Reduce your patients Post-Operative Pain and Swelling with the *TENS 3900*

From

MEDICAL FINANCE RESOURCES

TENS 3900

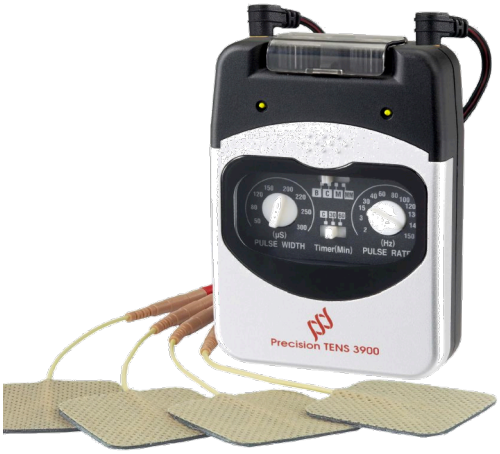
For treatment of Post-Operative Pain and swelling

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.**

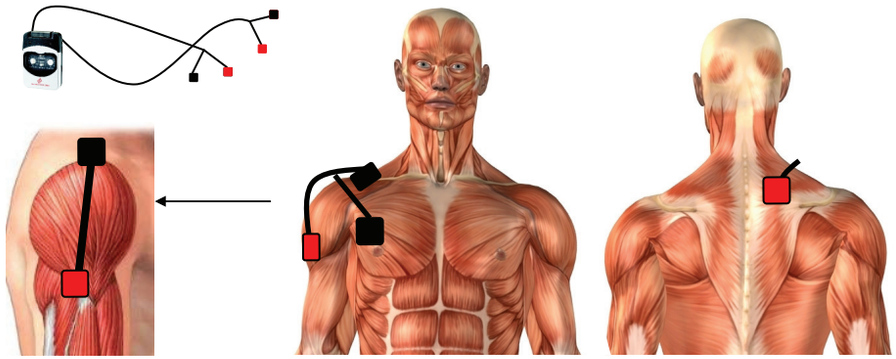


Our representatives educate patients and staff for proper usage of TENS on a per case basis, ensuring that patients receive maximum results after surgical procedures.

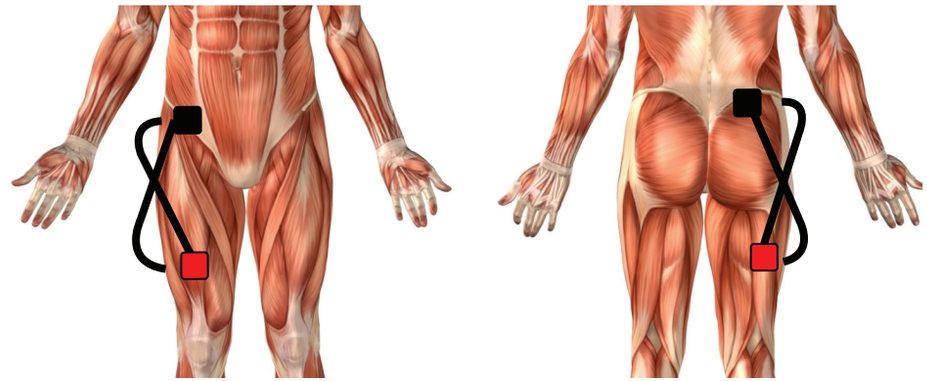
medicalfinanceresources.com 119 Main street South River, New Jersey 08882 (888) 214-2455

ELECTRODE PLACEMENT CHARTS

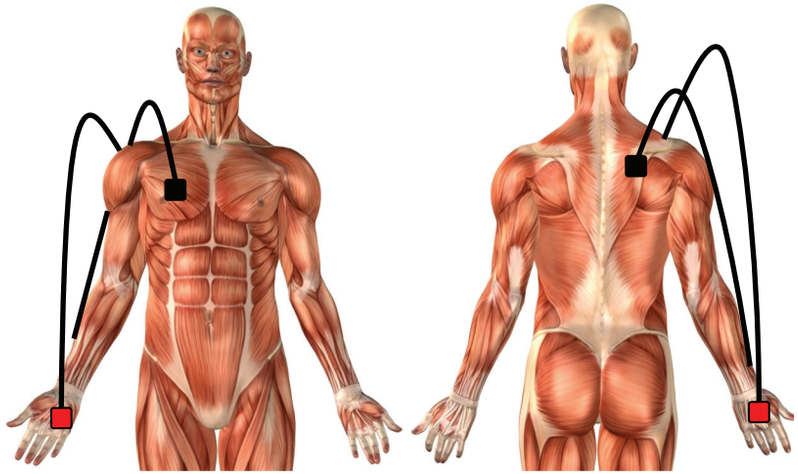
SHOULDER



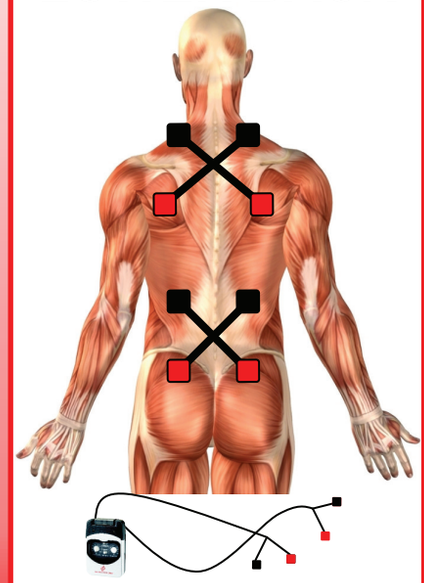
HIP PROCEDURE



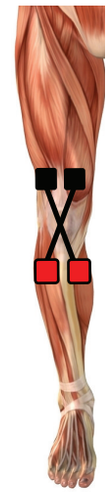
WRIST, ARM, ELBOW & UPPER ARM



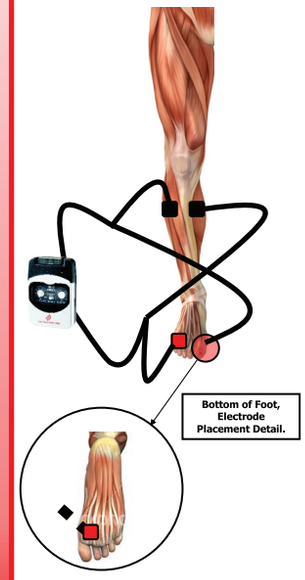
UPPER & LOWER BACK



KNEE



FOOT



Electrode Care

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

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

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

Removal

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

Care and Storage

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

Important

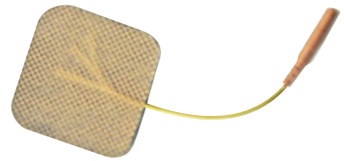
1. The electrodes are intended for single-patient use only.
2. Do not apply to broken skin. Should rash occur, discontinue use.

