The Effect of Transcutaneous Electrical Nerve Stimulation (TENS) on the Pregnancy Rate in Women Undergoing Assisted Reproduction Techniques and Embryo Transfer

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Abstract

**Background:** To evaluate the effect of TENS on the pregnancy rate in women undergoing assisted reproduction techniques (ART) and embryo transfer.

**Objective:** This study was designed by comparing a group of patients receiving TENS shortly before embryo transfer with placebo control group.

**Materials and methods:** A prospective, randomized single blinded placebo-controlled study was designed. After obtaining the informed consent from those who had good quality embryos, 233 patients who were undergoing ART, were signed in to the following two groups (117 in experimental- 116 in placebo control groups).

Conventional TENS (100Hz, 50µsec biphasic asymmetrical pulse) was applied by two channel over the groin and the mid part of anterior iliac spine to symphysis of pubis. 20 minutes in supine position before embryo transfer. In the control group, embryos were transferred without any supportive therapy.

Sperm parameters (count, viability, motility, normal morphology) and embryo quality were measured based on WHO criteria. Clinical pregnancy was defined by the presence of a fetal sac during an ultrasound examination 6 weeks after embryo transfer. X² and MANOVA were used for variables differences and Eta² for correlation.

**Results:** Clinical pregnancies were documented in 36 of 117 patients (30.8%) in the TENS group, whereas pregnancy rate in the placebo control group was 19.8% (23 out of 116), pregnancy rate was highly significant in TENS group (p<0.05). MANOVA did not show any differences of demographic, sperm parameters and number of egg by good embryo quality between two groups (P>0.05).

**Conclusion:** TENS seems to be a useful non invasive and easy applicable tool for improving pregnancy rates in ART protocol and embryo transfer.

**Keywords:** TENS; ART; Embryo transfer; Pregnancy rate

Introduction

For several years Transcutaneous Electrical Nerve Stimulation (TENS) has been used in some hospitals in Great- Britain and the United States several years ago as a pain relieving method during labour [2], for primary dysmenorrheal [3,4], and as a post operative pain control [1,5,6].

In recent years attention has been focused on the use of TENS and acupuncture in the area of reproductive medicine, especially for women who are undergoing In Vitro Fertilization (IVF) and Embryo transfer (ET) [7]. Studies had shown the acupuncture and TENS have the same current and both can cause endogenous opioid peptides secretions in the central nervous system (CNS), particularly ß- endorphin [1,8]. The neuropeptides influence gonadotropin secretion through their action on GnRH. It is logical to hypothesize the TENS and acupuncture may impact on the menstrual cycle and ovulation induction through these neuropeptides, gonadotrops, and gonadal steroids releasing in reproductive medicine and hormonal deficiency [1,9,10].

One theory on how TENS works is that it blocks pain in the spinal cord. Another is that stimulation with TENS causes natural pain relieving substances to be released, in other view TENS is thought to be alteration of body’s ability to receive or perceive pain signals rather than by having a control the visceral pain (e.g. uterine contraction or smooth muscle contraction) [2]. The other indication of TENS is the effect on the autonomic nervous system; sympathoinhibitory effects of TENS may impact on uterine blood flow. Specifically the effects of electric stimulation to increasing the blood flow in peripheral circulation [11,12]. TENS may also be indicated as a useful, noninvasive, no pharmacological treatment, safe, and easy to apply and remove, it has no side- effects, it does not interfere with consciousness. It is thought to excite receptors or nerve fibers which, complicated interaction with materials such as serotonin and endorphins, blocks pain impulses [1,4]. According to past investigations, hi- TENS induces central changes in the endorphinergic, serotonergic and possibly substance p-ergic systems [1]. Relating to the type of pain fibers involved, some authors mention only type IV (c) fibers being stimulated by TENS, whereas

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**Conflict of Interest:** None declared.

