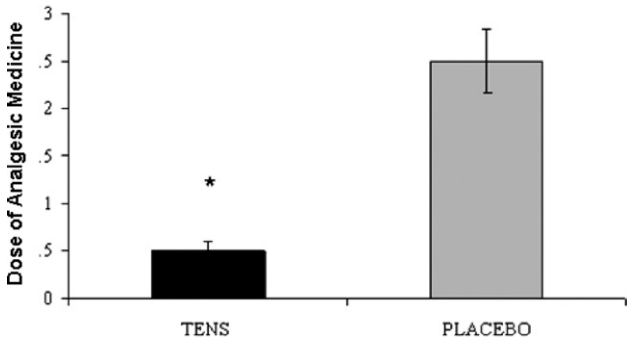

Figure 3. Mean number of doses of analgesic medicine for transcutaneous electrical nerve stimulation (TENS) (n = 20) and placebo TENS (n = 20). *$P = .001$.

times also showed no significant differences between groups ($P = .6$ and $P = .5$, respectively). Table 1 summarizes the basic characteristics of the groups.

The amount of time subjects waited between their arrival at PACU after the surgery and beginning of stimulation with TENS averaged 14 minutes and did not differ between treatments ($P = .67$). Subject activity before TENS did not differ given that all patients stayed at rest in bed.

Pain Outcomes (Numerical Rating Scale/ NRS)

The mean pain intensity was not different between groups at 2 hours postoperative time point before TENS, averaging 5.2 ± 1.8 for the active TENS group and 5.3 ± 2.5 for the placebo TENS group ($P = .654$). After the assigned treatment, the mean NRS score 2, 4, 8, and 24 hours after TENS were significantly lower in the active TENS group when compared with the placebo TENS group ($P = .028$, $P = .022$, $P = .006$, and $P = .001$, respectively). The pain intensity evaluation done after TENS application (2 and 4 hours after surgery) showed a reduction in pain intensity only in the active TENS group. Outcome data are depicted in Tables 2 and 3.

Request for Pharmacological Analgesia

Fig 3 shows that there were significant differences in the total amount of analgesic intake. The patients included in the active TENS group requested less analgesic medicines than placebo TENS group ($P = .001$). On average, subjects in the active TENS and placebo TENS groups consumed 0.5 and 2.5 doses of dipyrone, respectively, which indicates that some of the patients allocated in the TENS group did not request additional medication.

TENS-Related Questions

No subject reported that TENS sensation was irritating or uncomfortable, and all subjects stated it reduced their pain. About 95% of the subjects, both active and placebo, reported that they would use TENS again in a future postsurgical period to treat their pain.

Discussion

The aim of the study was to investigate the hypoalgesic effect of high-frequency TENS after unilateral inguinal herniorrhaphy. To this end, the effect of 100 Hz TENS was investigated over the first postoperative 24-hour period. Outcomes of this study showed that active TENS significantly reduced pain intensity and analgesic requirements when compared with placebo TENS. We chose to assess postoperative pain after inguinal herniorrhaphy because it is easily standardized, easy to enlist patients, and the pain it produces is usually not severe. To our knowledge, this is the first study showing the effectiveness of TENS in reducing postoperative pain after inguinal herniorrhaphy. In contrast to the current study, both Gilbert et al[16] and Smedley et al[41] showed no effect of TENS on postoperative pain or analgesic intake in patients undergoing unilateral inguinal herniorrhaphy. These 2 studies used 70-Hz frequency TENS delivered at 180-μs pulse duration and a sensory intensity, similar to the current study. However, the surgical procedures used by Gilbert et al[16] and Smedley et al[41] were different from the current study. The current study used the Lichtenstein technique, whereas the other 2 studies used the Shouldice method. The Shouldice method uses a straight incision

Table 3. Mean Pain Scores for TENS and Placebo TENS Groups

Group	Postoperative Period	Before TENS (Average ± SEM)	After TENS (Average ± SEM)	P Value
TENS	2 h after surgery	5.2 ± 1.8	1.4 ± 1.2	.007*
	4 h after surgery	3.7 ± 1.3	0.9 ± 0.8	.007*
Placebo TENS	2 h after surgery	5.3 ± 2.5	5.0 ± 3.4	.216
	4 h after surgery	5.0 ± 3.1	4.7 ± 3.7	.713

Wilcoxon matched-pair, signed-rank test, *$P < .05$. TENS, transcutaneous electrical nerve stimulation.

parallel to the inguinal ligament, a nylon darn repair of the posterior inguinal wall, and closure with subcuticular polyglycolic acid. The Shouldice method likely influences postoperative pain intensity making it more severe. Aytaç et al[2] compared the outcomes after Lichtenstein open mesh repair (n = 121) and Shouldice repair (n = 120) for the surgical treatment of unilateral inguinal hernias. The need for analgesic medication after mesh repair was lower and the time for return to work was shorter in the Lichtenstein group compared with Shouldice group ($P < .05$). According to Sikorszki et al,[38] Lichtenstein's method has become the gold standard because of its highly favorable results: simple technique, minimal postoperative pain, recurrence rate below 1%, short hospital stay, very low complication rate, and early return to physical activity.

