

# The Effect of Location of Transcutaneous Electrical Nerve Stimulation on Postoperative Opioid Analgesic Requirement: Acupoint Versus Nonacupoint Stimulation

Lei Chen, MD\*, Jun Tang, MD\*, Paul F. White, PhD, MD, FANZCA\*, Alexander Sloninsky, MD†, Ronald H. Wender, MD†, Robert Naruse, MD†, and Robert Kariger, MD†

\*Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas; and †Department of Anesthesiology, Cedars-Sinai Medical Center, Los Angeles, California

Transcutaneous electrical nerve stimulation (TENS) has been used as a complementary (supplemental) therapy to opioid analgesics for pain relief after surgery. Simultaneous stimulation at a classical Chinese acupoint site and periincisional dermatomes significantly decreases the postoperative analgesic requirement. This sham-controlled study was designed to assess the relative effectiveness of acupoint versus nonacupoint stimulation on the postoperative hydromorphone (HM) requirement, the incidence of opioid-related side effects, and the overall recovery profile. One hundred women undergoing total abdominal hysterectomy or myomectomy procedures with a standardized general anesthesia were randomly assigned to one of four postoperative analgesic treatment regimens ( $n = 25$  each): Group I = sham-TENS (no electrical current) at the Zusanli (ST36) acupoints, Group II = nonacupoint-TENS at the shoulders, Group III = dermatomal-TENS at the level of the surgical incision, and Group IV = acupoint-TENS at the Zusanli acupoints. The frequency of TENS was set in the standard dense-and-disperse mode of 2/100 Hz. The intensity of stimulation was set at 0 mA for patients in Group I and at 9–12 mA for patients in Groups II, III, and IV. A patient-controlled analgesia (PCA) device programmed to deliver bolus doses of HM 0.2–0.4 mg IV on demand with a minimal lockout interval of 10 min was used to quantify the postoperative opioid analgesic requirement. Standard 100-mm visual analog scales

were used to assess pain, as well as sedation, fatigue, and nausea, at specific intervals after surgery. The numbers of PCA demands and delivered bolus doses, requirements for supplemental medication, and any opioid-related side effects were recorded. In the first 24 h postoperatively, the opioid requirements in Groups III and IV were decreased by 37% and 39%, respectively, compared with the control (sham) group and 35% and 38%, respectively, compared with Group II. The duration of PCA usage and the incidences of nausea and dizziness were also significantly decreased in Groups III and IV compared with Groups I and II. We conclude that periincisional dermatomal and Zusanli acupoint stimulation were equally effective in decreasing the postoperative opioid analgesic requirement and in reducing opioid-related side effects. Both of these positions were more effective than the nonacupoint (shoulder) location. **Implications:** The location of the stimulating electrodes seems to be an important determinant of the efficacy of transcutaneous electrical nerve stimulation in decreasing the need for opioid analgesics in the postoperative period. This study demonstrates that transcutaneous electrical nerve stimulation applied at the dermatomal level of the skin incision is as effective as Zusanli acupoint stimulation, and both were more effective than stimulation at a nonacupoint (shoulder) location.

(Anesth Analg 1998;87:1129–34)

**P**atient-controlled analgesia (PCA) using opioid analgesics has become the treatment of choice for the management of acute postoperative pain (1). However, the use of PCA with opioid analgesics is associated

with well known side effects, including nausea, vomiting, urinary retention and ileus, pruritis, constipation, and even ventilatory depression (2). In addition, PCA therapy has been associated with serious mishaps (3) and potentially life-threatening complications (4).

The effect of transcutaneous electrical nerve stimulation (TENS) on postoperative pain and the need for opioid analgesic medication is controversial (5–8). However, a study found that when TENS was applied simultaneously at both the dermatome corresponding to the surgical incision and a classical Chinese acupoint site on the hand (Hegu) (9), a >50% decrease in the postoperative opioid analgesic requirement was produced after

This study was supported in part by funds from the Ambulatory Anesthesia Research Foundation of Texas.

