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Gonadotropin versus Follicle-Stimulating Hormone for Ovarian Response in Patients Undergoing in vitro Fertilization: A Retrospective Cohort Comparison

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ABSTRACT

Background: Poor ovarian responders generally refer to patients who respond poorly to ovarian stimulation for assisted reproductive techniques (ART) such as in-vitro fertilization (IVF) and hence experience low live birth rate. Various controlled ovarian stimulation (COS) protocols have been developed during the past 3 decades for IVF/ICSI to improve oocyte quality and ultimately live birth rate, to increase ovarian response in POR patients, and to reduce the risk of ovarian hyperstimulation syndrome. Both highly puri?ed human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) have been widely used for COS during IVF/ICSI. Their in?uence on treatment outcome in women undergoing IVF/ICSI hasbeen actively debated.

Objectives: To compare highly purified human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) in patients with poor ovarian response undergoing in vitro fertilization/intracytoplasmic sperm injection with a gonadotropin-releasing hormone antagonist protocol.

Methods: This retrospective cohort study included 60 patients with poor ovarian response (30 received hp-hMG and 30 received rFSH) undergoing in vitro fertilization/intracytoplasmic sperm injection with a gonadotropin-releasing hormone antagonist protocol. Pregnancy-related outcomes, ovarian response, oocyte, and embryo parameters were compared between the 2 groups. Additionally, serum insulin-like growth factor-1 and insulin-like growth factor binding protein-1 levels on the day of oocyte retrieval were compared between the 2 groups.

Results: The 2 treatments resulted in comparable numbers of oocytes retrieved and embryos, comparable oocyte retrieval rate, mature oocyte rate, and fertilization rate, and also comparable clinical pregnancy rates, implantation rates, and miscarriage rate. However, hp-hMG led to statistically insignificant higher viable embryo rate (54.0% vs 44.8%; $P = 0.174$) and live birth rate per pregnancy (16.7% vs 10%) versus rFSH. Finally, statistically significantly higher serum insulin-like growth factor-1 level (178.53 [13.70] ng/mL vs 164.93 [12.17] ng/mL; $P = 0.01$) and statistically insignificantly lower serum insulin-like growth factor binding protein-1 level (19.53 [3.56] ng/mL vs the lower insulin-like growth factor binding protein-1 level SD is (2.76 [20.83] ng/mL; $P > 0.05$) on the day of oocyte retrieval were associated with hp-hMG versus rFSH.

Conclusions: hp-HMG and rFSH did not lead to significantly different treatment outcomes in patients with poor ovarian response undergoing in vitro fertilization/intracytoplasmic sperm injection with a gonadotropin-releasing hormone antagonist protocol, although significantly higher serum insulin-like growth factor-1 level and insignificantly lower serum insulin-like growth factor binding protein-1 level on the day of oocyte retrieval associated with hp-HMG might suggest a beneficial endocrine environment. (*Curr Ther Res Clin Exp*. 2020; 81:XXX–XXX)

Introduction

Poor ovarian responders generally refer to patients who respond poorly to ovarian stimulation for assisted reproductive techniques (ART) such as in-vitro fertilization (IVF) and hence experience low

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live birth rate.[1] Poor ovarian response (POR) often indicates a reduced follicular response to ovarian stimulation leading to reduced number of retrieved oocytes.[2] Due to diversity of POR patients, a uniform definition of POR had been lacking until the publication of the Bologna criteria developed by the European Society of Human Reproduction and Embryology in 2011.[2] The Bologna criteria dictate the presence at least 2 of 3 features for diagnosis of POR, the 3 features being advanced patient age or presence of other POR risk factors, a previous episode of POR, and an abnormal ovarian reserve test.[2] Additionally, to diagnose POR, 1 cycle of stimulation is essential,[2] and the occurrences of 2 episodes of POR to maximal ovarian stimulation even in the absence of advanced age, POR risk factors, and abnormal ovarian reserve tests are also enough for a diagnosis of POR.[2] Estimated live birth rate for POR patients is <10% irrespective of the ovarian stimulation protocol used or age of the patients,[2] and it is estimated that POR patients accounted for about 9% to 24% of patients seeking ART.[3] Nowadays more women opt to postpone childbearing to a later age, and because prevalence of POR increases with age, a factor correlating significantly with ART outcomes,[1,2,4] the prevalence of POR patients is not expected to go down. It remains a challenge to improve ART outcomes for these patients,[4] and it is important to choose a suitable treatment protocol for the POR patients.

