ORIGINAL RESEARCH ARTICLE

Effectiveness of growth hormone in promoting endometrial growth in patients with endometrial dysplasia in frozen embryo transfer

DOI: 10.29063/ajrh2023/v27i3.4

*Yong Wu[#], Yuan Tian[#], Lili Zhang , Li Zeng , Ying Wang , Ruifeng Shao and Chihua He**

Jingzhou Hospital Affiliated to Yangtze University, Jingzhou, Hubei, 434020, China

***For Correspondence:** Email: *hchyzl@163.com*, Phone: (+86) 18107167959

Abstract

This study was designed to investigate the effect of growth hormone (GH) in promoting endometrial thickness, blood flow, and pregnancy outcome in patients with thin endometrium for frozen embryo transfer. Thirty-eight patients were recruited in the reproductive center of Jingzhou Hospital affiliated to Yangtze University who cancelled fresh embryo transfer due to thin endometrium and planned to undergo frozen-thawed embryo transfer (FET) from May 2019 to May 2020. The patients were randomly divided into the GH injection group (19 cases, endometrium preparation with hormone replacement therapy (HRT) and GH by subcutaneous injection) and the control group (19 cases, endometrium preparation with HRT). Both groups were similar in socio-demographic characteristics. After treatment, the thickness and volume of endometrium in the HRT & GH group were significantly increased ($p < 0.05$), and the growth rate was significantly higher than that in the control group ($p < 0.05$). The proportion of type A & B endometrium increased from 78.9% to 94.7% in the HRT & GH group. Moreover, the proportion of type I and II of endometrial blood perfusion in the HRT & GH group significantly increased compared with that before treatment. The human chorionic gonadotropin (hCG) positive rate (47.4 vs. 42.1%) and clinical pregnancy rate (36.8% vs. 31.6%) were slightly higher in the HRT&GH group than that in the control group. In conclusion, for patients with thin endometrium, HRT combined with subcutaneous injection of GH can increase the thickness and volume of the endometrium, improving the blood perfusion of the endometrium. This may play a positive role in improving endometrial receptivity and pregnancy outcome. *(Afr J Reprod Health 2023; 27 [3]: 32-39).*

Keywords: Growth hormone, endometrial dysplasia, embryo transfer

Résumé

Cette étude a été conçue pour étudier l'effet de l'hormone de croissance (GH) dans la promotion de l'épaisseur de l'endomètre, du flux sanguin et de l'issue de la grossesse chez les patientes présentant un endomètre mince pour le transfert d'embryons congelés. Trente-huit patients ont été recrutés dans le centre de reproduction de l'hôpital de Jingzhou affilié à l'Université du Yangtze qui a annulé le transfert d'embryons frais en raison d'un endomètre mince et prévu de subir un transfert d'embryons congelés-décongelés (FET) de mai 2019 à mai 2020. Les patients ont été répartis au hasard. dans le groupe injection de GH (19 cas, préparation de l'endomètre avec traitement hormonal substitutif (THS) et GH par injection sous-cutanée) et le groupe témoin (19 cas, préparation de l'endomètre avec THS). Les deux groupes présentaient des caractéristiques sociodémographiques similaires. Après le traitement, l'épaisseur et le volume de l'endomètre dans le groupe HRT & GH ont été significativement augmentés ($p < 0,05$), et le taux de croissance était significativement plus élevé que celui du groupe témoin ($p < 0,05$). La proportion d'endomètres de type A et B est passée de 78,9 % à 94,7 % dans le groupe THS et GH. De plus, la proportion de type I et II de perfusion sanguine de l'endomètre dans le groupe HRT & GH a augmenté de manière significative par rapport à celle avant le traitement. Le taux de gonadotrophine chorionique humaine (hCG) positive (47,4 contre 42,1 %) et le taux de grossesse clinique (36,8 % contre 31,6 %) étaient légèrement plus élevés dans le groupe HRT&GH que dans le groupe témoin. En conclusion, pour les patientes présentant un endomètre fin, le THS associé à une injection sous-cutanée de GH peut augmenter l'épaisseur et le volume de l'endomètre, améliorant ainsi la perfusion sanguine de l'endomètre. Cela peut jouer un rôle positif dans l'amélioration de la réceptivité de l'endomètre et de l'issue de la grossesse. *(Afr J Reprod Health 2023; 27 [3]: 32-39).*

