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Impact of transcutaneous electrical nerve stimulation (TENS) on endometrial thickness in the healthy women, a step to improve the female fertility

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Objective To determine the physiotherapeutic effect of transcutaneous electrical nerve stimulation (TENS) on endometrial lining thickness in healthy women at their childbearing age.
Methods This is a prospective randomized controlled clinical trial including 46 healthy women within their childbearing age during the first year of their marriage. Uterine blood flow and endometrial thickness (ET) are measured at day 13 of MC before TENS application and at the same day of the next cycle after six sessions of TENS were applied.
Results TENS significantly increases endometrial thickness from 5.80 ± 0.24 to 7.60 ± 1.57 mm. This has a beneficial effect to increase the rate of pregnancy as it properly prepares of the uterine lining for implantation of fertilizing ova mediated by the reduction of both resistance and pulsatility indices of uterine arteries. These findings were the regardless age and BMI of the participants.
Conclusion There are beneficial effects of TENS to increase endometrial thickness in healthy women at their childbearing age.
Keywords transcutaneous electrical nerve stimulation, female fertility, endometrial thickness, pulsatility index, resistance index.

Introduction

The technique of transcutaneous electrical nerve stimulation (TENS) is easy, safe and noninvasive.[1] At the same time, it is inexpensive, its application has no side effects as it is free of any pharmacological element and do not interfere with consciousness.[2] It emits mild electrical impulses that might be felt as a tingling sensation at the site. As it is widely applied in different therapeutic modality used in clinical practice, parameters such as intensity, rate, and duration of these electrical impulses can be adjusted according to the required purpose.[3] One of the main uses for TENS is those related to analgesic techniques where electrical pulses emitted primarily aim to provide a degree of symptomatic pain relief by stimulating sensory nerves and thereby exciting either the pain gate mechanism and/or endogenous opioid system.[4] In addition to its analgesic effects, TENS can modify the skin temperature and enhance blood flow, this observation led many studies to the impact of TENS on the peripheral vasculature and reproductive system.[5,6]

The human endometrium is a plastic tissue with a lot of blood vessels as spiral arteries, which are terminal branches of uterine arteries.[7] It is known that normal function of the reproductive system mostly depends on the organization of the blood flow in the endometrium and on its proper thickness.[8,9] Normally, these blood flow patterns changes during the menstrual cycle (MC), as new blood vessels are formed in the endometrium.[10] These changes in the vasculature pattern and in the endometrial thickness are variable as the endometrium is thin immediately after menstruation and gradually grows thicker then after.[11]

Materials and Methods

This study was conducted at the College of the Medicine\ University of Kufa and licensed private clinics as a prospective randomized controlled clinical trial including 46 healthy women within their childbearing age. It lasted for 14 months from April 2016 to May 2017. The study was approved by the ethical committee at the college and the participants were informed about the aim of the study and briefed about the techniques used, and their verbal approvals were collected.

The device used for TENS consists of a battery-powered simple stimulator along with one or two pairs of adhesive electrodes and their connecting leads. The parameters of the stimulation used in this study were 2 Hz for the frequency, 10–15 mA for the intensity and 0.6 ms for the pulse width.[12] The role that was strictly followed throughout the study is not to increase the intensity to a level that hurts (always stay under the point of discomfort).[5,10]

All participants have undergone for six sessions of TENS, each lasted for 30 min. The applications were done on a day of 2, 4, 6, 8 12 and 13 of the MC. The electrodes of TENS were applied to specific points over the skin of participants after being properly prepared.[13,14] These points were selected according to dermatosomatic segments of sympathetic outflow that innervate the uterus (T_{12}–L_2 and S_2–S_3).[15,16] These points are five; three of them on both sides of body (Sanyinjiao SP-6, Zusanli ST-36, and Guilai ST-29) and two of them on midline of the body (Zhoncji REN-3 and Guanyuan REN- 4) (Figure 1).