We suggest that the differences between studies are related to the severity of postoperative pain; TENS is more effective with lower levels of postoperative pain. In support, Benedetti et al[3] assessed effectiveness of TENS on postoperative pain for patients undergoing thoracic surgical procedures (n = 324) by assessing the time for the first analgesic request and the total medication intake during the first 12 hours. TENS was not effective in the posterolateral thoracotomy group, which produced severe pain, but was useful as an adjunct to other medications in the muscle-sparing thoracotomy, costotomy, and sternotomy groups, which produce moderate pain. This indicates that TENS is useful after thoracic surgical procedures only when postoperative pain is mild to moderate, being ineffective for severe pain.

Frequently, TENS is used as a complementary therapy to analgesic medication, psychological interventions, and physical therapeutic procedures to offer postoperative comfort to the patients reducing the pain intensity and duration.[1,5,27] Our data show a reduction in analgesic intake with active TENS, which is a common finding for studies examining effectiveness of postoperative pain being confirmed in a recent systematic review.[4]

We hypothesized that TENS used in combination with some analgesic drugs would decrease the analgesic requirement necessary to produce pain relief, and thus reduce the risk of their side effects such as nausea, dizziness, pruritus, sedation, vomiting, and respiratory complications.[20,30,31] Wang et al,[45] comparing the effect of high-frequency (100 Hz) and low-frequency (2 Hz) TENS in 101 gynecological patients undergoing lower abdominal procedures, showed that 100-Hz TENS decreased the hydromorphone requirement by 65% (sham 23%) and reduced the duration of PCA therapy, as well as the incidence of nausea, dizziness, and pruritus. This suggested that high-frequency TENS significantly decreased the PCA opioid requirement and opioid-related side effects after low intra-abdominal surgery. Similarly, animal studies show that TENS in combination with analgesic medications enhances analgesic effect requiring a lower analgesic dose to produce the same analgesic effect.[8,40] We therefore suggest that TENS can be used as an analgesic therapy after inguinal herniorrhaphy or, at least, can be administrated in combination with analgesic drugs as a multimodal analgesic system, permitting greater reduction of the postoperative pain intensity, decreasing analgesic drug intake and decreasing development of drug-related side effects. We conclude that TENS is a valid and safe option for pain relief in patients with liver or kidney disease, particularly if these organs have dysfunction of metabolism and excretion of analgesic drugs, which is a contraindication to the drug therapy. It has become apparent that TENS is a useful nonpharmacological treatment for pain and may have significant clinical effects and benefits for valid to moderate postoperative pain in a specific type of patient population. The opioid alkaloids are extensively metabolized mainly in the liver and predominantly excreted via the kidney.[17] Thus, TENS may be particularly useful for patients that have liver or kidney disease. Although TENS uses endogenous opioids, these are degraded at the site of release in the central nervous system. TENS offers a safe alternative and adjunct treatment for pain relief after surgery.[17]

The reduction in pain by TENS is expected to increase functional activity after surgery. In fact, in patients after thoracotomy, high-frequency TENS not only decreased opioid requirements, it also increased the spirometric breath function.[32] Specifically, the FEV_1, FVC, and PaO_2 were increased and $PaCo_2$ was decreased after treatment with TENS when compared with the placebo control group. Similarly, after abdominal surgery, high-frequency TENS reduces pain during walking and deep breathing and increases walking function.[32]

Our findings also showed that most patients judged TENS as a comfortable therapy and would use TENS again in the case of a new surgery. Kaplan et al[21] reported that most patients show satisfaction when they use the TENS. In the study by Hamza et al,[18] patients said that the massage-like effect caused by TENS was comfortable and improved the quality of sleep. Moreover, about 75% of the patients in the same study indicated that they would use TENS again in another surgical procedure, as found by Chen et al.[9]

The current study showed that active TENS had a greater effect than placebo. We were, however, unable to determine the extent of the placebo effect in the current study as we did not have a "no TENS" control group. However, an adequate placebo and sufficient blinding of the subjects is suggested, since 95% of all subjects, both active and placebo, said they would use TENS for a future surgical procedure.