Mots-clés: Hormone de croissance, dysplasie endométriale, transfert d'embryon

Introduction

Embryo quality and endometrial receptivity are two key factors for a successful pregnancy in *in vitro* fertilization and embryo transfer (IVF-ET) method[1]. In general, endometrial thickness and morphology are the leading indicators in the clinical evaluation of endometrial receptivity[2]. In clinical work, a considerable number of patients have been cancelled for transplantation because of endometrial

thinness, due to the absence of an effective method for the treatment of endometrial thinness. Hormone therapy, uterine blood perfusion elevation and other methods have been applied to increase endometrial thickness, to improve the endometrial receptivity and clinical pregnancy rate[3,4]. Several reports indicate that the intrauterine infusion of growth hormone (GH) could improve the clinical pregnancy rate of patients with thin endometrium[5,6]. However, only a few reports have documented the effects of the subcutaneous injection of GH on improving endometrial receptivity. This study was designed to investigate the effect of HRT combined with subcutaneous injection of GH on endometrial receptivity and pregnancy outcome in the freeze-thaw embryo transfer (FET) to provide some reference for the clinical treatment of patients with thin endometrium.

Methods

Patients

A total of 38 patients whose fresh embryo transfer plans were cancelled due to thin endometrium and instead underwent FET in the reproductive center of Jingzhou Hospital Affiliated to Yangtze University from May 2019 to May 2020 were recruited. The inclusion criteria were the thickness of endometrium on trigger day less than 7 mm; age < 40 years old; *In vitro* fertilization (IVF) or intracytoplasmic sperm injection & embryo transfer (ICSI-ET) performed due to female fallopian tube factors or male factors, and frozen transplantable embryos; and normal uterine cavity. The exclusion criteria included patients with abnormal liver and kidney functions; co-existing uterine myomata, presence of intrauterine adhesions and other intrauterine malformations, hypothyroidism, hyperthyroidism, and thrombotic diseases.

The study was approved by the medical ethics association of Jingzhou Hospital affiliated to Yangtze University. Informed consent was obtained from all the participants on the basis of full knowledge. All the patients who met the criteria were randomly divided into the combined group (19 cases, endometrium preparation with hormone replacement therapy (HRT) and GH by subcutaneous injection) and the control group (19 cases, endometrium preparation with HRT).

Process

Oral administration of Progynoya

The time axis of the hormone treatment was shown in Figure 1. HRT was used for endometrium preparation in all patients for 14-20 days. A 6 mg Estradiol valerate tablet (Progynoya, Bayer, Germany) was given daily from the third day of menstruation (M3) for eight to ten days. After that, the endometrium thickness was detected using B-scan ultrasonography. If the thickness was less than 8 mm, Progynoya was increased to 8 mg daily for three days. Another B-scan ultrasonography was performed, and if the endometrium thickness was found to be still less than 8 mm, Progynoya was increased to 10 mg per day for three days. After the third B-scan ultrasonography, Progynoya was maintained at a maximum dose of 10 mg per day until the day of hormone replacement luteal transformation.

The luteal transformation was performed when the endometrium thickness was ≥ 8 mm, and there was no increase in endometrium thickness for 3-5 days. The luteal transformation can also be performed if the endometrium thickness was still less than 8 mm after 20 days of Progynoya treatment. Two high-quality cleavage stage embryos of grade I ~ II were transplanted on the fourth day of luteal transformation, or one blastocyst with a quality level at 4bc or above was transplanted on the 6th day of luteal transformation.

During the luteal transformation, and till to 42 days after embryo transfer (E42), the dosages of Progynoya were maintained before luteal transformation. After that, the oral dosages were reduced by 2mg/d every 3 days.

