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Effects of Changing GnRH Agonist to Antagonist or Vice Versa on M2 Oocytes, Clinical Pregnancy and Live Birth Rates in Two Consequent IVF Cycles

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Abstract

Objectives: The objective of this study was to investigate the impact of changing the ovarian stimulation protocol from gonadotropin-releasing hormone (GnRH) agonists to antagonists, or vice versa, on the outcomes of in vitro fertilization (IVF) in the same groups of patients.

Materials and Methods: This study was a cohort study of women with infertility who had a history of two consequent IVF cycles due to an unsuccessful previous attempt and were recruited between 2016 and 2019. The patients were treated with either an agonist or antagonist protocol in the first or second round. They were categorized into two groups based on whether the second round was the same as the first one or different. The primary outcomes included the number of M2 oocytes, the number of transferred embryos, the chemical pregnancy rate, and the clinical pregnancy rate. The secondary outcome was the live birth rate. Statistical analyses were performed using SPSS version 26 software.

Results: A total of 39 women and 78 cycles with a history of infertility, with a mean age of 29.72 (5.36, SD), were evaluated in two groups: same (17, 43.6%) and different (22, 56.4%) protocols. Primary infertility was the most frequent type of infertility, recorded in 31 (79.6%) individuals. No significant differences were found between the two groups in terms of mean endometrial diameter ($P=0.820$), HCG administration ($P=0.069$), mean stimulation duration ($P=0.931$), mean total dose of administered gonadotropins ($P>0.05$), and embryo transfer types ($P= 0.051$). Also, no significant differences were found in the primary outcomes between the same and different protocol groups ($P>0.05$). The live birth rate also showed no significant difference as a secondary outcome ($P = 0.954$).

Conclusions: This study found no significant difference in IVF outcomes when switching between GnRH agonist and antagonist protocols or using the same protocol for consecutive rounds.

Keywords: Gonadotropin-Releasing Hormone, Pregnancy, In vitro fertilization

Introduction

Increased prevalence of infertility, decreased birth rates and advances in assisted reproductive technology (ART) have led to increasing use of such technologies worldwide, to the point that as high as 5% of children in several countries are now born with the help of medically assisted reproduction methods, e.g. in vitro fertilization (IVF) (1,2).

Prevention of premature Luteinizing hormone (LH) surge during ovarian stimulation is of great importance in ensuring embryo viability and survival and constitutes a key step in achieving a successful IVF. The introduction of gonadotropin-releasing hormone (GnRH) agonists for blockading premature LH surge has drastically increased the success rates of IVF, and these agents have been commonly employed for this purpose over the past decades. Such agents bind to GnRH receptors on the pituitary gland and, after an initial stimulation of LH and follicle stimulating hormone (FSH) release, inhibit the secretion of GnRHs and consequently result in desensitization (3,4). However, the use of GnRH agonists is associated with a delay until desensitization occurs, causes considerable side effects, and increases the risk of ovarian hyperstimulation syndrome (OHSS) (5,6).

In recent decades, the introduction of GnRH antagonists has provided an alternative to GnRH agonists for use in the IVF process. GnRH antagonists competitively block GnRH receptors, which leads to an immediate, rapid, dose-related inhibition of gonadotropin release (7,8). Employing such agents reduces costs, treatment duration,

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Key Messages

- Switching ovarian stimulation protocols does not impact IVF outcomes, providing flexibility for treatment.
- Consistent results suggest protocol choice can be individualized without compromising success rates.

and the risk of ovarian hyperstimulation syndrome, especially in hyper responders, thereby providing better patient compliance (9,10).

