

Study on The Pregnancy Outcome and Serum Biochemical Indexes of Cryo Embryo Transfer by Pelvic Floor Biomimetic Electrical Stimulation in Patients with Thin Endometrium

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Abstract

To observe the pregnancy outcome of cryo embryo transfer thin endometrium treated by pelvic floor biomimetic electrical stimulation. Methods: six patients with thin endometrium were randomly divided into two groups, 30 in each group. The patients in both groups were given artificial cycles (taking estradiol valerate tablets (bujiale, Bayer Pharmaceutical Co., Ltd.) 3 mg in the morning and 3 mg in the evening from the third day of menstruation, adding luteal support after 12 days of continuous use). After being purified, the observation group was massaged with pelvic floor muscles every day for 15 minutes at a frequency of 50 Hz, and the acupoints were selected as perineum the endometrial thickness, type, blood flow and clinical pregnancy rate of progesterone were compared between the two groups.

Results: after the treatment of pelvic floor bionic electrical stimulation, the blood flow of type I and type II III in the observation group was significantly decreased compared with that in the control group ($P < 0.05$); after the treatment of pelvic floor bionic electrical stimulation, the thickness of the endometrium in the observation group was significantly higher than that in the control group ($P < 0.05$); after the treatment of pelvic floor bionic electrical stimulation, the number of type a endometrium in the progesterone group was higher than that in the control group, but the difference was not statistically significant ($P > 0.05$); the clinical pregnancy rate in the observation group was significantly higher than that in the control group, and the difference was statistically significant ($P < 0.05$). After treatment, serum biochemical indexes of patients showed significant changes. Thromboxane A2/Prostacyclin (TXA2/PGI2) and Inhibin B (INHB) in observation group were higher than in control, while serum anti thyroid peroxidase antibody (TPOAb) in observation group was lower than in control group.

Conclusion: the combination of estrogen and progesterone combined with pelvic floor massage can improve the endometrial thickness and blood flow of thin endometrial patients undergoing Fe 'cycle, and improve the pregnancy rate.

Keywords: pelvic floor massage; frozen thawed embryo transfer; pregnancy outcome; thin endometrium

Introduction

In recent years, with the continuous development of assisted reproductive technology, how to further improve the embryo implantation rate and clinical pregnancy rate has become a common clinical concern (Liu et al.2008;Vanda and Ivan,2009;Fernández-Shawan Cercas,2015;Brezinová and Oborná,2004). Frozen

thawed embryo transfer (FET) can increase the cumulative pregnancy rate and reduce the occurrence of ovarian hyperstimulation in varying degree(Oriefet al.2015;ergievaet al.1984;Mcnamee and Huang,1997). At the same time, due to the fact that FET costs less, takes less time and is easy to operate compared with the process of fresh embryo oocyte retrieval, it is generally accepted by patients and clinicians that thin endometrium means that the thickness of endometrium is lower than the "threshold

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thickness" that enables patients to obtain pregnancy (Matsumoto et al. 1984; Cheung et al. 2011). At present, the commonly accepted clinical view is that the endometrial thickness is less than 7 mm when the follicle matures, which is defined as thin endometrium (Ndrickx et al. 1987; Gravesherring et al. 2008).

Clinically, its etiology and pathogenesis are complex. 60% of the clinical pregnancy rate is caused by the thin endometrium of the patient's children. Thin endometrium can not only affect the implantation of embryo, but also increase the risk of spontaneous abortion or embryo abortion to a certain extent, and also cause infertility and amenorrhea (Saillenfait et al. 1993; Danielsson and Danielson, 1990; Gibson and Becker, 1970). The change of endometrial receptivity caused by the thin endometrium is an important reason for the low pregnancy rate. The thickness is the most simple and measurable index to evaluate its receptivity, and the appropriate thickness is closely related to pregnancy. Under certain conditions, pregnancy rate is positively correlated with intimal thickness, but not with age and embryo quality.

