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The application of progesterone-primed ovarian stimulation protocol in patients with ovarian endometriosis combined with diminished ovarian reserve

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Abstract

Purpose The aim was to investigate the value of the application of a progesterone-primed ovarian stimulation (PPOS) protocol in patients with ovarian endometriosis (OEM) combined with diminished ovarian reserve (DOR).

Materials and methods A retrospective analysis of 95 patients with OEM combined with a DOR who underwent in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) was conducted between March 2020 and February 2024 at the Reproductive Center of Xuzhou Central Hospital. Patients were divided into two groups on the basis of the ovarian stimulation protocol used: the PPOS group ($n=60$, 60 cycles) and the GnRH agonist downregulation group ($n=35$, 35 cycles). General data, ovarian stimulation outcomes, and pregnancy outcomes were compared between the two groups.

Results There were no statistically significant differences between the two groups in terms of general data ($P>0.05$). Compared with the PPOS group, the GnRH agonist group presented significantly more Gn days and higher Gn dosages ($P<0.05$). However, there were no significant differences between the groups in terms of the number of oocytes retrieved, metaphase II oocyte rate, fertilization rate, cleavage rate, high-quality embryo rate, or cycle cancellation rate ($P>0.05$). Additionally, no significant differences were observed in the embryo transfer parameters, endometrial thickness, embryo implantation rate, clinical pregnancy rate, ectopic pregnancy rate, or early miscarriage rate ($P>0.05$).

Conclusions In patients with OEM combined with DOR, the PPOS protocol had pregnancy outcomes comparable to those of the downregulation protocol, with the added advantage of being more cost-effective.

Keywords Progesterone-primed ovarian stimulation protocol, Ovarian endometriosis, Diminished ovarian reserve, Downregulation protocol, Infertility, In vitro fertilization

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Introduction

Endometriosis (EM) is a chronic, inflammatory, and immune-related disorder that affects approximately 10–20% of women of reproductive age, with up to 50% of EM patients experiencing infertility. The disease is characterized by the presence of active endometrial-like tissue outside the uterine cavity, leading to symptoms such as dysmenorrhea, chronic pelvic pain, infertility, and organ dysfunction [1]. Ovarian endometriosis (OEM) is the most prevalent form of endometriosis, and a significant proportion of affected individuals require assisted reproductive technology to achieve pregnancy. According to current guidelines, preoperative treatment with GnRH analogues for 3–6 months is recommended to increase clinical pregnancy rates among patients with endometriosis [2–3]. However, in patients with OEM combined with diminished ovarian reserve (DOR), gonadotropin-releasing hormone agonist (GnRHa) downregulation may result in excessive suppression of the pituitary gland, leading to reduced ovarian responsiveness and an increased rate of cycle cancelation. Progesterone-primed ovarian stimulation (PPOS), a relatively new stimulation protocol, has shown potential advantages for these patients. Progesterone reportedly alleviates the symptoms of endometriosis, improves the ovarian response, and effectively suppresses premature LH surges, thus preventing early ovulation [4]. On the basis of these considerations, the PPOS protocol may be a more suitable option for ovarian stimulation in patients with OEM combined with DOR. This study aimed to assess the effect of the PPOS protocol compared with that of the GnRHa downregulation protocol on pregnancy outcomes in this specific patient population.

Materials and methods

Materials

From March 2020 to February 2024, 95 patients with OEM combined with DOR who underwent IVF/ICSI-ET at the Reproductive Center of Xuzhou Central Hospital were included in this retrospective study. The study was approved by the Ethics Committee of Xuzhou Central Hospital, and informed consent was obtained from all patients. The inclusion criteria were as follows [5]: (1) aged between 25 and 41 years; (2) a previous diagnosis of ovarian endometrioma confirmed through laparoscopic or open surgery, followed by ovarian cystectomy for endometriosis; (3) diminished ovarian reserve (DOR) diagnosed on the basis of the following criteria, with at least two of the following parameters being met: ① a follicle-stimulating hormone (FSH) level between 10 and 25 IU/L; ② an antral follicle count (AFC) of 5–7; and ③ an anti-Müllerian hormone (AMH) level between 0.5 and 1.1 ng/ml. The exclusion criteria were as follows: (1) uterine abnormalities (such as uterine malformations, adenomyosis, or fibroids), endometrial disorders (including endometritis, endometrial polyps, or intrauterine adhesions), or hydrosalpinx, which may interfere with embryo implantation; (2) comorbid thyroid disorders, diabetes, hyperprolactinemia, polycystic ovary syndrome, or other endocrine or metabolic disorders; (3) chromosomal abnormalities in either partner; (4) a history of severe organ dysfunction, malignancy, or thrombosis; and (5) intaking any concomitant treatment during the study period.

