The effects of acupuncture after thyroid surgery: A randomized, controlled trial

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Background. Acupuncture is a safe and well-tolerated treatment for pain relief. Previous studies supported the effectiveness of several acupuncture techniques for postoperative pain. The aim of this randomized, controlled trial was to evaluate the efficacy of acupuncture in reducing pain after thyroid surgery.

Methods. We randomized 121 patients to a control group (undergoing only standard postoperative analgesic treatment with acetaminophen) and an acupuncture group, undergoing also either electroacupuncture (EA) or traditional acupuncture (TA). Pain was measured according to intraoperative remifentanil use, acetaminophen daily intake, Numeric Rating Scale (NRS), and McGill Pain Questionnaire on postoperative days (POD) 1–3.

Results. Acupuncture group required less acetaminophen than controls at POD 2 (P = .01) and 3 (P = .016). EA patients required less remifentanil (P = .032) and acetaminophen than controls at POD 2 (P = .004) and 3 (P = .008). EA patients showed a trend toward better NRS and McGill scores from POD 1 to 3 compared with controls. EA patients had a lower remifentanil requirement and better NRS and McGill scores than TA patients. No differences occurred between TA patients and controls.

Conclusion. Acupuncture may be effective in reducing pain after thyroid surgery. EA is more useful; TA achieves no significant effects. (Surgery 2014;156:1605-13.)

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Thyroidecomy represents one of the most frequent procedures in endocrine surgery. Postoperative pain in patients undergoing thyroidecomy is the result of superficial incision, tissue dissection, and neck position during surgery. It needs appropriate control during the first days after the procedure. Administration of opioids and/or nonopioid drugs is often required, with frequent worsening of anesthetics-induced nausea and vomiting, and other side effects.

Alternative medicine may offer additional options for adequate management of postoperative pain. Acupuncture, a component of traditional Chinese medicine, is a well-known alternative and widely used treatment for pain, especially in Asian countries. In recent years, an increased use of acupuncture has been observed also in Western countries; the National Institutes of Health and the World Health Organization have recognized the safety and efficacy of the procedure for the treatment of neck pain. Thus, several clinical trials evaluating the efficacy of acupuncture as adjuvant method for postoperative analgesia have been published.

Conflicting results have been reported, probably owing to the heterogeneity in acupuncture techniques that may consistently vary according to the site, timing and type of stimulation. In fact, electric, chemical, or physical stimulations have been also used in several studies to increase the effectiveness of the procedure. This randomized, controlled trial evaluated the effectiveness of acupuncture in reducing pain in patients undergoing thyroid surgery.

MATERIALS AND METHODS

The present prospective, randomized, controlled, observer-blinded trial included a consecutive series...
of Caucasian patients undergoing total thyroidec-
tomy for benign disease, enrolled between May 2011
and December 2012 at the Endocrine Surgery Unit,
University of Padua, Italy.

The study protocol was designed according to
Helsinki declaration principles and approved
by the local Institutional Ethic Committee; this
trial was also registered at ClinicalTrials.gov
(NCT01579786). All patients gave the informed
consent. Patients were randomized by a closed en-
nvelope method to a control group, undergoing
standard postoperative analgesic treatment
(including acetaminophen ≤3,000 mg/day), or
an acupuncture group, undergoing electroacu-
puncture (EA) or traditional acupuncture (TA)
according to the availability of a dedicated electric
stimulator in addition to standard postoperative
analgesic treatment (Fig 1).

