Discussion on the Efficacy of Vascular Smooth Muscle Technology in the Treatment of Thin Endometrial Infertility

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*vascular smooth muscle technique; thin endometrial infertility; endometrial thickness*
Abstract

Objective: To clarify the efficacy of vascular smooth muscle technology in the treatment of thin endometrial infertility, and to provide a theoretical basis for the further diagnosis and treatment of thin endometrial infertility. Methods: In accordance with the inclusion and exclusion criteria, 2015.01-2020.01 selected thin endometrial infertility patients undergoing freeze-thaw embryo transfer at the Female Pelvic Floor Urinary Reconstructive Center in Dalian Municipal Women and Children’s Medical Center were selected according to different treatment methods. For the two groups, pure estrogen therapy was used as the control group, and vascular smooth muscle technology combined with estrogen therapy was used as the study group. All patients' endometrial thickness and pregnancy and delivery were recorded before and after treatment. Results: 1. The endometrial thickness of the study group was significantly larger than that of the control group after treatment, the difference was statistically significant (P <0.05); 2. 80 patients in the study group, 13 cases of successful pregnancy and delivery, 5 cases of biochemical pregnancy; the endometrial changes of the 50 patients in the control group was not obvious after treatment, none of the endometrial thicknesses reached the embryo transfer standard, and none were transplanted. Conclusion: Vascular smooth muscle technology can effectively increase the thickness of endometrium, with the aim of assisting to improve the pregnancy success rate of thin endometrial infertility through vascular smooth muscle technology.

Introduction

With the increase of infertility patients year by year, currently the widespread development of assisted reproductive technology has successfully treated some infertility patients, but for some infertility caused by thin endometrium, there is still no effective
treatment. As one of the important factors affecting women's pregnancy rate, the thin endometrium is increasing year by year. The pathogenesis is not completely clear, it may be secondary or primary\(^1\). At present, the clinical treatment methods of thin endometrium are mainly drug treatment and surgical treatment. High-dose estrogen treatment is the most common clinically used drug treatment, but the therapeutic effect is still controversial, some patients still have no obvious curative effect, the treatment method showed a lack of response\(^2\), and was eventually informed that there might be no fertility opportunities. Finding new and effective treatments is an urgent task for patients, family members and medical workers. In recent years, with the rapid development of electrophysiology rehabilitation science and technology, treatment methods using electrophysiology as the main intervention method have attracted everyone's attention. The purpose of this study is to explore the efficacy of pelvic floor rehabilitation technology based on vascular smooth muscle technology in the treatment of thin endometrial infertility, and to promote the development of pelvic floor rehabilitation technology, with a view to providing diagnosis and treatment of thin endometrial infertility reference.

Materials And Methods

1. Research data: According to the following inclusion and exclusion criteria, 2015.01-2020.01 collected cases of thin endometrial infertility patients undergoing freeze-thaw embryo transfer at the Female Pelvic Floor Urinary Reconstructive Center in Dalian Municipal Women and Children’s Medical Center. The methods were divided into two groups, the conventional estrogen treatment method was used as the control group, and the vascular smooth muscle technology combined with estrogen treatment was used as the study group. All patients signed the informed consent.

1.1 Inclusion criteria: (1) Age: 25-30 years old, BMI: 18-24 kg / m\(^2\), 3 years of primary
infertility. (2) A comprehensive infertility test has been performed, excluding infertility caused by other reasons (including routine semen examination of the male, tubal patency examination of the female, basic sex hormone examination, B-ultrasound monitoring of ovulation and exclusion of polycystic ovary syndrome, Endometriosis, etc.). (3) The thickness of endometrium on the day of HCG injection before treatment was ≤7mm. (4) Proposed freezing and thawing embryo transfer (FET).

1.2 Exclusion criteria: (1) Those with organic lesions in the uterus and ovaries, such as endometrial polyps, uterine fibroids, endometriosis, ovarian cysts, etc. (2) Patients with organic diseases such as genital malformation, congenital gonadal dysgenesis, and uterine amenorrhea. (3) Patients with gynecological inflammation, systemic infection, blood system and other diseases. (4) Contraindications to low-frequency electrical stimulation (such as the installation of a pacemaker, lack of local sensation and electrical allergies, mental and psychological disorders, neurological diseases such as epilepsy, acute infectious diseases, malignant tumors, etc.). (5) Those who cannot follow the doctor’s order.

2 Instruments and methods

2.1 Apparatus: French neuromuscular stimulation therapy instrument PHENIX 8 PLUS (Guangzhou ShanShan Medical Instrument Limited Company). B-K ultrasound equipment (model: 1202; manufacturer: B-K Medical ApS; manufacturer address: Mileparken34, DK-2730 Herlev, Denmark).