Methods

Down-regulation protocol

On Days 1 to 3 of the menstrual cycle, 3.75 mg of triptorelin acetate (Daptan, Ferring Pharmaceuticals, Switzerland) was administered as a GnRHa in one to three injections for downregulation, with subsequent administrations repeated every 28 days. Following the final dose on Day 28, a vaginal ultrasound was conducted to assess the number and size of the antral follicles, and the serum levels of FSH, luteinizing hormone (LH), and oestradiol (E2) were measured. Downregulation was considered complete when the follicular diameter was ≤ 10 mm, the serum FSH level was < 5 mIU/mL, the LH level was < 5 mIU/mL, and the E2 level was < 50 pg/mL. Recombinant FSH (r-FSH, Gonal-F, Merck Serono, Germany) was then administered at a dose of 150–225 IU, either alone or in combination with human menopausal gonadotropin (HMG, Lizhu Pharmaceutical Company), for ovarian stimulation. The dosage was adjusted on the basis of the ovarian response. After ultrasound confirmation of the presence of follicles ≥ 18 mm (for one follicle) or ≥ 17 mm (for two follicles) in diameter, 0.25 mg of recombinant human LH (rLH, Aizer, Merck Serono, Switzerland) was administered subcutaneously to trigger ovulation. Oocyte retrieval was performed 36–37 h later under ultrasound guidance.

PPOS protocol

On Days 2 to 4 of the menstrual cycle, oral medroxyprogesterone acetate (MPA; Hubei Fangtong Pharmaceutical Co., Ltd.) was administered at a dosage of 8 mg/day until the trigger day. Intramuscular injections of human menopausal gonadotropin (HMG) were given at a dose of 150–225 IU on the basis of the patient's follicular growth and hormone levels for ovarian stimulation. When ultrasound confirmed that the dominant follicle reached a diameter of ≥ 18 mm (for 1 follicle) or ≥ 17 mm (for 2 follicles), 0.25 mg of recombinant human luteinizing hormone (rLH, Merck Serono) was subcutaneously injected to trigger ovulation. Oocyte retrieval was performed 36–37 h later under vaginal ultrasound guidance.

IVF/ICSI-ET and luteal phase support

On the day of oocyte retrieval, semen from the male partner was obtained via masturbation. On the basis of semen analysis, fertilization was performed using either conventional in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). Fertilization status was assessed on Day 2, and the presence of two pronuclei (2PN) confirmed normal fertilization. After 48 h of embryo culture, cleavage was observed. Embryo and blastocyst grading were conducted using the Istanbul Consensus [6] and Gardner blastocyst grading system [7].

For the downregulation protocol group, luteal phase support was initiated postprocedure with an intramuscular progesterone injection (60 mg/day) and oral oestradiol valerate and dydrogesterone tablets (Fentam, Abbott Laboratories, containing 2 mg of oestradiol and 10 mg of dydrogesterone, 2 tablets per day). Luteal support was continued for 3–5 days, after which fresh embryo transfer was performed on the basis of the patient's physical condition, endometrial thickness, hormone levels, and embryo quality. In cases of fresh embryo transfer, 1–2 embryos were transferred under ultrasound guidance, and luteal support was continued. If fresh transfer was not performed, the embryos were cryopreserved, and frozen-thawed embryo transfer was scheduled.

For the PPOS protocol group, embryos were cryopreserved after formation, and frozen-thawed embryo transfer was performed at a later date as part of the scheduled procedure.

Frozen embryo transfer

A downregulation and hormone replacement therapy cycle protocol was employed for endometrial preparation. On Days 1–2 of the menstrual cycle, a single dose of 3.75 mg triptorelin (Daptan) was administered for downregulation, with additional injections given as needed (1–3 doses). After the final dose of triptorelin, the administration of oestradiol valerate (1 mg per tablet, twice daily) and dydrogesterone (10 mg per tablet, twice daily) was initiated on Day 28 and continued for 7 days. The dosage was adjusted on the basis of the endometrial thickness. When the endometrial thickness reached ≥ 8 mm, 60 mg/day of intramuscular progesterone was administered, along with oral dydrogesterone tablets (1 tablet, twice daily), for 3–5 days to promote endometrial transformation. Luteal phase support was maintained following embryo transfer.