Our findings showed significant reductions in postoperative pain using high-frequency TENS at sensory intensity (strong but comfortable tingling sensation, with no muscle contraction). In a systematic review, Bjordal et al[4] showed that there was a significant difference in analgesic consumption between groups receiving an adequate strong, submaximal electrical stimulation and groups given a nonoptimal (above sensory threshold) electrical stimulation.

A possible limitation in our study is that pain rating index was assessed by means of NRS only at rest. Evalua-

tions of pain intensity during movement and functional tasks were not performed in the current study but should be included in future investigation. Previously, several studies showed improvement in pain during walking, deep breathing,[32] and movement.[32,42] There is also an improvement of walking and breathing function in postoperative subjects with total knee replacement or thoracotomy, respectively.[32,42] However, TENS had no effect on resting pain after surgery[31] or visceral pain resulting from uterine contractions in patients after cesarean section.[42] These data together suggest that pain with movement is likely to be reduced by TENS in addition to resting postoperative pain. This would suggest that patients should recover faster after surgery by increasing activity, resulting in faster discharge from the hospital, as previously shown.

Although we did not evaluate expectancy of treatment in the current study, we believe it is important to determine the degree to which belief in the efficacy of the therapy delivered influences outcome. Hamza et al[18] reported that about 80% of the patients in active groups believed that TENS reduced their pain, against only 24% in the control (nonplacebo) group, supporting the notion that there was an increased satisfaction with treatment in the active group. This further supports the notion that an adequate placebo group be used to assess efficacy of TENS.

This double-blinded, randomized, placebo-controlled study showed that high-frequency TENS was an efficacious therapy to reduce postoperative pain intensity and analgesic consumption after herniorrhaphy, which produces mild to moderate pain. We reinforce that the absence of complications and adverse effects of TENS compared with conventional opioids and nonopioid analgesics makes TENS a safe and reliable therapeutic procedure.

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Transcutaneous Electrical Nerve Stimulation for Postlaparotomy Pain

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This study was designed to evaluate the transcutaneous electrical nerve stimulation (TENS) postoperative program administered by a physical therapy department. A surgeon, a physical therapist, a recovery room nurse, and unit nurses participated in the program which included preoperative evaluation and patient education, application of sterile electrodes parallel to the incision in the operating room, TENS activation in the recovery room, follow-up visits, and data collection. Seventy-five patients who underwent laparotomy and received TENS at the most comfortable machine settings were compared by chart review to 75 patients who had undergone similar surgical procedures performed by the same surgeon before TENS postoperative pain management had been instituted. The TENS was applied for an average of five days; machine settings of intensity, frequency, and pulse width tended to be midrange. The TENS group took significantly less pain medication, but the length of hospital stay was not significantly different. Patients with TENS rated their pain on 10-point scales as more intense than uncomfortable. This study demonstrated that a well-structured interdisciplinary program of postoperative TENS management can reduce the amount of pain medication taken by patients after laparotomy.

Key Words: *Pain, postoperative; Transcutaneous electrical nerve stimulation.*

Transcutaneous electrical nerve stimulation (TENS) is a technique for controlling pain that is undergoing increased clinical application in physical therapy. The December 1978 issue of PHYSICAL THERAPY provided background, theory, and guidelines for the use of TENS. Santiesteban and Sanders have provided further suggestions for establishing a postsurgical TENS program.[1]

A program of TENS is reported to be a noninvasive, nonaddictive method of relieving postoperative pain.[2-11] Commercially manufactured units that are small, portable, and battery-operated are used to generate a low-frequency, pulsed electrical current through the skin. The patient usually reports a sensation from this current that blocks or alters the ongoing perception of pain. Wolf has given perspectives on several current theories used to explain the effectiveness of pain relief from TENS.[12]

Many studies have shown that patients in a postoperative TENS program do not report as much pain and do not need as much pain medication in the postoperative period as patients not in a TENS program.[2-11] Postoperative complications of ileus and atelectasis have been reported to be less frequent with TENS application, and the number of days in intensive care and the total hospital stay have been reduced.[4, 6, 7, 11] Other beneficial effects have also been suggested, such as improved range of motion, activity level, alertness, function, sleep patterns, and healing in the postoperative period.

The purpose of this paper is to describe how a program for the use of TENS for postlaparotomy pain was instituted and evaluated by the Physical Therapy Department at St. Margaret Memorial Hospital. Although the literature supported TENS as an effective modality in relieving postoperative pain and complications, a controlled introduction of TENS for postoperative pain was instituted by our physical therapy department to determine whether TENS

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could produce the reported beneficial effects when used according to our protocol with our particular patient population.