The endpoints were the intraoperative pain
(measured by remifentanil consumption during
anesthesia) and postoperative pain, measured by
Numeric Rating Scale (NRS), the McGill Pain
Questionnaire, and analgesic (acetaminophen)
consumption.13,14

Exclusion criteria were age <18 or >80 years;
American Society of Anesthesiologists score >2;
presence of severe arthritis or osteoporosis of the
spine; myofascial pain or fibromyalgia; previous
neck and head surgery or traumatic injuries; severe
neurologic, respiratory, or cardiovascular diseases;
psychiatric diseases; history of drug addiction;
alcoholism; and chronic or recent use of analgesic,
neuroleptic drugs, or tranquilizers (benzodiaze-
pine, antidepressants inhibiting the reuptake of
serotonin or hypnotics).15

Acupuncture was performed by 2 experienced
acupuncturists (S.Z. and H.G.), approximately
30 minutes before surgery and in the morning of
postoperative day (POD) 1, using Hwato needles
(40 mm long, 0.30 mm thick) inserted bilaterally
and superficially (5 mm), at Hegu-LI4 and
Neiguan-Pc6 points. LI4 is located between the
first and the second metacarpal bones on the
dorsal hand region; Pc6 is located on the anterior
side of the forearm, 2 cun (about 5 cm) proximal
to the palmar wrist crease, between the tendons of
the muscle palmaris longus and the muscle flexor
carpi radialis (Fig 2). The stimulation of these
points has been previously reported to achieve
antinociceptive effects on cervical region after thy-
roid surgery.16 Sessions lasted 30 minutes; in TA
patients, needles were stimulated manually at the
insertion until feeling De-Qi sensation (a sensation
of numbness and distension) and every 10 minutes;
in EA patients, needles were stimulated using a
dedicated electric stimulator (Agistim Duo
Sedatelec, Irigny-Lyon, France); the stimulus was
delivered in continued waves at the intensity of
6–8 Volts and a frequency of 25 Hz.

Surgery was performed by or under the direct
supervision of the same surgeon (M.I.) with the
standard technique and a mild hyperextension of
the neck; the procedure was carried out under
general anesthesia with orotracheal intubation,
performed by the same team of anesthesiologists.
Surgeons and anesthesiologists were blinded to the
randomization of each patient.

A standardized intravenous anesthetic protocol
was used: Anesthesia was induced with fentanyl
(100 µg), propofol 1% (2.5 mg/kg), and cisatra-
curium (0.2 mg/kg). It was maintained with
remifentanil, propofol 1% (5 mg/kg/h), and cis-
catracurium (2 µg/kg/min); remifentanil was
titrated from 0.05 to 1 µg/kg/min to obtain a
bispectral index ranging between 40 and 60,17
monitored by a dedicated device (BIS View, Aspect
Medical system, Norwood, MA).

Postoperative analgesia during the first 24 hours
after surgery was provided by a standardized drug
treatment including intravenous ketorolac
(30 mg) and acetaminophen (3,000 mg) adminis-
tration in all patients. In the following PODs, oral
acetaminophen, at doses of 500 mg in tablets up to
a maximum of 3,000 mg/day, was self-administered
by the patient according to the need to obtain pain
relief.

Demographics (including age, sex, and patient
weight), disease type (euthyroidism or hyperthy-
roidism according to preoperative laboratory data),
weight of the removed thyroid, duration of surgery,
remifentanil consumption (measured as µg/kg/
min), subjective perception of postoperative pain,
and self-administered acetaminophen daily consumption were recorded and compared.

Postoperative pain was assessed in the morning on PODs 1–3 by NRS and the Italian Version of McGill Pain Questionnaire. NRS measures the pain intensity, ranging from 0 (no pain) to 10 (worst possible pain); the McGill Pain Questionnaire measures the quantity and quality of pain, using descriptive words selected to capture the patient’s pain experience, and converting in a numerical score, ranging between 0 (minimal pain score) and 20 (maximal pain score). Acetaminophen consumption was measured from POD 1 to 3 according to the number of required doses, converted to milligrams per day.

Independent observers not present during treatment and blinded to randomization handled all data, including the recording sheets with the remifentanil and acetaminophen consumption, the NRS, and the McGill Pain Questionnaire. After the discharge, the survey was completed directly by the patients or by phone interview.

Statistical significance (α) for a 2-tailed test was set at .05, a power (1-β) at 0.90, and an expected standardized effect size at 0.60, the consequent sample size required was 58 patients per group. Data are presented as absolute numbers or median (interquartile range). Statistical analysis was performed using Fisher’s exact test, Student’s t test, Kruskall–Wallis analysis of variance, Mann–Whitney U test, and Bonferroni correction for multiple comparisons, as appropriate.