Oral administration of asprin

Aspirin enteric coated tablets (100 mg per day) (Bayer, Germany) were oral administrated from the third day of menstruation (M3) to 14 days after the embryo transfer (E14).

Subcutaneous injection of GH and progesterone

On the first day of HRT (M3), 4 IU GH (Polyethylene Glycol Recombinant Human Somatropin Injection, Changchun GeneScience

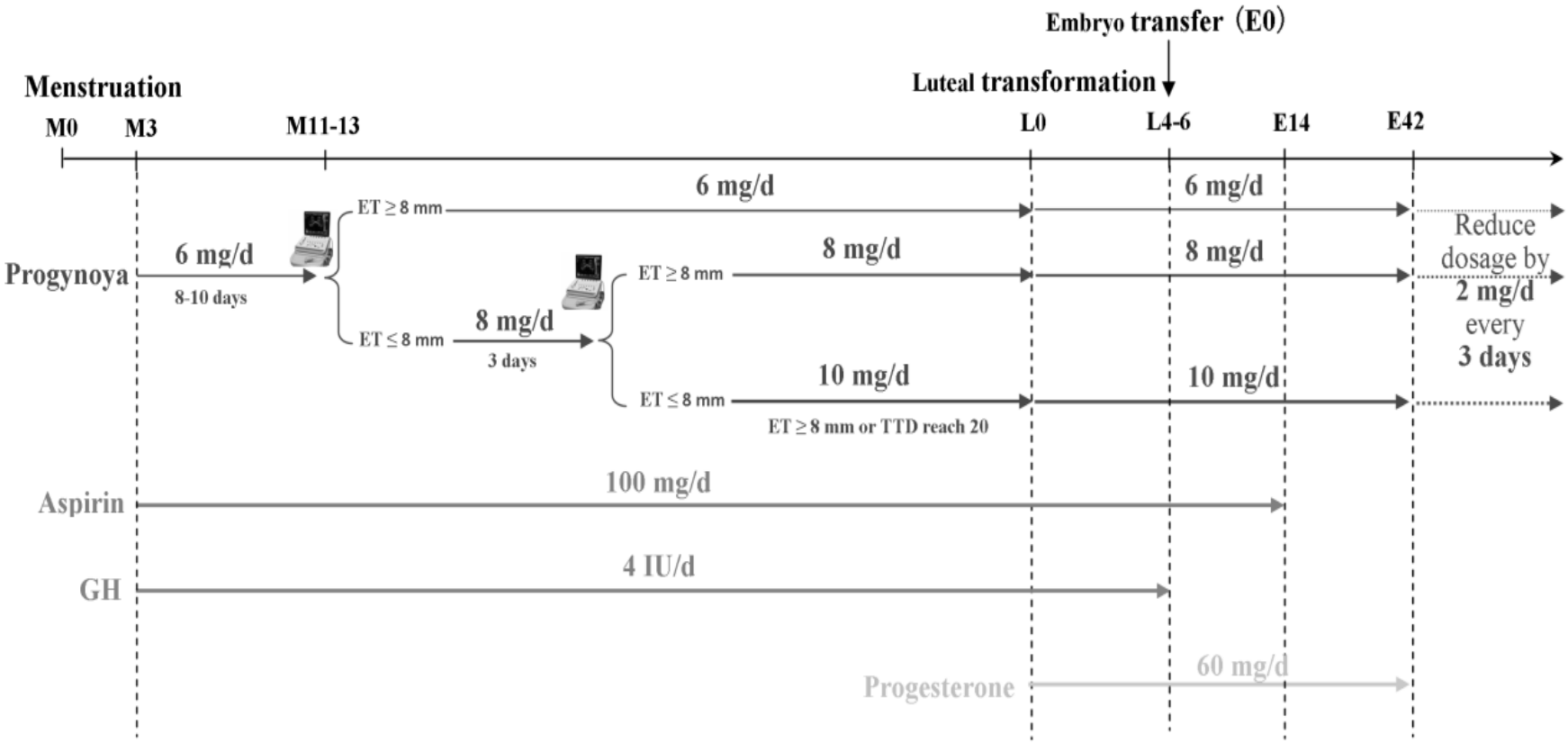

Figure 1: Hormone treatment for the patients. M0, menstruation day 0; L0, luteal transformation day 0; E0, embryo transfer day 0. TTD, total Progynoya treated days

