Auricular acupuncture for treatment of preoperative anxiety in patients scheduled for ambulatory gynaecological surgery: a prospective controlled investigation with a non-randomised arm

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ABSTRACT

Objective Auricular acupuncture (AA) is a promising alternative treatment for situational anxiety. The aim of this pilot investigation was to test the acceptability and feasibility of AA as a treatment for preoperative anxiety (PA) in preparation for a subsequent randomised controlled trial.

Methods AA was offered for treatment of PA to female patients who were scheduled for ambulatory gynaecological surgery. In patients who agreed, indwelling fixed needles were applied bilaterally at the points MA-IC1, MA-TF1, MA-SC, MA-AH7 and MA-T the day before surgery. Patients who declined AA but agreed to be examined constituted the control group (no intervention). State anxiety (primary outcome) was measured using the State-Trait-Anxiety Inventory (STAI) before AA (time I), the evening before surgery (time II) and immediately before surgery (time III). Anxiety was measured with a 100 mm visual analogue scale (VAS-100); heart rate, blood pressure and serum cortisol were also quantified.

Results Data from 62 patients (32 with AA and 30 with no intervention) were analysed. Whereas preoperative anxiety was reduced after AA the evening before surgery ($P<0.01$), anxiety levels in the control group increased from the first to the last measurement ($P<0.001$). Secondary outcomes were comparable between the patients from both groups.

Conclusions AA was acceptable and feasible as a treatment for preoperative anxiety. The results were used for the sample size calculation of a subsequent randomised controlled clinical trial.

Trial registration number NCT02656966; Results.

INTRODUCTION

Patients undergoing surgery often experience acute psychological distress in the preoperative period, including feelings of uncertainty, loss of control and decreased self-esteem, anticipation of postoperative pain, as well as the fear of separation from their family.[1] All these symptoms, known as preoperative anxiety syndrome, may have a profound effect on patients, not only influencing their quality of life but also the course and outcome of their surgical procedure.[2–6] However, pharmacological therapy for preoperative anxiety is associated with numerous medico-biological and economical adverse effects.[7 8] Moreover, in patients undergoing surgical procedures in an ambulatory care setting, the use of sedative drugs for premedication should be critically discussed.[9]

Auricular acupuncture (AA) is a complementary medicine technique, which has already been used to treat situational anxiety in clinical settings.[10–13] In 1987, Lewis and Litt found auricular acupressure and relaxation methods to be as effective as diazepam for premedication in 90 patients scheduled for surgery under general anaesthesia; those alternative treatments were associated with a reduced autonomous stress reaction as well as fewer side effects compared with diazepam treatment.[10] Karst *et al*[11] confirmed these results using the same model of situational anxiety in 67 patients scheduled for dental extraction. The authors compared AA with intranasal midazolam, placebo acupuncture and no treatment. Michalek-Sauberer *et al*[12] reported AA

to be more effective than sham acupuncture and no intervention at achieving anxiolysis in a sample of 182 patients scheduled to undergo dental procedures. In a recently published randomised investigation, Luo *et al*[13] found auricular acupressure to be superior to placebo acupressure for the reduction of preoperative anxiety in patients undergoing gynaecological surgery. The data from experimental research suggest that, due to unique neuroanatomical conditions, auricular stimulation exerts anxiolytic effects through involvement of cranial nerves,[14] which leads to the modulation of brain areas involved in the stress response such as the limbic system, locus coeruleus and hypothalamus.[15–17]

Given these findings, it seems possible that auricular stimulation might serve as an effective replacement for benzodiazepines, which are still widely used in Europe to treat preoperative anxiety as part of a standard premedication before surgery.[7]

This aim of this pilot investigation was to test the acceptability and feasibility of outcome measurements following AA as a simple, non-pharmacological treatment of preoperative anxiety in comparison with no intervention. Furthermore, we anticipated that the results should provide the necessary data to calculate the required sample size for a subsequent randomised controlled trial (RCT).