Endometrial thickness (ET) measurement was done using transabdominal ultrasonography that measures the thickest echogenic area from one basal endometrial border across the endometrial canal to the other basal surface.[17] On the other hand, the pulsed Doppler curves measures both pulsatility index (PI) and resistance index (RI) of uterine arteries on right and left sides. The PI value was calculated according to formula; PI = $(A - B)$/mean, and resistance index formula; RI = $(A - B/A)$, where A is the peak systolic Doppler shift, B is the end diastolic shift frequency and mean is the maximum Doppler shifted frequency over the cardiac cycle.[18] These measurements (ET, PI and RI) were done at day 13 of the MC before the use of TENS technique (pre-teens) and at the same

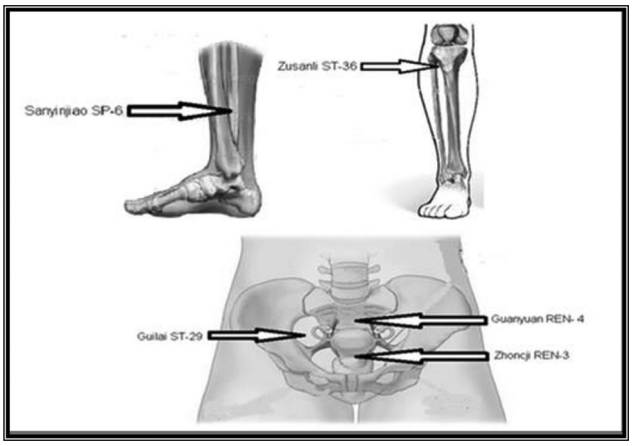

Fig 1. **Sites of the five TENS points: SP-6 (Sanyinjiao), ST-36 (Zusanli), ST-29 (Guilai), REN -3 (Zhoncji) and REN -4 (Guanyuan).**

day of the next MC after the application of the six sessions of TENS. In general, the normal ET that is important to prepare the uterus for a pregnancy state ranges from more than 6 to less than or equal to 10 mm.

Additionally, the participants were subdivided into two groups according to their age and into three subgroups according to their body mass index (BMI).[19] The correlation of these two variables were considered for the different parameters tested.

Results

The results of this study showed the range of age was between 15 and 42 years, BMI was 16.9–40.16, hemoglobin was 11–14 and RBS was 90–158 (Table 1). TENS application shows the significant increase of ET and the significant decrease of both RI and PI of uterine arteries (Table 2). Participants with age less than 25 years have none significant increase in their ET, RI, and PI (Table 3). The impact of the BMI of the participants on the effect of TENS application is not significant on ET, RI, and PI of both left and right side uterine arteries (Table 4). There is no significant correlation between changes in the ET and the change in RI and PI of both uterine arteries in the post-TENS application that measured by Pearson correlation (Table 5).

Discussion

Previous studies have been focused on using TENS for pain relief mechanism especially postoperatively or during labor.[1,2] However, in the last few years, some studies have been performed to test the effect of TENS in reproductive field. Among these are studies related to the uterine blood flow and endometrial thickness and subsequent pregnancy rate in infertile women.[3,5] Hence, the idea of this study is to study the effect of TENS on healthy women within childbearing age immediately after the first year of their marriage, before being infertile. Infertility is defined as the inability of couples to conceive after the end of the first year of their marriage.[20]

It focused on using TENS to prepare the uterus for implantation of fertilized ova by its effect on increase growing and thickness of endometrium due to increasing uterine blood flow.[3,6,21] The ET significantly increases along with a significant decrease in RI and PI of the uterine arteries in the post-TENS application. The mechanism underlying these effects is through their action on increasing production and secretion of endogenous opioid peptides, particularly B-endorphin in the central nervous system (CNS), that has inhibitory signal on vasomotor center. This will inhibit uterine sympathetic

Table 1. **The characteristic of participants**

Subjects' characteristics ($n = 46$)	Mean ± SD	Range
Age (years)	22.63 ± 6.41	15–42
Body mass index (kg/m^2)	26.87 ± 4.95	16.9–40.16
Hemoglobin (g/dl)	12.56 ± 1.08	11–14
Random blood sugar (mg/dl)	103.23 ± 15.86	90–158