Pregnancy follow-up

Serum β-HCG levels were quantitatively measured 14 days postembryo transfer to determine pregnancy status. A β-HCG level ≤ 5 mIU/ml was considered indicative of implantation failure, whereas a level > 5 mIU/ml was considered to indicate a biochemical pregnancy. Clinical pregnancy was confirmed between 28 and 35 days posttransfer through transvaginal ultrasound, with the presence of a gestational sac and embryonic heartbeats indicating a clinical pregnancy.

Observational indicators

General data

The following patient characteristics were collected for both groups: age, duration of infertility, BMI, antral follicle count (AFC), and baseline hormone (FSH, LH, and E2) levels, as well as anti-Müllerian hormone (AMH) levels.

The number of oocytes retrieved was defined as the total number of oocytes obtained. The number of metaphase II (MII) oocytes referred to the number of mature oocytes, defined as those at metaphase II of meiosis that had extruded the first polar body. The number of usable embryos was the total number of embryos available for transfer (both fresh and frozen). The number of Day 3 (D3) high-quality embryos was recorded as the number of high-quality embryos on the third day after fertilization. The MII oocyte rate was calculated as the ratio of MII oocytes to the total number of oocytes retrieved. The fertilization rate was calculated as the ratio of fertilized oocytes to the total number of oocytes retrieved and expressed as a percentage. The cleavage rate was the ratio of normally fertilized embryos that underwent cleavage to the total number of normally fertilized oocytes, expressed as a percentage. The D3 high-quality embryo rate was the ratio of D3 high-quality embryos to the total number of normally fertilized embryos (2PN) that had undergone cleavage, expressed as a percentage. The cycle cancellation rate was calculated as the number of cycles with no usable embryos divided by the total number of oocyte retrieval cycles, expressed as a percentage. The embryo implantation rate was the ratio of the number of embryos that were implanted to the total number of embryos transferred, expressed as a percentage. The clinical pregnancy rate was calculated as the ratio of clinical pregnancies to the total number of embryo transfer cycles, expressed as a percentage. The early miscarriage rate was calculated as the ratio of early miscarriages to the total number of clinical pregnancy cycles, expressed as a percentage. The ectopic pregnancy rate was calculated as the ratio of ectopic pregnancies to the total number of clinical pregnancy cycles, expressed as a percentage.

Clinical and laboratory indicators

These indicators included the number of days of gonadotropin (Gn) use, total gonadotropin dosage, number of oocytes retrieved, MII oocyte rate, fertilization rate, cleavage rate, D3 high-quality embryo

Table 1 Comparison of the general data between the two groups

	Down-Regulation Group	PPOS Group	*p*
Number of Cycles	35	60	
Age, years	34.14 ± 4.02	35.58 ± 4.42	0.117
AFC	5.83 ± 1.10	5.80 ± 1.22	0.909
Duration of Infertility, years	4.03 ± 2.74	3.33 ± 2.02	0.160
BMI (kg/m^2)	22.74 ± 2.69	23.02 ± 2.78	0.629
AMH (ng/ml)	0.93 ± 0.25	0.85 ± 0.23	0.096
Baseline Hormones			
FSH (mIU/ml)	9.22 ± 3.11	10.51 ± 3.29	0.062
LH (mIU/ml)	3.96 ± 1.51	3.88 ± 1.72	0.685
E2 (pg/ml)	49.30 ± 28.45	44.17 ± 24.99	0.361

Note: PPOS, Progesterone Priming Ovarian Stimulation; BMI, Body Mass Index; AMH, Anti-Müllerian Hormone; AFC, Antral Follicle Count; FSH, Follicle-Stimulating Hormone; LH, Luteinizing Hormone; E2, Estradiol

Table 2 Comparison of ovarian stimulation and laboratory indexes between the two groups