METHODS

Design and participants

This prospective open clinical study was conducted at University Medicine Greifswald from December 2015 to April 2016. The local ethics committee approved the study protocol. Patients were recruited according to the following eligibility criteria: American Society of Anaesthesiologists physical status I to II; scheduled for elective ambulatory gynaecological surgery under standardised general anaesthesia with a duration of surgery ≤60 min; aged between 19 and 55 years; able to fill in the study questionnaires; and without previous use of opioid or psychotropic medication, current psychiatric disorders or local skin infection at the sites of acupuncture. Patients were excluded when intraoperative complications (haemorrhage requiring transfusion of >6 units of packed red cells, or cardiovascular instability requiring catecholamines) or failures to follow the standardised schema of general anaesthesia occurred, as well as if patients took opioid medication ≤6 months before surgery or developed local auricular/systemic infection or a severe intercurrent disease during the study.

During the standard preoperative anaesthesiology examination, patients were informed, in writing, about the aim and procedures of the study. Afterwards, patients were asked if they wanted to participate and receive AA as treatment for preoperative anxiety before ambulatory surgery. Patients who declined AA were asked to take part in a routine internal audit of perioperative anxiety without any intervention and without any change in routine clinical care for ambulatory patients. Patients in this non-randomised arm constituted the control group receiving 'no intervention' in this investigation (figure 1). Written informed consent was obtained from each participant.

Auricular acupuncture

A licensed acupuncturist, with >5 years' experience of AA, applied indwelling fixed 'New Pyonex' needles (length 1.5 mm, diameter 0.22 mm; Seirin Corp,

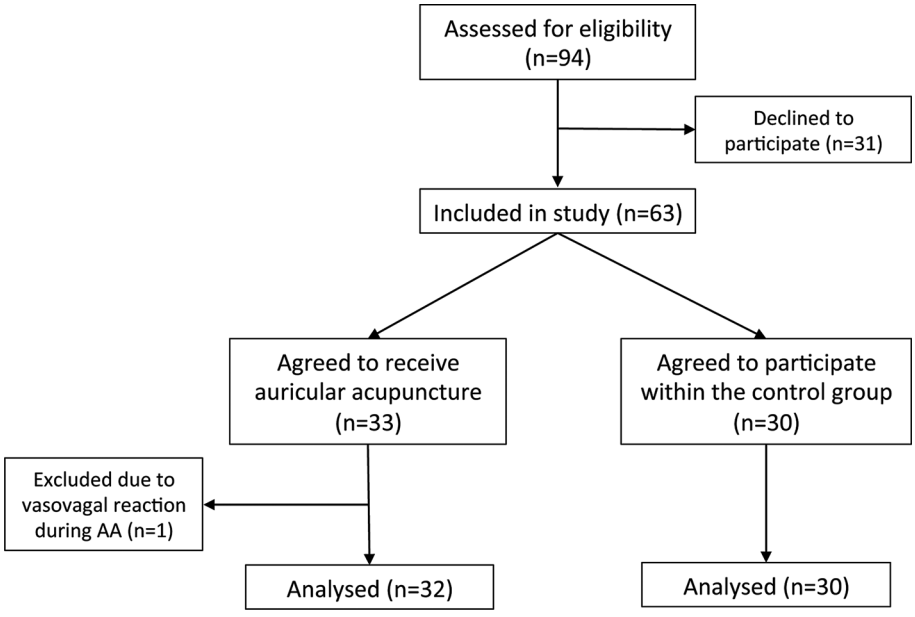

Figure 1 Study flow diagram. Patients meeting the eligibility criteria were asked to participate in the study. Those who declined auricular acupuncture (AA) as treatment for preoperative anxiety were asked to participate in a routine internal audit of perioperative anxiety during standard clinical care (control group with no intervention).