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

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

Electrode Placement

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



Adjustment Control

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

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

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

Medical Finance Resources

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119 Main St., South River, NJ 08882
www.medicalfinanceresources.com

Your Clinical Specialist

If you think your Clinical Specialist has provided you with exceptional service, please let your physician know!

TENS 3900

3 Modes, Timer, Safety Amplitude Cap

Microprocessor Technology

HOW THE TENS 3900 WORKS

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

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

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*

Matt Holowecky
119 Main Street
South River, NJ 08882
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 _____

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

Paul F. White, PhD, MD, FANZCA

Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas

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.

(Anesth Analg 2005;101:S5–S22)

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

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

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

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0003-2999/05

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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Postoperative TENS Pain Relief After Knee Surgery: Objective Evaluation

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ABSTRACT: A comparison was made between the pain-relieving effect of placebo-transcutaneous electrical nerve stimulation (TENS), high frequency TENS, and epidural analgesia with dilute local anesthetics in 15 patients with open knee surgery. Assessment of pain was compared with the patients' ability to contract their quadriceps muscle; the ability was measured with integrated EMG (IEMG) before and after the different treatments.

The results showed that placebo-TENS had no significant effect on either pain perception or on IEMG. High frequency TENS given for 15 min to 20 min decreased pain perception by 50% at rest and by 11% after quadriceps contraction. High frequency TENS increased muscle contraction ability by 305%, compared with the initial contraction before treatment. Epidural injection of a dilute local anesthetic decreased pain perception by 90% at rest and by 67% after contraction, and increased muscle contraction ability by 1,846%.

TENS undoubtedly has a place in the postoperative pain treatment, although its effect is not as strong as that of epidural analgesia with local anesthetics. TENS, however, is easy to administer, lacks side effects, and can be administered by the patients themselves.

Introduction

A good postoperative pain treatment is of utmost importance for rapid recovery. Pain interferes with normal muscle function[1] and increases stress.[2] The traditional method for postoperative pain relief has been the use of systemic analgesics, such as morphine and related drugs. These drugs may cause nausea, respiratory depression, and unwanted sedation of the patient. Continuous epidural analgesia is a good alternative for two to three days of postoperative pain relief.[3] A selective block of only the pain-mediating nerve fibers without blocking the motor fibers is possible.[2,3] Reinjections, however, often have to be given at least every second hour for proper pain relief. Furthermore, tachyphylaxis to the local anesthetic agent sometimes appears, and the pain relief gradually becomes shorter and less effective. Alternatives to this method, preferably one that the patients can administer themselves, are thus required. Transcutaneous electrical nerve stimulation might be such a modality.

To evaluate the efficacy of TENS treatment postoperatively, most investigators have recorded the reduction in narcotic requirement in a TENS group compared to a control group.[4-9] Other clinical data such as frequency of postoperative complications, length of hospitalization, pulmonary function, and range of motion also have been used.[4,6,10-14] Some authors employ different pain-grading scales to quantify the patient's pain perception.[5,15] Since pain is a very complex sensation composed of a variety of physiological, psychological, and environmental factors, other more objective parameters also are desirable.

Inability to normally contract the muscles around a tissue-damaged area due to pain is a common clinical finding.[16,17] Many authors have observed that by blocking, pain, muscle function, and joint mobility can be improved.[18-21]

In an earlier study,[1] we estimated the change in maximum voluntary muscle contraction after major knee surgery before and after pain-relieving measures. This was done by calculating the amplitude of IEMG during maximum voluntary contraction before and after blocking postoperative pain with an injection of a dilute local anesthetic solution into the epidural space (20 ml 0.25% lidocaine with adrenaline 2.5 μg/ml). Muscle function improved significantly and the amplitude of the IEMG from the quadriceps muscle increased an average of 27 times.

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The purpose of this study is to compare the pain-relieving effect of high frequency TENS with that of epidural analgesia with a dilute local anesthetic in patients who had undergone knee surgery. Subjective rating of the amount of pain was assessed as well as the ability to contract the quadriceps muscle measured (objectively) by EMG and IEMG. Many workers have shown a linear relationship between IEMG and muscle tension.[22-27] We also compared the effect of placebo-TENS treatment with actual TENS. The study was approved by the Ethical Committee at the Karolinska Institute, Stockholm, Sweden.

Materials and Methods

The study included 15 patients having undergone knee surgery the day before the tests were performed. They were informed of the purpose of the experiment and gave their informed consent. The group consisted of 12 men, age 19 to 53 (mean, 31.8 years) and three women, age 19 to 27 (mean, 22.7 years).

The surgical procedure was reconstruction of the anterior cruciate ligament (ACL) using the medial third of the patellar tendon[28] in 12 cases. The three remaining cases involved an open meniscectomy in one, an open lateral release and open shaving of the patella in another, and in one a medial collateral ligament repair and resection of a meniscus ganglion. The operations were performed under epidural anesthesia by the same surgeon. After closure of the wounds, sterile pregelled TENS electrodes, 3 cm × 20 cm, were applied to the skin on the medial and lateral sides of the knee. This is a recommended electrode placement after knee surgery.[29-32]

The epidural catheter was left in place after the operation for refilling the dilute local anesthetics every second hour for pain relief, but from three hours before the experiment was carried out, no reinjections of local anesthesia were allowed. All patients consequently had a significant pain level at the time of the start of the study which was carried out in the morning of the first postoperative day.

The operated knee was protected by a posterior splint and kept in about 45° of flexion. Two pairs of surface EMG electrodes (Beckman) were applied 12 cm to 14 cm proximal to the superior border of the patella. EMG signals were fed to a polygraph (Grass model 78 with preamplifiers and integrators model 7P3B), and after amplification, the signals from one of the electrode pairs were rectified and time-averaged (time constant, 0.2 sec). EMG and IEMG were recorded by the ink-writer of the polygraph. The patients were carefully instructed how to contract their quadriceps muscle and hold it isometrically for 5 sec.

