

Preoperative anxiety management: acupuncture vs. pharmacological treatment – A prospective study

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Abstract. – OBJECTIVE: Acupuncture, both auricular and somatic, is a widely adopted and well-tolerated treatment for preoperative anxiety. The aim of our study was to compare the effectiveness of acupuncture with pharmacological treatment in reducing preoperative anxiety in patients undergoing cholecystectomy or TEP.

MATERIALS AND METHODS: We randomized 120 patients in a control group PT (where patients underwent pharmacological treatment with Midazolam) and in an acupuncture group (here patients received somatic acupuncture SA and auricular acupuncture AA). Anxiety reduction was measured by intraoperative consumption of Propofol and Fentanyl and preoperatively by the Italian Version of the State-Trait Anxiety Inventory questionnaire (STAI).

RESULTS: Propofol consumption in the somatic (SA) and auricular (AA) acupuncture groups was found to be lower compared to patients that did not receive any treatment. SA and AA patients required less Propofol than the PT group ($p=0.0019$ and $p=0.0016$ respectively) and patients that underwent SA treatment used less Fentanyl than the PT group ($p=0.002$). No difference was measured when comparing SA to AA ($p=0.15$) and AA to PT ($p=0.16$).

CONCLUSIONS: Acupuncture is a safe and well-tolerated procedure that reduces preoperative anxiety. Both somatic and auricular acupuncture are more effective than pharmacological treatment in the intraoperative period. AA is easier to implement than SA.

Key Words:

Preoperative anxiety, Acupuncture, Midazolam, Propofol, Fentanyl, TEP, Cholecystectomy.

Introduction

Anxiety is one of the most important clinical manifestations of mental disorders and is associ-

ated to significant complications and disabilities. In the European Union it is the most prevalent psychiatric condition with over 60 million people affected. This condition, if chronic, interferes with daily life and predisposes to other serious health conditions¹. Anxiety can be characterized as “state anxiety” and “trait anxiety”. State anxiety indicates a transient emotional state of an individual with subjective feelings of tension, apprehension and worry. Trait anxiety represents an individual’s predisposition to respond with a rise in the intensity of anxiety to situations perceived as dangerous.

Preoperative anxiety (PA) affects more than 90% of adult patients before surgery and 40.5% of these experience severe anxiety². In the preoperative period, feelings of uncertainty about the future, loss of self-control and anticipation of post-operative pain are frequent. All these symptoms can affect the quality of life but also the results of surgery³.

Pharmacologic and alternative procedures have been used to decrease PA.

Pharmacological treatments used to reduce anxiety are anxiolytics, antidepressants or monoamine oxidase inhibitors. Midazolam is a benzodiazepine (BDZ) which is widely used in hospitals for the treatment of preoperative anxiety and for the sedation of patients undergoing various diagnostic/therapeutic procedures and in intensive care units. Intravenously Midazolam has an onset time of about 2 minutes, a 45-60-minute duration of action; it can be administered about half an hour before surgery intramuscularly in adults and by mouth in the pediatric population. Respiratory and cardiovascular functions are modified after its injection. The intraoperative anesthetic

treatment and the duration of hospitalization in the recovery room are also affected. BDZ often causes a longer persistence in the hypnotic effect caused by the other anesthetic agents (Propofol) resulting in prolonged anesthesia. In elderly patients it can cause increased anxiety, disorientation and agitation⁴.

Acupuncture has been recognized by the World Health Organization as an effective treatment for some medical conditions⁵ and it is used during surgery not only to control anxiety^{2,3} but also for post operative pain⁶.

Several studies have shown that acupuncture is a safe therapeutic approach to treat PA, with rare adverse effects. Fleckenstein et al⁷ used the HT 7 (Shaofu) acupuncture point to reduce anxiety and discovered that patients that did not receive the acupuncture treatment exhibited an increased cortisol level and heart rate.

Bae et al⁸ showed that PA therapy that uses true acupuncture is statistically more effective than sham acupuncture.

Auricular acupuncture developed by Paul Nogier around 1950 and based on the stimulation of cranial nerves has been used in several randomized controlled trials (RCTs) to treat preoperative anxiety. AA has shown to be more effective than an array of control procedures, including placebo and sham acupuncture and as effective as BDZ³.

No study in literature has ever compared both somatic (SA) and auricular acupuncture (AA) to treatment with benzodiazepines (PT).

The objective of this study was to compare the effectiveness of SA and AA to the effectiveness of PT in reducing preoperative anxiety (PA) in patients undergoing cholecystectomy or TEP (Totally Extraperitoneal Hernia Repair).