We believe that the most effective use of TENS depends on the competence, the commitment, and the coordination of an entire team that includes the patient, his family, the physician, the physical therapist, the operating room staff, the recovery room staff, and the nursing staff. The successful implementation of a protocol is therefore contingent on knowledgeable staff members who value TENS as an effective method of pain management. Our hypothesis was that patients who received the postoperative TENS program would require less postoperative pain medication than patients who had undergone similar operations who did not receive the TENS program.

METHOD

Educational Program for Staff

A format was developed for the education of all medical professionals involved with the TENS postoperative program. The format included specific goals and behavioral objectives relating to knowledge of the theory and correct use of TENS. The physical therapy staff provided a uniform educational program on a continuing basis through in-service training that included lecture, demonstration, and practice sessions. These group sessions were followed by individual discussions as needed. Staff physicians were informed of the postoperative TENS program, and if they were interested, further information was provided to them individually.

TENS Program

Referral procedure and introduction. Physicians interested in the use of TENS for postoperative pain were requested to make routine preoperative referrals to physical therapy for assessment and postoperative TENS. The physicians were relied on to introduce the concept of TENS use for pain control to the patients and to indicate that pain medications also were available as needed.

Preoperative visit. During the preoperative visit, the therapist explained to the patient (and family, if present) the rationale for TENS therapy after surgery, how TENS worked to control pain, and what the patient should expect from TENS therapy after surgery. The therapist identified the parts of the TENS equipment* and demonstrated how to turn the unit on and off, adjust the intensity, and change the batteries. A trial application of TENS to the approximate area of incision was made. The patient experienced the sensation of TENS and was encouraged to practice using the equipment. At this time, the most comfortable and effective intensity, pulse width, and frequency of TENS were determined and recorded. The patient was instructed in recording postoperative TENS use and also was taught deep breathing and leg exercises. The patient was then asked to demonstrate these tasks. Supplementary written educational materials were given to the patient and included a pamphlet on TENS and a sample recording sheet for times when the unit would be used during the postoperative procedure.

The therapist recorded the baseline data at this time on a preoperative assessment form that included 1) brief medical and pain history, 2) current pain medication and effectiveness, 3) TENS machine settings, 4) patient acceptance of TENS, 5) patient description of the TENS sensation, and 6) findings of a physical examination. The TENS machine used had settings from 0 to 10 for intensity, frequency, and pulse width and corresponded to values of 0 to 90 V for intensity, 10 to 100 pps for frequency, and 120 to 340 μsec for pulse width.

Operating room procedure. An ample supply of sterile disposable electrodes† was maintained in the operating room by the physical therapist. Normal procedures were followed except that after the surgery the electrodes were cut to approximately the same length as the incision and were placed parallel and adjacent to the incision. A telfa pad was sometimes placed over the electrodes to prevent them from being pulled loose when the dressings were changed.

Recovery room procedure. Whenever possible, the physical therapist attached the lead wires from the electrodes to the TENS unit in the recovery room before the patient fully awakened. The units were set at the preoperative pulse width, frequency, and intensity levels that had produced a comfortable sensation in the patient during the preoperative visit. Documentation of this procedure was made on a TENS recovery room record.

Postoperative procedure. On the first postoperative visit, the therapist reviewed the use of the TENS unit with the patient. The physical therapist also reviewed the operation of the unit with the nursing staff and outlined the procedures for checking the batteries and the electrode placement. At this time, the nurses were once again encouraged to use TENS as a method of pain control. An extra set of batteries was left at the nurses' station to be used if necessary. Any change in

* MicroCeptor II, Medgeneral, 10800 Lyndale Ave S, Minneapolis, MN 55420.

† Stimtech stimflex/S1, Codman & Shurtleff, Inc, Randolph, MA 02368.

TABLE 1

Surgical Procedures for Number of Patients in TENS Group and Comparison Group

Surgical Procedure	TENS	Comparison	Total
Cholecystectomy	26	26	52
Inguinal hernia repair	13	13	26
Cholectomy	9	9	18
Gastric and pancreatic surgery	9	9	18
Abdominal hernia repair	5	5	10
Hiatal hernia repair	2	2	4
Other abdominal surgery	11	11	22
TOTAL	75	75	150

TENS settings or in the patient's condition was reported to the physical therapist.