Both highly purified human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) have been widely used for controlled ovarian stimulation (COS) during IVF or intracytoplasmic sperm injection (ICSI).[4,5] Their influence on treatment outcome in women undergoing IVF/ICSI has been actively debated.[4,5] Numerous studies have investigated and compared the treatment outcomes of hp-hMG with rFSH, most of which were conducted with a gonadotropin-releasing hormone (GnRH) agonist protocol.[4,6–12] Several meta-analyses of randomized controlled trials in unselected populations reported favorable clinical outcomes in terms of slightly higher live birth rate associated with hp-hMG versus rFSH,[9,10,12] and such favorable outcomes were more pronounced in patients under IVF than ICSI.[11] There have been several studies comparing hp-hMG with rFSH in patients undergoing IVF/ISCI with a GnRH antagonist protocol, and they reported different findings.[5,13–15] hp-hMG contains FSH, luteinizing hormone (LH) and human chorionic gonadotropin (hCG),[4] and 1 meta-analysis and a later study did not reveal any benefit of adding LH to rFSH in women undergoing IVF/ICSI using a GnRH antagonist protocol.[16,17] Until now, there has been no study comparing the effectiveness of hp-hMG versus rFSH in POR patients undergoing IVF/ISCI with a GnRH antagonist protocol, and because POR patients account for 9% to 24% of patients seeking ART,[3] a study comparing hp-hMG versus rFSH is necessary and could potentially provide some guidance for choosing a proper gonadotropin for COS for these POR patients. Here we report the results of a retrospective cohort study comparing Hp-HMG (Menopur; Ferring Pharmaceuticals, Saint-Prex, Switzerland) and rFSH (Puregon; MSD Pharmaceuticals, Bandra, India) in patients undergoing IVF/ICSI using a GnRH antagonist protocol.

Materials and Methods

Patients and study design

This retrospective cohort study was conducted in the Reproductive Medicine Center, Xiangyang Central Hospital, The Affiliated Hospital of Hubei University of Arts and Science. Records of all patients undergoing IVF/ICSI using a GnRH antagonist protocol between May 2015 and October 2017 were reviewed to identify eligible POR patients to be included in the current study. This study was reviewed and approved by the Ethics Committee of the hospital.

Eligible patients must have a diagnosis of POR consistent with the Bologna criteria developed by the European Society of Human Reproduction and Embryology[2]; more specifically, they must possess at least 2 of the 3 following features: age ≥40 years or with other risk factors for POR, ≤3 oocytes retrieved from the previous IVF/ICSI cycle using a conventional stimulation protocol, and antral follicle count <7 or anti-Mullerian hormone <1.1 ng/mL.[2] Additional exclusion criteria included women with an infertility diagnosis of male factor, tubal factor, minimal or mild endometriosis, or unexplained infertility.

Thirty consecutive eligible POR patients using hp-hMG (the Hp-hMG group) and 30 consecutive eligible POR patients using rFSH (Gonal-F; Merck-Serono (Darmstadt, Germany), or Puregon) (the rFSH group) for COS during an IVF/ICSI cycle with a GnRH antagonist protocol between May 2015 and October 2017 were included in the study.

All patients included in the study underwent an IVF/ICSI cycle with a GnRH antagonist protocol according to Bosch et al.[15]

Main outcome measures

Main outcome measures included clinical pregnancy (defined as the presence of a gestational sac with positive heartbeat as imaged with sonography 4 to 5 weeks after embryo transfer) rate per embryo transfer, live birth rate per pregnancy, miscarriage rate per pregnancy, implantation rate per embryo transfer, and embryo transfer rate per oocyte retrieved. Additionally, mean number of >14 mm follicles on the day of hCG administration, mean number of oocytes and mature oocytes (ie, metaphase II) retrieved, mean number of fertilized oocytes, mean number of good quality embryos (grade I or II) and cryopreserved embryos, oocyte retrieval rate per >14 mm follicle, mature oocyte rate, fertilization rate, viable embryo rate per oocyte retrieved, and percentage of moderate or serious ovarian hyperstimulation syndrome were also compared between the 2 groups of patients. Finally, serum estradiol (E_2) on the day of hCG administration, serum insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-1 (IGFBP-1) levels on the day of oocyte retrieval before oocyte pickup were measured and compared between the 2 groups.