Accepted for publication July 9, 1998.

Address correspondence and reprint requests to Dr. Paul F. White, Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, 5161 Harry Hines Blvd., Room CS2.202, Dallas, TX 75235-9068. Address e-mail to pwhite@mednet.swmed.edu.

lower abdominal surgery. This study also reported that the intensity of the electrical stimulation was an important determinant of the opioid-sparing effect of TENS therapy. A greater intensity (9–12 mA) of electrical stimulation was more effective in decreasing the postoperative analgesic requirement than a low intensity of stimulation (4–5 mA) when used as an adjuvant to IV PCA. However, it is unclear whether the analgesic-sparing effect was produced by the electrical stimulation at the acupoint or the periincisional dermatomes. Factors that could influence the effectiveness of TENS therapy as a supplement to opioid analgesics include the site, frequency, and duration of electrical stimulation.

This randomized, single-blind, sham-controlled study was designed to test the hypothesis that the site of the electrical stimulation influences the opioid-sparing effect of TENS therapy. In women undergoing major gynecologic surgery, TENS stimulating electrodes were applied at a classical Chinese acupoint (Zusanli), a nonacupoint (shoulders), or the dermatome corresponding to the surgical incision, and the effect of each therapeutic modality on the severity of pain, the postoperative PCA analgesic requirement, the incidence of opioid-related side effects, and the recovery profiles in the early postoperative period were compared with a sham (control) treatment.

## Methods

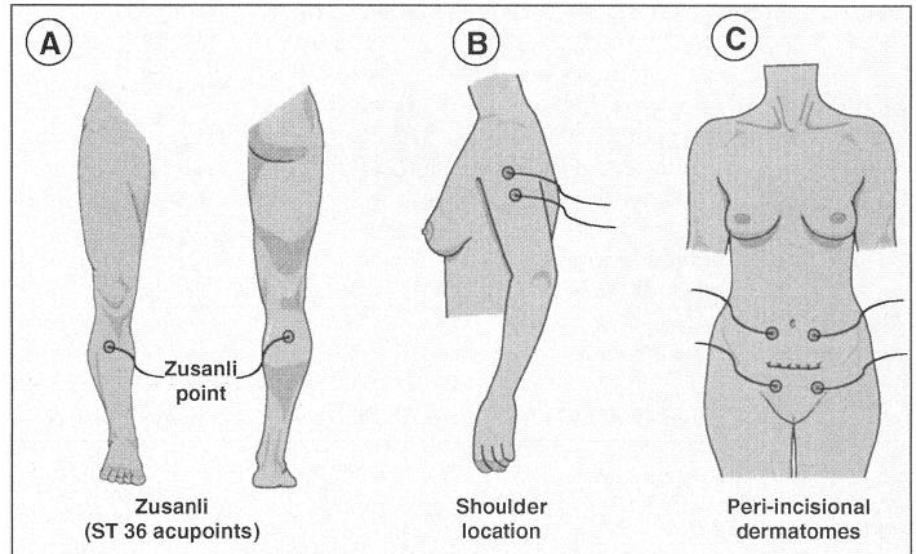
After we obtained written, informed consent, 100 ASA physical status I or II female patients scheduled for elective abdominal hysterectomy or myomectomy procedures were enrolled in this study. The study protocol was approved by the institutional review board at Cedars Sinai Medical Center. The patients were randomly assigned to one of four treatment groups: Group I = sham (no electrical current) stimulation at the Zusanli points, Group II = nonacupoint electrical stimulation at the shoulders, Group III = electrical stimulation at the dermatomal levels corresponding to the abdominal incision, and Group IV = electrical stimulation at the Zusanli acupoints. All patients received a PCA device containing a standardized solution of hydromorphone (HM; 1 mg/mL). The operational aspects of the PCA device (LIFE CARE® PCA Plus II infuser; Abbott Laboratories, North Chicago, IL) and the TENS stimulator (HAN LY257; Healthtronics, Singapore) were explained to each patient during the preoperative visit and were reviewed with the patient before initiating the therapy in the postanesthesia care unit (PACU). Patients with a history of narcotic (opioid) abuse or extreme sensitivity to opioid-related side effects, previous experience with acupuncture-like therapies, as well as those with clinically significant cardiovascular, pulmonary, renal, hepatic, and neurologic diseases were excluded from participating in this study.