Several studies have compared the efficacy and side effects of GnRH agonists and antagonists, but they have yielded inconsistent results (11). In a meta-analysis, Al Inany et al concluded that GnRH agonist regimens are associated with slightly better pregnancy rates, compared with antagonist regimens (12), while in another meta-analysis by Kolibianakis et al, authors demonstrated that live birth rates do not significantly differ between GnRH agonists and antagonists (13). Moreover, few studies have assessed the effects of changing the stimulation protocol on IVF outcomes. In a recent study, Wald et al demonstrated that changing stimulation protocol does not result in improved laboratory outcomes. A slight improvement in laboratory outcomes was seen when the same stimulation protocol was repeated (1). Nonetheless, few data are available regarding the effects of changing the protocol from GnRH agonists to antagonists, or vice versa, on some of the outcomes of IVF and no one has assessed the change impact on live birth in two consequent IVF cycles. Considering the increasing use of cycles of IVF worldwide, and the need for increasing the efficacy of IVF protocols, especially in repeated cycles in one patient who are hopeful and interested in continuing infertility treatments, further research is warranted in this field.

This study aimed to investigate the effects of changing ovarian stimulation protocol on three items together for the first time: the number of M2 oocytes, rates of clinical pregnancy, and live birth in the same patients. Namely, we did not focus on the priority of GnRH agonist or antagonist protocol or compare them but the purpose was the changing effect from one to another in any direction on the same patient on M2, clinical pregnancy and live birth.

Materials and Methods

Study Design and Setting

This study employed a mixed retrospective and prospective cohort design from registered data and follow up the conceived women for live birth, at a single center, Milad Infertility Center in Mashhad, Iran.

Participants

Eligible patients included those with a history of infertility, had undergone two consecutive IVF cycles, and had experienced an unsuccessful attempt in the previous cycle. Exclusion criteria consisted of age over 42 years, incomplete records, IVF intervals exceeding 5 years, and a history of receiving regimens other than GnRH agonists or antagonists. This study included 39 infertile patients (78 cycles) from April 2016 and September 2019.

Exposure and Outcomes

The exposure of interest was the change in ovarian stimulation protocol between the two IVF cycles, either from agonist to antagonist or vice versa. The primary outcomes of this study included the number of M2 oocytes, the number of transferred embryos per transfer, the chemical pregnancy rate (positive beta-HCG in serum 16 days after transfer), and the clinical pregnancy rate (detectable fetal heart rate in transvaginal ultrasound). The secondary outcome was the live birth rate (the proportion of alive babies after 24 weeks of gestation) during follow-up. Patients who received the same regimen in both IVF cycles (agonist-agonist or antagonist-antagonist) formed the "same protocol" group. Those who received different regimens in their second IVF cycle (agonist-antagonist or antagonist-agonist) constituted the "different protocol" group. Thus, four sub-groups were formed: 1) agonist-agonist, 2) antagonist-antagonist, 3) agonist-antagonist, and 4) antagonist-agonist. The "same protocol" group included sub-groups 1 and 2, while the "different protocol" group consisted of sub-groups 3 and 4.

Data Collection and Measurements

Patient data such as age, body mass index (BMI), infertility duration, type and cause of infertility, IVF regimens, stimulation type and dose, endometrial line diameter, and type of transferred embryo (fresh or frozen transfer) were obtained from medical records and live birth in follow up.

Potential Bias

The study's mixed retrospective and prospective data collection may have introduced potential bias. However, efforts were made to minimize bias by adjusting the analysis for potential confounders.

Sample Size

The study included a total of 39 patients (78 cycles).

Statistical Analysis

Qualitative variables were summarized using absolute frequencies and percentages and compared with the chi-square test. Quantitative data were presented as mean ± standard deviation (SD) or median (interquartile range) and compared using the Mann-Whitney test. Statistical analyses were performed using SPSS software version 26 (SPSS Inc., Chicago, Illinois, USA). A P value of <0.05 was considered statistically significant.

Results

In total, 39 women and 78 cycles with a history of infertility,

and a mean age of 29.72 (5.36, SD), were evaluated in two groups of the same 17 (43.6%) and different 22 (56.4%) protocols. The same group included 5 (29.4%) agonist-agonist and 12 (70.6%) antagonist-antagonist. Also, the different group included 8 (36.4%) agonist-antagonist and 14 (63.6%) antagonist-agonist. The mean BMI of patients was 24.96 (3.47, SD) kg/m^2. The mean duration of infertility was 4.92 (3.77, SD) years. Primary infertility was the most frequent type of infertility, recorded in 31 (79.6%) individuals. Furthermore, the infertility cause in 17 (43.6%) cases was unexplained. Regarding demographic characteristics, there were no statistical differences between the two groups of study ($P>0.05$) (Table 1).