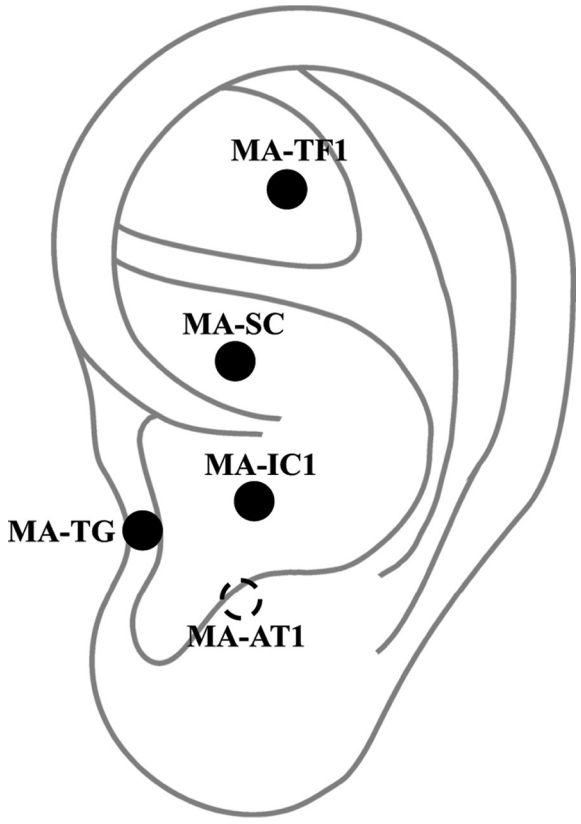

Figure 2 Localisation of the auricular acupuncture points used to treat preoperative anxiety: MA-SC, Kidney; MA-TF1, Ear Shenmen; MA-IC1, Lung; MA-AT1, Subcortex; MA-TG, Adrenal gland.

Shizuoka City, Japan) bilaterally at the following five ear acupuncture points: MA-IC1 (Lung), MA-TF1 (ear Shenmen), MA-SC (Kidney), MA-AT1 (Subcortex) and MA-TG (Adrenal gland, figure 2), according to the AA nomenclature of the WHO[18] and French classification.[19] The choice of acupuncture points was based on the methodology of our randomised controlled study of the treatment of situational (exam) anxiety in medical students,[20 21] as well as the AA patterns from previous investigations.[10–13]

Before needle insertion, the skin was disinfected with alcohol swabs. Patients were instructed by the acupuncturist to stimulate the auricular needles for 3–5 min if they felt anxious. AA needles were placed the day before surgery, immediately after the preoperative anxiety level was assessed for the first time (figure 3). The needles remained in situ until the next day and were removed after surgery, right before being discharged home.

General anaesthesia and postoperative analgesia

All patients in the study received standardised general anaesthesia. Anaesthesia was performed using propofol 2–3 mg/kg, sufentanil 0.02 µg/kg and mivacurium 0.2 mg/kg as muscle-relaxing agents, if tracheal intubation was required. Lung ventilation was either manually or mechanically controlled to keep end-tidal carbon dioxide at 4.5–5.3 kPa throughout the surgery. Anaesthesia was maintained using either continuous infusion of propofol 4–8 mg/kg/hour or the volatile anaesthetic sevoflurane with end-tidal concentration 1.5–2 volume % in a 40% oxygen-air mixture.

Perioperative PONV (postoperative nausea and vomiting) prevention was provided according to departmental-internal standard using PC6 acupuncture and dexamethasone 0.01 mg/kg. Treatment of postoperative pain included either acetaminophen 4×1 g or metamizole 4×1 g daily, supplemented by injections of piritramide (opioid analgesic with 0.7 potency of morphine) 0.01–0.015 mg/kg if required.