All patients received midazolam 1–2 mg IV for premedication immediately before entering the operating room. Anesthesia was induced with fentanyl 1–2  $\mu$ g/kg IV and thiopental 4 mg/kg IV and was maintained with desflurane 3%–5% and nitrous oxide 67% in oxygen. Tracheal intubation was facilitated with vecuronium 0.1–0.15 mg/kg IV, and residual neuromuscular blockade was reversed with a combination of neostigmine 0.05–0.075 mg/kg and glycopyrrolate 0.005–0.01 mg/kg IV at the end of the operation. No additional opioid analgesic medications were administered during the intraoperative period.

On arrival in the PACU, the PCA device was connected to the patient's IV line and programmed to deliver 0.2–0.4 mL (0.2–0.4 mg) bolus doses of HM on demand, with a minimal lockout interval of 10 min and a maximal hourly dose of 6.0 mg. The patients were randomly assigned to one of four different TENS treatment groups to supplement standard PCA therapy. In Groups I and IV, the stimulating pads were placed bilaterally at the Zusanli acupoints (ST36); in Group II, the stimulating electrodes were placed bilaterally at the deltoid region of the shoulder, and in Group III, the stimulating pads were positioned across the surgical incision site at adjacent dermatomal levels. The patients in Group I were told that they may not be able to feel the electrical stimulation. Although the device was nonfunctional, the in-use light on the TENS device flashed in the usual manner when activated by the patient. The placement positions of the cutaneous stimulating electrodes at the Zusanli acupoints (Groups I and IV), the shoulders (Group II), and the skin incision (Group III) are illustrated in Figure 1. The frequency of stimulation was set in the standard dense-and-disperse (D-D) mode at a frequency setting of 2/100 Hz (i.e., alternatingly stimulating at 2 Hz and 100 Hz every 3 s). The intensity of the electrical stimulation was set at 0 mA for Group I and at 9–12 mA (depending on the patient's ability to tolerate the electrical stimulation) for Groups II, III, and IV. The TENS therapy was initiated when the patient arrived in the PACU and continued for a period of 30 min. The device automatically shuts off at the end of each 30-min treatment interval. The patient was instructed to use the TENS device every 2–3 h while awake, as well as at bedtime and on waking in the morning.

Supplemental bolus doses of HM 0.5–1 mg were administered IM if the patient was unable to achieve adequate pain relief from the PCA device. PCA therapy was discontinued when the patient no longer required IV therapy (i.e., when the pain was controllable with oral analgesic drugs). The TENS therapy was discontinued when the patient was able to control their pain with oral analgesic medication consisting of acetaminophen and/or oxycodone. The number of

**Figure 1.** The locations of the transcutaneous electrical nerve stimulation pads in the sham (Group I) and acupoint (Group IV) groups (A), in the nonacupoint group (Group II) (B), and in the incisional dermatome group (Group III) (C).



PCA demands (i.e., button presses) and delivered bolus doses in the PACU and at each subsequent 8-h interval were recorded by a blind observer (who was not aware of the TENS treatment group). In addition to assessing the postoperative analgesic requirement, opioid-related side effects and requirements for supplemental medications (e.g., antiemetics, antipruritics, analgesics) were recorded during the 72-h postoperative observation period. Opioid-related side effects (e.g., nausea and vomiting, pruritis) were treated according to a standardized protocol if the symptoms were present on successive nursing visits or if the patient complained of persistent symptoms.