Materials and Methods

The present prospective, randomized, controlled, observer-blinded study included a consecutive series of 120 patients [41 (34.2%) females, 79 (65.8%) males], that would undergo cholecystectomy or TEP⁹. The patients were enrolled between July 2016 and January 2020 at the Surgery Unit of Santa Maria del Carmine Hospital, Rovereto, Italy.

The study protocol was designed according to the Declaration of Helsinki principles and approved by the local Institutional Ethic Committee. All patients gave informed consent.

Patients were randomized by means of closed envelope method to a control group, Group A (N = 22, pharmacological treatment (PT) (Midazolam 0.04-0.07 mg/kg im 30 minutes before surgery) and to an acupuncture group where patients received either somatic acupuncture (SA), Group B (N=32) or auricular acupuncture (AA), Group C (N=30). Another group, Group D (N = 36, no treatment), had no treatment.

The Primary endpoint was the evaluation of the level of intraoperative relaxation (measured indirectly through the consumption of Propofol and Fentanyl during anesthesia). The secondary endpoint was the reduction of preoperative anxiety measured using the Italian Version of State-Trait Anxiety Inventory questionnaire (STAI)¹⁰. The STAI questionnaire used for preoperative anxiety^{11,12}, consists of forty questions and was administered to patients upon admission to evaluate Trait Anxiety; State Anxiety and its variation were evaluated before and 30 minutes after the treatments (PT, SA, AA).

The following exclusion criteria were adopted: a score of more than 2 ASA (American Society of Anesthesiologists), myofascial pain or fibromyalgia, severe neurologic, respiratory or cardiovascular diseases, psychiatric diseases, a history of drug addiction, alcoholism and chronic or recent use of neuroleptic drugs or tranquilizers (benzodiazepine, antidepressants that inhibit the reuptake of serotonin or hypnotics).

Somatic acupuncture was performed by 4 experienced acupuncturists (S.Z., A.L., R.D. and S.V.), approximately 30 minutes before surgery, using Hwato[®] (Suzhou, Jiangsu, China) needles (25 mm long, 0.20 mm thick) inserted bilaterally and superficially (5 mm), at the Hegu-LI4 and Neiguan-Pc6, Zusanli-St36, Yintang-Ex1 and Baihui-GV20 acupoints. 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 2 cm) from the palmar wrist crease, between the tendons of the muscle palmaris longus and the muscle flexor carpi radialis. St36 is located 3 cun (about 5 cm) from the depression under the patella to the side of the patellar ligament and 1 cm from the anterior crest of the tibia. Ex1 is located halfway between the two eyebrows. GV20 is located at the intersection of the line connecting the apexes of the two auricles and the median line of the head, 7 cun directly above the posterior hairline. The stimulation of these points has been previously reported to achieve a relaxing effect^{8,13}. Sessions

lasted 30 minutes; in SA patients, needles were stimulated manually every 5 minutes at the insertion until they felt the De-Qi sensation (a sensation of numbness and distension). The AA group was treated with auricular acupuncture the same day of the surgery through the insertion of the New PyoNex® (Sodeshi-cho, Shizuoka, Japan) semi-permanent needles; these needles are 0.2 mm in diameter and 0.6 mm in length according to a scheme defined as the Triad Relax (Shenmen, Sensory Master and Callous Body) points³ (Figure 1). Surgical operations were performed by or under the direct supervision of the same surgeon (A.V.) using the standard techniques. The procedures were carried out under general anesthesia with orotracheal intubation and were performed by the same team of anesthesiologists. The Surgeons and anesthesiologists were blinded to the randomization of each patient. A standardized intravenous anesthetic protocol was used: Anesthesia was induced with Fentanyl (3-5 mcg/Kg), Propofol 1% in TCI modality with a target of between 4 and 5 mcg/ml at the effector site and Rocuronium 0.8 mg/Kg. The effects of acupuncture and PT were evaluated by measuring the amount of Propofol and Fentanyl administered during the interventions. The depth of anesthesia was monitored with the BIS (BIS View, Aspect Medical system, Norwood, MA)¹⁴ and ranged between 40 and 60 to ensure an adequate hypnotic state. This parameter was used together with the hemodynamic (blood pressure, heart rate) and respiratory (End-Tidal CO₂, SatO₂) values that



Figure 1. Auricular acupuncture points.

are routinely measured during general anesthesia.

