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ORIGINAL ARTICLE

Progestin-primed ovarian stimulation versus GnRH antagonist protocol in ICSI cycles in patients with different ovarian reserve: A retrospective cohort study

Short title: Progestin-primed ovarian stimulation versus GnRH antagonist protocol in ICSI cycles in patients with different ovarian reserve

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ABSTRACT

Objective. To compare the ICSI cycle outcomes in PPOS Vs. conventional GnRh antagonist protocol.

Patients and Methods. In this retrospective cohort study, 200 patients who were administrated gonadotropins for ovarian stimulation from the second or the third day of menstruation cycle were included in this study. When the follicular diameter reached 13-14 mm, GnRH antagonist was started in the group A, while in the group B,10 mg norethisterone acetate was taken daily orally. The retrieved oocytes were fertilized in vitro by intracytoplasmic sperm. Both groups underwent freeze-all and delayed embryo transfer. The primary outcome is the clinical pregnancy rate. The secondary outcomes included the duration, dosage & form of ovarian stimulation, the number & quality of oocytes retrieved which means mature and well-functioning oocytes, the number of MII oocytes, and the number and quality of embryos.

Results. A total of 200 women were recruited, with 100 in the PPOS group and 100 in the GnRH antagonist group. The PPOS group had lower clinical pregnancy rate compared with the GnRH antagonist protocol group. PPOS group showed also, lower number of oocytes retrieved, lower number of M II oocytes however, they had better quality of oocytes and lower rate of class A embryos when compared with the GnRH antagonist protocol group.

Conclusions. Compared with PPOS, GnRH antagonist protocol had higher clinical pregnancy rate. PPOS may be suitable for oocyte or embryo cryopreservation, but should not totally replace GnRH antagonist for patients undergoing in vitro fertilization (IVF).

Key words

Norethisterone acetate; Cetrorelix; Dydrogesterone; GnRh antagonist; Progestin-primed ovarian stimulation.

Introduction

In vitro fertilization (IVF) is a widely used and effective treatment for infertility [1]. The first and critical step for IVF or intracytoplasmic sperm injection (ICSI) is controlled ovarian stimulation (COS). Luteinizing hormone (LH) surge and ovarian hyperstimulation syndrome (OHSS), which result from multi-follicular development and high oestradiol levels, have always been the focus of various COS protocols [2, 3].

For several years, the conventional COS protocol was commonly associated with gonadotropin-releasing hormone (GnRH) analogues to prevent a premature LH surge [4]. Despite their overall effectiveness, the LH surge occurs in 3-10% of all in vitro fertilization (IVF) cycles [4, 5].

Furthermore, the utilization of GnRH analogues is burdened by high costs and poor adherence to the daily subcutaneous administration [5].

The GnRH antagonist protocol (GnRH-ant) has been proven to effectively block premature pituitary LH secretion during COS [6]. It has been the first choice of COS in patients with normal ovulation and those with polycystic ovary syndrome (PCOS) [6, 7].

Pregnancy outcomes have improved with progress in embryo vitrification techniques, which may be associated with improved endometrial receptivity, as in frozen-thawed embryo transfers, endometrial priming may be achieved with the use of estrogen and progesterone, and endometrial growth can be controlled more exactly in COH cycles [8].

Progesterone-primed ovarian stimulation (PPOS) has been adopted as an innovative regimen for ovarian stimulation. Progesterone reduces GnRH's pulsatility from the hypothalamus, thus inhibiting the LH release associated with increased estradiol levels. Therefore, a new strategy for COS, i.e., PPOS, was gradually investigated [9].

In 2015, Kuang [8] first used Medroxyprogesterone acetate (MPA) for LH suppression in COS, which resulted in similar outcomes with short agonist protocol. Subsequent studies also demonstrated the efficacy of progesterone in preventing LH elevation during ovarian stimulation. In contrast to GnRH analogues, the use of progestin for LH suppression is associated with the promising advantages of oral administration, user convenience, and low cost [10]. Concomitantly, however, the endometrium is not allowed for fresh embryo transfer because early exposure to the progesterone would result in endometrial advancement [11].

To overcome the adverse effect of the progesterone on endometrium, one strategy is to freeze all the embryos and defer the embryo-transfer in a future frozen-thawed replacement cycle (FET). This was enabled by the development of advanced cryopreservation techniques [11].

Thanks to the economic and clinical convenience, the PPOS protocol has gained considerable popularity nowadays. Several investigations about the use of PPOS protocol in

different ovarian reserve patients had been reported. Nevertheless, information about the effectiveness of progestins compared to GnRH analogues in various populations of patients is limited; for instance, information pertaining to whether PPOS has the same effect or is safer than the conventional COS protocols in all patient populations is limited.