Pharmaceuticals Co., Ltd.), dissolved with 1 mL sterilized water was injected subcutaneously in the abdomen until the day of transplantation (L0). Progesterone from Guangzhou baiyunshan Ming xing pharmaceutical (Guangzhou, China) was given by intramuscular injection at the day of luteal transformation (60 mg per day), and lasted until 42 days after embryo transfer (E42).

Measurement of endometrial thickness and subendometrial blood flow

Endometrial thickness and subendometrial blood flow were measured in both the groups during previous ovulation and on the day of luteal transformation (L0). The median long axis section of the uterus was determined to detect the endometrial thickness (the maximum distance between the interface of the anterior and posterior myometrium and the endometrium perpendicular to the midline of the uterine cavity) and subendometrial blood perfusion. In the shell volume mode, select the thickness of the subintimal region of 1 mm, and obtain the blood flow parameters of the shell volume. According to the blood perfusion of endometrial and subendometrial, it can be divided into type I (blood flow signal seen in the endometrial area and close to the midline of uterine cavity), type II (blood flow signal seen in the endometrial area but ≤ 1/2 single layer of endometrial), and type III (blood flow signal seen in sub-endometrial area). The endometrial flow resistance index (RI), pulsatility index (PI) and the ratio of systolic to diastolic velocity (S/D) were measured.

Follow up

The blood β-hCG was determined 12 days after embryo transfer (E12). Clinical pregnancy (including ectopic pregnancy) was detected as a gestational sac by transvaginal B-scan ultrasonography 4-weeks after embryo transfer (E28). Early abortion is defined as the abortion that occurs during 12 weeks of pregnancy.

Parameters

The general information was collected from the two groups of patients. Endometrial thickness/morphological data and subendometrial blood flow data before and after treatment, as well as pregnancy outcome of FET after treatment (embryo implantation rate, clinical pregnancy rate, and early abortion rate), were recorded.

Statistical analysis

All data were analyzed using SPSS 18.0. t-test was used for comparison of measurement data and χ^2 for comparison of counting data inspection. $p < 0.05$ was set as statistically significant.

Results

General information

A total of 38 patients with a thin endometrium (< 7 mm) were included in this study, of which 19 were assigned to the HRT & GH group and 19 in the control group. GH was injected subcutaneously 16-26 times, with an average of 21 ± 4.7 times. A total of 55 embryos were transplanted, including 28 in the HRT & GH group and 27 in the control group.

As shown in Table 1, there were no significant differences between the two groups with respect to age, infertility duration, physiological FSH (β-FSH), anti-Mullerian hormone (AMH), body mass index (BMI), days of estrogen use (referring to the days of estrogen use during endometrial progesterone transformation), the average number of embryos transferred, and proportion of embryos transferred at different stages ($p > 0.05$) .

Endometrial condition

Before treatment, the endometrial thickness of the HRT & GH group was significantly less than that of the control group ($p < 0.05$), but there was no significant difference in the endometrial volume or its classification ($p > 0.05$) (Table 2). After treatment, the thickness and volume of endometrium in the HRT & GH group were significantly increased ($p < 0.05$). Moreover, the growth rate of endometrial thickness and volume was also significantly higher than that in the control group ($p < 0.05$) (Table 2). The proportion of type A & B endometrium in the HRT & GH group (94.7%) was increased compared to that before the treatment (78.9%), but no significant difference ($P > 0.05$) was found (Table 2).