The unit remained on constantly for the first two days postoperatively. During this time, the physical therapist saw the patients twice daily to evaluate their pain and functioning. The TENS unit was also examined to determine if it was functioning properly, and the settings were recorded. After 48 hours, the patients adjusted the amplitude and duration of TENS as needed for pain and were asked to document these factors. The patients were also asked to record the amount of pain they were having. The therapists asked the patients twice daily to rate how uncomfortable and how intense their pain was. The discomfort was measured by asking the patient to rate how uncomfortable his pain was by choosing a point along a diagonal line with numbers from 0 to 10 on the left and the following words across from the numbers: 0—absent, 2—uncomfortable, 4—upsetting, 6—miserable, 8—excruciating, and 10—worst imaginable. The intensity of the pain was measured by showing the patient another diagonal line with numbers 0 to 10 on the left and asking the patient to choose a point along the scale that rated how strong the pain was. The words on the right of this line corresponding to the numbers were as follows: 0—none, 2—mild, 4—moderate, 6—marked, 8—severe, and 10—most intense possible. These scales were based on work that suggested that sensory and affective verbal descriptors provide a valid scaling method that can discriminate between sensory intensity and affect, or discomfort.[13, 14]

Nurses and physical therapists continued to monitor and encourage correct usage of TENS and to assist in recording the needed information. Discontinuation of TENS was based on painless activity, or on other conditions deemed appropriate by the physician. When TENS was discontinued during the weekend or evening, the nurses turned off the unit and disconnected the lead wires. The electrodes were left in place, however, in case the unit was needed again. The time, date, and reason for discontinuation were noted.

Discharge Summary

A final data collection was made and a discharge summary completed by the therapist. Data included the patient's and the therapist's opinion of the effectiveness of TENS and reasons why TENS was considered effective or not effective. Information regarding medication usage and days in the hospital was obtained from the medical records.

Comparison of Groups

Information from the medical records over a 10-month period of 75 patients using TENS who had undergone laparotomies were compared with 75 patients who had undergone similar operations performed by the same surgeon before the TENS program had been instituted. (The numbers of different surgical procedures are presented in Tab. 1.) There were 50 women and 25 men in the TENS group and 42 women and 33 men in the comparison group. The mean age of both groups was 57 years.

The doses of pain medication taken postoperatively were chosen to reflect a comparison of postoperative pain in each group. The amounts in milligrams of meperidine hydrochloride given intramuscularly were available from the medication record sheets. Doses rather than amount of pain medication were chosen as the basis for comparison. It was assumed that the total amount of pain medication that patients receive is determined by their physiological characteristics, such as age and size, as well as the amount of pain they experienced; whereas, doses represent the number of times medication is requested or required and therefore more accurately reflect the levels of pain.

Meperidine hydrochloride was the most commonly used postoperative pain medication. Most doses of meperidine hydrochloride were 75 mg with occasional doses of less for older or smaller patients. Pain medication was ordered for every three or four hours as needed. Occasionally, other pain medications were used instead of, or in addition to, meperidine hydrochloride and were also counted. The medications included in the counts of other pain medication doses were propoxyphene hydrochloride, propoxyphene napsylate with acetaminophen, acetaminophen, oxycodone hydrochloride, pentazocine hydrochloride, and morphine sulfate.

RESULTS

The average length of postoperative stay was 9.4 days for the TENS group and 9.2 days for the comparison group. A comparison of the amounts of pain medication taken by the TENS group and the comparison group is presented in Figure 1. The daily means with standard deviations and p values are

TABLE 2

Mean Doses of Meperidine Hydrochloride (mg) Taken by TENS and Comparison Group

Post Surgical Day	TENS Group		Comparison Group		*p*
	$\bar{X}$	*s*	$\bar{X}$	*s*	
1	0.96	0.91	1.13	0.89	.11
2	1.79[a]	1.67	2.37	1.75	.02
3	1.04[a]	1.39	1.65	1.96	.02
4	0.57[a]	1.08	0.93	1.48	.05
5	0.39	1.06	0.71	1.45	.06
Cumulative Average	4.75[a]	4.40	6.80	6.10	.01

[a] Significant at .05 level or less.

TABLE 3

Mean Doses of Other Pain Medication (mg) Taken by TENS and Comparison Group

Post Surgical Day	TENS Group		Comparison Group		*p*
	$\bar{X}$	*s*	$\bar{X}$	*s*	
1	0.12	0.46	0.04	0.20	.09
2	0.20[a]	0.52	0.41	0.95	.04
3	0.35	0.81	0.56	1.09	.09
4	0.24[a]	0.75	0.65	1.21	.01
5	0.19[a]	0.51	0.45	1.00	.02
Cumulative Average	1.09[a]	2.04	2.10	3.20	.01

[a] Significant at .05 level or less.

presented in Tables 2 and 3. The TENS group took less meperidine hydrochloride each day of the five-day postoperative period and therefore less pain medication cumulatively for the period. The day of surgery was considered Day 1. Days 2 and 3 were the days when the most merperidine hydrochloride was required by both groups; and the differences in the amount of meperidine hydrochloride between groups were significant on Days 2, 3, and 4 at the .05 level using a one-tailed independent test on the mean doses for comparison.