The purpose of this cohort study was to investigate whether PPOS has the same results of LH suppression in COS and achieves similar pregnancy outcomes with conventional protocols.

Patients and Methods

Settings

This retrospective cohort study was conducted at ICSI center in El-Madina Women Hospital, Alexandria, Egypt, between January 2022, and January 2023.

Written informed consent was obtained from all enrolled patients with infertility undergoing their first ovarian stimulation cycle for ICSI.

The inclusion criteria were as follows: Female aged 20–45 years, spontaneous menstrual cycle (25–35 days), and single cycle of IVF or ICSI procedure. The exclusion criteria were: Endometriosis, uterine anomalies and hydrosalpinx, basal oestradiol levels above 80 pg/ml, recurrent implantation failure, presence of a functional ovarian cyst and any contraindications for COS or systemic disease such as renal failure. A total of 200 women (100 in each group) were enrolled in this study.

Study Protocol

On the second or third day of the menstrual period, transvaginal ultrasonography was done to exclude any uterine, tubal abnormalities or ovarian cysts.

Stimulation started by 75–300 IU of subcutaneous highly purified human menopausal gonadotropin (hMG, Meriofert) and or subcutaneous FSH (Recombinant Follitropin Alfa (Gonal f). They were administered daily starting from day 2 or 3 of the menstrual cycle (MC). When follicles reached 13-14 mm, cases were divided into two groups according to the pituitary suppression method.

Group A: GnRH antagonist (GnRH-ant) protocol: The GnRH antagonist named cetrorelix (Cetrotide, 0.25 mg, Merck-Serono) was administered till the end of stimulation.

While in Group B: PPOS protocol: Tablets containing 10 mg oral Norethisterone acetate (Steronate, 5 mg) were started till the end of stimulation.

The dosage of gonadotropins was adjusted according to serum E2 levels and follicle sizes.

In both groups, when three or more dominant follicles reached 17-18 mm in diameter, a trigger was administered for final oocyte maturation by intramuscular (IM) hCG (10,000 IU) injections. Oocyte retrieval was performed 35 h after administering the trigger.

Oocyte collection and embryo culture

Standard insemination or ICSI was performed within one hour of retrieval. On the third day, embryos were examined for the number and regularity of blastomeres and the degree of embryonic fragmentation. Embryos from normal and high responder patients were extended

to day 5 when more than 5 good quality embryos achieved on day 3. The top-quality embryos were frozen by vitrification on day 3 or day 5.

The viable embryos included all top-quality cleavage embryos (including grade I and grade II, 8-cell blastomere embryos) and good morphological blastocysts [12].

Endometrium preparation and frozen embryo transfer

All patients in the PPOS group and in the GnRH-ant group underwent frozen embryo transfer (FET) which was conducted during the second menstrual cycle after the oocyte pickup (OPU) cycle.

For endometrial preparation in FET cycles, HRT was preferred by giving the recipients cyclic estrogen–progestin (CycloProgynova, Bayer) for one cycle before the ET cycle. Recipients started 2 mg E2 valerate tablets three to four times a day starting from the second day of an induced menstruation. Endometrial preparation was considered adequate when endometrial thickness ≥ 7mm. Vaginal progesterone was added at a dose of 400 mg twice a day, after at least 10 days of E2 and when endometrial thickness became more than 7 mm. Blastocyst transfers were done on the sixth day and cleavage stage embryos were transferred on the fourth day of P administration. Medications were continued until a negative pregnancy test 17 days after ET, or between the seventh and tenth week of gestation when pregnancy was achieved (Confirmed by B-hCG and transvaginal ultrasound).

Outcome measures and definitions

The primary outcome measure was the clinical pregnancy rate. Secondary outcome measures included: The total number of oocytes retrieved, number of metaphase two (MII) oocytes, percentage of good quality embryos, the duration and dosage of stimulation drugs.

The implantation rate was defined as the number of gestational sacs visualised on ultrasound examination divided by the number of embryos transferred [13].

Biochemical pregnancy was defined as serum β-hCG level ≥ 5 IU/l 2 weeks after embryo transfer [13].

Clinical pregnancy was defined as at least one gestational sac on ultrasound 4 weeks after embryo transfer [13].

The cumulative live birth rate (CLBR) was calculated as the delivery of a living newborn after the 24th gestational week divided by the number of enrolled patients [13].

The OHSS was classified into three grades (mild (grade 1 and 2), moderate (grade 3), and severe (grade 4 and 5) according to the modified Golan classification [13].

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. **(**Armonk, NY: IBM Corp**)**. Categorical data were represented as numbers and percentages. **Chi-square test** was applied to compare between two groups. Alternatively, **Fisher Exact or Monte Carlo correction** test was applied when more than 20% of the cells have expected count less than 5. For continuous data, they were tested for normality by the **Kolmogorov-Smirnov**. Quantitative data were expressed as range (minimum and maximum), mean, standard deviation and median for normally distributed quantitative

variables **Student t-test** was used to compare two groups while. On the other hand for not normally distributed quantitative variables **Mann Whitney test** was used to compare two groups. Significance of the obtained results was judged at the 5% level.

