Cover page:

Official title of the study:

The Effect of Complementary Medicine (CAM) Treatments on Common Symptoms in Hospitalized Patients

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Background

Cholecystectomy due to gallstones is one of the most common operations in general surgery.[1] Nowadays, this type of surgery is usually done electively in the laparoscopic method (LC – Laparoscopic Cholecystectomy), in Israel and worldwide.[2] In recent years, ERAS (enhanced recovery after surgery), an international association of experts in the fields of surgery, anesthesia, and other allied health professions, has led a process of formulating guidelines, based on research evidence, in order to improve peri-operative care.[3] This trend reflects an interventionist approach and a global perspective on the public health level in the context of surgery which, among others, highlights the need to address peri-operative symptoms.

The state of preoperative anxiety may affect the course of surgery usage of anesthetics[4], and the recovery period that follows in different aspects, such as pain[5,6], wound healing[7], nausea and vomiting[8], duration of hospitalization and recovery[9], immune system status.[10] Preoperative anxiety is usually evaluated using the VAS-A (Visual Analog Scale for Anxiety) questionnaire, which is based on the patient's own reporting and is a reliable, simple and quick method, particularly when the time available for interaction with the subject is limited, as is the case in the HRA (Holding Room Area), a waiting room in which patients stay for 15-50 minutes before surgery.[11-14]

Between 11% and 80% of adult patients undergoing surgery, report experiencing significant (moderate-to-high) preoperative anxiety.[15,16] A controlled, randomized clinical trial on 360 surgical patients showed that 70% of the subjects experienced moderate-to-high levels of anxiety approximately one hour before the surgery, despite being treated with the standard-of-care (SoC), which involves administering anxiolytics prior to the surgery at the discretion of the anesthesiologist.[17]

Anxiolytics are often administered before surgery, either orally or by intravenous injection. Several studies have proven the efficacy of using anxiolytics as part of premedication before surgery, including midazolam[18], gabapentin[19], diazepam[20] and oxazepam.[21] However, data obtained from several other studies cast doubt on their effectiveness.[22,23] Several studies have demonstrated the effectiveness of different complementary medicine treatments, including reflexology, in reducing preoperative anxiety and anxiety before other medical procedures.[17,24,25]

Reflexology is a touch treatment method which is based on the theory that the entire body is represented in reflex points located on the soles of the feet (or the palms of the hands). A number of studies have examined the impact of reflexology treatments on indices of stress, anxiety and relaxation.[17,26,27]

A handful of studies compared reflexology treatments with sham reflexology treatments (general foot massage without applying direct pressure to formal reflex points), to counteract the expected placebo effect.[28,29] Such studies are important in order to isolate the treatment's placebo effect and highlight the specific effect, if any, of real reflexology.

Since elective LC is a very common operation, and due to the significance of preoperative anxiety in the context of potential postoperative complications and morbidity, we have examined the effect of reflexology as well as sham reflexology in parallel with SoC treatment which currently involves administration of anxiolytics, on this issue.

Methods

1. Type of study and study population

We conducted a single-blinded clinical intervention randomized controlled trial. Trial methods and results were reported according to the 2010 guidelines for Consolidated Standards of Reporting Trials (CONSORT) for non-pharmacologic interventions.[30]
The trial involved 300 patients awaiting an elective LC, who agreed to participate in the trial and were randomly allocated into three equal groups. Group 1 received the SoC treatment (anxiolytics) at the discretion of the anesthesiologist (n=100). Group 2 received reflexology treatment on top of SoC (n=101), and Group 3 received sham reflexology treatment in addition to SoC (n=99) (see Figure 1). The study was single-blinded because while patients in the study arms that involved reflexology did not know whether they were being treated with real reflexology or sham reflexology, and the treatment was described to them as medicinal foot massage rather than reflexology, the therapists, however, did know whether they were giving real or sham reflexology treatment.

Inclusion criteria: (1) Patients aged 18 years undergoing LC who consented to the study.
Exclusion criteria: (1) Patients with a history of obstructive sleep apnea; (2) Contraindication for benzodiazepines; (3) Hemodynamic instability; (4) Patients with feet ulcers; (5) Patients undergoing a LC together with another surgical procedure.