Outcome measures

The primary outcome measure was preoperative anxiety, measured before the AA intervention or at a comparable time point in the control group (time I), in the evening of the day before surgery (time II) and immediately before surgery (time III, figure 3) using the state form of the German version of the STAI, ranging from 20 (= no anxiety) to 80 (= maximum imaginable anxiety).[22] Secondary outcome measures were anxiety level, measured using a 100 mm VAS (VAS-100; 0 = no anxiety and 100 = maximum imaginable anxiety) at time points I, II and III, as well as heart rate and blood pressure, which were registered throughout the course of the study. Serum cortisol was measured at time point II using a competitive immunoassay on

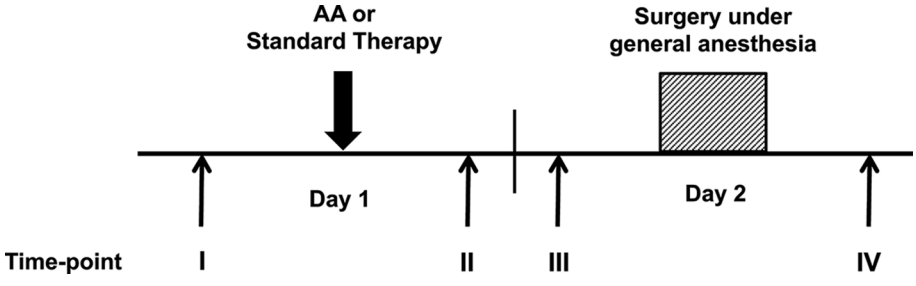

Figure 3 Timeline of outcome measurement. I: afternoon of the day before surgery; II: evening of the day before surgery; III: morning of the day of surgery; IV: discharge home in the afternoon. Auricular acupuncture (AA) was performed in the afternoon of the day before surgery using indwelling fixed needles, which remained in situ and were removed after surgery immediately before discharge. Preoperative anxiety was measured using the State-Trait-Anxiety Inventory (STAI) and a 100 mm visual analogue scale (VAS-100) at time I, II and III. Serum cortisol was measured at time point III (immediately before surgery).

Table 1 Patients' characteristics

	Auricular acupuncture (n=32)	No intervention (n=30)
Age (years)	37±10	36±9
Body mass (kg)	71±16	72±17
Height (cm)	167±7	168±7
Body mass index (kg/m^2)	24.4±6.8	25.4±5.8
Trait anxiety	44±11	41±10

Data presented as mean±SD.

the basis of ADVIA-Centaur chemiluminescence technology (Siemens Healthcare Diagnostics, Eschborn, Germany) according to the guideline of the German Medical Association on Quality Assurance in Medical Laboratory Examinations.[23]

Statistical analysis

The aim of this pilot investigation was to generate data for the sample size calculation of a subsequent RCT. Since the state anxiety data (measured with STAI) was assumed to be nearly normally distributed among 30 subjects, the sample size was set to 30 for each group (AA and 'no intervention'). Analysis of the primary outcome was performed using analysis of variance (ANOVA) for repeated measures with the between-subject factor GROUP (AA vs no intervention) and within-subject factor TIME (measurement time points I to III). Post-hoc comparison, as well as the analysis of secondary outcome measures, was performed using Student's t-test (for normally distributed data) and the Wilcoxon signed rank test (for skewed data) within each group. IBM SPSS Statistics Software (Version 22.0) was used for data analysis. P values were corrected for multiple comparisons using the Holm-Bonferroni procedure and adjusted P values <0.05 were regarded as significant. All data are presented as mean±SD unless otherwise stated.