2.2 Method

2.2.1 Study group treatment: vascular smooth muscle technology combined with estrogen treatment for 3 consecutive courses. 1) Vascular smooth muscle technology: PHENIX 8 PLUS therapy device is used to start treatment after menstruation is clean. Each menstrual cycle is treated continuously for 20 days, once a day, hemodynamic activation
and hemodynamic acceleration programs are selected for a total of 40 minutes. The specific method is as follows: Raise the bed of the treatment bed by 30°, lie on the treatment bed flat, place the vaginal probe and electrode pads, relax both hands on both sides of the body, and adjust the current intensity to the maximum tolerability of the treatment. 2) Biofeedback therapy: The same treatment method as vascular smooth muscle technology, instruct patients to contract and relax the pelvic floor muscles according to the biofeedback training module displayed by the equipment. **Control group treatment:** oral estradiol valerate (estrogen) 2 mg, 3 times a day. Take it from the 5th day of the menstrual cycle, stop taking it for 1 week after taking it for 21 days, and use it for 3 cycles. Oral progesterone capsules 200 mg / d for 14 days after ovulation.

**Ovulation-stimulating therapy:** All patients first use gonadotropin-releasing hormone agonists and gonadotropins in the usual way. Human chorionic gonadotropin (10 IU) was injected intramuscularly when there was at least one dominant follicle diameter ≥18 mm.

### 2.2.2 Efficacy observation:

Compare the endometrial thickness of the two groups before and after treatment with the maximum follicular diameter ≥18mm (the day of human chorionic gonadotropin injection), and follow-up of pregnancy and delivery.

**1) Determination of endometrial thickness:** Obtain the largest longitudinal section of the uterus, measure the maximum distance between the anterior wall of the uterus, the posterior wall of the uterine muscle layer and the endometrium, and take the average of three measurements.

**2) Follow-up of pregnancy and childbirth:** Follow-up of biochemical pregnancy, clinical pregnancy and childbirth.

### 3. Statistical methods

Statistical analysis was performed using spss21.0 statistical software. Measurement data that conform to the normal distribution were expressed as mean ± standard deviation,
and t test was used; $X^2$ test was used for count data. $P < 0.05$ was considered statistically significant.

Results

1. Collecting patients: 144 patients who compliant the inclusion and exclusion criteria were collected, of which 130 patients completed the treatment and follow-up work, including 80 patients in the research group and 50 patients in the control group.

2. Endometrial thickness comparison: (1) Comparison between groups: There was no significant difference in endometrial thickness between the two groups of patients before treatment ($P > 0.05$). The endometrial thickness of the study group was significantly larger than that of the control group after treatment ($P < 0.05$); (2) Comparison within the group: The endometrial thickness of the study group after treatment was significantly greater than that before treatment, and the difference was statistically significant ($P < 0.05$); the comparison of endometrial thickness of patients in the control group before and after treatment ($P > 0.05$). (Table 1).

Table 1 Comparison of endometrial thickness between the two treatment groups
| Group       | Research Group | Control Group |
|------------|----------------|---------------|
| Before     | After          | Before        | After        |
| Intimal Thickness (mm) | 3.39±1.84     | 4.59±1.76     | 3.34±1.28    | 3.92±0.93 |

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P_{\text{within research group}} = 0.023
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P_{\text{within control group}} = 0.255
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P_{\text{Inter-group before treatment}} = 0.892
\]
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P_{\text{Inter-group after treatment}} = 0.039
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3. **Follow-up of pregnancy and childbirth:** 80 patients in the study group, 13 cases of successful pregnancy and childbirth, and 5 biochemical pregnancy; the endometrial changes of the 50 patients in the control group were not obvious after treatment, none of the endometrial thicknesses reached the embryo transfer standard, and none of them were transplanted.

**Discussion**

In recent years, the number of infertility patients has increased year by year, and research on the etiology that affects women's pregnancy rate and corresponding treatment methods has become a hot issue. Successful embryo implantation must have two conditions: a well-developed embryo and a receptive endometrium, both of which are indispensable. In female infertility, thin endometrium is a more important factor.