Demographics (including age, sex, and patient weight), type and duration of surgery, Propofol (measured as mg/Kg/h) and Fentanyl consumption (measured as mcg/kg) were recorded and compared.

Data are presented as absolute numbers or as median \pm standard deviation (SD). Statistical analysis was performed using Fisher's exact test, Student's *t*-test, the Kruskal-Wallis analysis of variance, the Mann-Whitney U test, the Tukey test and the Bonferroni correction for multiple comparisons, as appropriate. A *p*-value <0.05 was considered statistically significant. The software used for analyses was R[®] version 3.4.0.

Results

120 patients were randomly assigned to four Groups. The Acupuncture groups were composed of 62 patients (30 AA and 32 SA). Pharmacological treatment in the control group was administered to 22 patients, whereas 36 patients received no treatment. No adverse events were attributed to acupuncture. No local complications such as bleeding, hematoma, or infection occurred after the procedure; treatment was well tolerated in all cases. The baseline characteristics of each group are shown in Table I. The control and acupuncture groups were homogeneous when considering age, patient weight, type of surgery, duration of the operative procedure, STAI Trait, STAI State before and after treatment and STAI State variation (before and after treatment). When comparing the acupuncture groups (Group B and C) to Group D that did not receive any treatment, the Propofol consumption in the first two groups was found to be statistically significant or close to significance ($p=0.04$ and $p=0.05$).

Pharmacological Treatment vs. SA and AA

Analysis of the primary endpoint in the subgroups showed that patients in the SA and AA groups required less Propofol than the PT group ($p=0.0019$ and $p=0.0016$ respectively) (Figure 2). No statistical difference between the SA and the AA groups ($p=0.99$) in Propofol consumption was noticed. Only patients that received SA used less Fentanyl than the PT group ($p=0.002$). No difference in the use of Fentanyl was observed when comparing SA to AA ($p=0.15$) and AA to PT ($p=0.16$).

Table 1. Main preoperative parameters and results (median ± standard deviation).

Characteristic	Control group		Acupuncture group		p-value	
	NoBDZ	PT	Auricular	Somatic	SA vs. PT	AA vs. PT
Sex M/F	22/14	14/8	27/5	16/14	0.573	0.109
Age	55.6 ± 17.4	53.6 ± 15.1	59 ± 13.7	59.1 ± 15.5	0.382	0.402
Weight	72.4 ± 13.3	76.6 ± 13.3	76.2 ± 12.1	74.4 ± 12.9	0.809	0.993
Cholecystectomy/TEP	21/15	10/12	13/19	16/14	0.784	0.779
Operation time	47.1 ± 23.6	41.7 ± 18.9	40.5 ± 18.8	45.7 ± 19.6	0.842	0.993
STAI Trait	44.3 ± 3.4	44.8 ± 3.5	46.2 ± 3.4	46.7 ± 5.7	0.329	0.552
STAI State before treatment	41.3 ± 4.5	44.1 ± 4	43.1 ± 4.7	44.2 ± 5.1	0.999	0.666
STAI State after treatment		43.5 ± 3.9	41.2 ± 3.9	42.3 ± 6.3	0.677	0.234
STAI Variation		0.4 ± 4.6	1.8 ± 4.2	1.9 ± 4.9	0.490	0.500
Propofol Consumption	0.2 ± 0.10	0.2 ± 0.04	0.14 ± 0.05	0.14 ± 0.03	0.0019	0.0016
Fentanyl Consumption	0.32 ± 0.15	0.39 ± 0.09	0.33 ± 0.13	0.28 ± 0.07	0.002	0.16

Discussion

The use of acupuncture in the perioperative period (including in this definition the preoperative, intraoperative and postoperative phases of surgical procedures) has a history of more than 50 years as reported in a recent review by Acar¹⁵.

Several studies investigated the role of acupuncture, both auricular¹⁶ and somatic, in reducing PA. A recent study¹⁷ demonstrated that acupressure of the Shenmen-HT 7 and Neiguan-Pc 6 points in 14 infertile women could reduce “unpleasant body feelings and sensations”. Acupuncture treatment, as observed in experiments using rats, significantly reduced anxiety through the increase in protein synthesis necessary for synaptic plasticity within the hippocampus¹⁸. Preoperative anxiety was investigated also in a study by

Wunsch et al³. In patients awaiting gynecologic surgery, bilateral auricular acupuncture using the Shenmen, Sensory Master, Callous Body points (amongst others) reduced anxiety compared to patients who did not undergo any treatment. In the intraoperative period the role of acupuncture as an adjuvant to general anesthesia in decreasing the doses of anesthetic is controversial^{19,20} and it is not possible to conclude that acupuncture reduces anesthetic consumption²¹. Greif et al²² and Taguchi et al²³ showed that auricular acupuncture may reduce desflurane requirement (11% and 8% respectively) but Morioka et al²⁴ and Kvorning et al²⁵ did not find a decrease in the inhalation of anesthetics using somatic acupuncture.