The TENS group of patients also took significantly less other pain medications on postoperative Days 2, 4, and 5. The TENS group consistently had more patients each day who required no meperidine hydrochloride or other pain medication.

Table 4 presents the average doses of all pain medication (meperidine hydrochoride and other pain medications together) taken by patients with similar surgical procedures for the five-day postoperative period. The amount of reduction demonstrated by the TENS group in the average doses of the pain medication required is shown as a percentage representing the average difference in the amount taken by the two groups over the amount taken by the group of patients who did not receive TENS. As can be seen in the third column of Table 4, the average doses taken by the group of patients who received the TENS after hiatal and abdominal hernia repair were 76 percent less during the five-day postoperative period than the average doses of the comparison group. The second most successful group by surgical procedure was the cholecystectomy with a 38 percent reduction in average doses for the TENS group. The least successful group was those with cholectomy surgeries; the reduction in average doses taken by the TENS group was only 8 percent.

The TENS unit was used an average of 4.6 days ($s \pm 1.7$) postoperatively. Figure 2 indicates the percentage of patients remaining on TENS each postoperative day. After Day 5, only 15 percent of the patients were still using TENS. At the time of discon-

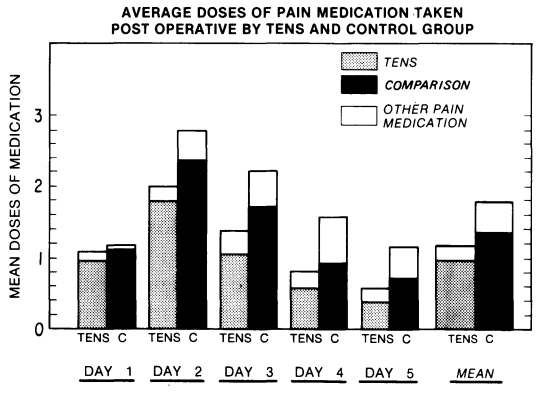

Fig. 1. Average doses of pain medication taken during the five-day postoperative period by TENS group and comparison group.

TABLE 4

Average Doses and Amount of Reduction in Average Doses of Pain Medication Taken Five Days Postoperatively by Patients with Similar Surgical Procedures

Surgical Procedure	Average Doses (mg)		Amount of Reduction in Average Doses by TENS Group (%)
	TENS Group	Comparison Group	
Hiatal and abdominal hernia repair	1.85	7.85	76
Cholecystectomy	5.81	9.42	38
Other abdominal surgery	5.00	7.91	37
Gastric and pancreatic	6.78	9.11	26
Inguinal hernia	4.23	5.07	17
Cholectomy	7.33	7.99	8

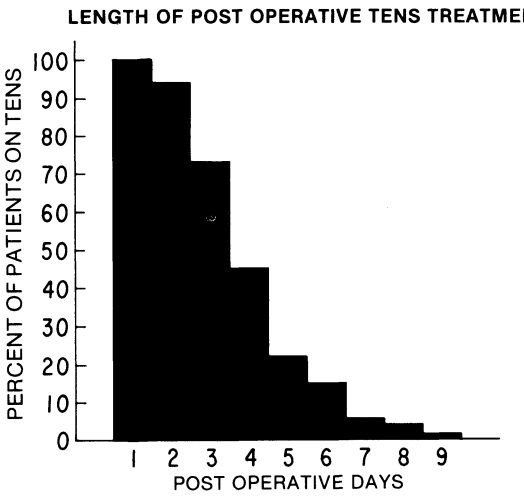

Fig. 2. Percentage of patients on TENS for each postoperative day.

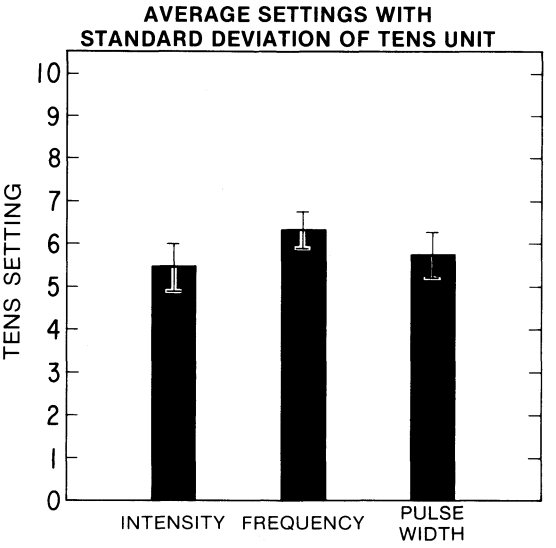

Fig. 4. Average intensity, frequency, and pulse width settings used for the TENS during the postoperative period.

tinuation of TENS, the physical therapists administering the postoperative treatments subjectively reported that TENS had been effective on 83 percent of the patients, not effective on 10 percent, and questionably effective in 7 percent of the reported cases. On a subjective 4-point scale of attitude toward TENS, most patients were positive toward the treatments.