Kunicki\(^3\) et al believe that about 1/3-2/3 of human embryos eventually fail to implant due
to uterine receptivity abnormalities, and the thickness of the endometrium is an important indicator for evaluating receptivity. The diagnostic criteria for thin endometrium are still not clear. Some scholars believe that the thickness of the endometrium is 6 to 8mm. Most researchers tend to endometrial thickness ≤7mm[4]. Most scholars agree that thin endometrium refers to the day when human chorionic gonadotropin or luteal support is given in assisted reproduction technology. The thickness of the endometrium measured under ultrasound is ≤7mm, which is infertility. One of the most common causes of women with asthma[5]. The successful development of assisted reproduction technology has successfully rescued many infertility patients, but some patients with thin endometrial infertility due to the thin thickness of the endometrium, a variety of treatment methods are ineffective, resulting in unacceptable embryo transfer. Because the pathogenesis is not completely clear, the etiology is complicated, and although there are many treatment methods, there is no one method that is universally applicable and the effect is accurate. Usually, the disease duration of this part of the thin endometrium patients who do not respond is as long as several years or even ten years. Try many treatments that can be implemented have ended in failure. Clinical diagnosis of the disease is usually performed by ultrasound and hysteroscopy. Treatments for this type of disease include a large number of estrogen, aspirin, chinese medicine and the latest stem cell treatment, granulocyte colony-stimulating factor and other treatment methods. However, the efficacy is still not satisfactory, and some patients are ineffective for the above treatment schemes, and they are at risk of losing their mothers[6,7]. Miwa[8] and others first pointed out the pathophysiology of thin endometrium: slow growth of glandular epithelium, high resistance to uterine arterial blood flow, vascular dysplasia, and reduced expression of vascular endothelial growth factor. In recent years, with the rapid development of
electrophysiology rehabilitation science and technology, treatment methods using electrophysiology as the main intervention method have attracted everyone's attention. Pelvic floor rehabilitation technology has been widely used in gynecological diseases and reproductive endocrine diseases, and has achieved good results[9]. In clinical practice, pelvic floor rehabilitation technology is a new type of physical therapy, which can reflect and simulate the body's electrophysiological environment, and respond to the body through low-frequency bioelectrical stimulation, which mainly includes electrical stimulation therapy, biofeedback therapy, kegel training method, and et al. Vascular smooth muscle technology appears as a new technology in the medical field. Previous studies have confirmed that vascular smooth muscle technology can promote the contraction and relaxation of vascular and lymphatic smooth muscle, significantly improve the circulation speed of blood and lymph fluid, and improve the blood and oxygen supply of tissues. The amount of harmful substances in the tissue at the same time, and effectively improve the physiological status of the tissue. The main pathophysiology of thin endometrium is the poor local blood supply of the endometrium and the poor environment of the surrounding immune fluids, whether vascular smooth muscle technology can increase uterine blood circulation, provide nutrition for endometrial growth, increase endometrial thickness, and improve pregnancy rate has become the focus of this study. Many scholars at home and abroad have actively participated in clinical application research on pelvic floor rehabilitation technology. Bodombossou-Djobo[10] and others have found that low-frequency electrical stimulation biofeedback therapy for thin endometrium can significantly increase the thickness of the endometrium. The increase in pregnancy rate was not significant. Kunicki[2]stimulation can increase the thickness of endometrium in patients with thin endometrial infertility and increase the
pregnancy rate. Our study found that the vascular smooth muscle technology combined with estrogen treatment significantly thickened the endometrium, and the endometrial changes did not change after estrogen treatment alone, obvious or almost no change; 13 cases of successful pregnancy and childbirth in the study group, 5 cases of biochemical pregnancy; 50 patients in the control group did not reach the embryo transfer standard due to endometrial thickness after treatment, neither of them were transplanted, and the pregnancy rate in the study group was obvious improve. The analysis may lead to the following three reasons: Firstly, the patients in the group were severely ill, and the endometrial conditions were extremely poor, the thin endometrial infertility patients included in this study were subjected to a variety of methods in reproductive center of our hospital, those who did not see any effect in treatment, the thinnest intimal thickness was only 2mm, and patients and their families even lost hope, due to the severe infertility, although the endometrium was thickened, the effect was not significant, and only 18 cases met the transplant conditions; Secondly, because the treatment time of the patient is only 3 courses, the time is short; finally, the number of patients included in the study is small, and the sample size needs to be expanded for further research.

Pelvic floor rehabilitation technology uses bioengineering technology, bioinformatics principles, and high-tech therapeutic instruments to develop personalized treatment plans. Compared with traditional drug treatment and surgical treatment, pelvic floor rehabilitation technology is a non-toxic side effect, non-invasive the bionic physical therapy method with accurate curative effect opens up a brand-new treatment method for such patients. In the future, it is necessary to expand the sample size, extend the treatment time, and screen patients for enrollment to further improve the research. The results of this research will be used in clinical work to help improve the pregnancy success rate of patients with thin endometrial infertility, reduce the burden on families and
society, maintain stability and harmony in families and society, and save suffering from infertility a tortured family has good economic and social benefits. At the same time, it will help expand the therapeutic field of pelvic floor rehabilitation technology, promote the implementation and development of new technologies and new projects, and lay a solid foundation for the application of biomimetic technology in people's lives.

Conclusion

Vascular smooth muscle technology can effectively increase the thickness of endometrium, with the aim of assisting to improve the pregnancy success rate of thin endometrial infertility through vascular smooth muscle technology.

Declarations

1. Ethical Approval and Consent to participate:

This article has been obtained ethical approval and consent to participate.

2. Consent for publication:

This article has been obtained consent for publication.

3. Availability of supporting data:

This article has been obtained availability of supporting data.

4. Competing interests:

No competing interests in this article.

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6. Authors' contributions:

Zhongmin Wang was responsible for designing and supervising projects. Caixia Sun was responsible for implementing projects, collating data, and writing article.
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