Before the treatment, the endometrial blood flow parameter S/D in the HRT & GH group was

Table 1: General information of the enrolled patients

	HRT & GH	HRT	*P* Value
Numbers	19	19	/
Age	30.632 ± 2.432	30.263 ± 3.280	0.686
Infertile Duration (Years)	4.316 ± 1.493	4.368 ± 1.739	0.930
β-FSH (U/L)	6.374 ± 1.763	6.268 ± 1.372	0.837
AMH (ng/ml)	5.068 ± 2.161	4.947 ± 2.626	0.891
BMI	21.158 ± 1.714	21.389 ± 1.650	0.695
Days of estrogen use	15.947 ± 1.810	15.947 ± 2.223	1.000
Number of D5 embryos transferred	1.474 ± 0.513	1.421 ± 0.507	0.331
Cleavage Stage	47.4% (9/19)	42.1% (8/19)	/
Blastocysts	52.6% (10/19)	57.9% (11/19)	/

GH, growth hormone; HRT, hormone replacement treatment; FSH, follicle stimulating hormone; AMH, Anti-Mullerian hormone; BMI, body mass index; Data were expressed as mean ± standard deviation.

Table 2: Comparison of endometrium between the two groups before and after treatment

	GH & HRT (19)		HRT (19)	
	Control	Treatment	Control	Treatment
Endometrial thickness (mm)	5.547 ± 0.598^{A}	7.021 ± 0.898^{B}	5.811 ± 0.704^{A}	6.111 ± 0.916^{A}
Endometrial Volume (mL)	1.242 ± 0.440^{Aa}	2.095 ± 0.424^{B}	1.389 ± 0.458^{A}	1.426 ± 0.456^{Ab}
Type A	47.4% (9/19)	68.4% (13/19)	47.4% (9/19)	57.9% (11/19)
Type B	21.1% (4/19)	21.1% (4/19)	21.1% (4/19)	15.8% (3/19)
Type C	31.5% (6/19)	10.5% (2/19)	31.5% (6/19)	26.3% (5/19)

Data were expressed as mean ± standard deviation. $^{A, B}$, $p < 0.01$; $^{a, b}$, $p < 0.05$.

Table 3: Blood flow parameters

	GH & HRT (19)		HRT (19)	
	Control	Treatment	Control	Treatment
PI	1.100 ± 0.213	1.068 ± 0.250	1.111 ± 0.141	1.079 ± 0.227
RI	0.663 ± 0.116	0.611 ± 0.094	0.642 ± 0.107	0.632 ± 0.095
S/D	2.726 ± 0.292^{A}	2.416 ± 0.281^{B}	2.568 ± 0.267^{A}	2.389 ± 0.313^{AB}
II	5.3% (1/19)	21.1% (4/19)	10.5% (2/19)	10.5% (2/19)
III	94.7% (18/19)	78.9% (15/19)	89.5% (17/19)	89.5% (17/19)

PI, pulsatility index; RI, resistance index; S/D, ratio of systolic to diastolic flow rate. Data were expressed as mean ± standard deviation. $^{A, B}$, $P < 0.01$

Table 4: Assisted pregnancy outcomes of the patients enrolled

		GH & HRT (19)	HRT (19)
Cleavage Stage	HCG Positive Rate	44.4% (4/9)	37.5% (3/8)
	Clinical Pregnancy Rate	22.2% (2/9)	37.5% (3/8)
	Embryo Implantation Rate	16.7% (3/18)	25% (4/16)
	Early Abortion Rate	0% (0/9)	12.5% (1/8)
Blastocysts	HCG Positive Rate	50.0% (5/10)	45.5% (5/11)
	Clinical Pregnancy Rate	40% (4/10)	45.5% (5/11)
	Embryo Implantation Rate	40% (4/10)	45.5% (5/11)
	Early Abortion Rate	10% (1/10)	0% (0/11)

Note: 2 embryos were transferred in the cleavage stage, and single embryo transfer was performed in the blastocysts stage.

significantly higher than in the control group ($p < 0.05$) (Table 3). However, there was no significant difference in the other parameters ($p > 0.05$). After treatment, the proportion of type I and II endometrial blood perfusion in the HRT & GH group was significantly increased compared to that before the treatment ($p < 0.05$). However, there was no significant difference from the control group

after the treatment ($p > 0.05$). We also observed that there was no significant difference in other parameters before and after the treatment within the group or between groups after treatment ($p > 0.05$) (Table 3).