Pelvic floor bionic electrical stimulation refers to put electrodes under the perineum to irritate and make uterine vascular smooth muscle contraction and relaxation, which could increase pelvic floor, vagina, endometrium and uterine muscle blood liquid circulation to increase tissue nutrition and improve endometrial receptivity. In our study, to further explore the applications of pelvic floor bionic electrical stimulation in treatment of thin endometrium, we used pelvic floor bionic electrical stimulation in treatment processions of 60 patients to observe its outcome in cryo embryo transfer.

1. Objects and methods

1.1 research object

From March 2015 to August 2016, 60 cases of thin endometrial patients requiring FET were treated in the reproductive Department of the Second Affiliated Hospital of Shandong University of traditional Chinese medicine

1.2 diagnostic criteria

Diagnosis of thin endometrium: at present, there is no uniform standard for thin endometrium in clinical practice. According to the previous literature, in the natural cycle of patients, when the LH peak day and the maximum follicle diameter line ≥ 18 mm (ovulation day), the thickness of the endometrium of the ovary ≤ 7.0 mm³ is included in the standard and excluded from the standard: it conforms to the diagnosis of thin endometrium; the

basic endocrine of the menstrual period is normal; In recent 3 months, no hormone drugs were used; in recent 3 months, there was no OHSS. Exclusion criteria: patients with heart and blood vessel diseases and mental disorders; patients over 40 years old or with low ovarian response; patients who cancelled the cycle due to various factors on the transplantation day; patients who refused to accept the study.

1.3 Treatment

60 patients were divided as control and observation group, and patients in observation group were arrayed to accept pelvic floor bionic electrical stimulation. Pelvic floor bionic electrical stimulation: U8 Phenix equipment (France) was used to patient treatment. Treatment stick was disinfected and slowly insert into vagina of patients, and two electronic slices were pasted on bilateral groin and lumbar sacral of patients. Whole treatment is at 50HZ for 15 min every day.

2. Observation method

B-ultrasound was performed on the 15th day of menstrual cycle (the day of adding progesterone)

2.1 thickness of intima

In the sagittal plane of the uterus, the thickness of two layers of endometrium perpendicular to the midline was measured for three consecutive times, and the average value was recorded.

2.2 type of intima

Type A: three-line structure, the outer layer and the middle layer are strong echo, the other parts are low echo type B: uniform medium intensity echo, the middle strong echo is discontinuous; type C: uniform strong echo, no three-line structure

2.3 blood flow pattern of intima:

There was no intimal or subintimal blood flow under B-ultrasound; type III: only existed in the intima

2.4 serum biochemical indexes test

TXA2/PGI2, INHB and TPOAb diagnostic kit were used to detect TXA2/PGI2, INHB and TPOAb.

3. Results

3.1 Baseline data of two groups of patients

The baseline of patients in observation and control groups has no significant difference, including in age, infertility years and body mass index (Fig.1, $P > 0.05$).

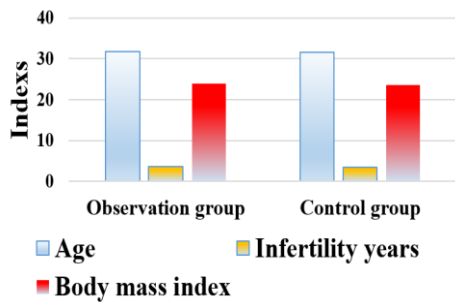


Figure 1. there was no significant difference between the two groups ($P > 0.05$). including age, infertility years, body mass index. See Fig.1 for details.

3.2 comparison of endometrial thickness and structure between two groups

By comparison, the thickness of endometrium in the observation group was higher than that in the control group on the day of adding progesterone ($P < 0.05$) see from Fig.2 . The number of type a endometrium in the observation group was higher than that in the control group on the day of adding progesterone ($P > 0.05$) see from Fig.3. The difference between the two groups was statistically significant ($P > 0.05$). See Fig.4 for specific results.