Registration of quadriceps muscle contraction ability was made by recording EMG and IEMG during maximum voluntary contraction. Three contractions were performed in each of the following trials: before treatment; after 15 min to 20 min treatment with placebo-TENS; after 15 min to 20 min actual TENS; and after epidural injection of 20 ml of 0.25% lidocaine with adrenaline (2.5 μg/ml).

Peak amplitudes from the two highest IEMG registrations were averaged and noted. Unintegrated EMG was used as a check for artifacts in the recordings.

For psychological pain assessment, a category-ratio scale developed by Borg was used.[33] A slight modification of the scale, with numbers varying from 0 to 20, was used in this experiment[34] (Fig. 1). Assessment of pain at rest and after muscle contraction was made in connection to the trials described above.

Before the experiments started, another pair of TENS electrodes, 5 cm × 5 cm, were placed on the back of the patient, on either side at the level of L3-L4, ie, the dermatome corresponding to the knee region.[29,30] The knee and back TENS electrodes were connected to a Tenzcare® stimulator (model 6240 3M). This transcutaneous nerve stimulator is battery-powered and has dual channels, delivering pulses of rectangular constant current. The amplitude spans from 0 mA to 70 mA. The pulse rate can be varied from 4 Hz to 185 Hz (rate normal mode) and the pulse width from 30 μsec to 200 μsec.

Placebo-TENS

The patient was told that the stimulation might or might not be perceived as a tingling sensation depending on technique. The apparatus was switched on to the lowest level and the lamp started to twinkle. This was carried out so that the patient could see that the apparatus was on. The apparatus was then put aside and secretly shut off. During placebo-TENS, the patients were asked if they could feel the electrical current. Several patients said that they noted pulsations around the knee joint.

Actual TENS

The TENS intensity was gradually increased and the patient told the physician when the amplitude reached pain level; subsequently the intensity was lowered slightly to a comfortable level. Adjustments were made by the examiner for knee and back electrodes respectively, during the stimulation time. The pulse rate was, as an average, set to 100 Hz and pulse width to 160 μsec; these values are reported by several authors to give the best stimulation with high frequency TENS.[9,35-39] The amplitude usually varied between 30 mA and 40 mA, and the stimulating time from 15 min to 20 min.

The protocol for the experiment can be summarized as follows: 1) Grading of pain based on the Borg scale; EMG and IEMG registration of maximum isometric quadriceps contraction of the operated leg; and pain grading immediately after contraction. 2) Placebo-TENS for 15 min to 20 min; pain grading at rest; EMG registration of quadriceps contraction; and immediate grading of pain after contraction. 3) TENS (high frequency) 15 min to 20 min

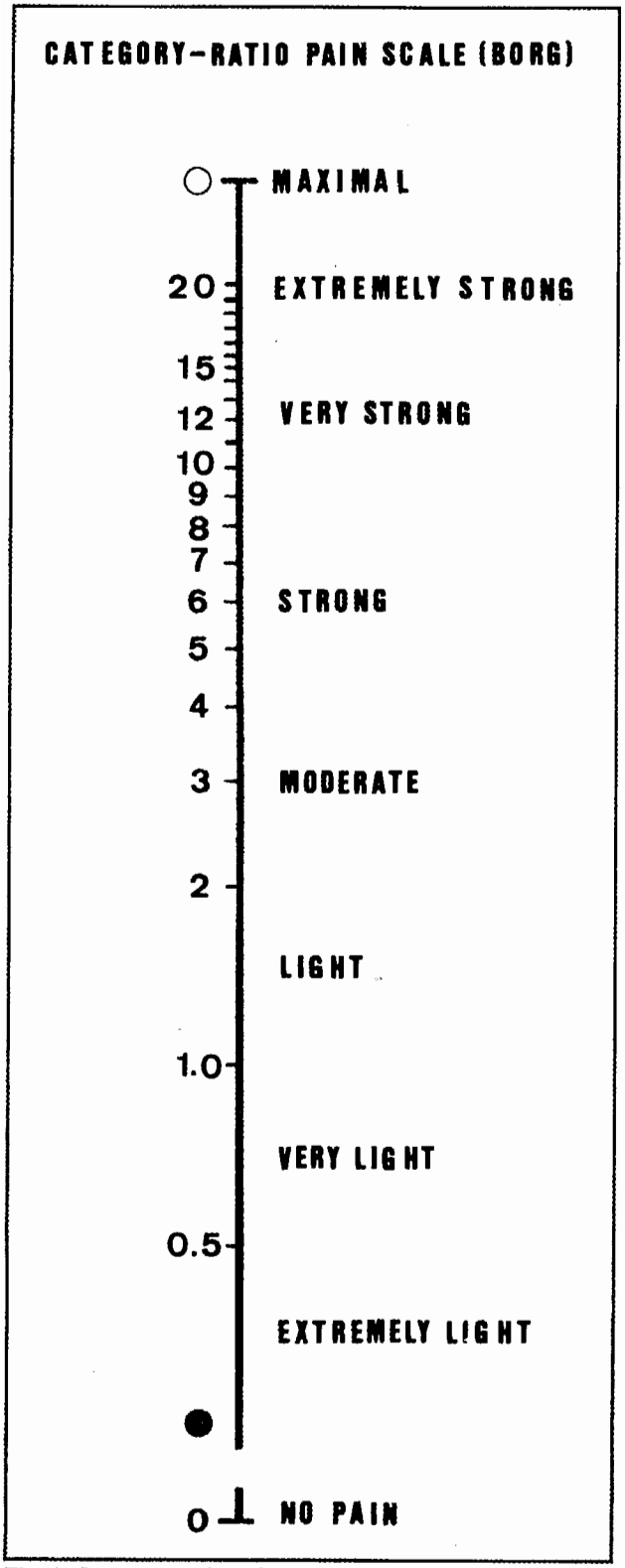

Fig. 1: Category-ratio pain scale (Borg).

(both knee and back); pain grading at rest; EMG registration during quadriceps contraction; immediate pain grading after contraction. 4) Injection of local epidural anesthesia (20 ml of 0.25% lidocaine with adrenaline 2.5 μg/ml); pain grading 20 min after epidural injection (during rest); EMG registration during quadriceps contraction; and immediate pain grading after contraction.