The mean endometrial diameter in the second round of IVF was 9.197 (1.12, SD) mm, and there were no statistical differences between the two groups ($P=0.820$). HCG was administrated for 28 (71.8%) participants as the most common type of trigger, and there was not any significant difference between the study groups ($P=0.069$). The mean stimulation duration was 10 (9-11) days which was not statistically different between the same and different groups ($P=0.931$). The mean total dose of administrated gonadotropins was 2188 IU (819.32, SD). The total dose of administrated gonadotropins did not differ significantly ($P>0.05$). Also, there were no significant differences between the two study groups regarding the embryo transfer types, including fresh embryo and freeze embryo types ($P=0.051$) (Table 1).

The primary results, which included the number of M2 oocytes, number of transferred embryos, chemical pregnancy rate, and clinical pregnancy rate, were compared between the same and different protocol groups. The results showed no significant differences between the two groups for any of the primary outcomes ($P>0.05$). Similarly, there were no significant differences in the live birth rate between the two groups as secondary result ($P=0.954$) (Table 2).

Discussion

Traditionally there is a thought that which is better for taking home a baby: agonist protocol or antagonist. But asides from the existing answers about the priority of one protocol over another or equivalent effect on outcomes in various studies (11-14), a new question for us in this article was about the patients who failed in the first IVF cycle: Which is better? *Whether "changing" the stimulation protocol in the second round or not?* If the patient has not a well-qualified response in the first IVF round then it would be better to change it for trying another manner for the prevention of premature LH surge or more qualified gametes.

In this study which is the first in its nature, we evaluated the effects of "changing" ovarian stimulation protocol on the outcomes in women with a history of infertility, including 17 (43.6%) women who received the same regimen (agonist-agonist and/or antagonist-antagonist) as their first IVF round (same protocol group), and 22

Table 1. The Baseline Characteristics of the Same and Different Groups

Characteristics		Same Protocol No. (%) or median (IQR) (n = 17)	Different Protocol No. (%) or median (IQR) (n = 22)	*P* Value
Age (y)		30 (5.22)	29.8 (5.47)	0.889[a]
BMI (kg/m^2)		25.34 (3.70)	24.53 (3.00)	0.413[a]
Infertility duration (y)		4 (2.87-6)	4 (2-5)	0.391[b]
Infertility type	Primary	15 (88.2)	16 (72.7)	0.234[b]
	Secondary	2 (11.8)	6 (27.3)	
Infertility causes	Male cause of infertility	4 (23.5)	4 (18.2)	0.933[b]
	Tubal factor	2 (11.8)	2 (9.1)	
	Ovarian factor	3 (17.6)	3 (13.6)	
	Mix	2 (11.8)	2 (9.1)	
	Unexplained factor	6 (35.3)	11 (50)	
Endometrial diameter (mm)		8.65 (8-10)	9 (7.45-10)	0.820[b]
Trigger type	HCG	9 (52.9)	19 (86.4)	0.069[c]
	Deca	2 (11.8)	1 (4.5)	
	Deca + HCG	6 (35.3)	2 (9.1)	
Stimulation duration (days)		10 (9-11)	10 (9-11)	0.931[b]
Gonadotropin dose (IU)		2139.70 (949.83)	2226.13 (723.97)	0.749[a]
Embryo transfer type	ET	8 (47.1)	17 (77.3)	0.051[b]
	FET	9 (52.9)	5 (22.7)	

BMI, body mass index; ET, fresh embryo transfer; FET: freeze embryo transfer.
[a] Independent sample test; [b] Mann-Whitney U test; [c] Chi-square.