Endocrine profiles

Serum FSH, LH, E_2, progesterone, and testosterone levels were measured using Elecsys electrochemiluminescence immunoassays (Roche Diagnostics, Mannheim, Germany) according to the manufacturer's instructions.

Serum IGF-1 and IGFBP-1 levels on the day of oocyte retrieval before oocyte pickup were measured with a commercially available antibody-based ELISA (Raybiotech; Norcross, Georgia). The lower limits of detection for IGF-1 and IGFBP-1 were 0.276 ng/mL and 1.86 ng/mL, respectively. Concentrations of IGF-1 and IGFBP-1 in the study were above the lower limits of detection.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences for Windows 10.0 (IBM-SPSS Inc, Armonk, NY). Descriptive measures (mean [SD]) were used to express continuous variables. Additionally, frequencies of categorical variables were expressed with absolute numbers and relative numbers and also in the form of percentage. The χ^2 test and t test were used to compare categorical variables and continuous variables between the 2 groups, respectively. Statistical significance was acceptable with a P value < 0.05.

Table 1
Demographic and baseline characteristics of the patients in the highly purified human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) groups.*

Characteristic	hp-hMG (n = 30)	rFSH (n = 30)	*P* value
Age (y)	34.43 (5.722)	35.10 (5.604)	0.65
Duration of infertility (y)	6.97 (3.783)	6.17 (3.621)	0.406
BMI	22.137 (1.410)	22.390 (1.683)	0.53
AFC	4.53 (1.852)	3.80 (1.955)	0.141
Basal FSH (IU/mL)	7.4853 (2.955)	7.9670 (2.165)	0.474
LH (IU/mL)	8.6623 (2.886)	8.1247 (2.080)	0.411
E_2 (pg/mL)	43.5230 (15.970)	47.8007 (22.495)	0.399
P (ng/mL)	0.5127 (0.248)	0.6890 (0.530)	0.104
T	0.3270 (0.303)	0.2450 (0.151)	0.190
PRL (ng/mL)	17.9933 (8.858)	20.3227 (13.800)	0.440

AFC = antral follicle count; BMI = body mass index; FSH = follicle-stimulating hormone; LH = luteinizing hormone; E2 = estradiol; P = progesterone; T = testosterone; PRL = prolactin.
* Values are expressed as mean (SD).

Results

A total of 60 POR patients were included in the current retrospective study, 30 received hp-hMG and 30 received rFSH for COS during IVF/ICSI with a GnRH antagonist protocol. One patient in the hp-hMG group and 1 patient in the rFSH group were excluded due to no oocyte retrieval. There was no exclusion of other patients in either of the groups.

Demographic and baseline characteristics

The 2 groups of patients had comparable demographic and baseline characteristics such as age, duration of infertility, body mass index, antral follicle count, recurrent pregnancy loss, basal serum FSH, LH, E_2, progesterone, and testosterone levels (Table 1).

Ovarian response, oocyte, and embryo parameters from retrieval to transfer

The 2 groups of patients had comparable durations of gonadotropin stimulation and consumed comparable doses of gonadotropin (Table 2). They also had similar E_2 concentrations, endometrial thicknesses, and numbers of >14 mm follicles on the day of hCG administration (Table 2).

Average numbers of total, mature (ie, metaphase II), and fertilized oocytes retrieved (2.90 [1.470] vs 2.70 [1.579], and 2.53 [1.167] vs 2.13 [1.137], 2.30 [1.119] vs 1.80 [0.997], respectively; all *P* values > 0.05) and average numbers of good and cryopreserved embryos (1.83 [1.02] vs 1.50 [0.974], 2.03 [1.098] vs 1.57 [0.935], respectively, both *P* values > 0.05) were comparable between the hp-hMG and the rFSH groups (Table 2). Additionally, there was no significant difference in oocyte retrieval rate per >14 mm follicle (77.0% vs 77.1%), mature oocyte rate (87.4% vs 77.8%), or fertilization rate (90.8% vs 85.7%) between the hp-hMG versus the rFSH group (Table 2).