Standard 100-mm visual analog scales (VAS) were used to assess the patient's level of sedation (0 = awake and alert to 100 = almost asleep), fatigue (0 = well rested to 100 = exhausted), discomfort (0 = extremely comfortable to 100 = extremely uncomfortable), pain (0 = no pain to 100 = worst pain imaginable), and nausea (0 = no nausea to 100 = severe nausea). Pain referred to the adverse feelings associated with the surgical incision, whereas discomfort referred to more global "whole body" feelings. The VAS assessments were performed before the midazolam premedication was administered (baseline) and at 24-h, 48-h, and 72-h intervals after the operation. A postoperative global pain assessment questionnaire was completed 72 h postoperatively.

An *a priori* power analysis determined that 25 patients in each group should be sufficient to detect a decrease of  $\geq 30\%$  in the PCA opioid analgesic requirement during the first 24 h after surgery based on the results of the preliminary study (9) ( $\alpha = 0.05$ ,  $\beta = 0.20$ ,  $SD = 5.3$ ). The patients' age, weight, and height; duration of surgery; PCA demands and delivered doses; postoperative analgesic usage; VAS scores; and recovery times were analyzed using one-way analysis of variance. If significant

differences were found, multiple comparisons were performed using Student's *t*-test with Bonferroni's adjustment. The incidence of side effects and the requirements for supplemental medications were compared among the four groups using the  $\chi^2$  test. Data are presented as mean values  $\pm$  SD, with *P* values  $< 0.05$  considered statistically significant.

## Results

The four TENS treatment groups were comparable with respect of both demographic and clinical variables. There were no significant intergroup differences in the patients' age, weight, height, surgical time or intraoperative opioid usage (Table 1).

The number of PCA demands and delivered doses of HM during the first 24 h postoperatively was significantly decreased in Groups III and IV compared with Groups I and II (Table 2). As a result, the total dosage of HM administered in the first 24 h after the operation was significantly decreased in Groups III ( $6.8 \pm 4.2$ ) and IV ( $6.5 \pm 3.5$ ) compared with Groups I ( $10.7 \pm 5.0$ ) and II ( $10.5 \pm 6.2$ ) (Table 2). In addition, the duration of PCA device use was significantly shorter in Groups III and IV than in Groups I and II (Table 3). However, there were no differences among the four groups with respect to the number of patients requiring supplemental injections of opioid or nonopioid oral analgesics (Table 2). There were also no significant differences in the length of the PACU stay, the duration of TENS usage, and the length of hospitalization among the four groups (Table 3).

The incidences of nausea and dizziness during the first 24 h after surgery, as well as the incidence of

**Table 1.** Demographic Data for the Four Treatment Groups

	Group I Sham	Group II Nonacupoint	Group III Dermatomal	Group IV Acupoint
<i>n</i>	25	25	25	25
Age (yr)	45 ± 12	44 ± 13	44 ± 13	43 ± 13
Weight (kg)	68 ± 15	72 ± 14	69 ± 16	70 ± 12
Height (cm)	172 ± 7	171 ± 8	169 ± 9	171 ± 8
Type of operation (H/M)	10/15	15/10	14/11	15/10
Duration of operation (min)	113 ± 33	112 ± 35	114 ± 34	108 ± 29
Intraoperative fentanyl (μg)	133 ± 38	142 ± 32	134 ± 39	134 ± 36

Values are means ± SD or *n*.  
H = hysterectomy, M = myomectomy.