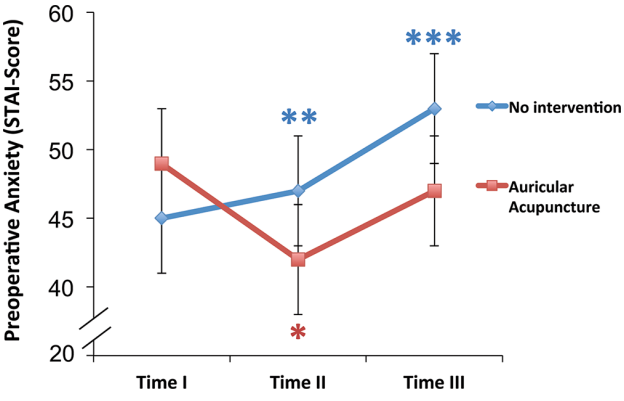

Figure 4 Preoperative anxiety, measured in patients who received auricular acupuncture (AA) and untreated patients on the day before surgery prior to AA or at a comparable time in the control group (time I); in the evening of the day before surgery (time II); and immediately before surgery (time III) using the state form of the German version of the State-Trait-Anxiety Inventory (STAI). *P<0.01time I vs time II in AA group. **P<0.001 time III vs time II in 'no intervention' group. ***P<0.01 time III vs time I in 'no intervention' group; P values presented are post Holm-Bonferroni correction.

Table 2 Preoperative anxiety and serum cortisol concentration

	Timing of outcome measurement	Auricular acupuncture (n=32)	No intervention (n=30)
State anxiety	I (before)	49±15	44±12
	II (evening after intervention)	42±13	47±11
	III (before surgery)	47±14	53±12
VAS-100 (mm)	I	50 (13.75–75)	50 (10–57.5)
	II	30 (15–50)	50 (30-65)
	III	30 (15-70)	57.5 (30–80)
Serum cortisol (ng/ml)	III	375±153	390±150

Data presented as mean±SD or median (IQR).
VAS-100, visual analogue scale 100 mm.

RESULTS

Of 94 eligible patients, 63 agreed to participate and were included in the investigation. One patient reacted with a vasovagal faint during the AA intervention and was excluded (figure 1). The time lapse between AA and surgery the next day was 22.5±2.7 hours (mean±SD). The demographic parameters and trait anxiety of the 32 patients who chose to receive AA were comparable to those of 30 participants who consented only to the audit for anxiety (table 1).

There were no significant differences in preoperative anxiety between the study groups at any of the three time points of outcome measurement, although the course of preoperative anxiety differed between the groups, as indicated by the interaction effect of GROUP*TIME (P<0.001) (figure 4). In patients who received no intervention, anxiety (STAI) increased through the course of the study and was significantly greater at time III versus time I (P=0.002) and versus time II (P<0.001) (figure 4, table 2).

In participants who received AA, preoperative anxiety decreased after the AA intervention (time II) compared with baseline (time I): P=0.006 (table 2 and figure 4). The next day, immediately before surgery (time III), anxiety increased in comparison with time II: P=0.013 (figure 4, table 2).

Heart rate, blood pressure and serum cortisol were comparable between the study groups.

State anxiety, which will be the primary endpoint in our subsequent RCT (with three study arms: verum AA, placebo AA and no intervention), was used to calculate the required sample size. Assuming a variability in anxiety of 11 (SD, table 2), 60 patients per group are needed to demonstrate an estimated minimal clinically important difference between groups of 20% at a significance level of 0.05 and power of 85%, taking into account a proposed Bonferroni adjustment for multiple comparisons between

three anticipated experimental groups. In order to compensate for the expected dropout rate of 10%, the size of these groups will be further inflated to 67 patients each.

DISCUSSION

The aim of this open non-randomised pilot clinical investigation was to test the acceptability and feasibility of outcome measurements and the methodology of AA as a simple non-pharmacological treatment for preoperative anxiety in comparison with no intervention.

All participants except one tolerated AA treatment well and indicated they would wish to receive it again before a future surgical procedure. One participant reacted with vasovagal syncope after AA stimulation, exemplifying a rare hyperactive vagal response that is documented in the literature.[24 25] Since all patients received AA by a licensed doctor in the supine position, the occurrence of this adverse event was easily brought under control with no further complications for the patient. However, the possibility of vasovagal reactions after auricular stimulation should be kept in mind for all future AA treatments and the acupuncturist should always be prepared to handle such situations promptly.