	Down-Regulation Group	PPOS Group	*p*
Number of Cycles	35	60	
Gn Duration (Days)	10.74 ± 2.15	8.28 ± 1.39	<0.001
Gn Dose (U)	2898 ± 798.8	1880 ± 471.0	<0.001
Number of Oocytes	4.00 ± 1.53	3.52 ± 1.50	0.137
MII Oocyte Rate (%)	86.43(121/140)	86.26(182/211)	0.963
Fertilization Rate (%)			
IVF Fertilization Rate (%)	84.74(100/118)	84.38(162/192)	0.930
ICSI Fertilization Rate (%)	81.82(16/22)	84.21(16/19)	0.376
Cleavage Rate (%)	86.21(100/116)	85.96(153/178)	0.951
Day 3 Quality Embryo Rate (%)	63.00(63/100)	61.44(94/153)	0.802
Cycle Cancellation Rate (%)	2.86(1/35)	3.33(2/60)	0.898

Note: PPOS, Progesterone Priming Ovarian Stimulation; Gn, Gonadotropin; MII, Metaphase II; IVF, In Vitro Fertilization; ICSI, Intracytoplasmic Sperm Injection

rate, cycle cancellation rate, endometrial thickness, and number of embryos transferred.

Clinical outcomes

The clinical outcomes included the embryo implantation rate, clinical pregnancy rate, early miscarriage rate, and ectopic pregnancy rate.

Statistical analysis

Statistical analysis was performed using SPSS 19.0 software. Continuous data were analysed using the t test and are presented as the means ± standard deviations. Categorical data were analysed using the χ^2 test and are expressed as percentages (frequency/total number) [% (n/N)]. A P value < 0.05 was considered to indicate statistical significance.

Table 3 Comparison of first embryo transfer and pregnancy outcomes between the two groups

	Down-Regulation Group	PPOS Group	*p*
Number of Cycles	34	58	
Number of Embryos Transferred	1.74 ± 0.45	1.67 ± 0.47	0.532
Endometrial Thickness (mm)	8.97 ± 1.47	8.93 ± 1.50	0.902
Embryo Implantation Rate (%)	23.73(14/59)	26.80(26/97)	0.670
Clinical Pregnancy Rate (%)	38.24(13/34)	37.93(22/58)	0.977
Ectopic Pregnancy Rate (%)	0(0/13)	4.55(1/22)	0.435
Early Miscarriage Rate (%)	15.38(2/13)	13.64(3/22)	0.886

Note: PPOS, Progesterone Priming Ovarian Stimulation

Results

Comparison of the general data

There were no significant differences in age, the duration of infertility, BMI, the AFC, the AMH level, or baseline hormone levels (FSH, LH, and E2) ($P > 0.05$) between the two groups (Table 1).

Comparison of ovarian stimulation and laboratory outcomes

Compared with the downregulation group, the PPOS group had a significantly shorter duration of Gn treatment and a significantly lower total Gn dose ($P < 0.05$). However, there were no significant differences in oocyte retrieval, the MII oocyte rate, the fertilization rate, the cleavage rate, blastocyst quality on Day 3, or the cycle cancellation rate ($P > 0.05$) between the two groups (Table 2).

Embryo transfer and pregnancy outcomes

A total of 58 patients in the PPOS group underwent embryo transfer (all frozen embryo transfer), whereas 34 patients in the downregulation group underwent embryo transfer. There were no significant differences in the number of embryos transferred, endometrial thickness, implantation rate, clinical pregnancy rate, ectopic pregnancy rate, or early miscarriage rate ($P > 0.05$) between the two groups (Table 3).

Discussion

EM is a benign disease that exhibits biological characteristics similar to those of malignant tumours, including invasiveness and metastasis. The ovaries are the most commonly affected organs in women with endometriosis, with OEM occurring in approximately 17–44% of EM patients. Active endometrial tissue is ectopically located on the ovarian cortex, where it undergoes cyclic bleeding, rupture, encapsulation, adhesion, and fibrosis in response to menstrual cycle changes. This process ultimately leads to the formation and progression of ovarian endometriotic cysts [8]. The cysts exert a space-occupying effect on the surrounding