Although the hp-hMG group had numerically higher viable embryo rate per oocyte retrieved versus the rFSH group, the difference did not reach statistical significance (50.4% vs 44.8%; $P = 0.174$) (Table 2).

Neither group had occurrence of moderate or severe ovarian hyperstimulation syndrome requiring hospitalization and/or paracentesis (Table 2).

As to pregnancy-related outcomes, the 2 groups had comparable clinical pregnancy rates (30.8% vs 29.4%), implantation rates per transferred embryo (62.3% vs 61.7%), and miscarriage rate per pregnancy (33.3% vs 30.0%) (Table 3). Additionally, although the hp-HMG group had numerical higher number of embryos transferred per >14 mm oocyte (54.0% vs 44.8%) and live birth rate per pregnancy (16.7% vs 10%) versus the rFSH group, neither difference reached statistical significance (both *P* values > 0.05) (Table 3).

Serum IGF-1 and IGFBP-1 levels on the day of oocyte retrieval before oocyte pickup

Serum IGF-1 level was significantly higher in the hp-hMG group versus the rFSH group on the day of oocyte retrieval before oocyte pickup (178.53 [13.70] ng/mL vs 164.93 [12.17] ng/mL; $P = 0.01$), on the other hand, lower serum IGFBP-1 level was associated with the hp-HMG group versus the rFSH group, although the difference was not statistically significant (19.53 [3.56] ng/mL vs 20.83 ng/mL; $P > 0.05$).

Discussion

In this retrospective cohort study, we compared the effects of hp-hMG versus rFSH used for COS by retrospectively examining treatment outcomes of 30 consecutive POR patients receiving hp-hMG for COS and 30 consecutive POR patients receiving rFSH for COS while undergoing IVF/ICSI using a GnRH antagonist protocol. We found no significant difference in the 2 groups regarding ovarian response, oocyte, and embryo parameters from retrieval to

Table 2
Ovarian response, oocyte, and embryo parameters from retrieval to transfer of the patients in the highly purified human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) groups.*

Parameter	hp-hMG (n = 30)	rFSH (n = 30)	*P* value
Duration of stimulation (d)	9.20 (1.448)	9.23 (1.478)	0.93
Total Gn (IU)	2721.67 (612.961)	2570.83 (395.943)	0.263
Estradiol concentration on the day of hCG administration (pg/mL)	790.90 (319.586)	751.13 (330.30)	0.637
Endometrial thickness on the day of hCG administration (mm)	9.297 (2.0962)	9.370 (2.2530)	0.897
No. of >14 mm follicles on the day of hCG administration	3.77 (1.569)	3.50 (1.503)	0.504
No. of oocytes retrieved	2.90 (1.470)	2.70 (1.579)	0.614
No. of mature oocytes† retrieved	2.53 (1.167)	2.13 (1.137)	0.184
No. of fertilized oocytes	2.30 (1.119)	1.80 (0.997)	0.073
No. of good embryos	1.83 (1.02)	1.50 (0.974)	0.201
No. of cryopreserved embryos	2.03 (1.098)	1.57 (0.935)	0.082
Oocyte retrieval rate per >14 mm follicle	87/113 (77.0)	81/105 (77.1)	0.979
Mature oocyte† rate	76/87 (87.4)	63/81 (77.8)	0.101
Fertilization rate	69/76 (90.8)	54/63 (85.7)	0.351
Viable embryo rate per oocyte retrieved	61/113 (54.0)	47/105 (44.8)	0.174
Rate of moderate or serious OHSS per cycle	0 (0.0)	0 (0.0)	–

Gn = gonadotropin; hCG = human chorionic gonadotropin; OHSS = ovarian hyperstimulation syndrome.
* Values are expressed as mean [SD] or n /N (%).
† Metaphase II.

Table 3
Pregnancy-related outcomes of the patients in the highly purified human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) groups.*

Outcome	hp-hMG (n = 30)	rFSH (n = 30)	*P* value
Embryos transferred per >14 mm oocyte	61/113 (54.0)	47/105 (44.8)	0.174
Clinical pregnancy rate per cycle initiated	12/39 (30.8)	10/34 (29.4)	0.900
Implantation rate per transferred embryo	38/61 (62.3)	29/47 (61.7)	0.950
Miscarriage rate per pregnancy	4/12 (33.3)	3/10 (30.0)	0.867
Live birth rate per pregnancy	2/12 (16.7)	1/10 (10)	0.650

* Values are presented as n/N (%).