It is not possible to draw a definitive conclusion after reviewing the literature because of poor methodological quality and because most of the studies are not double-blinded and placebo-controlled.

Currently our study is the first randomized and prospective study that compares auricular and somatic acupuncture with benzodiazepines for preoperative anxiety.

Preoperative anxiety evaluated using the STAI questionnaire showed no advantage in using acupuncture. The intraoperative period was evaluated comparing the consumption of Fentanyl and Propofol, anesthetic drugs whose infusion was based on clinical and Bispectral parameters. The Bispectral index is influenced by the patient’s relaxation and is indicative of the depth of anesthesia. For this reason, BIS is considered an indirect index of relaxation; similarly, the infusion of Fentanyl and Propofol that are administered based on the BIS can also be used as an index of relaxation.

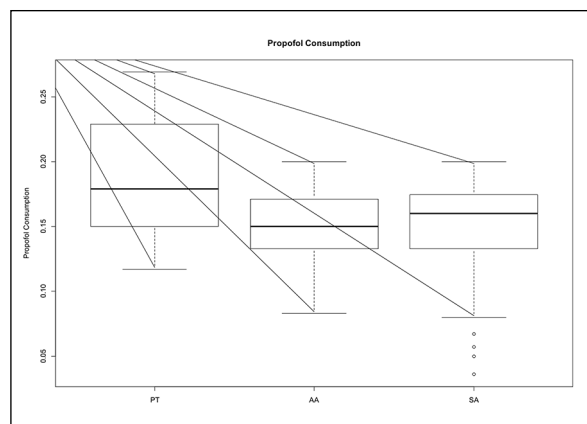


Figure 2. Propofol consumption in control (PT), auricular (AA) and somatic (SA) acupuncture groups.

Our results demonstrate that acupuncture is a safe and well-tolerated procedure; analysis of the subgroups reveals that acupuncture is more effective than pharmacological treatment in the intraoperative period. SA patients showed lower Fentanyl consumption compared to the PT control group ($p=0.002$) and both SA and AA patients showed lower Propofol consumption compared to PT patients ($p=0.0019$ and $p=0.0016$ respectively).

In our opinion and, as other studies²⁶ show, the effect of acupuncture on preoperative anxiety evaluated with the STAI questionnaire cannot be considered conclusive.

The absence of a statistically significant difference in preoperative anxiety measured with the STAI in our study could be explained by the fact that the questionnaire was administered before entering the operating room. The patient would have been too distracted by the imminent surgery to be able to effectively answer the questionnaire. Furthermore, the SA group answered the questionnaire too close to the end of the treatment.

The present study has some limitations. Firstly, drugs were administered during surgery by different anesthesiologists; however, none of them knew the type of treatment performed to reduce anxiety preoperatively. Secondly, a possible limitation could be the use of Fentanyl and Propofol consumption to evaluate intraoperative relaxation; these drugs have however been widely used in many clinical trials. Furthermore, patients were operated using two standardized surgical techniques and were continuously monitored with the BIS and hemodynamic parameters; for this reason, the only differences in the consumption of drugs can be explained by the anxiolytic treatment received preoperatively.

The state of relaxation achieved with acupuncture under general anesthesia cannot be influenced by consciousness and may therefore be seen as indicative of the effectiveness of acupuncture treatment.

Patients without risk factors or severe diseases were used and for this reason this study is not completely representative of usual clinical situation. Another limitation is the lack of double-blinded randomization; however, although patients were aware of the type of treatment used, they had no knowledge of the differences between the types of acupuncture used. In addition, as demonstrated in studies on animals, the psychological effect could be excluded.

Conclusions

In conclusion, as other studies in the literature also show, acupuncture has proven to be an adequate, safe and effective alternative to the treatment of preoperative anxiety. Auricular acupuncture is more suitable for the treatment of elderly and complex patients with important pharmacological therapies because it is easy to use and can also be performed before the surgical procedure, when patients are admitted to the hospital department.

Conflict of Interest

No sponsorships or competing interests have been disclosed for this article.

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