Assisted pregnancy outcomes

Day 5 blastocyst transfer was performed in both groups. There was no significant difference in the hCG positive rate, clinical pregnancy rate, embryo implantation rate of blastocyst transfer, and total embryo transfer between the two groups ($p > 0.05$) (Table 4). The hCG positive rate (47.4 vs. 42.1%) and clinical pregnancy rate (36.8% vs. 31.6%) of the combined group was slightly higher than that in the control group (Table 4).

Discussion

Endometrial receptivity is a complex process that provides the embryo an opportunity to attach, invade, and develop, culminating in a new individual and continuation of the species[7]. It is closely related to the thickness, morphology, and blood flow state of the endometrium[8]. At present, transvaginal Doppler ultrasound has been widely used in assisted reproductive technology (ART) to observe the endometrial state of patients. However, there are very few studies on the relationship between endometrial blood flow parameters and endometrial receptivity, in addition to endometrial thickness and morphology, with no unified standard.

The pathogenesis of thin endometrium remains unclear. Thinness may be due to endometrial injuries, such as mechanical injury caused by various uterine cavity operations[9], or congenital dysplasia. When the endometrial basal layer is severely damaged, the number of endometrial stem cells is reduced, the cell function becomes abnormal, endometrial regeneration ability is seriously reduced, and the responsiveness to estrogen stimulation is reduced or not responsive. This leads to thin endometrium, thus providing no support for embryo implantation. Though pregnancies have been reported at 4 and 5 mm, it is apparent that an endometrial thickness < 6 mm is associated with a trend towards lower probability of pregnancy[10]. Currently, there are no reasonable and effective methods available for treating thin endometrium. The well-accepted treatment with thin endometrium included (1) hormone approach, such as estradiol administration adjustment[11,12], human chorionic gonadotropin priming in the follicular phase[13,14], or GnRH agonist during luteal phase[15]; (2) vascular approach, using sildenafil citrate[16], aspirin[17], pentoxifylline-tocopherol[18], or electrostimulation[19]; (3) growth factor approach, like granulocyte colony-stimulating factor[20,21] or platelet-rich plasma[22,23]. Therefore, treatment of thin endometrium remains challenging for clinicians, as lack of solid evidence impedes support of one therapeutic option versus the other. Only some patients are found to benefit from these treatments.

GH is secreted by the anterior pituitary, which participates in cell growth and metabolism. GH regulates the secretion of insulin-like growth factor (IGFs) in the endometrium by binding with GH receptor to promote endometrial thickening, vascular enrichment, and gland growth. At the same time, GH also promotes the expression of multiple inflammatory cytokines in the endometrium, coordinates the balance of multiple cytokines, and improves endometrial receptivity, thus increasing the pregnancy rate. In this study, GH was injected subcutaneously in combination with artificial cycles patients with thin endometrium, and perform FET assisted pregnancy therapy was performed. The results showed that the endometrial thickness and endometrial volume were significantly increased in the HRT & GH group after treatment, and the growth rate was significantly higher than that in the control group. The proportion of type A+B endometrium in the HRT & GH group was significantly higher than before the treatment (94.7% vs. 78.9%).

Among the cases included in this study, the endometrium of the control group before treatment was slightly thicker than that of the HRT & GH group. The results showed that the patients in the HRT & GH group with worse basic conditions showed similar embryo implantation rate (25.0% vs. 25.9%), clinical pregnancy rate (36.8% vs. 31.6%), and blastocyst transfer pregnancy rate (42.9% vs. 37.5%) compared with the control group after treatment.

The effect of GH on thin endometrium was verified in a rat model, which demonstrated that GH could promote regeneration and repair of thin endometrium[6]. Few studies indicated that co-treatment with GH would improve the endometrial thickness and possibly receptivity among infertile

women[5]. This effect might be obtained by increasing endometrial blood perfusion and the expression of genes and proteins related to endometrial receptivity, such as vascular endothelial growth factor (VEGF) and integrin beta 3 (ITGB3) together with insulin-like growth factor 1 (IGF-1), however the exact mechanisms in the endometrium remain to be clarified.