The preoperative anxiety of patients who received AA was reduced by about 14% in the evening before surgery, in comparison with anxiety levels before the AA intervention. Preoperative anxiety immediately before surgery nearly reached the baseline anxiety level measured before the AA intervention. In the group with no intervention, however, preoperative anxiety levels continuously increased from the first time point of measurement, through the evening before surgery, and remained increased by about 20% immediately before surgery, when compared with the anxiety levels assessed at baseline.

These findings are in agreement with the results of previous investigations of AA and situational anxiety.[10–13 20 21] For example, Karst *et al*[11] reported that state anxiety scores decreased by about 18% from baseline after AA treatment of dental anxiety. Likewise, Michalek-Sauberer *et al*[12] demonstrated a reduction in STAI state anxiety levels by about 15% from baseline after AA in 61 patients undergoing dental procedures.

Trait anxiety scores were comparable in patients who received AA and patients receiving no intervention. The mean value of trait anxiety in this sample was higher than the mean in the general female population of this age (37±11; $P<0.001$) (table 2), but below the critical cut-off for diagnosis of a specific phobia.[22] This finding is in line with the results of a study by Carr et al[26] where almost half of the sample of 80 women undergoing gynaecological surgery reported trait anxiety scores ≥45.[18] This is probably due to the particular nature of gynaecological conditions, which are associated with high rates of psychological morbidity and vulnerability.[27]

The main limitation of the present investigation is that the patients were not randomly allocated to receive AA versus no intervention. Moreover, the effects of AA should be examined in comparison with a comparable placebo treatment as in previous studies.[11–13 21] In addition, future studies should assess stress-specific biomarkers such as cortisol, catecholamines and salivary α-amylase or continuous monitoring of heart rate variability and electrodermal activity in order to support self-reporting of anxiety levels. However, the present study was designed only to test the acceptability and feasibility of our AA methodology and to yield preliminary data to calculate the necessary sample size for further randomised controlled investigations.

CONCLUSION

AA was well accepted by patients as a treatment for preoperative anxiety. The chosen outcome measurements were feasible and have facilitated the calculation of the sample size for a subsequent RCT.

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Contributors TIU conceived the study. JKW, CK and AM recruited the patients. CK performed the auricular acupuncture. JKW, HH, TH, AP and TIU collected the data. JKW analysed the data. KH interpreted the data. All authors contributed to the writing of the manuscript approved the final version accepted for publication.

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Competing interests None declared.

Patient consent Obtained.

Ethics approval Ethics Committee of University Medicine Greifswald (reference no. BB 158/15); the trial was registered at clinicaltrials.gov (registration no. NCT02656966) and was carried out in accordance with the principles of the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Asilioglu K, Celik SS. The effect of preoperative education on anxiety of open cardiac surgery patients. *Patient Educ Couns* 2004;53:65–70.
2 Markland D, Hardy L. Anxiety, relaxation and anaesthesia for day-case surgery. *Br J Clin Psychol* 1993;32(Pt4):493–504.
3 Pritchard MJ. Managing anxiety in the elective surgical patient. *Br J Nurs* 2009;18:416–9.
4 Biddiss E, Knibbe TJ, McPherson A. The effectiveness of interventions aimed at reducing anxiety in health care waiting spaces: a systematic review of randomized and nonrandomized trials. *Anesth Analg* 2014;119:433–48.