Results

The studied cases were divided into 2 groups, group A included participants received GnRH-ant protocol, and group B included participants received PPOS protocol, and each group was subdivided into 3 subgroups according to the AMH serum level as showed in table (1).

1. Group (1) including poor responders with AMH < 1.2.
2. Group (2) including normal responders with AMH 1.2 – 3.5.
3. Group (3) including high responders with AMH > 3.5.

Both figure (1) and table (2) show the outcomes of COS in poor responders in the two studied groups. The PPOS protocol yielded a similar number of total retrieved oocytes, M2 oocytes, injected oocytes and class A embryos when compared to GnRH-ant protocol (PPOS: 6.8 ± 4.8, 4.8 ± 5, 5.9 ± 4.8, 2.9 ± 2.3 vs. GnRH-ant: 5.2 ± 3.4, 4.6 ± 3.3, 4.9 ± 3.4, 2.5 ± 2.5 , respectively , P > 0.05), also the duration of stimulation needed was comparable between the two groups (PPOS: 10.1 ± 2.2 vs. GnRH-ant: 10.1 ± 1.9, p > 0.05). However, the dose of gonadotropins used and the quality of oocytes were higher in PPOS protocol than in GnRH-ant one (PPOS: 6 ± 0.2, 64% vs. GnRH-ant: 5.8 ± 0.4, 24%, respectively, P < 0.05), and the percentage of M2 oocytes/total retrieved oocytes was significantly higher in GnRH-ant (84.8 ± 16.9), than in PPOS protocol group (65.3 ± 23.6), p < 0.05. Whereas, the clinical pregnancy rate was significantly higher in GnRH-ant group than in PPOS group (64% vs. 26.7%, respectively, p < 0.05).

Among the normal ovarian reserve participants as showed in table (3) and figure (1), GnRH-ant group had significantly higher numbers of total oocytes retrieved, M2 oocytes, percentage of M2 oocytes/total oocytes, injected oocytes, class A embryos and also higher clinical pregnancy rate when compared to the PPOS protocol. (GnRH-ant: 15.6 ± 5.6, 13 ± 5.1, 82.5 ± 12.9, 14.1 ± 5.2, 7 ± 4.2, 84.2%, PPOS: 11.3 ± 7, 7.5 ± 4.7, 68.6 ± 18, 9.3 ± 6, 3.9 ± 3.1, 40.9%, respectively, p <0.05). However, the dose and duration of gonadotropins used for stimulation, the quality of oocytes and the quality of embryos shared the same values in both groups. (PPOS: 5.3 ± 0.8, 10 ± 1.8, 43.2%, 0.64 ± 0.31, GnRH-ant: 5.1 ± 0.7, 9.6 ± 1.4, 35.1%, 0.69 ± 0.26, respectively, p > 0.05).

In high responder participants of the two studied groups, the outcomes were illustrated in table (4) and figure (3). The quality of oocytes was significantly better in PPOS protocol group than in the other group with a percentage of 50%, p < 0.05, while M2 oocytes/total retrieved oocytes was significantly higher in GnRH-ant protocol group (GnRH-ang: 75.6 ± 24.1, PPOS: 62 ± 23.8, p < 0.05). On the other hand, all other findings including the dose and duration of gonadotropins used, total number of retrieved oocytes, M2 oocytes, injected oocytes, class A embryos, the quality of embryos, and finally, the clinical pregnancy rates shared the same values when being compared between the two groups. (PPOS: 4 ± 1, 10.2 ± 1.6, 21.8 ± 11.2, vs. 13.8 ± 8.9, 16.5 ± 9.2, 8.6 ± 5.9, 0.73 ± 0.25, 69.2%, GnRH-ant: 3.8 ± 0.8, 9.7 ± 2.4, 23.2 ± 7.6, 18.1 ± 8.1, 19.3 ± 8, 10.4 ± 7, 0.66 ± 0.25, 77.8%, respectively, p > 0.05).

Discussion

In the current study, we retrospectively compared the clinical and laboratory outcomes of two COS protocols (PPOS using steronate vs. GnRH antagonist using cetrorelix) which were successfully used in patients with different ovarian reserve. It showed that using PPOS protocol in poor responders gave a comparable result when compared to the GnRH-ant protocol as regards the doses and duration of stimulation, the quality of oocytes, number of retrieved oocytes, M2 oocytes, injected oocytes, and class A embryos with a higher M2/total oocytes ratio. However, it gave a lower clinical pregnancy rate with no clear cause.