In this study, endometrial blood flow parameters were measured at least twice in all patients, including PI, RI, S/D, and endometrial blood perfusion typing. Uterine histology confirmed that the blood vessels of the innermost myometrium were more abundant than those on the outer myometrium. The blood flow perfusion of the endometrium and subendometrium directly reflects the microcirculation of the embryo implantation site and play an important role in endometrial receptivity[24]. In this study, the S/D of endometrial blood flow parameters in the HRT & GH group was significantly different from that in the control group before treatment. The difference disappeared after treatment, with an increase in the types I and II of endometrial blood flow perfusion. These results suggested that the intrauterine perfusion GH in thin endometrial patients not only improved the endometrial thickness and morphology, but also improved its receptivity. However, there was no significant difference in the endometrial blood flow parameters PI, RI, and S/D before and after treatment in the HRT & GH group. It was considered that the endometrium might be seriously damaged in patients with thin endometrium, including the endometrial cells and blood vessels, and the regeneration and repair might be very difficult or minimal. However, as long as the best condition can be achieved, embryo implantation can also be realized. The number of samples included in the study was limited, and thus the results can only serve as a reference.

In conclusion, intrauterine perfusion of GH to the endometrium promoted endometrial development, increased endometrial thickness and blood flow, improved the endometrial microenvironment, and reduced endometrial blood flow resistance, thereby improving the endometrial receptivity. Thus, it can be concluded that the intrauterine infusion of GH could be one of the treatment options for patients with thin endometrium for improving the pregnancy rate and clinical outcome. However, due to the small experimental design and sample size, the results of this study have certain limitations, which warrants further confirmed by the randomized controlled trials.

Contributions of authors

#These authors contributed equally to this article. Conceptualization, Yong Wu and Chihua He; Methodology, Lili Zhang and Li Zeng; Data analysis, Ying Wang and Ruifeng Shao; Supervision, Chihua He; Writing-Original Draft Preparation, Yong Wu and Yuan Tian; Writing-Review and Editing, Chihua He, Funding Acquisition, Yong Wu.

Acknowledgements

This study was supported by grants from Jingzhou Medical Health Science and Technology Planning Project (Grant no. 2022HC69).

References

1. Paulson RJ, Sauer MV and Lobo RA. Embryo implantation after human in vitro fertilization: importance of endometrial receptivity. Fertil Steril. 1990;53(5): 870-4.
2. Opolskiene G, Sladkevicius P and Valentin L. Ultrasound assessment of endometrial morphology and vascularity to predict endometrial malignancy in women with postmenopausal bleeding and sonographic endometrial thickness >or= 4.5 mm. Ultrasound Obstet Gynecol. 2007;30(3):332-40.
3. Chang K and Lubo Z. Review article: steroid hormones and uterine vascular adaptation to pregnancy. Reprod Sci. 2008;15(4):336-48.
4. Kara AS, Guzel AI and Onderoglu L. Evaluation of uterine perfusion in postmenopausal women receiving hormone replacement therapy. Clin Exp Obstet Gynecol. 2014;41(5):521-4.
5. Altmae S and Aghajanova L. Growth Hormone and Endometrial Receptivity. Front Endocrinol (Lausanne). 2019;10:653.
6. Li W, Cao Z, Yu X and Hu W. Effect of growth hormone on thin endometrium via intrauterine infusion. Ann Transl Med. 2021;9(16):1325.
7. Lessey BA and Young SL. What exactly is endometrial receptivity? Fertil Steril. 2019;111(4):611-7.
8. Zaidi J, Campbell S, Pittrof R and Tan SL. Endometrial thickness, morphology, vascular penetration and velocimetry in predicting implantation in an in vitro fertilization program. Ultrasound Obstet Gynecol. 1995;6(3):191-8.
9. Shufaro Y, Simon A, Laufer N and Fatum M. Thin unresponsive endometrium--a possible complication of surgical curettage compromising ART outcome. J Assist Reprod Genet. 2008;25(8):421-5.