RESULTS

The Consolidated Standards of Reporting Clinical Trials flow chart for the study is provided in Fig 1. We identified 167 consecutive eligible patients; the majority (83%) agreed to participate in the study. Nineteen patients were withdrawn because they refused surgery after enrolment (n = 4), rescinded consent to participate in the trial (n = 6), or did not fill out the questionnaires assessing pain control (n = 9). The remaining 121 randomly assigned patients were evaluable for the endpoints of the study: 62 patients in the control group and 59 patients in the acupuncture group (27 EA and 32 TA cases).

No adverse events were attributed to acupuncture. In particular, no local complications such as bleeding, hematoma, or infection occurred after the procedure; treatment was well tolerated in all cases.

Table I outlines the baseline characteristics of each group. No differences were found between control and acupuncture patients concerning demographics, patient weight, disease type, thyroid weight, or duration of the operative procedure.

Standard care versus acupuncture. Patients undergoing acupuncture required less acetaminophen than controls only at POD 2 (P = .010) and 3 (P = .016). Otherwise, no differences occurred.
between the control and acupuncture groups concerning remifentanil consumption ($P = .388$); NRS score at the POD 1 ($P = .118$), 2 ($P = .486$), and 3 ($P = .281$); McGill score at POD 1 ($P = .164$), 2 ($P = .534$), and 3 ($P = .251$); and acetaminophen consumption at the POD 1 ($P = .658$; Table II; Fig 3).

**Standard care versus EA and TA.** Subgroup analysis showed that EA patients required less remifentanil ($P = .032$), and had a lesser acetaminophen consumption at POD 2 ($P = .004$) and 3 ($P = .008$) compared with controls, without any significant difference in analgesic requirement at POD 1 ($P = .272$; Table II; Fig 4).

A trend toward significant lower NRS score at POD 1 ($P = .097$), 2 ($P = .054$), and 3 ($P = .072$) was found in EA patients compared with controls. Similarly, a trend toward significant lower McGill score occurred in EA patients compared with controls at POD 1, 2, and 3 ($P = .081$, .058, and .061, respectively).

No differences were found between TA patients and controls concerning each of the examined outcomes. EA patients had a lesser remifentanil consumption ($P = .025$), lower NRS score at POD 2 ($P = .008$), and lower McGill score at POD 2 ($P = .003$) and 3 ($P = .029$) compared with TA patients.

**DISCUSSION**

Acupuncture has been used in China and East Asia for >2,500 years; in recent years, it has been recognized as a safe, well-tolerated, and effective analgesic procedure by international health care institutions.5,6

Multiple physiologic models have been proposed to explain the analgesic effects of acupuncture stimulation9: it modulates the transmission of nervous signaling in the nociceptive pathways, activating the mesencephalic reticular formation, inhibiting the dorsal horn of spinal cord and the parafascicular thalamic nuclei; it increases the endorphin release at both spinal and supraspinal levels.18

Recently, several clinical trials have suggested the efficacy of acupuncture as an adjuvant method for postoperative analgesia7,8,19; however, conflicting results have been reported also.10-12 It is difficult to achieve a definitive conclusion from reviewing the literature; the main challenge is related to the language of publications (most papers have been published only in Chinese); furthermore, most studies reach only a low level of evidence, because of methodologic bias and lack of standardized procedures. In fact, several variants of the traditional method have been used to increase the acupuncture
efficacy; EA is among the most used adjunct both in clinical and experimental models.20 EA is a modified acupuncture technique that utilizes electrical stimulation; it is considered more efficient than manual TA in pain relief. In fact, the application of low-intensity continuous electric stimulation to acupuncture is more effective in inducing nervous reflex responses and releasing endogenous opioids in the central nervous system, with subsequent increased analgesic effects.20-22

Previous papers have suggested a role for acupuncture in analgesia after thyroidectomy.16,23 To the best of our knowledge, the present study is the first prospective, randomized, clinical trial in the English literature focusing on acupuncture efficacy in pain control after thyroid surgery. Our results confirmed that acupuncture is a well-tolerated procedure. It was effective in reducing pain after thyroidectomy, as demonstrated by a significant reduction of acetaminophen consumption at POD 2 and 3. However, no evident differences were observed in terms of self-perceived pain as shown by NRS and McGill Questionnaire, and these results may be explained by the efficacy of the standard care for pain control.