**Table 2.** Postoperative PCA and Oral Analgesic Dosage Requirements in the Four Treatment Groups

	Group I Sham	Group II Nonacupoint	Group III Dermatomal	Group IV Acupoint
PCA demands ( <i>n</i> )				
In PACU	10 ± 7	10 ± 10	6 ± 4*†	6 ± 5*†
Total in 24 h	84 ± 49	80 ± 59	45 ± 34*†	45 ± 29*†
PCA deliveries ( <i>n</i> )				
In PACU	4 ± 2	4 ± 4	2 ± 2*†	2 ± 1*†
Total in 24 h	30 ± 16	29 ± 19	18 ± 13*†	17 ± 9*†
Hydromorphone (mg)				
In PACU	1.0 ± 0.6	1.1 ± 1.1	0.6 ± 0.5*†	0.5 ± 0.4*†
24-48 h	5.1 ± 4.7	4.7 ± 3.1	3.0 ± 1.9*†	2.8 ± 1.3*†
Total in 24 h	10.7 ± 5.0	10.5 ± 6.2	6.8 ± 4.2*†	6.5 ± 3.5*†
Supplemental analgesic medication ( <i>n</i> )				
0-24 h	3 ± 2	4 ± 2	3 ± 2	3 ± 3
24-48 h	5 ± 3	6 ± 4	5 ± 4	4 ± 4
Oral analgesics ( <i>n</i> )				
Acetaminophen (g in 24-72 h)	4.6 ± 3.0	4.3 ± 2.7	3.5 ± 2.3	3.9 ± 2.6
Oxycodone (mg in 24-72 h)	55 ± 36	51 ± 32	42 ± 27	46 ± 31

Values are means ± SD.  
PCA = patient-controlled analgesia, PACU = postanesthesia care unit.  
\* *P* < 0.05 versus Group I.  
† *P* < 0.05 versus Group II.

**Table 3.** Recovery Times for Patients in the Four Treatment Groups

	Group I Sham	Group II Nonacupoint	Group III Dermatomal	Group IV Acupoint
Time in PACU (min)	147 ± 34	149 ± 35	145 ± 32	145 ± 33
Duration of PCA therapy (h)	38 ± 9	37 ± 9	30 ± 8*†	31 ± 10*†
Duration of TENS therapy (h)	35 ± 8	36 ± 10	31 ± 7	32 ± 8
Days in the hospital (d)	4 ± 2	3 ± 2	3 ± 1	3 ± 2

Values are means ± SD.  
PACU = postanesthesia care unit, PCA = patient-controlled analgesia.  
\* *P* < 0.05 versus Group I.  
† *P* < 0.05 versus Group II.

dizziness 24-72 h after the operation were significantly reduced in Groups III and IV compared with Groups I and II (Table 4). The incidence of nausea 24-72 h after surgery was also significantly reduced in Group III compared with Group II (Table 4). The VAS sedation score at 24 h after surgery was significantly smaller in Groups III and IV (35 ± 25 and 31 ± 25, respectively) compared with Groups I and II (56 ± 29 and 53 ± 31, respectively).

On the follow-up global pain assessment questionnaire, 88%-96% of the patients reported that their postoperative pain was "adequately" treated (Table 5). Only one patient in Group IV complained about feeling "uncomfortable" electrical stimulation from the TENS device. The number of the patients who felt that TENS decreased their postoperative pain was significantly larger in Groups III and IV compared with Groups I and II (Table 5). Of interest, more than half of

**Table 4.** Postoperative Side Effects in the Four Treatment Groups

	Group I Sham	Group II Nonacupoint	Group III Dermatomal	Group IV Acupoint
Nausea				
0-24 h	22 (88)	22 (88)	15 (60)*†	16 (64)*†
24-72 h	19 (76)	20 (80)	13 (52)†	14 (56)
Vomiting				
0-24 h	8 (32)	8 (32)	6 (24)	5 (20)
24-72 h	4 (16)	5 (20)	2 (8)	2 (8)
Dizziness				
0-24 h	20 (80)	19 (76)	11 (44)*†	12 (48)*†
24-72 h	19 (76)	17 (68)	10 (40)*†	10 (40)*†
Itching				
0-24 h	13 (52)	12 (48)	9 (36)	10 (40)
24-72 h	11 (44)	9 (36)	6 (24)	9 (36)
Required antiemetics				
0-24 h	11	12	9	13
24-72 h	8	8	7	11
Required antipruritics				
0-24 h	3	4	1	1
24-72 h	2	2	1	3
Required sedative-anxiolytics				
0-24 h	3	2	3	2
24-72 h	5	5	3	5

Values are n (%).