These findings coincides with Tzu-ChingKao[a] et al,[14] who underwent a single-center retrospective study, which enrolled the PORs (defined by the Bologna criteria) undergoing COS with PPOS or flexible GnRH antagonist protocol during January 2018 to December 2021. They compared the incidence of premature LH surge (LH > 10 mIU/mL) and the outcome of oocyte retrieval between the PPOS group and the GnRH antagonist group by using a total of 314 women with 54 in the PPOS group and 260 in the GnRH antagonist group. The PPOS group had lower incidence of premature LH surges compared with the GnRH antagonist protocol group (5.6% vs 16.9%, *P* value 0.035). There was no significant difference between the two groups regarding the number of oocytes retrieved (3.4 vs 3.8, *P* value 0.066) and oocyte retrieval rates (88.9% vs 88.0%, *P* value 0.711).

Also, our study coincides with Xiaoyu Tu et al,[15] who underwent a retrospective cohort study involving patients aged ≥35 years and DOR undergoing their first IVF/ICSI cycle: 139 and 600 patients underwent the PPOS and mild stimulation protocols, respectively. The primary outcomes were cumulative clinical pregnancy rate (CCPR) and cumulative live birth rate (CLBR). The secondary outcomes were the number of oocytes retrieved and top-quality embryos with the result of no significant difference of baseline characteristics between the two groups. Although a greater amount of total gonadotropin (1906.61 ± 631.04 IU vs.997.72 ± 705.73 IU, P<0.001) and longer duration of stimulation (9 (10–7) vs. 6 (8–4),P<0.001) were observed in the PPOS group, the number of retrieved oocytes (3 (6–2) vs.2(4–1), P<0.001) and top-quality embryos (1 (2–0) vs. 1 (2–0), P=0.038) was greater in the PPOS group than the mild stimulation group. However, it differs from our study as there was no significant difference in conservative CCPR, conservative CLBR, optimistic CCPR, and optimistic CLBR between the two groups (all P>0.05).

They concluded that the PPOS protocol is an effective alternative to the mild stimulation protocol for advanced-age patients with DOR, as it provides comparable reproductive outcomes and better control of premature LH surge. Further, more oocytes and top-quality embryos were obtained in the PPOS group, which had a positive association with conservative CCPR and CLBR.

On the other hand, in normal responder participants, GnRH antagonist protocol was associated with better results in most of IVF success rates - number of retrieved oocytes, M2 oocytes, injected oocytes, class A embryos, M2/total oocytes and clinical pregnancy rate - with the exception of the quality of oocytes which was not significantly better in participants received PPOS protocol.

Our study differs from Sule Yildiz et al,[16]**.** A retrospective cohort study was performed at private assisted reproductive center to compare between PPOS and traditional GnRH-ant which showed that the duration of stimulation was 11 (10–11) days in both groups. Total gonadotropin consumption was similar. Pituitary suppression was started on day 7 and lasted for 5 days in each group. There were no premature ovulations in any group. The

fPPOS yielded a significantly higher number of cumulus oocyte complexes than GnRH antagonist cycles (33 (21–39) vs. 26 (18–36), respectively). Likewise, the fPPOS generated significantly more metaphase II oocytes than GnRH antagonist cycles (24 (17–34) vs. 21 (15–28), respectively).

Furthermore, in higher responder participants GnRH-ant protocol and PPOS protocol had a comparable result in regard to the total number of retrieved oocytes, M2 oocytes, injected oocytes, class A embryos, percentage of good-quality embryos, and clinical pregnancy rate. Nevertheless, the PPOS protocol was superior as regards the quality of oocytes, while M2/total oocytes ratio was significantly higher in GnRH-ant protocol.

Our study coincides with Zhuo-Ni Xiao et al,[16] who performed a retrospective cohort study to investigate whether progestin-primed ovarian stimulation (PPOS) can be an alternative as gonadotrophin-releasing hormone antagonist (GnRH-ant) protocol for infertile women with polycystic ovary syndrome (PCOS) during IVF/ICSI. Basic characteristics such as infertility duration, age, and body mass index (BMI) were comparable in both groups. No significant difference was found in the number (mean ± SE) oocytes retrieved (20.2 ± 1.4 for PPOS vs 20.7 ± 0.6 for GnRH-ant protocol) or high-quality embryos (7.5 ± 0.8 for PPOS vs 7.6 ± 0.4 for GnRH-ant protocol) between the groups. The FSH dosage, ovarian stimulation duration, and ovarian hyperstimulation syndrome incidence were comparable between the groups. There was no significant difference in the clinical pregnancy rate (57.1% for PPOS vs 60.7% for GnRH-ant protocol) or live birth rate (42.9% for PPOS vs 46.4% for GnRH-ant protocol) of the first embryos transfer cycle between the two groups. In the cost-effectiveness analysis, the PPOS protocol was strongly dominant over the antagonist protocol.