Statistics

As a statistical method, the non-parametric "sign-test" of Dixon and Mood was used.[40]

Results

Pain Grading

All comparisons are expressed in percent of initial scoring at rest before the experiment. Twelve out of 15 patients reported increased pain when initially contracting the quadriceps muscle. Mean increase in pain grading was 29%, range −33% to +100% ($p<.01$) (Fig. 2). After 15 min to 20 min of placebo-TENS, the pain experienced was not significantly changed, a mean +19% of initial grading during rest. After contraction of the quadriceps muscle the mean increase in pain scoring had augmented to +31%; 13 patients suffered from increased pain ($p<.01$).

After high frequency TENS for 15 min to 20 min, pain grading decreased to a mean of 50% as compared with initial scoring. Fourteen of the 15 patients had reduction of pain and one reported no change ($p<.001$). When the patients had performed a maximum isometric contraction

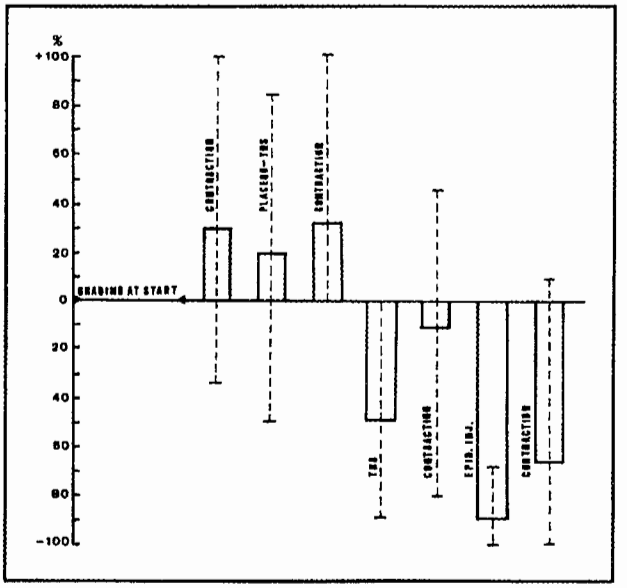

Fig. 2: Pain grading, in percent, of the initial score at rest during the different phases of the experiment. Rectangles represent the average, and broken lines represent the range.

of the quadriceps muscle, the mean reduction of pain experienced was not significant, −11% as compared with initial grading at rest.

Injection of a dilute local anesthetic into the epidural space brought about a reduction in mean pain scoring of −90.0% ($p<.001$). In one patient the catheter had slipped out subcutaneously and did not function.

Maximum isometric contraction of the quadriceps muscle led to somewhat reduced pain relief after epidural injection, but compared with initial scores at rest, 13 patients still reported less pain. Mean pain score was −67% compared with pre-trial value ($p<.001$).

IEMG

All comparisons are expressed in percent of the peak IEMG value from maximum quadriceps activation before treatment (Fig. 3).

After 15 min to 20 min of placebo-TENS, nine out of 15 patients showed a decrease in maximum voluntary contraction as revealed from IEMG (not significant). One patient performed the same, five patients increased their IEMG; the mean change was +1%.

When 15 min to 30 min of high frequency TENS had been given, 12 patients had an increased IEMG activity during quadriceps contraction ($p<.01$). Mean increase was 305%. Twenty minutes to 30 min after epidural injection with local anesthetics, the mean increase of IEMG was 1,846%. One catheter did not function, one patient developed an almost total motor block, but the remaining 13 augmented their IEMG ($p<.001$).

Relation Pain—IEMG

When pain scoring and IEMG were compared during the different stages of the experiment, it was found that as pain scoring decreased, IEMG increased, as could be expected. The correlation between the mean pain scoring and the mean IEMG was high; $r = -0.99$.

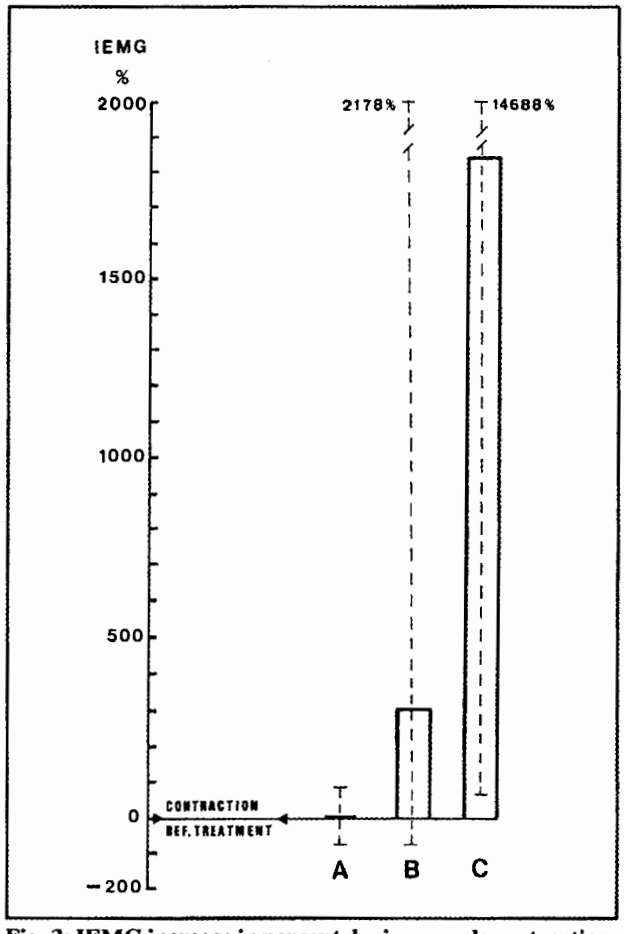

Fig. 3: IEMG increase in percent during muscle contraction. A) contraction after placebo TENS; B) contraction after TENS; C) contraction after epidural injection. (Rectangles represent the average, and broken lines represent the ranges.)