Table 2. **Effect of TENS on endometrial thickness and resistance and pusatility indices for uterine arteries on both sides**

Variables		Pre-TENS ($N = 46$)	Post-TENS ($N = 46$)	*P*-value
ET (mm)		5.80 ± 0.24	7.60 ± 1.57	<0.05
RI of uterine arteries	Left	0.91 ± 0.04	0.80 ± 0.01	<0.05
	Right	0.88 ± 0.02	0.80 ± 0.01	<0.05
PI of uterine arteries	Left	3.27 ± 0.24	2.33 ± 0.07	<0.05
	Right	3.12 ± 1.52	2.40 ± 0.59	<0.05

ET, endometrial thickness; RI, resistance index; PI, pulsatility index; TENS, transcutaneous nerve stimulation.

Table 3. **The effect of age on post-TENS measurements of endometrial thickness and resistance and pusatility indices for uterine arteries on both sides**

Variables		Age (years)		*P*-value
		<25 ($N = 32$)	≥25 ($N = 14$)	
ET (mm)		7.62 ± 1.56	7.57 ± 1.65	>0.05
RI of uterine arteries	Left	2.38 ± 0.57	2.24 ± 0.39	>0.05
	Right	2.40 ± 0.60	2.39 ± 0.57	>0.05
PI of uterine arteries	Left	0.80 ± 0.05	0.78 ± 0.05	>0.05
	Right	0.80 ± 0.05	0.79 ± 0.03	>0.05

ET, endometrial thickness; RI, resistance index; PI, pulsatility index; TENS, transcutaneous nerve stimulation.

Table 4. **The effect of body mass index on post-TENS measurements of endometrial thickness and resistance and pusatility indices for uterine arteries on both sides**

Variables		Body mass index (kg/m^2)			*P*-value
		Normal ($N = 17$)	Overweight ($N = 17$)	Obese ($N = 12$)	
ET (mm)		7.70 ± 1.86	7.00 ± 1.22	8.33 ± 1.30	>0.05
RI of uterine arteries	Left	0.82 ± 0.06	0.78 ± 0.05	0.78 ± 0.04	>0.05
	Right	0.80 ± 0.05	0.78 ± 0.04	0.80 ± 0.04	>0.05
PI of uterine arteries	Left	2.49 ± 0.62	2.27 ± 0.49	2.17 ± 0.29	>0.05
	Right	2.48 ± 0.75	2.42 ± 0.59	2.25 ± 0.21	>0.05

ET, endometrial thickness; RI, resistance index; PI, pulsatility index; TENS, transcutaneous nerve stimulation.

Table 5. **Post-TENS pearson correlation between endometrial thickness and resistance and pusatility indices for uterine arteries on both sides**

Parameter	Post-TENS	*r* (Pearson correlation)	*P*-value
RI of uterine arteries	Left	−0.116	>0.05
	Right	−0.129	>0.05
PI of uterine arteries	Left	−0.224	>0.05
	Right	−0.223	>0.05

TENS, transcutaneous nerve stimulation; RI, resistance index; PI, pulsatility index, *r* = Pearson correlation.

tone as a result of inhibiting excessive α motor neuron activity and stimulating the Ia afferent nerve of the muscle that is the antagonist to the spastic muscle, thereby decreasing blood flow impedance by reducing uterine arteries spasticity. This inhibition is accomplished by peripheral stimulating of large diameter afferent fibers (Aβ) fibers which activate local inhibitory mechanisms in the dorsal horn of the spinal cord that lead to the presynaptic inhibition of nociceptive afferent fibers (Aδ) and C fibers, all these will result in increasing the uterine blood flow and subsequently, improve growth and thickness of the endometrium.[22] These results are agreed with previous studies.[3,23]