Shaogen Guan et al,[1] searched published randomized controlled trials (RCTs) about PPOS on Cochrane Library, PubMed, Embase, and Web of Science to investigate the effectiveness of PPOS and its suitability for infertile patients with different ovarian reserve functions. Subgroup analysis was performed for different ovarian reserve patients which showed that the clinical pregnancy rates and live birth or ongoing pregnancy rates with the PPOS protocol were not different from those with the control group. In the diminished ovarian reserve (DOR) subgroup, the PPOS protocol had a lower rate of premature LH surge (RR = 0.03, 95% CI = 0.01 to 0.13, $p < 0.001$). The PPOS protocol had a lower rate of ovarian hyperstimulation syndrome (OHSS) (RR = 0.52, 95% CI = 0.36 to 0.76, $p < 0.001$, I^2 = 0.00%).

The secondary outcomes showed that the number of oocytes retrieved, MII oocytes, and viable embryos was higher than that of the control protocol in DOR patients ((MD = 0.33, 95% CI = 0.30 to 0.36, $p < 0.001$), (MD = 0.30, 95% CI = 0.27 to 0.33, $p < 0.001$), (MD = 0.21, 95% CI = 0.18 to 0.24, $p < 0.001$)) and normal ovarian reserve (NOR) patients ((MD = 1.41, 95% CI = 0.03 to 2.78, $p < 0.001$), (MD = 1.19, 95% CI = 0.04 to 2.35, $p < 0.001$), (MD = 1.01, 95% CI = 0.21 to 1.81, $p = 0.01$)).

Our before and after self-controlled study demonstrated that PPOS protocol couldn't only suppress the LH surge, but also improve the quantity and quality of oocytes through improving the folliculogenesis, particularly in patients with diminished ovarian reserve, suggesting that PPOS is a comparable protocol to GnRH antagonist and ideal ovarian stimulation protocol for patients with DOR.

Conclusion

This study demonstrated that PPOS protocol couldn't only suppress the LH surge, but also improve the quantity and quality of oocytes particularly in patients with diminished ovarian reserve, suggesting that PPOS is a comparable protocol to GnRH antagonist for patients

with DOR. PPOS showed poor clinical pregnancy rate when compared with GnRH-ant protocol for all types of patients according to the ovarian reserve.

Authors contributions: M.E owners the idea of the study, gave the stimulation protocols to the participants, OPU, and analyzed and interpreted the patient data regarding the studied parameters. D.E was responsible for writing the manuscript and data analysis. M.E and H.H were contributors in collecting the data. N.A MD was responsible for embryology laboratory findings. All authors read and approved the final manuscript.

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Disclosure of interest: The authors declare that they have no competing interests.

Ethical approval: This study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript is in line with the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals.

This study was approved from the Ethics committee, faculty of medicine, Alexandria university. The number is: 0306026

Informed consent: none

Data sharing: none

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Table 1. Descriptive analysis of the studied cases according to AMH in each group.

	AMH	No.	Mean ± SD.	Median (Min. – Max.)
Cetrotide	**<1.2**	**25**	0.72 ± 0.32	0.82 (0.19 – 1.13)
	1.2 - 3.5	**57**	2.17 ± 0.62	2.10 (1.20 – 3.48)
	>3.5	**18**	5.98 ± 2.33	4.50 (3.62 – 10.10)
	Total	**100**	2.49 ± 2.06	1.90 (0.19 – 10.10)
PPOS	**<1.2**	**30**	0.66 ± 0.29	0.71 (0.20 – 1.18)
	1.2 - 3.5	**44**	2.20 ± 0.66	2.31 (1.20 – 3.30)
	>3.5	**26**	6.0 ± 2.01	6.05 (3.76 – 12.10)
	Total	**100**	2.73 ± 2.34	2.25 (0.20 – 12.10)
Total	**<1.2**	**55**	0.69 ± 0.30	0.72 (0.19 – 1.18)
	1.2 - 3.5	**101**	2.18 ± 0.64	2.18 (1.20 – 3.48)
	>3.5	**44**	5.99 ± 2.12	5.90 (3.62 – 12.10)
	Total	**200**	2.61 ± 2.20	2.10 (0.19 – 12.10)

SD: Standard deviation.

Table 2. Comparison between the two studied groups according to different parameters in AMH <1.2 (n = 55).