Subgroup analysis revealed even more convincing results, suggesting a more clear effectiveness of EA. In our study, EA patients showed lower intraoperative and postoperative pain than controls and TA patients, at least at POD 2 and 3.

Intraoperative pain was evaluated by the consumption of remifentanil, an analgesic drug titrated according to the intraoperative clinical signs and the bispectral index. The bispectral index provides a continuous monitoring of the depth of anesthesia, that is influenced by pain17,24; thus, remifentanil consumption may be considered an indirect index of intraoperative pain.

EA patients required less remifentanil than controls and TA patients. Bias related to the team of anesthesiologists could not be excluded, although it might be unlikely because the anesthesiologists delivering the drug were blinded to the randomization. A further limitation could be the potential inaccuracy of remifentanil consumption in intraoperative pain monitoring, because it is only an indirect index and may be biased by the influence of pharmacokinetic factors; however, it is widely used in clinical trials because of lack of further direct and reliable evaluative index of intraoperative nociception.17,24

Postoperative pain was evaluated by NRS, McGill Pain Questionnaire and, indirectly, by acetaminophen requirements. NRS and McGill questionnaire are reliable and validated methods for perceived pain evaluation. NRS describes the

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<th>Table II. Pain control outcomes after total thyroidectomy in 121 patients randomized to control or acupuncture groups</th>
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<td><strong>Outcome</strong></td>
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<td><strong>Total</strong> (n = 59)</td>
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<td>EA (n = 27)</td>
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<td>TA (n = 32)</td>
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<td><strong>Remifentanil consumption</strong> (mg/kg/min)</td>
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<td><strong>NRS</strong></td>
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<td><strong>McGill score</strong></td>
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Results expressed as median values (interquartile range). EA, Electroacupuncture; TA, traditional acupuncture; POD, postoperative day.
The intensity of pain, and the McGill questionnaire explore its multifactorial nature. EA patients had a significantly lesser acetaminophen consumption than controls at POD 2 and 3 ($P = .004$ and $P = .008$, respectively). Similarly, a trend toward lower NRS and McGill score was found at POD 1–3 in EA patients compared with controls. Furthermore, NRS and McGill score at POD 2 and 3 were significantly lower in EA than TA patients; no significant differences were found between TA patients and controls, concerning each examined outcome.

However, some limitations to the present study should be noted. It focused on a highly selected population, including only patients with benign thyroid diseases and without associated risk factors that are not representative of usual clinical practice. The selection was performed to obtain a homogeneous population; patients with thyroid malignancies and associated comorbidities were not included to avoid potential bias from more extensive surgery (nodal dissection) and interferences in pain perception, respectively.

A further limitation was the lack of double-blinded randomization; in fact, patients were aware of the treatment received; thus, a placebo effect cannot be excluded. However, although the trial was not designed for a subgroup analysis, different outcomes in EA and TA patients were detected. Patients were not obviously conscious of the technical differences between the procedures, thus, they might be considered blinded. Furthermore, acupuncture has proven analgesic effects on animal models, allowing to exclude a primary role of psychological factors on its efficacy.

Interestingly, the efficacy of acupuncture was less evident at POD 1; no differences in acetaminophen requirement were found. There was a trend in favor of EA patients detected according to the NRS and McGill score. The limited efficacy might be due to baseline analgesic treatment administered to all patients during the first 24 hours after surgery, possibly interfering with the outcomes on POD 1.

