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Research paper

Transcutaneous electrical acupoint stimulation alleviates the anxiety levels of IVF: A prospective, randomized and controlled study

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ABSTRACT

Introduction: It is recognized that all over the world, infertile women undergoing in vitro fertilization (IVF) experience high levels of stress, but most remain undiagnosed and untreated. This study explored whether transcutaneous electrical acupoint stimulation (TEAS) could relieve anxiety levels in infertile women.

Methods: A total of 360 infertile women with tubal blockage were randomized into four groups: control group, TEAS–2 Hz group, TEAS–100 Hz group and TEAS-2/100 Hz group. After excluding patients who did not complete embryo transfer, 84, 84, 80 and 86 cases respectively remained in the above groups. Anxiety levels were measured using the Spielberger's State Trait Anxiety Inventory (STAI) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS).

Results: We found that 2/100 Hz TEAS treatment significantly decreased the levels of state anxiety and preoperative anxiety ($P < 0.05$). In addition, there were indications that a100 Hz TEAS treatment could decrease the scores of APAIS.

Conclusions: TEAS using a frequency of 2/100 Hz could help to alleviate state anxiety and preoperative anxiety levels.

The trial was registered at Chinese Clinical Trial Register (ChiCTR) with the identifier ChiCTR-TRC-14004493.

1. Introduction

In vitro fertilization (IVF), as an important assisted reproductive technology (ART), is chosen by more and more infertile couples, and is linked to over 400,000 babies born worldwide each year [1]. The treatment of IVF is usually stressful for infertile women and the emotional experiences of the IVF patient has drawn more and more attention in recent years [2]. Based on the Spielberger's State Trait Anxiety Inventory (STAI), anxiety levels in infertile women have been shown to be significantly elevated during the IVF cycle [3]. Psychiatric disorders have been found in 30.8% of infertile women and 10.2% of men undergoing IVF treatment, and mood disorder is present in 26.2% of females and 9.2% of males, suggesting that the psychiatric and mood disorders are common in both women and men undergoing IVF treatment [4]. In China, 23.2% of infertile women undergoing IVF or intracytoplasmic sperm injection (ICSI) were found to have anxiety disorders [5]. However, the majority of infertile couples with the psychiatric or mood disorder are undiagnosed and untreated [4]. A meta-analysis found that there was a negative correlation between stress distress and pregnancy outcomes with ART [6]. The increased depression and anxiety scores of women during IVF treatment have notably been correlated with the lower number of oocytes and women with higher anxiety or depression scores on the day of *trans*-vaginal oocyte retrieval (TVOR) have been shown to have significantly lower pregnancy rates [7].

Abbreviations: APAIS, Amsterdam preoperative anxiety and information scale; ART, assisted reproductive technology; COH, controlled ovarian hyperstimulation; CONSORT, consolidated standards of reporting trials; CPR, clinical pregnancy rate; ET, embryo transfer; IR, implantation rate; ICSI, intra-cytoplasmic sperm injection; IVF, in vitro fertilization; LBR, live birth rate; NPY, neuropeptide Y; STAI, Spielberger's state trait anxiety inventory; STRICTA, standards for reporting interventions in clinical trials of acupuncture; TEAS, transcutaneous electrical acupoint stimulation; TVOR, trans-vaginal oocyte retrieval

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Consequently, it is necessary to provide effective and safe treatment to decrease the anxiety levels of infertile women undergoing IVF and to improve their quality of life and pregnancy outcome [8].

Transcutaneous electrical acupoint stimulation (TEAS), as a new and non-invasive acupuncture treatment, avoids the discomfort, bleeding or pain induced by the skin needling in the traditional acupuncture treatment and increases the reproducibility of acupuncture-like stimulation [9,10]. TEAS has significant advantages in alleviating mood disorders [11,12]. TEAS has also shown to be a safe, easy and noninvasive technique for nursing home staff to improve depressive mood in old people [11]. The combination of acupressure and TEAS has been found to also significantly reduce depressed mood and improve sleep quality in hemodialysis patients [12]. The aim of the study was to see whether TEAS could also relieve anxiety levels of infertile women during the period from TVOR to embryo transfer (ET) in IVF treatment.

2. Methods

2.1. Subjects

In a six-month period (April 21, 2014 to October, 20, 2014), 486 infertile women with tubal blockage referred to Reproductive Medicine Center of Zhejiang Province, China (Department of Reproductive Endocrinology, Women's Hospital, School of Medicine, Zhejiang University, China) for IVF were screened. Among the patients screened, 121 women did not meet the inclusion criteria, and 5 women declined to participate. Finally, 360 infertile women with tubal blockage were included in the study. The long protocol for controlled ovarian hyperstimulation (COH) was used as previously described [13]. The subjects were randomized into one of four groups: a control group, a TEAS–2 Hz group, a TEAS–100 Hz group or a TEAS-2/100 Hz group using a randomization chart constructed in Microsoft Excel with a proportion of 1:1:1:1. The random allocation sequence was concealed until the interventions were assigned. A nurse enrolled the participants and assigned them to their groups. The IVF clinicians and laboratory staff were blinded to the group assignment. The ET treatment was conducted three days after TVOR. In the statistical analysis, 6, 6, 10 and 4 cases respectively in the control group, TEAS–2 Hz group, TEAS–100 Hz group and TEAS-2/100 Hz group were excluded, as these patients did not complete ET (Fig. 1).