Table 4
Serum insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-1 (IGFBP-1) levels of the patients in the highly purified human menopausal gonadotropin (hp-hMG) and recombinant follicle-stimulating hormone (rFSH) groups on the day of oocyte retrieval before oocyte pickup.

Parameter	hp-hMG (n = 30)	rFSH (n = 30)	*P* value
IGF-1 (ng/mL)	178.53 (13.70)	164.93 (12.17)	0.01*
IGFBP-1 (ng/mL)	19.53 (3.56)	20.83 (2.76)	> *0.05*

* Values are presented as mean (SD).

transfer, and also pregnancy-related outcomes, although the hp-hMG group had numerically higher viable embryo rate per oocyte retrieved and live birth rate per pregnancy versus the rFSH group. These differences were not statistically significant. Of particular interest was the finding that statistically significantly higher serum IGF-1 level and statistically insignificantly lower serum IGFBP-1 level on the day of oocyte retrieval before oocyte pickup were associated with hp-hMG versus rFSH.

Various COS protocols have been developed during the past 3 decades for IVF/ICSI to improve oocyte quality and ultimately live birth rate, to increase ovarian response in POR patients, and to reduce the risk of ovarian hyperstimulation syndrome.[18] There is no single protocol that could fit all patients and the same protocol could often lead to different outcomes in different patients; therefore, individualized treatment protocols are recommended.[18,19] Therefore, studying the effects of various COS protocols in different populations is important because it could help to individualize treatment protocols for different patients based on their predicted treatment response.[19] POR patients accounted for about 9% to 24% of patients seeking ART[3] and live birth rate for these patients was estimated to be <10% irrespective of the ovarian stimulation protocol used or age of the patients.[2] Improving ART outcomes for POR patients remains a great challenge,[4] and it is important to choose a suitable treatment protocol for these patients

Whether using hp-hMG for COS leads to superior treatment outcomes versus rFSH in patients undergoing IVF/ICSI has long been a topic of constant debate.[4,5] Ultimately, it boils down to whether presence of exogenous LH activity, especially hCG-driven LH bioactivity, would be beneficial because hp-hMG contains FSH, LH, and hCG, and the majority of hp-hMG's LH bioactivity is driven by hCG.[4] Many studies have been conducted on this topic, most of which were conducted with a GnRH agonist cycle and they reached different conclusions regarding whether hp-hMG for COS led to superior or comparable treatment outcomes versus rFSH.[4,6–12] Several studies compared hp-hMG with rFSH in patients undergoing IVF/ISCI with a GnRH antagonist protocol and reached somewhat different conclusions.[5,13–15] In addition, 1 meta-analysis did not reveal any benefit of adding LH to rFSH in women undergoing IVF/ICSI using a GnRH antagonist protocol.[16] However, another meta-analysis of 7 trials (6 using a GnRH agonist and 1 using a GnRH antagonist) did find higher implantation rate and clinical pregnancy rate associated with recombinant LH in combination with rFSH versus rFSH alone in women of advanced reproductive age (ie, ≥35 years),[20] although a later randomized controlled trial found no such benefit associated with adding recombinant LH to rFSH in women aged ≥35 years when a GnRH antagonist protocol was used.[17] Because women of advanced reproductive age constitute a large portion of POR patients,[17] these results were more relevant to our study. Our results of comparable ovarian response, oocyte retrieval, and transfer and pregnancy-related outcome associated with hp-hMG versus rFSH were more consistent with Vuong et al[17] and were also consistent with several earlier studies on this topic in general population of women undergoing IVF/ICSI using an antagonist protocol.[13,21,22] Our results on ovarian response, oocyte retrieval, and embryo transfer and pregnancy-related outcomes seemed to support the notion that the choice of hp-hMG or rFSH for COS had little influence on IVF/ICSI outcomes in POR patients, and such choice should depend more on cost, availability, and convenience.[13]