**Ethical Approval:** The study was approved by the Ethics Committee ofт...
others reported stimulation of both type (III) (A∆d) and type IV (c) fibers. The nature of the involved pain conducting fibers will determine the choice of TENS mode which has to be used. The combination of parameters in conventional or hi- TENS provides stimulation of group two (Aßb) fibers, which cause analgesia primarily by spinal segmental mechanisms. Which inhibit type IV (c) fibers and type (III) (Aαd) fibers. These stimulation parameters are: low intensity, high frequency (above 100 Hz) with a pulse width of start duration (50-80µs) [2,3]. Using hi- TENS also induces central changes in the endorphinergic, serotoninergic and possibly substance p- ergic systems [1]. According to investigations, high frequency uterine contractions on the day of ET hinder IVF- ET outcome, possibly by expelling embryo out of uterine cavity [13], and reducing the degree of difficulty of embryo transfer will increases the pregnancy rate [13-15]. Now the definitive role of TENS in the treatment of female infertility is yet to be established and its potential impact centrally on the hypothalamic – pituitary- ovarian axis and peripherally on the uterus systemically examined [10,16]. In the present study we evaluate the effect of TENS on the pregnancy rate in those women who are undergoing embryo transfer in assisted reproduction technique (ART) by comparing with control group, receiving no TENS.

Materials and Methods

A prospective study was designed and a total of 233 randomly chosen healthy women who undergoing IVF/ ET treatment were enrolled in three groups; 117 women with the mean (SD) age of 31.20(3.85) years as the experimental group receiving 20 minutes TENS shortly before embryo transfer, 116 women with the mean (SD) age of 30.91(4.60) years receiving placebo no TENS as the control group in embryo transfer.

The overall age of the subjects ranged from 20 to 45 years. Only women with good quality of embryo were included in the study and patients with amenorrhea, endometriosis, and poly cystic ovaries (PCO) were excluded. All women underwent a stimulation protocol for induction of ovulation (IO), down regulated with GnRH agonist (1.2mg per day nasally or 1.0mg per day as a sub coetaneous injection; Suprecur or Superfact; Hoechst, Frankfurt, Germany). Down regulation was followed by stimulation with recombinant FSH (Gonal F, Serono, Geneva, Switzerland or Purogen, Organon, Oss, Nederland). Monitoring was performed via vaginal ultrasound scans and serum estradiol measurements. When adequate stimulation was achieved, 10000 IU of hCG (Profasi, Serono or Pregnyl, Organon) was administered. Oocyte retrieval by transvaginal ultrasonography guidance was performed 36 hours after hCG administration. Those oocytes that extruded the first polar body, indicating the metaphase II state, were injected with sperm. Intra cytoplasmic sperm injection (ICSI) was performed as described by Palermo et al. [17]. Fertilization was confirmed 16 to 20 hours after injection by visualization of two pronuclei. Embryos were graded using Bolton’s definition. The cavity [13], and reducing the degree of difficulty of embryo transfer will increases the pregnancy rate [13-15]. Now the definitive role of TENS in the treatment of female infertility is yet to be established and its potential impact centrally on the hypothalamic – pituitary- ovarian axis and peripherally on the uterus systemically examined [10,16]. In the present study we evaluate the effect of TENS on the pregnancy rate in those women who are undergoing embryo transfer in assisted reproduction technique (ART) by comparing with control group, receiving no TENS.

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Clinical pregnancy was defined as the presence of a fetal sac during an ultrasound examination 6 weeks after ET. None of the subjects takes supportive medication.

Statistical methods

The X²(Chi- square) tests were used to compare differences of clinical pregnancy rate in both groups. MANOVA was used to compare the variables differences and Eta2 test to analyze the correlation between Age of females, sperm parameters and clinical pregnancy. All procedures were carried out using SPSS for windows V11.5. The type 1 error rate was set to 0.05 for hypothesis test.

Results

A total of 233 patients were recruited for this study. The mean (SD) age of women in the TENS experimental group was 31.20(3.85), in placebo control group 30.91 (4.60).

Clinical pregnancies were documented in 36 of 117 patients (30.8%) in the TENS experimental group, whereas pregnancy rate in placebo was 19.8% (23 out of 116), pregnancy rate was highly significant in the TENS experimental group (p<0.05).

In MANOVA did not show any statistically significant differences of sperm parameters and number of egg by good quality among the groups (P>0.05) (Table 1). In the X²(Chi- square) tests, the expected frequency of pregnancy in placebo group was (23 vs. 29.4) (Table 2), and our results showed the pregnancy rate in the TENS experimental group significantly higher than placebo control group (p<0.038). The Eta2 test, showed the correlation between age of female and rate of pregnancy with coefficient determination (R = 0.389) and applying TENS was associated with significant increase in pregnancy rate in women younger than 40 years (P<0.05) but not in women older than 40 years.

The pregnancy rate had correlation with sperm parameters, the coefficient determinations are; sperm count(R= 0.610), sperm motility(R= 0.390), and sperm abnormality (R= 0.456).