ovarian tissue, disrupting normal ovarian architecture. Cystic fluid, which lacks a surrounding wall, stimulates the local ovarian microenvironment, resulting in the release of inflammatory mediators, growth factors, reactive oxygen species, and free iron. These substances cause varying degrees of fibrosis in ovarian tissue, reduced angiogenesis in the ovarian cortex, and loss of functional ovarian tissue, ultimately impairing ovarian function, decreasing ovarian responsiveness, and negatively affecting oocyte quality [9]. Schubert et al. [10] reported that, compared with patients with other benign ovarian cysts, patients with OEM presented increased fibrotic tissue around the cyst wall; a significant reduction in follicle density; a decrease in primordial follicles; and an increase in the numbers of primary, secondary, antral, and growing follicles. The excessive activation of primordial follicles may be a key factor contributing to follicular depletion in patients with OEM [11]. Additionally, patients with endometriotic cysts often have reduced AFCs and AMH levels, which are positively correlated with cyst size and number [12–13]. Importantly, several factors significantly influence ovarian function following endometrioma removal, including the surgical technique, the surgeon's skill level, the awareness of fertility preservation, and the economic conditions of the country or region. According to a study by Gaetano Riemma and colleagues [14], the use of thermal haemostatic methods such as bipolar electrocoagulation during endometrioma excision may cause thermal damage to surrounding normal ovarian tissue, potentially compromising ovarian function. On the other hand, microsurgical techniques, such as ovarian suturing, are designed to minimize mechanical and vascular injury, offering enhanced protection of ovarian function. However, in cases of severe haemorrhage, thermal haemostatic methods may be unavoidable [14].

Currently, GnRHa-based downregulation protocols are the preferred treatment for patients with endometriosis and infertility. GnRHa binds to gonadotropin-releasing hormone receptors, interfering with the hypothalamic–pituitary–ovarian axis to inhibit the release of FSH, LH, E2, and prolactin. This suppression also inhibits neovascularization and oxidative stress in endometriotic lesions, promoting the atrophy of these lesions and creating a more favourable environment for oocyte maturation [15]. Furthermore, GnRHa pretreatment can increase the expression of endometrial receptivity markers such as integrin avβ3, HOXA10, MEISI, and leukaemia inhibitory factor, modulate NK cell activity, and reduce local inflammation. These effects improve endometrial thickness, receptivity, embryo implantation rates, clinical pregnancy rates, and live birth rates [16]. However, in patients with DOR, the use of GnRHa in downregulation protocols may result in excessive pituitary suppression, reducing ovarian responsiveness. The long treatment cycle and high Gn dosage further increase the psychological and economic burdens on patients. Alternative stimulation protocols, such as natural cycle, microstimulation, short, and antagonist protocols, are commonly used in patients with DOR. However, these protocols often involve challenges such as asynchronous follicle development, premature LH surges, the luteinization of follicles before oocyte retrieval, and early follicular release, which are critical issues to address in ovarian stimulation for patients with DOR. Therefore, selecting an optimized stimulation protocol is crucial for improving clinical pregnancy rates in EM patients with DOR.

The PPOS protocol is a more physiologically mimicking approach to ovarian stimulation. Yu et al. [17] conducted a meta-analysis of 14 studies involving 4182 patients with DOR and reported that the PPOS protocol was an effective ovarian stimulation protocol for patients with DOR. In this protocol, medroxyprogesterone acetate (MPA) acts on the hypothalamus without causing pituitary suppression, thereby not interfering with endogenous progesterone secretion. It effectively suppresses LH surges during stimulation, preventing premature follicular release. A 2021 meta-analysis revealed that in patients with DOR, PPOS resulted in a lower incidence of early LH surges and ovarian hyperstimulation syndrome (OHSS) than did the GnRH antagonist protocol, GnRHa protocol, and natural cycle protocol [18]. Compared with microstimulation protocols, the PPOS protocol significantly reduces the occurrence of early LH surges, improves oocyte retrieval rates and embryo quality, and is positively correlated with cumulative pregnancy rates and live birth rates [19–20]. The weak downregulatory effect of MPA on the ovaries helps maintain a state of low E2, which inhibits the growth of ectopic endometrial tissue. Additionally, the anti-inflammatory properties of MPA contribute to improving the immune-inflammatory environment in the pelvis. Research has shown that MPA treatment for 8 days in endometriosis patients results in a 36% decrease in luciferase activity and a 50% reduction in the protein level of the chemokine RANTES in endometrial stromal cells [21].