Discussion

The factors that influence pain perception are multiple and vary individually. They include physical as well as psychological factors.[39,41] In this study, we noted that even if the surgical procedure is identical in 12 cases, the individual pain scorings vary considerably. Even though the patients, from the test-leader's point of view, seemed to suffer almost equally, judged by pallor, cold sweating, rapid breathing, and other signs of pain, pre-treatment pain scores varied considerably—from 4 to 16 on the Borg scale. It was therefore impossible to make a direct comparison between different patients' pain grading. We used change in pain relief in percent of the patients' own initial perception and grading. We also compared patients' subjective pain grading with objective IEMG recording.

The ideal design of an experiment such as this would, of course, be to change the sequence of treatments between the groups, ie, to start with actual TENS in one-third of the patients, with epidural injection in one third, and placebo-TENS in one-third. This order of procedure was, however, impossible to carry out from a practical point of view. To start with epidural analgesia would block all pain, thus making placebo-TENS and actual TENS totally unnecessary and impossible to judge the effect. If we had started with actual TENS, which could be presumed to be more potent than placebo-TENS, and allowed it to be perceived by the patients, it would have been immaterial to try "mock therapy" (placebo) afterward. In the order used in the experiment, no patient expressed any doubts that he/she was really treated with TENS during placebo-TENS. Several patients declared that they felt pulsations around the knee joint even if it was explained that the

treatment might or might not be perceived.

If a more potent treatment is to be used before a less potent one, the different tests must be timed so that they cannot influence each other. In our case this would have meant an experimental time of six to seven hours, which we considered unethical. In addition, it also could be expected that the time factor of pain could influence the experiment in a non-acceptable manner.

After placebo-TENS, some patients reported somewhat less pain than during earlier muscle contraction. This could either be due to the fact that placebo-TENS did have some effect, or to the fact that the patients were resting the leg while the placebo-TENS was given (time factor). It has been reported that 17% to 33% of patients treated with placebo-TENS feel an improvement.[11,15,42] The effect of placebo-TENS was, however, not measured quantitatively. In our study, three of the patients (20%) had some pain relief from placebo-TENS, but in the majority, no significant pain change occurred.

Pain grading after high frequency TENS decreased an average of 50% as compared to initial value. Compared to preceding scores (contraction after placebo-TENS), the score dropped over 80% as a mean. This substantial reduction of pain could hardly be due to the effect of rest only, but is probably caused by TENS pain-relieving effect. Reduction of pain after placebo-TENS was only 10% compared to previous scores. Even after muscle contraction there was still less pain than initially (−11%), and more than 40% less pain than during contraction after placebo-TENS. Parallel with diminished pain, muscle contraction power increased measure as IEMG voltage. This reduction of pain and improvement of contractability has been observed by several authors.[18-21] However, these authors have used various drugs as a means of pain relief.

When our patients received epidural anesthesia, pain grading decreased even more, to −90% of initial scoring. Fourteen of the 15 patients scored less than one in the Borg scale, ie, very slight or no pain. It is well known that epidural analgesia is effective as a pain relief, and it is used extensively, for example, during childbirth,[43] in acute back pain,[44-46] and for postoperative pain reduction.[2] Our main purpose was not to prove the pain-relieving effect of epidural injections, but to use it as a reference for comparing the pain-relieving effect of TENS and placebo-TENS. It is obvious that TENS did not have as strong a pain-reducing effect as epidural local anesthetics, but it did have an effect on pain perception which was statistically significant. The surgery preceding the experiments, ACL reconstruction,[28] is very pain inducing. The patients normally experience a great degree of pain the day after surgery, and are hardly able to contract their quadriceps.

The three patients who did not undergo ACL reconstruction were exposed to knee surgery of a similar pain degree. They also scored their initial postoperative pain equal to that of the ACL patients.

Conclusion

In 15 patients operated with open knee surgery, placebo-TENS had no significant effect on either pain perception or on muscle contractability measured as IEMG.

High frequency TENS given for 15 min to 20 min decreased pain perception by 50% at rest and by 11% during quadriceps contraction compared with pre-treatment assessment. It increased muscle contractability by 305% compared with contraction before treatment.

Epidural injection of a dilute local anesthetic solution decreased pain perception by 90% at rest and by 67% after muscle contraction. It augmented the maximum voluntary contraction by 1,846%. TENS undoubtedly has a place in postoperative pain treatment, although its effect is not as strong as that of epidural analgesia with local anesthetics. TENS, however, is easy to administer, lacks side effects, and can be handled by the patients themselves.

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Postoperative Pain Control after Shoulder Arthroscopy

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Abstract

Successful postoperative pain management after arthroscopic shoulder surgery allows patients to go home earlier, decreases the potential for hospital readmission, and facilitates rehabilitation. Optimal pain control considers the physiological and psychological states of the patient, the resulting alterations due to the surgery, and the technical and economic resources available during recovery. A comprehensive approach to pain control should include preoperative, intraoperative, and postoperative efforts. Efforts at postoperative pain reduction should begin preoperatively with the establishment of an excellent patient/physician relationship. Preoperative analgesia should be administered. Intraoperative efforts should include the administration of anesthetic medication intra-articularly. Postoperative management should include sleep medication, continuous cold-flow therapy, oral analgesics, and, if necessary, the use of narcotics.

Increasingly, orthopedic surgery is moving from an inpatient setting to an outpatient setting. This is especially true for arthroscopic and mini-open shoulder procedures. Uncontrolled postoperative pain interferes with initial rehabilitation.[1] In a study of >15,000 ambulatory surgical procedures, pain was responsible for 12% of the unplanned hospital admissions, and of these, 60% were orthopedic patients.[2] Acute postoperative pain in an ambulatory surgical setting is frequently undertreated,[3-5] especially after shoulder surgery, operations for hardware removal, and elbow arthroscopy.[3]

Epidemiologic studies suggest that shoulder pain ranks third among reasons patients visit a doctor,[6] and almost half of patients who seek orthopedic surgical treatment are between 19 and 64 years.[7,8] This group constitutes most wage earners, and they need to return to work as soon as possible.

Shoulder surgery often results in bone removal, extensive resection of bursal tissue, insertion of hardware, and soft tissue distension from irrigation fluid. Many patients are hospitalized overnight to control pain that results from this intervention. This may be because the postoperative pain is undertreated in the outpatient setting.