\* P < 0.05 versus Group I.

† P < 0.05 versus Group II.

**Table 5.** Responses to the Posttherapy Global Assessment Questionnaire Regarding Transcutaneous Electrical Nerve Stimulation in Each of the Four Treatment Groups

	Group I Sham		Group II Nonacupoint		Group III Dermatomal		Group IV Acupoint	
	Yes	No	Yes	No	Yes	No	Yes	No
Adequacy of pain relief	23	2	22	3	24	1	22	3
Felt treatment was uncomfortable	0	25	0	25	0	25	1	24
Felt treatment decreased pain	5	20	8	17	15	10*†	17	8*†
Felt treatment improved sleep	6	19	8	17	8	17	9	16
Use device after a future operation	25	0	24	1	25	0	25	0
Willing to pay extra to receive therapy	14	11	15	10	18	7	17	8

Values are n.

\* P < 0.05 versus Group I.

† P < 0.05 versus Group II.

the patients expressed a willingness to pay extra to receive TENS therapy after a future operation, including those in the sham TENS and nonacupoint (shoulder) groups (Table 5).

## Discussion

According to traditional Chinese medicine, the Zusanli acupoints are highly effective in relieving lower abdominal pain. In human volunteer studies, when TENS was applied at the Zusanli and Hegu acupoints, it produced marked increases (367%) in immunoreactive met-enkephalin-arg-phe (ir-MEAP) in the lumbar cerebrospinal fluid (10). The integration of Chinese acupuncture-based techniques with conventional

Western practices (e.g., TENS and PCA therapies) may make it possible to improve the control of acute postoperative pain (11). This study clearly demonstrates the benefits of using a nonpharmacologic complementary (or alternative) therapy in combination with PCA for controlling postoperative pain.

In a preliminary study (9), we demonstrated that concurrent stimulation at both a classical Chinese acupoint and the periincisional dermatomes with a high intensity (9-12 mA) of TENS produced a 50% decrease in the postoperative opioid analgesic requirement and also reduced opioid-related side effects. Because many factors can influence the effect of this nonpharmacologic therapy on postoperative pain, we designed this follow-up study to examine the effect of the specific

site of electrical stimulation (i.e., acupoint versus nonacupoint) on the opioid analgesic requirement and the incidence of opioid-related side effects. The current study demonstrates that electrical stimulation at either the dermatomal level of the skin incision or the Zusanli acupoint can significantly decrease the requirement for opioid analgesics in the postoperative period. The postoperative PCA requirement for HM was 35% and 38% less when the electrical stimulation was administered either at the dermatomes corresponding to the surgical incision or the Zusanli acupoint, respectively, compared with the nonacupoint (shoulder) group. Interestingly, there was no difference in the PCA opioid requirement when electrical stimulation was applied at the nonacupoint (shoulders) compared with a sham (no electrical current) treatment at the acupoint.

In comparing these findings with the preliminary study involving a similar patient population (9), it seems that simultaneous stimulation at both the dermatomal level corresponding to the skin incision and an acupoint can produce a greater opioid-sparing effect (62%) than stimulating either site alone. The failure to include a combination acupoint (Zusanli) and periincisional dermatome stimulation group is a deficiency in the design of this study. In the incisional dermatome and acupoint treatment groups, 60% and 68% of the patients, respectively, felt that TENS therapy decreased their pain, compared with only 20% and 32% of the patients in the sham and nonacupoint groups, respectively. Surprisingly, more than half of the patients in all groups indicated that they would be willing to pay extra to receive TENS therapy after a future operation. These data suggest that the availability of the TENS device provides a degree of patient comfort independent of its effect on the postoperative opioid analgesic requirement. This finding is consistent with the well known placebo effect produced by nonpharmacologic therapies. Unfortunately, we did not record the number of times that the patient actually activated the TENS device during the study period. The similar overall adequacy of pain relief in 88%–96% of the patients in all four treatment groups is a reflection of the combined efficacy of TENS and PCA therapies in controlling pain after lower abdominal surgery.