This study showed that uterine arteries on both sides are affected to the same extent by TENS application. This is because both have the same origin from the internal iliac artery.[24] Subsequently, a decrease in the RI and PI will increase uterine blood flow leading to optimal endometrial circulation which in turn will improve the growth and thickness of the endometrium.[12,23,25] This will increase the rate of conception by increasing chances of the fertilized ova to be implanted in the uterus.[26]

This in consistence with other studies like that of Randolph et al.[14,27] concluded a positive correlation between high endometrial thickness >8 mm and a higher rate of conception. Some researches stated that endometrial thickness of >7 mm was a predictive factor for pregnancy while thickness of <6 mm is associated with no pregnancy.[28,29] Some studies stated that the ideal ET for conception is 5–8 mm, while Isaksson et al.[30] identified the ideal range of ET is 9–11 mm. However, the majority of researches suggested the correlation of specific values of ET during ovulation and the likelihood of pregnancy. At the same time, our results were consistent with that of many other studies in that a reduced RI and PI of uterine arteries after TENS will increase uterine receptivity and lining thickness of endometrium.[13,24,31]

On contrary, Tsai et al.[32] found that endometrial thickness does not have useful prediction value and Kolibiianahis[33] showed that endometrial thickness cannot predict ongoing pregnancy. Going along with these findings were that of Ng et al.[34] reported no relationship between endometrial thickness, morphology and pregnancy outcomes. Furthermore, the findings of Schild et al.[35] disagreed with ours as they stated no association between uterine arterial blood flow and endometrial thickness.

The results of this study showed no significant impact of the participants' age on TENS effect for all the ET, RI and PI. These could be explained if we know that the uterus is affected less than ovaries with increasing age of women. So endometrial aging has a negative effect on changing ET. This is consistent with the findings of previous studies that endometrial aging was negatively associated with pregnancy outcome, while ET was positively associated with pregnancy outcome.[36–38]

This study showed that the change in BMI has no significant role in modulating the effect of TENS application on ET, RI, and PI. This seems logical as the effect of TENS is mediated by the CNS mechanisms mainly that mediated by endorphin (nevertheless, the variety of responses such as neurological, histochemical and neuropharmacological).[39] What further explains these findings is fact that the endometrium represents the vascular mucosal lining of the uterus. That is why the effect of obesity on the endometrium had received less attention.[40]

What further minimizes the effect of BMI in this study is that the participants pre- and post-TENS application was the same. Many other studies had concluded same results regarding the impact of the BMI.[41,42]

The results of this study confirmed the *r*-Pearson correlation between changes that occur in endometrial thickness after TENS application and PI, RI of both sides uterine arteries with no significant correlation at $P > 0.05$, this result does not mean that there was no relationship between two variables but the relationship does not reach significantly effective. Therefore, this result passed with the suggestion that increasing uterine arteries blood flow cause increasing the endometrial growth and thickness, not vice versa, that means the uterine blood flow increasing are the causes and increase endometrial thickness, however, this results of increasing endometrial thickness in agreeing with the previous study.[43]

Limitation of the study

We hoped to use eight points of stimulation instead of five, but the two-channel TENS device can only provide four electrodes. Considering that three of the five stimulation points were bilaterally located, two TENS units had been used simultaneously in this study. Here, another limitation is issued regarding the output pulses. Although the two units were started at the same time, their outputs signals cannot be guaranteed to be absolutely synchronous, to guarantee the uniformity of stimulation. In future studies, this could be managed using a TENS device with four channels instead of two which was not available at the time of his research.

Conclusion

This provides evidence-based findings for the use of TENS in assisted reproductive technique (ART), program to decrease time, cost and efforts. Furthermore, TENS application could be used to adjunct known medication like clomiphene and HCG administration that induced ovulation to decrease their side effects and to increase the chance of pregnancy. TENS technique is easy to perform, safe with low cost. It has the ability to prepare the uterus for pregnancy by increasing both the uterine blood flow and the endometrial thickness. Hence, it has a positive influence to increase the endometrial receptivity for implantation of fertilizing ova.

Conflict of Interest

The authors declare that there is no conflict of interests for this article.

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