The results of the pain intensity and discomfort scoring done twice daily by the patients receiving the TENS is shown in Figure 3. Patients receiving postoperative TENS consistently reported the mean discomfort less than the mean intensity of their pain. However, this difference was not significant. This subjective reporting of pain did show a consistent decrease in pain starting from a maximum on postoperative Day 2, when most pain medication was requested by both groups. Seventy-five percent of the patients receiving TENS were reported to be functioning out of bed on the day after surgery. Most patients in the TENS group carried out their breathing and exercise program, but no reliable data on the other group were available for comparison.

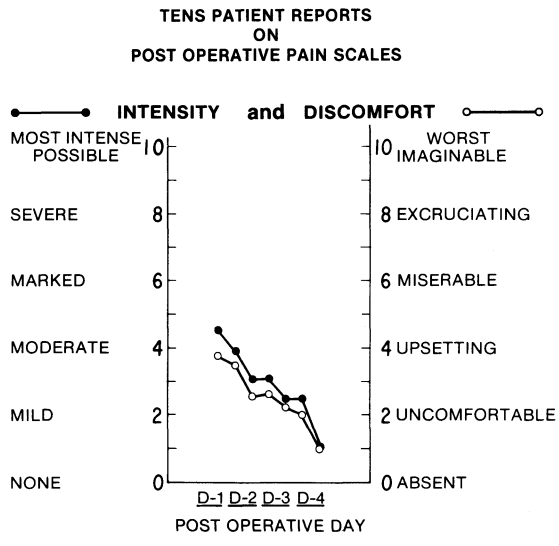

Fig. 3. Average of patients' subjective reporting of pain intensity and pain discomfort on 10-point scales (example of first four days only).

The TENS unit settings were near the midrange during this postoperative period, as shown in Figure 4. The mean settings were intensity 5.4 ($s \pm 0.6$), frequency 6.3 ($s \pm 0.4$), and pulse width 5.7 ($s \pm 0.5$). No corresponding machine outputs were measured; they were assumed to be near the middle of the ranges available on the machine.

DISCUSSION

Measuring pain and pain relief quantitatively is difficult and lacking in precision; however, we believe that TENS used postoperatively is effective in reducing the postoperative requirement for pain medications after laparotomy. The reduction in required pain medication was found to be significant despite the large variation in medication requirements as reflected in the large standard deviations. The TENS program also was subjectively considered by patients and therapists to be effective in the management of postoperative pain. These findings of reduced pain medication requirement and positive subjective opin-

ion agree with other studies on the postoperative use of TENS, although direct comparison is difficult because of the different methods of measuring, summarizing, and reporting medication use or program effectiveness. However, the reported decrease in pain and the reduction of medication requirements by patients using TENS are seen as consistent patterns. The second day after surgery was when the most pain was reported, when the most medication was taken, and when TENS appeared most effective.

The differences between patients with different surgical procedures in the amount of reduction in pain medication taken may have been due to differences in depth, amount, and location of surgery required. A possible explanation is that surgeries closer to the diaphragm may result in aggravated pain caused by the diaphragmatic movement. This type of pain may respond better to TENS modulation, but further study of this is needed for verification.

Because the purpose of this study was to evaluate a new clinical program, no evaluation of the placebo effect was included. Other studies have shown a significant placebo effect of postoperative TENS, as well as significant additional effects of TENS beyond the placebo effect.[2, 4, 5, 15] Although we did not attempt to separately measure the effects of all that may go into this aspect of treatment, we believed that such things as patient and staff education, team cooperation, belief in the treatment's effectiveness, and patient compliance may be key factors in determining the overall effectiveness. Direct comparison of surgical complications, such as ileus, atelectasis, or functional measures, were not made because of the difficulty in objectively measuring them. Other studies have shown significant reductions in complications after surgery when TENS was used.[6, 7] No attempt was made to alter or measure preoperative or intraoperative analgesics. Although pain medication intake is not the ultimate measure of pain, we believed that there was a strong relationship between decreased requirements for pain medication and patient perception of pain. We also assumed that decreased pain and decreased narcotic intake would allow patients to function better. The finding that the length of hospital stay did not differ between groups did not support this assumption. However, it is more likely that total hospital stay may be influenced by considerations other than pain. This aspect of care deserves further investigation.