2. Study objective

The primary study objective was to examine the effectiveness of a combined treatment of reflexology on top of SoC in comparison to a combined treatment of sham reflexology on top of SoC and in comparison to SoC treatment alone in reducing preoperative anxiety in elective LC.

3. Sampling method and study procedure

The study was conducted at the Bnai Zion Medical Center in Haifa. Participants were recruited between July 2016 and October 2019.

Patients that agreed to be included in the study were randomly assigned to one of the three study groups using a designated software (randomization.com) (see Figure 1). Patients were asked to rate their level of anxiety and their level of comfort using the Visual Analog Scale (VAS) and VAS-A (Visual Analog Scale for Anxiety) questionnaire at the surgery department and in the HRA. Subsequently, patients were told whether they had been assigned to the intervention group involving foot massage – without specifying whether it would be real or sham reflexology – or to the control arm.

4. Therapeutic approach protocol

The study included three treatment groups:

A. SoC (group 1) included premedication about two hours before the operation with the anxiolytics Oxazepam and Diazepam, according to the anesthesiology department protocol and at the discretion of the anesthesiologist, regardless of the study arm. It should be clarified that in some cases the anesthesiologist decided not to administer anxiolytics, or the patient chose not to receive them. In cases where premedication was administered, the instructions were to administer 10mg of Diazepam to patients under the age of 65, and 10mg of Oxazepam to patients over 65. This protocol is supported by the study conducted by Pomara et al.[23] which found that older patients taking diazepam tend to suffer from side effects of memory and psychomotor performance impairments.

B. Reflexology (group 2) intervention involved a 15-minute treatment in the induction room, provided by three reflexologists from the hospital staff. The reflexology protocol was developed through a Delphi method.[31]

C. Sham reflexology (group 3) intervention were given by two complementary medicine practitioners with knowledge in touch therapy (shiatsu) and included 15 minutes of gentle, nonspecific foot massage. Similarly to the true reflexology protocol, the protocol for this treatment was also determined in a consensus-reaching process among a group of four experienced reflexologists.

5. Assessment tools

The level of anxiety was evaluated both before and after the treatments, using the VAS-A questionnaire for anxiety and the VAS scale for the level of comfort (rated from 0 – not comfortable at all, to 10 – very comfortable). VAS Comfort questionnaires were used in order to support the assessment of anxiety by VAS-A. The control group was assessed at the same time points. The questionnaire was given to the patient at the surgery department by a study coordinator. At the HRA questionnaires were given by the nursing staff before and after the intervention, shortly before the patient was transferred to the operating room.
Baseline assessment was carried out at the entrance to the HRA through a VAS-A valid anxiety questionnaire for current anxiety level from 0—no anxiety, up to 10—maximum anxiety.[14] Similar to pain scale, it is common to divide the anxiety symptoms into categories; Low Anxiety (VAS-A≤4), Moderate to Severe Anxiety (VAS-A≥4), Severe Anxiety (VAS-A≥7).

7. Sample size calculation and statistical analysis

The calculation of the sample size was carried out using GPower software, which examines the sample size with reference to ANOVA variance analysis. The comparison between the three different groups, given a confidence level of 95%, power of 85% and an effect size that is considered medium according to Cohen's 0.25, alongside the definition of one unit of VAS as the low value for clinical significance[32], required a sample size of at least 45 subjects per group. Due to the intention to use stratification to analyze the data of those with a VAS-A score above 4 (moderate-to-high anxiety), age, sex, as well as according to the administration of anxiolytics, approximately 100 subjects were recruited to each group. Since the result distribution was not normal, a variance test was conducted using Kruskal-Wallis' non-parametric test to compare the average change in preoperative anxiety in the induction room. Due to multiple comparisons (between 3 groups), the p-value in these tests was 0.014 in order to overcome the false discovery rate (FDR), and $p<0.05$ for the purpose of bilateral comparison.[33] Of note, both per-protocol and intention-to-treat analyses were planned, but since there was no patient cross-over, there was no need to differentiate between the analyses.

8. IRB approval

The study was approved by the local IRB (Helsinki Committee), approval no. BNZ-0041-09.

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