10. Mahajan N and Sharma S. The endometrium in assisted reproductive technology: How thin is thin? J Hum Reprod Sci. 2016;9(1):3-8.
11. Chen MJ, Yang JH, Peng FH, Chen SU, Ho HN and Yang YS. Extended estrogen administration for women with thin endometrium in frozen-thawed in-vitro fertilization programs. J Assist Reprod Genet. 2006;23(7-8):337-42.
12. Liao X, Li Z, Dong X and Zhang H. Comparison between oral and vaginal estrogen usage in inadequate endometrial patients for frozen-thawed blastocysts transfer. Int J Clin Exp Pathol. 2014;7(10):6992-7.
13. Davar R, Miraj S and Farid Mojtahedi M. Effect of adding human chorionic gonadotropin to frozen thawed embryo transfer cycles with history of thin endometrium. Int J Reprod Biomed. 2016;14(1):53-6.
14. Papanikolaou EG, Kyrou D, Zervakakou G, Paggou E and Humaidan P. "Follicular HCG endometrium priming for IVF patients experiencing resisting thin endometrium. A proof of concept study". J Assist Reprod Genet. 2013;30(10):1341-5.
15. Qublan H, Amarin Z, Al-Qudah M, Diab F, Nawasreh M, Malkawi S and Balawneh M. Luteal phase support with GnRH-a improves implantation and pregnancy rates in IVF cycles with endometrium of <or=7 mm on day of egg retrieval. Hum Fertil (Camb). 2008;11(1):43-7.
16. Dehghani Firouzabadi R, Davar R, Hojjat F and Mahdavi M. Effect of sildenafil citrate on endometrial preparation and outcome of frozen-thawed embryo transfer cycles: a randomized clinical trial. Iran J Reprod Med. 2013;11(2):151-8.
17. Weckstein LN, Jacobson A, Galen D, Hampton K and Hammel J. Low-dose aspirin for oocyte donation recipients with a thin endometrium: prospective, randomized study. Fertil Steril. 1997;68(5):927-30.
18. Acharya S, Yasmin E, and Balen AH. The use of a combination of pentoxifylline and tocopherol in women with a thin endometrium undergoing assisted conception therapies--a report of 20 cases. Hum Fertil (Camb). 2009;12(4):198-203.
19. Bodombossou-Djobo MM, Zheng C, Chen S and Yang D. Neuromuscular electrical stimulation and biofeedback therapy may improve endometrial growth for patients with thin endometrium during frozen-thawed embryo transfer: a preliminary report. Reprod Biol Endocrinol. 2011;9:122.
20. Kunicki M, Lukaszuk K, Liss J, Skowronska P and Szczyptanska J. Granulocyte colony stimulating factor treatment of resistant thin endometrium in women with frozen-thawed blastocyst transfer. Syst Biol Reprod Med. 2017;63(1):49-57.
21. Sarvi F, Arabahmadi M, Alleyassin A, Aghahosseini M and Ghasemi M. Effect of Increased Endometrial Thickness and Implantation Rate by Granulocyte Colony-Stimulating Factor on Unresponsive Thin Endometrium in Fresh In Vitro Fertilization Cycles: A Randomized Clinical Trial. Obstet Gynecol Int. 2017;2017:3596079.
22. Zadehmodarres S, Salehpour S, Saharkhiz N and Nazari L. Treatment of thin endometrium with autologous platelet-rich plasma: a pilot study. JBRA Assist Reprod. 2017;21(1):54-6.
23. Kim H, Shin JE, Koo HS, Kwon H, Choi DH and Kim JH. Effect of Autologous Platelet-Rich Plasma Treatment on Refractory Thin Endometrium During the Frozen Embryo Transfer Cycle: A Pilot Study. Front Endocrinol (Lausanne). 2019;10:61.
24. Uysal S, Ozbay EP, Ekinci T, Aksut H, Karasu S, Isik AZ and Soylu F. Endometrial spiral artery Doppler parameters in unexplained infertility patients: is endometrial perfusion an important factor in the etiopathogenesis? J Turk Ger Gynecol Assoc. 2012;13(3):169-71.