Discussion

Past studies on IVF/ ET have focused on the implantation process including the induction and selection of the best- quality embryos using controlled ovarian hyper stimulation and embryo culture

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Placebo Control</th>
<th>TENS Experiment</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of patients</td>
<td>30.91(±4.6)</td>
<td>31.20(±3.85)</td>
<td>31.20(±3.85)</td>
<td>P&gt; 0.61</td>
</tr>
<tr>
<td>Sperm count (mil/ml)</td>
<td>67.14(±60.6)</td>
<td>58.83(±54.92)</td>
<td>58.83(±54.92)</td>
<td>P&gt; 0.24</td>
</tr>
<tr>
<td>Sperm motility (%)</td>
<td>27.89(±18.58)</td>
<td>26.42(±5.74)</td>
<td>26.42(±5.74)</td>
<td>P&gt; 0.40</td>
</tr>
<tr>
<td>Sperm morphology (%)</td>
<td>72.67(±24.41)</td>
<td>76.88(±14.12)</td>
<td>76.88(±14.12)</td>
<td>P&gt; 0.263</td>
</tr>
<tr>
<td>No. of embryos transferred</td>
<td>3.6(± 1.8)</td>
<td>3.2(± 2.6)</td>
<td>3.2(± 2.6)</td>
<td>P&gt;0.105</td>
</tr>
</tbody>
</table>

Table 1: The mean comparison of the age, sperm parameters and number of transferred embryos among the groups (MANOVA).
techniques, and little progress has been made to improve uterine receptivity [18]. High resolution ultrasound probes have enabled visualization of uterine contractility and provided insight into the importance of contractility in determining endometrial receptivity [13]. The acupuncture and TENS have the same current [19] and both in the day of ET significantly improves the reproductive outcome in infertile women because of endogenous opioid peptides secretion in the central nervous system (CNS), particularly; ß-endorphin [1,7,15]. The hypothalamic ß-endorphinergic system has inhibitory effects on the vasomotor center, and thereby a central inhibition of sympathetic activity [20], leads to decrease the tonic activity in the sympathetic vasoconstrictor fibers to the uterus and increase the uterine blood flow [10]. TENS may reduce uterine contractility and increase uterine blood flow, thus priming the uterus for implantation. This has the potential to improve implantation and pregnancy rate.

In this study we used conventional TENS (100Hz, 50usec biphasic asymmetrical pulse) 20 minutes before ET during IVF/ET compared with control and placebo group, the implantation and pregnancy rate was increased 11% in women with infertility. Our results are in agreement by Tomas et al. [14] who have explained the TENS current before ET during IVF/ET reduced the difficulty of embryo transfer and increase 7% the pregnancy rate.

The physical pain and complaints are more prominent in infertile women which are associated with lower productivity [21]. Some reports are shown that, 40% depression, 87% anxiety and 40% physical illness in the Iranian female [22]. In the other study, Karimzadeh et al. [23] showed that psychological impact of infertility in Iranian infertile female leads to psychological problems which affects the successful outcome in IVF. Therefore, conventional TENS provides stimulation of group II (Aδb) fibers, cause analgesia primarily by spinal segmental mechanisms, and inhibit the type IV(c) and type III (Aδd) fibers [19]. By this mechanism TENS relieves the physical pain of speculum and instrument setting during ET and reduces psychological physical pain feeling in this group. Chang et al. [15] indicated that the use of acupuncture reduce the anxiety and stress in infertile patients possibility through its sympathoinhibitory property and impact on ß-endorphin levels.

The most preferences of TENS to acupuncture are its non-invasive, safe, no side effect, easy to apply and remove, and TENS is battery- powered unit which send electrical impulses through the skin electrodes placed on or near the painful site. Some investigators indicated that non steroidal anti- inflammatory drugs (NSAIDS) may cause the reduction of uterine contractility and improve the pregnancy outcome after IVF/ET [24].

The preferences of TENS to pharmacological drugs are it has no side effect [3].

Further research is needed to demonstrate precisely how TENS causes physiological changes in the uterus, uterine blood flow impedance during ET on the endometrial and the reproductive system.

And more investigations are needed to explain the effect of TENS on the psychological status in infertile woman.

Conclusion

TENS seems to be a useful non invasive and easy applicable tool for improving pregnancy rate for ART protocol, psychologically prepared and relieve the pain of the patient during embryo transfer.

References