	Cetrotide (n = 25)	**PPOS (n = 30)**	**Test of Sig.**	**p**
Age (/years)				
Mean ± SD.	36.3 ± 5.8	33.4 ± 6.8	t= 1.675	0.100
Median (Min. – Max.)	38 (26 – 45)	33 (20 – 42)		
Total Dose of stimulation				
Mean ± SD.	5.8 ± 0.4	6 ± 0.2	U= 297.5	0.023*
Median (Min. – Max.)	6 (5 – 6)	6 (5 – 6)		
Stimulation Days				
Mean ± SD.	10.1 ± 1.9	10.1 ± 2.2	U= 361.0	0.810
Median (Min. – Max.)	10 (7 – 15)	10 (7 – 15)		
Total Oocytes				
Mean ± SD.	5.2 ± 3.4	6.8 ± 4.8	U= 287.0	0.134
Median (Min. – Max.)	4 (1 – 11)	6 (2 – 21)		
M2 oocytes				
Mean ± SD.	4.6 ± 3.3	4.8 ± 5	U= 374.50	0.993
Median (Min. – Max.)	4 (1 – 10)	3 (1 – 21)		
Percentage M2/Oocytes				
Mean ± SD.	84.8 ± 16.9	65.3 ± 23.6	U= 199.00*	0.003*
Median (Min. – Max.)	90.9 (50 – 100)	66.7 (25 – 100)		
Injected oocytes				
Mean ± SD.	4.9 ± 3.4	5.9 ± 4.8	U= 324.0	0.385
Median (Min. – Max.)	4 (1 – 11)	5 (1 – 21)		
Quality of oocytes				
Poor	19 (76%)	13 (43.3%)	χ^2= 5.981*	^{MC}p= 0.014*
Good	6 (24%)	17 (56.7%)		
Class A embryos				
Mean ± SD.	2.5 ± 2.5	2.9 ± 2.3	U= 315.50	0.303
Median (Min. – Max.)	1 (0 – 8)	3 (0 – 9)		
% Quality of embryos				

Mean ± SD.	0.62 ± 0.42	0.74 ± 0.30	U= 329.00	0.416
Median (Min. – Max.)	0.83 (0 – 1)	0.80 (0 – 1)		
Pregnant				
No	9 (36%)	22 (73.3%)	χ^2= 7.728	0.005*
Yes	16 (64%)	8 (26.7%)		

SD: Standard deviation t: Student t-test U: Mann Whitney test

χ^2: Chi square test MC: Monte Carlo FE: Fisher Exact

p: p value for comparing between the two studied groups

*: Statistically significant at $p \leq 0.05$

Table 3. Comparison between the two studied groups according to different parameters in AMH 1.2 – 3.5 (n = 101)

	Cetrotide (n = 57)	**PPOS (n = 44)**	**Test of Sig.**	**p**
Age (/years)				
Mean ± SD.	31.2 ± 5.9	32 ± 5.4	t= 0.698	0.487
Median (Min. – Max.)	32 (17 – 45)	32 (21 – 42)		
Total Dose of stimulation				
Mean ± SD.	5.1 ± 0.7	5.3 ± 0.8	U= 1012.0	0.073
Median (Min. – Max.)	5 (3 – 6)	5.5 (3 – 6)		
Stimulation Days				
Mean ± SD.	9.6 ± 1.4	10 ± 1.8	U= 1091.5	0.254
Median (Min. – Max.)	9 (7 – 13)	10 (7 – 13)		
Total Oocytes				
Mean ± SD.	15.6 ± 5.6	11.3 ± 7	U= 722.5*	<0.001*
Median (Min. – Max.)	15 (6 – 26)	11.5 (2 – 31)		
M2 oocytes				
Mean ± SD.	13 ± 5.1	7.5 ± 4.7	U= 533.50*	<0.001*
Median (Min. – Max.)	13 (3 – 24)	6.5 (1 – 20)		
Injected oocytes				
Mean ± SD.	14.1 ± 5.2	9.3 ± 6	U= 592.0*	<0.001*
Median (Min. – Max.)	13 (3 – 24)	9 (2 – 30)		
Percentage M2/ Oocytes				
Mean ± SD.	82.5 ± 12.9	68.6 ± 18	U= 644.0*	<0.001*
Median (Min. – Max.)	85.7 (50 – 100)	71 (33.3 – 100)		
Quality of oocytes				
Poor	37 (64.9%)	25 (56.8%)	χ^2= 0.686	0.407
Good	20 (35.1%)	19 (43.2%)		
Class A embryos				
Mean ± SD.	7 ± 4.2	3.9 ± 3.1	U= 718.50	<0.001*
Median (Min. – Max.)	7 (0 – 16)	3.5 (0 – 13)		

% Quality of embryos				
Mean ± SD.	0.69 ± 0.26	0.64 ± 0.31	U= 1133.0	0.405
Median (Min. – Max.)	0.80 (0 – 1)	0.65 (0 – 1)		
Pregnant				
No	9 (15.8%)	26 (59.1%)	χ^2= 20.561*	<0.001*
Yes	48 (84.2%)	18 (40.9%)		