Ethical permission to conduct the study was obtained from the Institutional Review Board of Reproductive Medicine, Women's Hospital, School of Medicine, Zhejiang University. The aim and methodology of the study were explained to the patients in detail. Voluntary participation was requested and informed consent was obtained from all of the participants. The subjects included in the study were infertile women with tubal blockage who were referred to the department for IVF. They were otherwise healthy women with regular menstrual cycles and normal sex hormone levels, and no other existing pelvic pathology. No structural abnormalities of the uterus or ovaries were found by vaginal ultrasound or laparoscopy. None of the women had received salpingectomy or ART therapy previously. We excluded the patients with neurological, mood or psychiatric disorders, the patients who were taking any anxiolytics, the patients who were receiving acupressure or acupuncture therapy, the patients with a history of smoking or drinking, or the patients who were not fluent in Chinese. All the partners of the women had normal spermiograms and sperm morphology. The present study adheres to the Consolidated Standards of Reporting Trials (CONSORT) statement [14], and Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [15,16]. The TEAS treatments were performed by two registered acupuncturists who had worked in Traditional Chinese Medicine (TCM) department for more than 5 years. The TEAS protocol was developed based on the clinical experience of our hospital, the TCM literature and consultation with six experts in Chinese medicine. The TEAS devices (HANS-100B) used in the study were provided by Nanjing Jisheng Medical Technology Co., Ltd, Nanjing, China.

2.2. Group and administration

Control group: The patients only followed the routine procedure of IVF treatment and no TEAS.

TEAS–2 Hz group: TEAS was firstly administered for 30 min, 24 h before TVOR, using a frequency of 2 Hz at the acupoints: SP10 (Xuehai, bilateral), SP8 (Diji, bilateral), LR3 (Taichong, bilateral), and ST36 (Zusanli, bilateral). At 2 h before ET, TEAS was administered for 30 min using a frequency of 2 Hz at the following acupoints: EX-CA1(Zigong, bilateral), RN4 (Guanyuan), PC6 (Neiguan, bilateral) and RN12 (Zhongwan). TEAS was applied to the patients through self-adhesive surface electrodes. The standard electrodes affiliated to the TEAS device were applied to the denuded skin and the intensity was set strong enough to elicit visible muscle contraction.

TEAS–100 Hz group: TEAS was administered for 30 min, respectively at 24 h before TVOR and 2 h before ET, using a frequency of 100 Hz. The acupoints used and the manipulation were exactly the same as the TEAS–2 Hz group above.

TEAS-2/100 Hz group: TEAS was administered for 30 min, respectively at 24 h before TVOR and 2 h before ET, using a frequency of 2/100 Hz. The acupoints used and the manipulation were exactly the same as the TEAS–2 Hz group above.

2.3. Measurement of anxiety

The levels of state anxiety, preoperative anxiety (including anesthesia related anxiety and surgery related anxiety) and the need-for-information were evaluated respectively on the morning of one day before TVOR (before the first TEAS treatment, defined as time-point T1) and on the morning of the day of ET (after the second TEAS treatment, defined as time-point T2) by four independent trained nurses who were out of the research team. They were all blinded to the group assignment. The levels of state anxiety were measured with the Chinese version of STAI, which is characterized by high reliability and good construct validity [17–19]. STAI includes 20 short items measuring state anxiety which refers to transitory emotional arousal or situational distress at a particular moment in time and the score of each item ranges from 1 to 4 and a higher score reflects a higher level of state anxiety [20]. The levels of preoperative anxiety and the need-for-information were measured with the Amsterdam Preoperative Anxiety and Information Scale (APAIS) and the score of each item ranges from 1 to 4 and higher scores reflect higher levels of preoperative anxiety and the need-for-information [19,21–23].

2.4. Sample size and data analysis

Power Analysis and Sample Size (PASS 11.0) was used to calculate the sample size. Power analyses performed prior to the study showed we should include at least 78 participants per group (allowing for a 20% loss to follow-up) for 90% power and $p = 0.05$ to detect a clinically significant change (10-point) in anxiety between groups.

Data were analyzed using the Statistical Package for Social Sciences (SPSS 19.0 for Windows). One-way analysis of variance (ANOVA) was used to evaluate statistical significances of continuous data. Chi-square test was used to compare categorical data. For all the hypothesis tests, a significance level was set at $P < 0.05$.

3. Results

3.1. The baseline characteristics

There were no significant differences among the control group, TEAS–2 Hz group, TEAS–100 Hz group and TEAS-2/100 Hz group on all the baseline characteristics ($P > 0.05$) (Table 1).