Our study demonstrated that an adequately managed program of TENS used for postoperative pain could reduce the amount of pain medication required after laparotomy. However, some questions remain about the cost effectiveness of this program relative to traditional medication, about criteria concerning which patients would most benefit from TENS, and about the importance of different methods of TENS application. Important factors for further study may include patient characteristics such as previous surgery, anxiety, pain tolerance, surgical conditions, and the total perception of postoperative care.

CONCLUSION

A well-managed program of TENS that stresses education and team coordination can be effective in managing postoperative laparotomy pain as measured by reduction in pain medication requirements. However, the pain control did not eliminate the use of some pain medication in addition to the TENS. Thus, TENS use may be one of several factors influencing postoperative pain.

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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 analgesics (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.

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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).

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).

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 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 Møiniche 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 nonsurgical 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 μg/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
Valdecoxib (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 valdecoxib (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 valdecoxib 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, 4–18 $\mu g \cdot kg^{-1} \cdot min^{-1}$, in combination with propofol, 30–90 $\mu g \cdot kg^{-1} \cdot min^{-1}$, 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 μg/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 μg/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 μg/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 μg/kg IV) reduced patient anxiety, sympathoadrenal responses, and intraoperative opioid analgesic requirement. Compared with propofol (75 $\mu g \cdot kg^{-1} \cdot min^{-1}$), dexmedetomidine (1 μg/kg followed by 0.4–0.7 $\mu g \cdot kg^{-1} \cdot h^{-1}$) 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 μg/kg followed by 0.4 $\mu g \cdot kg^{-1} \cdot h^{-1}$, 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 (remifentanil) 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 mg/kg IV followed by an infusion of 0.5 g/h) yielded a significant reduction in the postoperative analgesic requirement after abdominal hysterectomy. A bolus dose of magnesium (50 mg/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 mg/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 mg/kg followed by 10–15 $mg \cdot kg^{-1} \cdot h^{-1}$) 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 μg were administered in the subarachnoid or epidural spaces (236,248). Although peripherally administered neostigmine failed to produce postoperative analgesia, epidurally administered neostigmine (1 μg/kg) produced more than 5 h of pain relief after knee surgery (249). Neostigmine (10 μg/kg) also enhanced epidural local analgesia (250). Both epidural (60 μg) and spinal (1–5 μg) neostigmine enhanced morphine-induced neuraxial analgesia (251–254). In patients undergoing knee replacement surgery with intrathecal bupivacaine, adjunctive use of neostigmine (50 μg) was alleged to produce better postoperative analgesia than morphine (300 μg) (255). In addition, transdermal nitroglycerin enhanced spinal neostigmine-induced postoperative analgesia without increasing perioperative side effects (256). However, epidural neostigmine (75–300 μg) 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 nonpharmacologic 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 preemptive techniques involving both central and peripheral-acting analgesic drugs and devices.

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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 compromising 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.

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, acpuncture-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:

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

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 discectomi	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 ± 20 SD) less nausea and 29.4% (mean ± 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	Gynaechological	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 comfortable	No	
Forster	1994	Coronary bypass	45	TENS	6	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

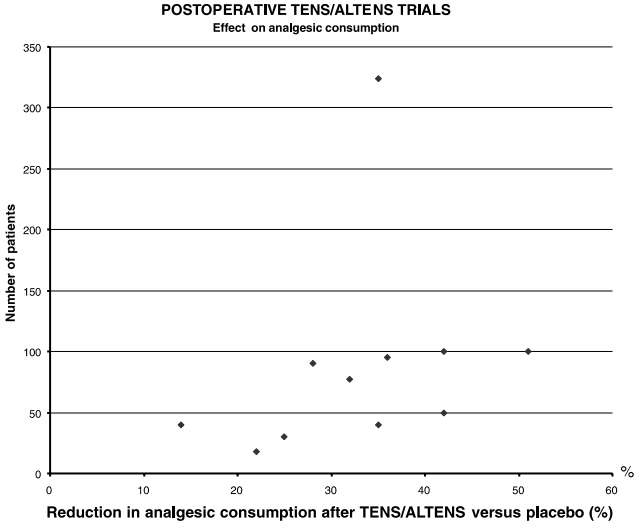

Fig. 1. Effect size plot for trials with optimal treatment procedure.

(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, submaxial 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 between 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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