SD: Standard deviation t: Student t-test U: Mann Whitney test

χ^2: Chi square test MC: Monte Carlo FE: Fisher Exact

p: p value for comparing between the two studied groups

*: Statistically significant at $p \leq 0.05$

Table 4. Comparison between the two studied groups according to different parameters in AMH >3.5 (n = 44)

	Cetrotide (n = 18)	**PPOS (n = 26)**	**Test of Sig.**	**p**
Age (/years)				
Mean ± SD.	28.2 ± 5	28.5 ± 4	t= 0.272	0.787
Median (Min. – Max.)	28.5 (20 – 35)	27 (24 – 38)		
Total Dose of stimulation				
Mean ± SD.	3.8 ± 0.8	4 ± 1	U= 204.0	0.450
Median (Min. – Max.)	4 (3 – 5)	4 (2.5 – 5)		
Stimulation Days				
Mean ± SD.	9.7 ± 2.4	10.2 ± 1.6	U= 174.0	0.144
Median (Min. – Max.)	9 (7 – 16)	10 (8 – 14)		
Total Oocytes				
Mean ± SD.	23.2 ± 7.6	21.9 ± 11.2	U= 209.50	0.558
Median (Min. – Max.)	22 (13 – 47)	22 (7 – 49)		
M2 oocytes				
Mean ± SD.	18.1 ± 8.1	13.8 ± 8.9	U= 168.0	0.115
Median (Min. – Max.)	18 (4 – 33)	12 (1 – 32)		
Percentage M2/ Oocytes				
Mean ± SD.	75.6 ± 24.1	62 ± 23.8	U= 147.0*	0.038*
Median (Min. – Max.)	89.7 (30.8 – 96.3)	64.6 (8.3 – 96.6)		
Injected oocytes				
Mean ± SD.	19.3 ± 8	16.5 ± 9.2	U= 181.50	0.209
Median (Min. – Max.)	18 (6 – 39)	12 (6 – 36)		
Quality of oocytes				
Poor	18 (100%)	13 (50%)	χ^2= 12.774*	<0.001*
Good	0 (0%)	13 (50%)		
Class A embryos				
Mean ± SD.	10.4 ± 7	8.6 ± 5.9		0.388

Median (Min. – Max.)	11 (3 – 25)	7 (2 – 20)	U= 198.0	
% Quality of embryos				
Mean ± SD.	0.66 ± 0.25	0.73 ± 0.25	U= 200.0	0.416
Median (Min. – Max.)	0.74 (0.28 – 1.0)	0.80 (0.25 – 1.0)		
Pregnant				
No	4 (22.2%)	8 (30.8%)	χ^2= 0.392	^{FE}p= 0.733
Yes	14 (77.8%)	18 (69.2%)		

SD: Standard deviation t: Student t-test U: Mann Whitney test

χ^2: Chi square test MC: Monte Carlo FE: Fisher Exact

p: p value for comparing between the two studied groups

*: Statistically significant at $p \leq 0.05$

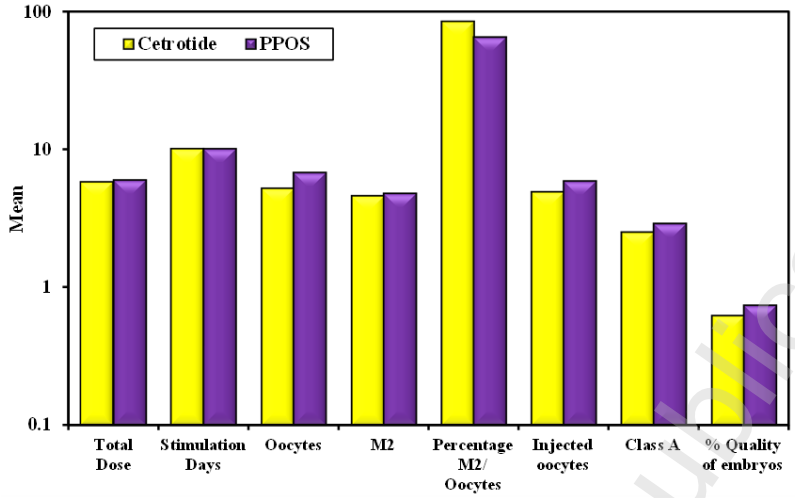

Figure (1): Comparison between the two studied groups according to different parameters in AMH <1.2 (n = 55)