In our experience, conventional analgesic therapy was effective in managing pain after thyroid surgery.

Fig 3. Outcomes of postoperative pain in the control and acupuncture groups.
surgery, because NRS and McGill score were always moderate in controls; the difference in analgesic drug requirement was minimal in all cases, but significant.

Acupuncture is a time-consuming procedure and requires specific devices and experienced operators; subsequently, it could not be considered a cost-effective alternative to drugs, at least in Western countries. However, because it causes no harm, acupuncture may be used as an adjunct to conventional pharmaceutical approaches, particularly in cases of hyperalgesia or when conventional techniques fail or are associated with severe drug-related adverse events.

In conclusion, our study suggests a role for acupuncture in pain management after thyroid operations. EA is effective in reducing intraoperative and postoperative pain; however, TA seems to achieve no relevant effects. Additional research should focus on the effects of different acupuncture techniques on larger and unselected surgical populations.

The authors thank Professor Gennaro Favia for help and useful suggestions during the preparation of the study.

REFERENCES
DISCUSSION

Dr Quan-Yang Duh (San Francisco, CA): I have a couple of comments and a couple of questions for you. The points that were chosen are exactly the same points that people use in China for actual operations; not just for postoperative care, but for doing surgery under acupuncture as well!

One of the questions I have for you is: Have you considered doing this preoperatively, not just postoperatively? Because there is some evidence that you can decrease the pain. Related to that: How do you treat the patient intraoperatively? Do you use local anesthesia or regional block in addition to acupuncture?

My third question is whether there are any differences in nausea, because acupuncture can be used also to reduce postoperative nausea.

Dr Maurizio Iacobone (Padua, Italy): Thank you for your questions. Acupuncture was performed both preoperatively and postoperatively; pain was measured both intraoperatively and postoperatively. Concerning your questions about local anesthesia, we have not used local anesthesia or locoregional blocks during neck surgery. Finally, we have no data concerning postoperative nausea, but I know that literature reports a lot of studies concerning the effects of this procedure. However, we have observed that a lot of patients declared a decreased anxiety after this procedure, although this issue was not assessed in our paper.

Dr Laurent Brunaud (Vandoeuvre les Nancy, France): I come back to the control group. If I have understood properly, those patients had no local cervical block, because it may be a potential bias. If you have a control group in which you can decrease the pain, it is more difficult to prove potential benefit for the acupuncture. I just want to make sure that you had no local anesthesia on your control group.

Dr Maurizio Iacobone: You are right; it could be a good idea to compare acupuncture and local anesthesia, but we did not use local anesthesia or locoregional blocks in the acupuncture or in the control group.

Dr Keith Heller (New York, NY): Very nice to see a randomized, prospective study. I particularly congratulate you on your honesty in the limitations of the study, because you have recognized the possible limits of this technique. My question is: Could you at least eliminate the placebo effect by
using as your control not a group with no needles but a group where the needles were put in a position where you would expect no effect? Assuming the patient and the anesthesiologist did not know which position was the useful position, you might be able to eliminate the placebo effect.

**Dr Maurizio Iacobone:** Thank you for your suggestion; it is the so called “sham acupuncture.”

**Dr Rachael Slotcavage** (Camden, NJ): I also wanted to address the placebo effect issue. Because obviously the patients cannot be blinded to the fact that they are receiving acupuncture, with the exception of the sham acupuncture issue, I was wondering if your group collected any data on whether the patients were preoperatively acupuncture naive or had any preconceived notions about the effectiveness of acupuncture therapy, because that might be another way to address the placebo effect.

Essentially, I was just wondering whether your group collected any data on patient’s preconceived notions on acupuncture prior to undergoing therapy.

**Dr Maurizio Iacobone:** We decided to exclude Asian patients from the study, because they may have preconceived notions about this procedure, because it is more widely used in those regions. In our country, acupuncture is not a common procedure, and it is not officially recognized or refunded by the public health system. Thus, although it cannot be excluded, I believe that most patients in our group had no previous or preconceived experiences concerning acupuncture.