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Acute pain results from mechanically, chemically, or thermally induced damage to tissue integrity.[9] With cellular damage, a variety of chemicals are released, including histamine, bradykinin, prostaglandins, serotonin, substance P, acetylcholine, and leukotrienes, which sensitize nociceptors to other noxious stimuli.[10-12] These chemical reactions stimulate the sensitive receptors, which are responsible for the

pain sensation. If pain is not adequately treated, it can result in the sensitization of the peripheral and central nervous system and lead to the development of chronic pain.[10,13,14] This article presents the preoperative, intraoperative, and postoperative pain control practices surgeons should apply to treat surgical pain adequately.

Factors Influencing Analgesic Needs

Pain is not only a sensory experience, but also a phenomenon with cognitive and affective components. Factors such as gender, age, culture, communication skills, and previous pain experiences may play a role in determining an individual's perception of pain.[15,16] For example, advancing age is associated with enhanced opioid sensitivity and decreases in opioid consumption.[17] Educating patients about what to expect before, during, and after surgery can decrease anxiety and therefore postoperative pain. Communication between physician and patient is key to a successful outcome.

Goals of Postoperative Pain Control

Outpatient surgery offers several advantages: 1) patients have more control of their postoperative care and consequently accept more responsibility for a successful outcome, 2) the stress and expense of a hospital stay are avoided, 3) patients can be hospitalized after outpatient surgery if required, and 4) the surgical team works together to send patients home postoperatively in an adequate condition.[18]

The pain management plan should be a collaborative effort among the physician, nursing staff, anesthesiology team, patient, and patient's family. Optimal pain control considers the physiological and psychological states of the patient, resulting alterations due to the surgery, and technical and economic resources available during recovery. Pain intensity is rarely constant. Movement and physical therapy may increase postoperative pain. Postoperative pain seems to have a circadian cycle, increasing at night,[17] and is usually greatest in the first 24 hours postoperatively. Postoperative pain has a natural history, and the goal of any pain control plan is to modify its course and lessen its development.

Preoperative Efforts

A rested state is important preoperatively. A good night's sleep prior to the day of surgery reduces anxiety. Anxiety causes more pain and may have a detrimental effect by increasing the perception of postoperative pain. Providing patients with sleeping medication one night before and after surgery has been shown to be effective.[19] This medication is an adjuvant to the analgesic protocol.

One approach to pain control is the use of preemptive analgesia. Preemptive analgesia refers to efforts to prevent pain before it starts, therefore reducing central sensitization. Kissin[20] reviewed this technique and concluded that the evidence from clinical and basic science studies validated the phenomenon of preemptive analgesia. Orthopedic surgeons are now developing preemptive protocols to achieve better postoperative pain control. The most frequently used techniques include local wound infiltration, joint inflation, and peripheral nerve blocks.

The routine infiltration of arthroscopic portals and incision sites is commonplace. The most commonly used drugs are lidocaine and bupivacaine. Combining these drugs with epinephrine can provide both adequate analgesia and some control of intraoperative bleeding. Preincisional local anesthetics block the sensitization of peripheral nociceptors and reduce hyperexcitability. This technique provides greater relief than using the same drugs in the postoperative period.[21,22]

Joint inflation with between 20 and 60 mL of lidocaine or bupivacaine is another option. These drugs have been demonstrated to have a better analgesic effect in the shoulder joint than morphine.[23]

The third most common technique is a peripheral nerve block such as interscalene and suprascapular nerve blocks. The peripheral nerve block can provide both preemptive analgesia and anesthesia. It has been reported that training in regional anesthesia is inadequate in many residency programs in the United States.[24,25] Certainly the training and practice of peripheral nerve blocks varies significantly from institution to institution; therefore, not all surgical centers can consistently provide this kind of anesthesia. Advantages of peripheral nerve blocks over general anesthesia in arthroscopic shoulder surgery include the ability to use hypotensive anesthesia with improved hemostasis during shoulder surgery, a reduction in intraoperative narcotic use, earlier patient discharge from the postanesthetic care unit, fewer unplanned hospital admissions, and a faster time to hospital discharge.[26] However, the disadvantages of peripheral nerve blocks include a longer procedure time and a significant incidence of block failure. Other complications include reflex sympathetic dystrophy[27] and the possibility of having intense pain (rebound pain) once the block wears off.[26]

Interscalene Nerve Block

An interscalene nerve block offers some advantages over general anesthesia for both open and arthroscopic surgical procedures. This block provides excellent intraoperative anesthesia, muscle relaxation, and postoperative analgesia.[28,29] Although sedation is sometimes needed during block placement, it is well accepted by patients.

However, the interscalene block, even when performed by highly trained and dedicated anesthesiologists, has complications. Bishop et al[27] reported a 3% interscalene block failure rate, 2.3% short-term complication rate (primarily sensitive neuropathies that resolved in a 9-week period), and 1 case of reflex sympathetic dystrophy. This low complication rate is unusual. Weber and Jain[30] reported a failure rate of 13%, while 92% of patients required additional opioid medication. The complication rate can be substantially higher if the interscalene block is performed by an inexperienced anesthesiologist.[27] Lewis and Buss[18] suggest that while an interscalene block may provide an additional measure of pain control combined with general anesthesia, the increased costs and risks are not justified by the marginal benefit.

Complications related to the interscalene block include recurrent laryngeal nerve block, ipsilateral hearing loss, Horner syndrome, vertebral artery injection, pneumothorax,

epidural injection, subarachnoid injection, and phrenic nerve block.[25,31] Since the phrenic nerve block occurs approximately 100% of the time, an interscalene block should never be done bilaterally, and is contraindicated in patients with severe chronic obstructive pulmonary disease.[31] Other complications reported to occur with interscalene blocks include cardiac arrest, grand mal seizures, high spinal blocks, hematomas, pneumothorax, phrenic nerve palsy, and respiratory distress.

The interscalene nerve block is an effective shoulder anesthetic technique. However, the best results demand a high level of expertise and familiarity. Complications associated with this technique are higher in the community setting, where focused attention to the technique may not be as available as in an academic institution.[30]

Suprascapular Nerve Block

The suprascapular nerve block is another type of peripheral nerve block. The suprascapular nerve arises from the superior trunk of the brachial plexus. It innervates up to 70% of the posterior shoulder joint and provides innervation to the acromioclavicular joint, subacromial bursa, and coracoclavicular ligament, along with the lateral pectoral nerve. It does not fully reach some portions of the posterior shoulder joint and the anterior inferior shoulder.