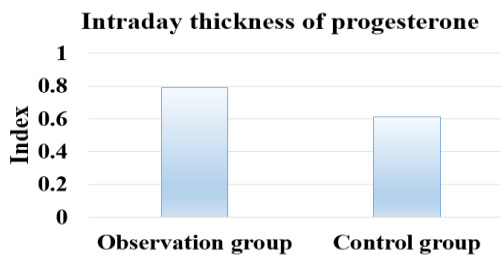


Figure 2. Comparison of progesterone days between the two groups

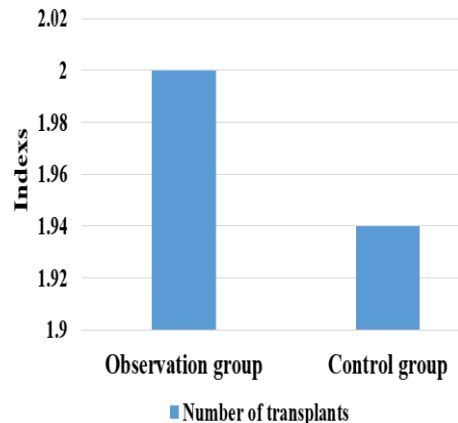


Figure 3. Comparison of endometrial thickness between the two groups

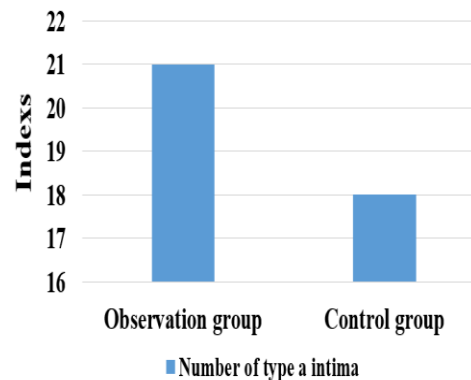


Figure 4. Comparison of endometrial structure between the two groups

Table 1. Comparison of serum biochemical indexes between the two groups

	Phase	TXA2/PGI2	INHB (pg/mL)	TPOAb(U/mL)
Control group	pretherapy	0.89 ± 0.09	73.21 ± 9.23	92.63 ± 15.34
	post-treatment	1.03 ± 0.07	95.32 ± 11.19	27.63 ± 4.09
Observation group	pretherapy	0.87 ± 0.06	72.25 ± 9.27	93.53 ± 14.46
	post-treatment	1.23 ± 0.13	125.33 ± 13.29	17.93 ± 3.17

Table 2. Comparison of pregnancy outcome between the two groups

Groups	Embryonic implantation rate	Clinical pregnancy rate
Control group	11/30 (37%)	9(30%)
Observation group	23/30(76.7%)	22(73%)

3.3 Comparison of serum biochemical indexes between the two groups

By comparison, serum biochemical indexes in the observation group, including TXA2/PGI2 and INHB, were higher than that in the control group, while TPOAb in observation group is lower than in control (all $P < 0.05$) see from Table 1.

3.4 Comparison of pregnancy outcome between the two groups

By comparison, embryonic implantation rate and clinical pregnancy rate were higher than that in

the control group, while TPOAb in observation group is lower than in control (Table 2, all $P < 0.05$).

3.5 Ultrasonographic characteristics of various structures in two groups of embryos

Embryo sac is also called gestational sac. It is the first sign of pregnancy observed in the uterus. It is a round sacculus. The wall of the sacculus is a regular halo. It is located between the decidua of the ovary on one side of the uterine cavity. The smallest diameter of this group is 16.03mm at the 5th week of pregnancy see from Fig.5. The amniotic sac gradually increased, while the yolk sac was free or attached to the amniotic sac wall, and the increased amniotic sac was squeezed on the side of the uterine cavity wall until the end of early pregnancy, the yolk sac gradually shrunk and no longer showed by ultrasound. Irregular yolk sac morphology in early embryogenesis as shown in Fig.6.