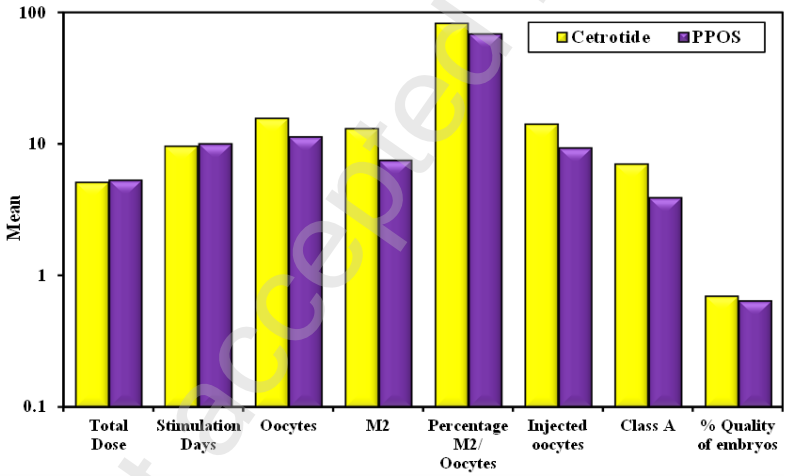

Figure (2): Comparison between the two studied groups according to different parameters in AMH 1.2 – 3.5 (n = 101)

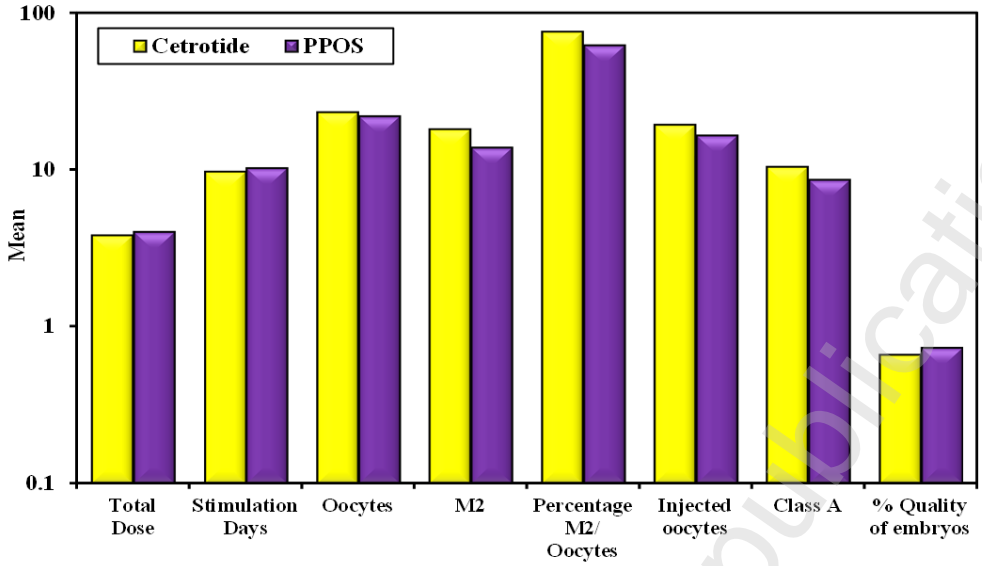

Figure (3): Comparison between the two studied groups according to different parameters in AMH >3.5 (n = 44)

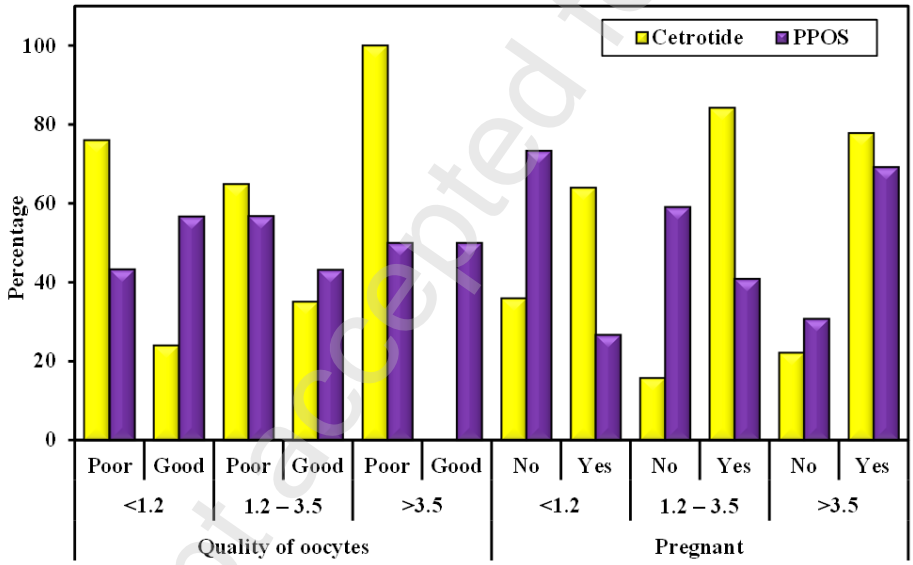

Figure (4): Comparison between the two studied groups according to different parameters