Ritchie et al[1] reported that preemptive suprascapular nerve blocks improved analgesia and 24-hour quality of life outcomes when used as an adjunct to general anesthesia for arthroscopic shoulder surgery. In contrast, Neal et al[32] reported that the suprascapular nerve block provided an average analgesia of 220 minutes, with great variation among individuals and no improvement in the 24-hour outcome.

Barber[33] reported a technique consisting of 1 injection with 20 to 25 mL of 0.5% bupivacaine administered before the start of the procedure. Although this technique does not prevent all postoperative pain, it decreases the intraoperative pain and delays the onset of pain for several hours. The reported risks of the suprascapular nerve block are rare (<1%), with pneumothorax being the most frequent.[27]

Regional blockade techniques have a number of common complications. These include persistent paresthesia, nerve damage, inadvertent intravascular injections, and local anesthetic toxicity. Cardiac toxicity with the use of bupivacaine is well documented.

Intraoperative Efforts

The extent and duration of surgery can greatly influence postoperative pain intensity and analgesic requirements. The reduction of surgical time and the use of minimally invasive techniques reduce postoperative pain.

Joint infiltration at the end of the procedure is an option for pain control. Although an intra-articular injection of morphine has been found to be beneficial in the knee,[34-36] Scoggin et al[23] did not report any beneficial effect of intra-articular and/or subacromial

morphine in the shoulder after arthroscopic surgery. The favorable response to morphine in the knee may be due to tourniquet use (not applicable to the shoulder).

Although bupivacaine appears to have a superior effect when administered intra-articularly inside the shoulder joint in comparison to morphine,[23] Singelyn et al[37] reported that a single dose of intra-articular bupivacaine does not provide a significant analgesic effect when compared to peripheral nerve blocks. This can be explained by a rapid washout of the local anesthetic into the adjacent soft tissues or by dilution of irrigating fluid.

Postoperative Efforts

Multimodal analgesia techniques may be more effective than a single analgesic, reduce opioid requirements, and decrease undesired side effects.

Postoperative Oral Medications

One of the most common postoperative medications is acetaminophen, an over-the-counter analgesic and antipyretic drug. This drug does not cause impaired platelet aggregation, cardiorenal effects, or impairment of bone and ligament healing. It increases the pain threshold by inhibiting the production of central prostaglandins, and it may not be suitable for blocking an inflammatory response. Acetaminophen selectively inhibits COX-3, which is a variant of COX-1 cloned recently from the canine central cortex. This isoform may play a role in the central analgesic and antipyretic effects of acetaminophen.[38-40] When acetaminophen is compounded with opioid drugs, it effectively relieves moderate to severe postoperative pain.[17]

Nonsteroidal anti-inflammatory drugs (NSAIDs) have effects on both isoforms of cyclooxygenase (COX-1, COX-2) or selectively block the formation of the isoform type 2 as well as prostaglandin synthesis. They are effective in reducing the sensitization of nociceptors, attenuating the inflammatory pain response, and preventing central sensitization. These drugs can reduce the need for opioid drugs by 20% to 40%.[41-43] The nonspecific forms of NSAIDs have potential adverse effects that make them unsuitable for use in patients with preexisting coagulation defects, preexisting renal dysfunction, myocardial dysfunction, and end-stage liver disease.

The COX-2-specific inhibitors have similar analgesic efficacy, and they offer the advantages of having no effect on platelet function and an improved gastrointestinal tolerability. However, one example of these drugs, celecoxib, is contraindicated in patients with a sulfa allergy. The use of COX-2 inhibitors can be related to other side effects that can make them unsuitable for chronic use, most commonly abdominal pain, diarrhea, and dyspepsia. There is a higher risk of myocardial infarction in some cases, as well as the potential for a rise in systolic blood pressure. Fluid retention and edema have also been observed with the use of COX-2 inhibitors.

Prostaglandin E2, among other protaglandins, is useful in the formation of new bone. Some NSAIDs, therefore, will have an adverse effect on bone formation, at least in part

interfering with the bone morphogenetic protein (BMP) signaling system. The use of NSAIDs has resulted in slower healing rates for bone fractures, higher nonunion rates, and weaker fracture unions in animals treated with these medications.[44,45] The BMP system has also been implicated during early tendon formation.[46,47] Therefore, disturbing the BMP system by using these drugs can also impair the early phase of tendon repair. These effects seem to be more significant with the use of COX-2 inhibitors. The inflammatory response during the first days after trauma is necessary for adequate and normal bone and soft tissue repair, and should not be inhibited. This acute period may last for the first 10 postoperative days.[48] After this period has elapsed, it is safer to use COX-2 inhibitors.

Opioids are frequently used to treat moderate to severe pain. They produce their analgesic effect by mimicking the action of endogenous opioid peptides in the central nervous system. Tramadol is a synthetic analog of codeine that acts as a central analgesic drug. Its side effects are vertigo, dizziness, and seizure.[49] Tramadol is frequently combined with acetaminophen and is effective for pain control.

Constant Infusion Devices

Constant infusion devices consist of multiport catheters inserted with a needle into the surgical site (subacromial space or glenohumeral joint) at the end of the procedure. These catheters are attached to pumps that infuse local anesthetics (bupivicaine or ropivacaine are most commonly used) at a constant rate.

Constant infusion pumps provide a consistent medication infusion rate over an extended period. Electric-powered pumps appear to be more consistent than other types. The elastic devices sometimes provide a quicker-than-expected basal rate (100%-150%) initially and then achieve the expected rate within 2 to 12 hours. There is an increased rate once again just before medication exhaustion.[50] Spring-powered pumps initially provide a quicker-than-expected basal rate (115%-135%), and this rate decreases to a less-than-expected rate (70%-75%) near reservoir exhaustion. However, there are no studies that explore the clinical significance of the variations of different constant infusion systems.[51-54]

The most effective medication for continuous infusion pumps is not clearly established. Savoie et al[55] tested bupivacaine 0.25% in the subacromial space and compared it to saline infusion. They evaluated pain by visual analog scale and tabulated the amount of nonnarcotic and narcotic medication. They concluded that a bupivacaine pain-control infusion pump is an effective means of decreasing postoperative pain. Borgeat et al[56] reported a trial involving ropivacaine 0.2% and bupivacaine 0.15%. They reported a similar analgesic effect, but ropivacaine was associated with better preservation of hand strength and less finger paresthesia. Harvey et al[57] also reported that the use of subacromial ropivacaine 0.2% patient-controlled analgesia provided effective postoperative pain control after subacromial arthroscopic decompression. Casati et al[58] found ropivacaine 0.2% and levobupivacaine 0.125% equivalent after shoulder surgery, but patients given levobupivacaine consumed less analgesic oral medication.