On the other hand, our study showed that compared to the rFSH group, the hp-hMG group had significantly higher serum IGF-1 level and statistically insignificant lower IGFBP-1 level on the day of oocyte retrieval before oocyte pickup, suggesting that hp-hMG and rFSH led to different endocrine environments. There have been very few studies mentioning whether hMG and rFSH used for COS resulted in different IGF-1 and/or IGFBP-1 levels in patients undergoing IVF/ICSI. It has been reported that hp-hMG/hMG and rFSH used for COS led to comparable serum or follicular fluid IGF-1 level at oocyte retrieval in women undergoing IVF/ICSI when a GnRH agonist protocol was used.[23,24] Our result on IGF-1 was inconsistent with these previous findings; however, a GnRH antagonist protocol was used in our study, and this might lead to the difference in the results. Of course, more studies of larger sample sizes are needed to verify our findings. If compared with patients receiving rFSH, patient receiving hp-hMG indeed had significantly higher serum IGF-1 levels and statistically insignificant lower IGFBP-1 levels on the day of oocyte retrieval and thus a higher IGF-1 to IGFBP-1 ratio. This may suggest that patients taking hp-hMG could have an endocrine environment beneficial for improving oocyte quality and this possibly could affect the clinical outcomes of the IVF/ICSI,[23,25] because it has been reported that serum IGF-1 to IGFBP-1 ratio on the day of oocyte retrieval was significantly higher in women who became pregnant versus those who did not and that serum IGF-1 to IGFBP-1 ratio could be an index of oocyte quality, a higher ratio reflecting better oocyte quality.[25] Neither IGF-1 nor IGFBP-1 level varies across menstrual cycles in normal-cycling women, suggesting that neither has an important role in normal reproductive processes in women; however, the scenario changes during COS, because both IGF-1 and IGFBP-1 levels vary in response to exogenous gonadotropin.[25] Further, compared with women who became pregnant, those who did not had higher serum IGFBP-1 levels, possibly reflecting premature luteinization, known to be associated with poor treatment outcomes for IVF.[25] In patients undergoing IVF, IGF-1 amplifies the action of FSH in the follicular fluid as evidenced by the report that during ART cycles, follicles with higher IGF-1 levels require lower FSH dose and shorter stimulation time.[26] IGFBP-1, on the other hand, acts as an anti-gonadotrophic factor and in-

hibits IGF-1 action.[26] It has been reported that both IGF-1 and IGFBP-1 could be indicators for oocyte maturity and quality,[25,27–30] and studies also showed that IGF-1 (exogenous or endogenous) was beneficial for preembryonic development and formation of the blastocyst.[25] Additionally, during IVF cycles, higher follicular fluid IGF-1 level on the day of oocyte pick up was associated with higher fertilization rate, cleavage, top-grade embryos, and also higher clinical pregnancy rate and embryo implantation rate, and as such follicular fluid IGF-1 level on the day of oocyte pickup was a marker of embryo quality and implantation rate and had correlation with clinical pregnancy rate in IVF cycles.[31] Because follicular fluid IGF-1 level correlated well with serum IGF-1 level,[25] it could be postulated that serum IGF-1 on the day of oocyte pickup could also be a marker of embryo quality and implantation rate. Our findings of statistically insignificant higher viable embryo rate and live birth rate per pregnancy, significantly higher serum IGF-1 level and statistically insignificant lower IGFBP-1 level on the day of oocyte retrieval before oocyte pickup associated with hp-hMG versus rFSH were consistent with these previous reports.

Our study was limited by the fact that it was a retrospective study because bias is common in retrospective studies; however, as patients in the hp-hMG and the rFSH groups in our study had comparable demographic and baseline characteristics (Table 1), bias in our study was minimized. Secondly, our study had a small sample size, and studies with larger sample sizes are needed to further elucidate our results. Preparation for a prospective study with a larger sample size is underway.

Conclusions

There was no significant difference in treatment outcomes (ie, ovarian response, oocyte, and embryo parameters; and pregnancy-related outcomes) between POR patients receiving hp-hMG versus rFSH for COS during IVF/ICSI cycles using a GnRH antagonist protocol. Compared with the rFSH group, patients in the hp-hMG group had significantly higher serum IGF-1 levels and statistically insignificant lower serum IGFBP-1 levels on the day of oocyte retrieval before oocyte pickup, suggesting an endocrine environment beneficial for oocyte development as well as embryonic implantation and development. More studies with larger sample sizes are needed.

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All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. X. Yang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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