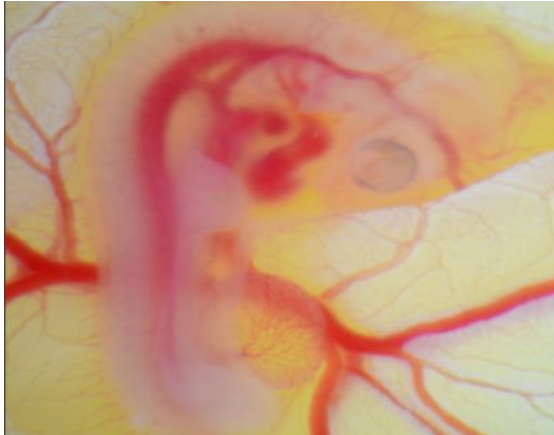


Figure 5. Sonographic characteristics of embryo structure in control group

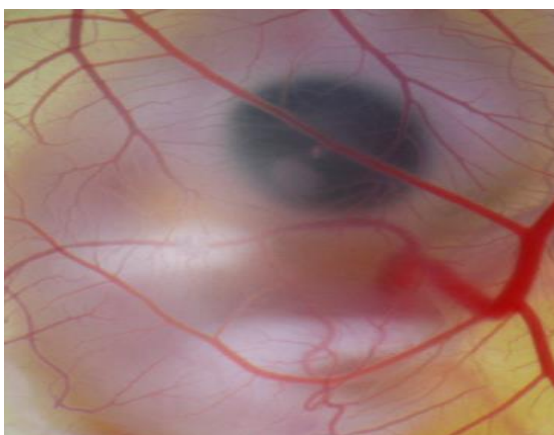


Figure6. Ultrasonographic characteristics of embryo structure in the observation group.

4 Discussion

With the development of if, the influence of pure technical factors on the clinical success rate is becoming smaller and smaller(Saillenfait

et al.1993;Danielsson and Danielson,1990; Gibson and Becker,1970). The main influencing factors are the embryo quality and endometrial receptivity of patients themselves. Studies have shown that endometrial thickness and endometrial blood flow are the most intuitive indicators to evaluate endometrial receptivity(Gardner et al.2003). Too thick or too thin endometrium and poor endometrial blood flow will affect embryo implantation. In previous studies on the influence of endometrial thickness on pregnancy, meta-analysis was carried out in nearly 5000 cycles(Lindgren et al.1984; Wilson and Ritter,1977; Chung and Yu,2013). It was found that the thickness of official endometrium in pregnant group was significantly higher than that in non pregnant group on the day of hCG, with an average difference of 0.4mm(Dimopoulou et al.2018). Endometrial blood flow is regarded as an index to evaluate endometrial receptivity by some scholars, which is positively correlated with endometrial receptivity and pregnancy rate(Nau et al.1981). It is believed that endometrial blood flow can reflect endometrial receptivity, and the pregnancy rate is inversely proportional to the resistance of subendometrial blood flow, and is directly proportional to the extent that the distribution of blood vessels is close to the endometrium(Lindenau et al.1996)

Thin endometrium is characterized by high arterial blood flow resistance, poor blood perfusion of endometrium, slow growth of glandular epithelium, resulting in poor blood supply of endometrium, thus affecting the thickness of endometrium, and finally the formation of thin endometrium(Wilson et al.1996). Therefore, improving the intimal blood flow and increasing the intimal thickness have become the focus of clinical attention. This study is simple, economical and applicable. The pelvic floor massager is selected to improve the pelvic floor blood flow, and then improve the cumulative pregnancy rate. The pelvic floor massager combines the traditional massage, rehabilitation, electrical stimulation and modern biofeedback information theory of our country. Its vibration source is the motor, At present, its mechanism is believed to affect metabolism by driving the passive contraction of muscle cells. The massage method can induce the contraction of pelvic floor muscles, promote the circulation of pelvic blood, increase the blood flow under the

endometrium, so as to improve the thickness and structure of the endometrium, regulate the function of gonad axis, improve the environment in the uterine cavity, and improve the receptivity of

the endometrium, so as to facilitate the implantation.

5. Conclusion

In conclusion, the application of pelvic floor biomimetic electrical stimulation intervention in FET cycle of patients with hypoplasia of endometrium can increase the blood circulation of endometrium and Subendometrium, improve the receptivity of endometrium, and increase the rate of embryo implantation. It is worth further promoting that pelvic floor biomimetic electrical stimulation refers to the electrode placed in perineum passing through different frequencies of current, Stimulating the contraction and relaxation of uterine vascular smooth muscle can increase the blood circulation of pelvic floor, vagina, endometrium and uterine muscle, increase tissue nutrition and improve the receptivity of endometrium.

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