A review published in 2021 indicated that the PPOS protocol or antagonist protocol may be more suitable for patients with endometriosis than the long protocol is. One reason for this could be that the PPOS protocol increases the expression of miR-6869-5p in the granulosa cells of follicular fluid in infertile patients while downregulating the expression of miR-4261. This affects the follicular microenvironment, stimulating follicle maturation and ovulation [22]. In patients with normal ovarian function and OEM, there was no significant

difference between the PPOS and long protocols in terms of the implantation rate, clinical pregnancy rate, ongoing pregnancy rate, or live birth rate. However, the PPOS protocol was associated with lower treatment costs [23]. A study by Mathieu d'Argent E et al. [24] revealed that, in patients with ovarian endometriosis who required fertility preservation surgery, there was no significant difference in the number of mature oocytes and cryopreserved embryos between the PPOS and antagonist groups. However, the PPOS protocol demonstrated a better cost-effectiveness ratio. In patients with severe EM, the PPOS protocol showed similar safety to both the long and antagonist protocols, with no adverse effects on neonatal outcomes [25]. Compared with the mild stimulation protocol, the PPOS protocol resulted in better ovulation induction and cumulative live birth rates, possibly due to the higher Gn dosage used in the PPOS protocol, which promotes follicular recruitment and growth [26]. Our study also demonstrated that, compared with the downregulation protocol, the PPOS protocol yielded similar oocyte retrieval rates, MII oocyte rates, fertilization rates, cleavage rates, embryo quality rates, and cycle cancellation rates. However, the PPOS protocol requires fewer Gn days and lower Gn doses, which may be related to the excessive suppression of the pituitary gland and reduced ovarian responsiveness caused by GnRHa in the downregulation protocol. The present study has several notable strengths. First, to the best of our knowledge, this is the first investigation to directly compare the PPOS protocol with a GnRH agonist downregulation protocol in patients with OEM combined with DOR. Second, all measurements were meticulously performed by a fellowship-trained reproductive physician, ensuring a high level of accuracy. Third, all procedures were performed by a highly experienced reproductive physician with specialized expertise in both the PPOS and GnRH agonist downregulation protocols, further enhancing the reliability of the findings. Nevertheless, it is important to acknowledge some limitations of this study. One limitation of this study is the relatively small sample size. Second, the reproductive outcomes of endometriosis can also be influenced by general proinflammatory conditions, such as those in obese patients [27–28]. Additionally, endometriosis is a chronic inflammatory and immune-mediated disease, and individual differences in metabolic and inflammatory states among patients inevitably influence oocyte quality and pregnancy outcomes. These factors may introduce bias into the results. Moreover, both groups of patients had a low number of oocytes retrieved, and none of the embryos underwent blastocyst culture, which could impact the objectivity of the findings. Therefore, future studies should aim to increase the sample size and further refine the research methodology to provide more robust and generalizable results.

Conclusion

On the basis of the findings of this study, the application of a high-progesterone-based ovarian stimulation protocol (PPOS) in patients with ovarian endometriosis and diminished ovarian reserve has significant advantages. The PPOS protocol reduces the amount and duration of GnRH agonist use, leading to time and cost savings while still achieving pregnancy outcomes similar to those obtained with downregulation protocols. It is a simple and safe ovarian stimulation regimen. The PPOS protocol could be considered the preferred option for assisted conception in this patient population. However, as the clinical prevalence of such patients is relatively low, further large-scale, controlled studies are necessary to validate these findings.

Abbreviations

PPOS	Progesterone-primed ovarian stimulation
OEMs	Ovarian endometriosis
DOR	Diminished ovarian reserve
IVF/ICSI-ET	In vitro fertilization/intracytoplasmic sperm injection-embryo transfer
EMs	Endometriosis
GnRHa	Gonadotropin-releasing hormone agonist
FSH	Follicle-stimulating hormone
AMH	Anti-Müllerian hormone
LH	Luteinizing hormone
E2	Estradiol
IVF	In vitro fertilization
ICSI	Intracytoplasmic sperm injection
BMI	Body mass index
AFC	Antral follicle count
Gn	Gonadotropin
MII	Metaphase II
MPA	Medroxyprogesterone acetate

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Author contributions

Qingqing Sun conceived and designed the study. Yijuan Cao performed the surgery. Juan Gu and Yaqing Xu conducted the statistical analysis. All authors reviewed and approved the final version of the manuscript.

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Data availability

The study results were included in this published article.

Declarations

Ethics approval and consent to participate

The patients were given informed consent about the above treatment and the study was approved by the Reproductive Medicine Ethics Committee of Xuzhou Central Hospital. All methods were carried out in accordance with relevant guidelines and regulations. None of the authors has any commercial associations or financial disclosures that might pose or create a conflict of interest with information presented in this article. No external funding was received.

Consent for publication
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Competing interests
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