The incidence of opioid-related side effects, such as postoperative nausea and dizziness, was significantly reduced in the incisional dermatome and acupoint stimulation groups compared with the sham and nonacupoint groups. In addition, the opioid-sparing effect may have contributed to a decrease in postoperative sedation. The reduction in these common postoperative side effects may be both the result of the decreased opioid

requirement and an effect of improved pain relief on postoperative nausea (12). Analogous to the findings with respect to their opioid-sparing effects, there were no differences between the periincisional dermatome and acupoint stimulation groups with respect to the incidences of opioid-related side effects during the 72-h study period. Importantly, both periincisional and acupoint stimulation decreased the duration of time that patients required PCA therapy to control their pain symptoms.

In conclusion, electrical stimulation applied at the dermatomal levels corresponding to the skin incision or the Zusanli acupoint produced comparable decreases in the postoperative PCA requirement and opioid-related side effects compared with nonacupoint and sham (nonelectrical) stimulation. These data demonstrate that the site of electrical stimulation is an important determinant of its pain-relieving efficacy after surgery. However, incisional dermatomal stimulation was as effective as acupoint stimulation in producing opioid-sparing effects after lower abdominal surgery.

## References

1. White PF. Use of patient-controlled analgesia for management of acute pain. *JAMA* 1988;259:243-7.
2. Joshi GP, White PF. Patient controlled analgesia. In: Ashburn MA, Rice LJ, eds. *The management of pain*. New York: Churchill Livingstone, 1998:577-611.
3. White PF. Mishaps with patient-controlled analgesia (PCA). *Anesthesiology* 1987;65:81-3.
4. White PF, Parker RK. Is the risk of using a "basal" infusion with patient-controlled analgesia therapy justified? *Anesthesiology* 1992;76:489-90.
5. McCallum MI, Glynn CJ, Moore RA, et al. Transcutaneous electrical nerve stimulation in the management of acute postoperative pain. *Br J Anaesth* 1988;61:308-12.
6. Stubbing JF, Jellicoe JA. Transcutaneous electrical nerve stimulation after thoracotomy: pain relief and peak expiratory flow rate—a trial of transcutaneous electrical nerve stimulation. *Anaesthesia* 1988;43:296-8.
7. Benedetti F, Amanzio M, Casadio C, et al. Control of postoperative pain by transcutaneous electrical nerve stimulation after thoracic operations. *Ann Thorac Surg* 1997;63:773-6.
8. Carroll D, Tramer M, McQuay H, et al. Randomization is important in studies with pain outcomes: systematic review of transcutaneous electrical nerve stimulation in acute postoperative pain. *Br J Anaesth* 1996;77:798-803.
9. Wang BG, Tang J, White PF, et al. Effect of the intensity of transcutaneous electrical stimulation on the postoperative analgesic requirement. *Anesth Analg* 1997;85:406-13.
10. Han JS, Chen XH, Sun SL, et al. Effect of low- and high-frequency TENS on Met-enkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF. *Pain* 1991;47:295-8.
11. Andersson S, Lundeberg T. Acupuncture: from empiricism to science—functional background to acupuncture effects in pain and disease. *Med Hypoth* 1995;45:271-81.
12. Andersen R, Krohg K. Pain as a major cause of postoperative nausea. *Can Anaesth Soc J* 1976;23:366-9.