5 Vaughn F, Wichowski H, Bosworth G. Does preoperative anxiety level predict postoperative pain? *Aorn J* 2007;85:589–604.
6 Van den Bosch JE, Moons KG, Bonsel GJ, *et al*. Does measurement of preoperative anxiety have added value for predicting postoperative nausea and vomiting? *Anesth Analg* 2005;100:1525–32.
7 Maurice-Szamburski A, Auquier P, Viarre-Oreal V, *et al*. Effect of sedative premedication on patient experience after general anesthesia: a randomized clinical trial. *JAMA* 2015;313:916–25.
8 Patel T, Kurdi MS. A comparative study between oral melatonin and oral midazolam on preoperative anxiety, cognitive, and psychomotor functions. *J Anaesthesiol Clin Pharmacol* 2015;31:37–43.
9 White PF, Eng M. Fast-track anesthetic techniques for ambulatory surgery. *Curr Opin Anaesthesiol* 2007;20:545–57.
10 Lewis GBH, Litt M. An alternative approach to premedication: comparing diazepam with auriculotherapy and a relaxation method. *Am J Acupunct* 1987;15:205.
11 Karst M, Winterhalter M, Münte S, *et al*. Auricular acupuncture for dental anxiety: a randomized controlled trial. *Anesth Analg* 2007;104:295–300.
12 Michalek-Sauberer A, Gusenleitner E, Gleiss A, *et al*. Auricular acupuncture effectively reduces state anxiety before dental treatment–a randomised controlled trial. *Clin Oral Investig* 2012;16:1517–22.
13 Luo L, Dai Q, Mo Y, *et al*. The effect of auricular acupressure on preoperative anxiety in patients undergoing gynecological surgery. *Int J Clin Exp Med* 2016;9:4065–70.
14 Usichenko T, Hacker H, Lotze M. Transcutaneous auricular vagal nerve stimulation (taVNS) might be a mechanism behind the analgesic effects of auricular acupuncture. *Brain Stimul* 2017;10:1042–4.
15 Kraus T, Hösl K, Kiess O, *et al*. Bold FMRI deactivation of limbic and temporal brain structures and mood enhancing effect by transcutaneous vagus nerve stimulation. *J Neural Transm* 2007;114:1485–93.
16 Frangos E, Ellrich J, Komisaruk BR. Non-invasive access to the vagus nerve central projections via electrical stimulation of the external ear: FMRI evidence in humans. *Brain Stimul* 2015;8:624–36.
17 Chen J, Barrett DW, He Y, *et al*. Anxiolytic-like behavioural effects of head electroacupuncture in rats susceptible to stress. *Acupunct Med* 2016;34:235–40.
18 WHO. *Third WHO regional working group on standardization of acupuncture nomenclature*. Seoul: World Health Organisation, 1987.
19 Nogier PFM. *Traité d'auriculotherapie*. Moulinlés-Metz: Maisonneuve, 1972.
20 Klausenitz C, Hesse T, Hacker H, *et al*. Auricular acupuncture for pre-exam anxiety in medical students: a prospective observational pilot investigation. *Acupunct Med* 2016;34:90–4.
21 Klausenitz C, Hacker H, Hesse T, *et al*. Auricular acupuncture for exam anxiety in medical students-a randomized crossover investigation. *PLoS One* 2016;11:e0168338.
22 Spielberger CD. *Manual for State-Trait Anxiety Inventory (STAI: form Y)*. Palo Alto, California: Consulting Psychologist Press, 1983.
23 Bekanntgaben der Herausgeber. Richtlinie der bundesärztekammer zur qualitätssicherung laboratoriumsmedizinischer untersuchungen. *Dtsch Arztebl* 2014;111:A1583–618.
24 Smith ML. Mechanisms of vasovagal syncope: relevance to postflight orthostatic intolerance. *J Clin Pharmacol* 1994;34:460–5.
25 Thakar A, Deepak KK, Kumar SS. Auricular syncope. *J Laryngol Otol* 2008;122:1115–7.
26 Carr E, Brockbank K, Allen S, *et al*. Patterns and frequency of anxiety in women undergoing gynaecological surgery. *J Clin Nurs* 2006;15:341–52.
27 Lalinec-Michaud M, Engelsmann F. Anxiety, fears and depression related to hysterectomy. *Can J Psychiatry* 1985;30:44–7.