To date there are no conclusive studies about which is the best anesthetic medication for continuous infusion pumps. Nevertheless, it is important to mention that continuous infusion pumps may not be effective in open shoulder surgery. Boss et al[59] reported that continuous subacromial infiltration with bupivacaine is ineffective in providing pain relief supplementary to patient-controlled analgesia after open rotator cuff repair and acromioplasty.

Recent evidence of the potential for chondrolysis after continuous intra-articular bupivacaine infusion suggests closer scrutiny of this modality in a joint is needed, although insertion of the infusion devices into areas without articular cartilage should avoid these concerns.[60]

Postoperative Sleep Agents

Pain can cause sleeplessness, which can lead to a vicious cycle of acute pain, anxiety, and additional sleep deprivation. The use of sleeping medication, at least during the first 24 postoperative hours, is advocated. Sleep disturbances may be related to hyperalgesic changes and to alteration of the effect of analgesic or sedative medications via opioidergic and serotoninergic mechanisms of action.[61,62] Sleep disturbances can alter the natural history of pain, so it is important to improve sleep quality and quantity. This improvement is related to an enhancement of patient overall health and quality of life.[63] Thus, the neurobiologic pathways that regulate sleep may also play a role in central pain processing.[64]

Physical Methods

Cryotherapy

The use of cold for analgesia is a practice dating from the time of Hippocrates in the 4th century BC. Ice was also used as a preoperative anesthetic agent in the Middle Ages. Cold therapy in the form of ice bags has been extensively used in athletic training since the 1960s.[65,66] The mechanism of action of cold is not clear. It is thought to act as an anesthetic agent, raising the pain threshold of the nerve fibers at low temperatures, with its early application reducing the initial hemorrhage, swelling, and inflammation by reflex capillary vasoconstriction. The major benefits of cryotherapy result from altered blood flow and decreased pain, muscle spasm, sensorimotor nerve conduction, and metabolism, as well as increased tissue stiffness. Furthermore, minor elevations in intra-articular temperatures can stimulate proteolytic enzyme activity, which has a detrimental effect on articular cartilage.[66-70]

Several methods exist for cold application: ice bags, reusable cold packs, and refrigeration devices.[70] In the first 48 hours after shoulder surgery, cryotherapy provides its major benefits by its anesthetic effects and by lowering the metabolic rate of the affected zone and preventing inflammation. Pain reduction has been reported after the application of cold between 50° and 60°F (10° to 15°C).[71] Singh et al[71] reported that continuous cold therapy was useful for both open and arthroscopic shoulder surgery. They confirmed a significant decrease in postoperative pain and an increase in overall

patient comfort and satisfaction. Patients slept longer and more comfortably and were able to reestablish their normal daily patterns.

In contrast, no observed decrease in subacromial and glenohumeral joint temperatures was observed in the immediate postoperative period after 90 minutes of cold therapy.[72] After applying cold therapy for 23 consecutive hours, however, Osbahr et al[73] found significant reduction in skin, subacromial, and glenohumeral temperatures. They observed an increase in temperature in these regions from 4 to 12 hours postoperatively and a relative thermostatic phase from 12 to 23 postoperative hours. The results of cold therapy on the shoulder depend on the tissue depth and the duration of surface cooling. This is because the cold temperature has to overcome a large, muscular mass that surrounds the joint. In contrast to other joints, circumferential cooling cannot be achieved. Although conflicting reports exist, cold therapy after shoulder arthroscopy is a common modality with apparent good subjective results.

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation provides a noninvasive method of reducing postoperative pain. While unable to relieve the most intense aspects of pain, it works as an important analgesic adjuvant. Likar et al[74] evaluated the use of transcutaneous electrical nerve stimulation for 3 days after shoulder surgery in a randomized clinical study. Reduced analgesic consumption and significantly lower pain scores were observed.

Summary

Efforts at postoperative pain reduction should begin preoperatively with the establishment of an excellent patient/physician relationship. Adequate counseling as to the nature of the condition and what the procedure entails should be provided. A good night's sleep preoperatively will decrease anxiety and postoperative pain perception. Preemptive analgesia should be administered, including portal and portal track infiltration, joint inflation with an analgesic/anesthetic drug, and peripheral nerve blockade (such as the suprascapular nerve block). Intraoperative efforts should include the administration of anesthetic medication intra-articularly. Postoperative management should include sleep medication, continuous cold-flow therapy, oral analgesics, and, if necessary, the use of narcotics and instillation of a local anesthetic/analgesic agent into the operative site via a pain pump. The use of NSAIDs should be postponed until after the 10th postoperative day in cases of tendon or ligamentous repair. Reduced intraoperative time, elimination of unnecessary bone and soft tissue manipulation, and meticulous surgical technique are also essential for postoperative pain reduction.

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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

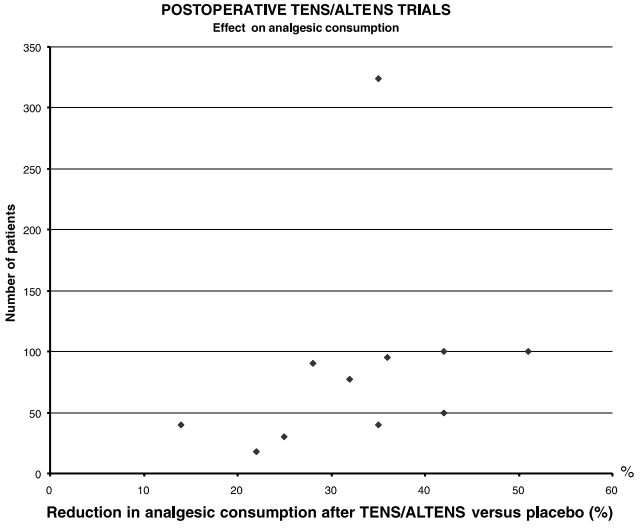

Fig. 1. Effect size plot for trials with optimal treatment procedure.

(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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