Table 2. Comparison of Primary and Secondary Outcomes Between the Same and Different Groups

Item	Total Mean (min-max) N = 39	Same Mean (min-max) n = 17	Different Mean (min-max) n = 22	*P* Value
Number of M2 oocyte	7 (4-11)	9 (5-14)	5.50 (3.75-9.25)	0.065[a]
Chemical pregnancy rate (%)	25.2 (0-100)	25(0-100)	25.3 (0-100)	0.826[b]
Number of transferred embryo	2 (2-3)	2 (1-3)	2 (2-3)	0.812[b]
Clinical pregnancy rate (%)	23.53 (0-100)	22.12(0-100)	24.61(0-100)	0.937[b]
Live birth rate (%)	19.73(0-100)	17.36(0-100)	21.50(0-100)	0.754[b]

BMI, body mass index; ET, fresh embryo transfer; FET: freeze embryo transfer.
[a] Mann-Whitney U test; [b] Chi-square.

(56.4%) women who received a regimen different (agonist-antagonist and/or antagonist-agonist) from their first IVF round (different protocol group). Both groups were matched in terms of their demographic characteristics. The primary results in the second IVF round included the number of M2 oocytes, number of transferred embryos, chemical pregnancy and clinical pregnancy rate, which were not significantly different between the two groups. Also, live birth rates, as the secondary outcome, were not significantly different between groups.

Several studies have compared the efficacy of GnRH agonists and antagonists in IVF, but they have yielded inconsistent results (11). The results of a meta-analysis by Al Inany indicate that the use of GnRH agonists, compared with antagonists, leads to slightly better pregnancy rates (12). However, in another meta-analysis, Kolibianakis et al reported similar live birth rates between GnRH agonist and antagonist regimens (13). According to these studies, GnRH agonist and antagonist protocols seem to have comparable effectiveness. Indeed, a study on first-time IVF cycles in good respondents reported similar pregnancy and live birth rates for either GnRH agonists or antagonists (14). The main goal of the current research was investigating the effects of "changing" ovarian stimulation protocol on the outcomes of two consequent IVF cycles; however, we also observed a similar efficacy between GnRH agonists and antagonists, which is in line with the findings a previous studies.

In another study by Yang et al on more than 18 thousand Chinese women who had completed their first IVF cycle, the cumulative live birth rate (CLBR) in the GnRH antagonist group was lower than that of the GnRH agonist group in suboptimal responders, but not in other patients (11).

Stimpfel et al. compared three ovarian stimulation protocols in patients with good prognoses (GnRH agonist, GnRH antagonist, or GnRH antagonist mild protocol in combination with gonadotropins). They reported no differences in live birth rate and miscarriages between the evaluated protocols, but rates of pregnancy and CLBR per cycle were significantly higher in the GnRH antagonist mild protocol (15). Contrarily, findings from several randomized clinical trials indicate that the antagonist protocol results in a lower number of retrieved oocytes, and subsequently, lower pregnancy rates compared to the long agonist protocol (18).

However, it has been argued that antagonist agents are sometimes incorrectly viewed as second-line treatment, and are more likely to be used in older women and patients with previously unsuccessful attempts, which could potentially lead to confounding bias. A study by Griesinger et al performed in Germany revealed that the proportion of GnRH antagonist cycles increases with consecutive treatment attempts, from 23% in the first to 48% in the tenth treatment (16). Similarly, Engel et al reported that GnRH antagonists are more often used in higher ranks of treatment and older patients (17).

As it is apparent that for many years the golden purpose of articles had been comparing GnRH agonist and antagonist together and priority of one protocol over another or vice versa. Moreover, few studies have focused on evaluating the effects of changing the stimulation protocol in consequent IVF cycles outcomes on the same group of patients in which they only focused on laboratory outcomes (1) or convert the GnRH agonist protocol to antagonist only (18), but not vice versa.

Recently, Wald et al showed that changing stimulation protocol is related to slightly less oocyte count, and careful attention must be done before switching protocols (1). Although in our study, concerning M2 oocytes numbers, there was no statistical difference between the same and different groups, it seems that in the same group with no changing stimulation protocol, the number of M2 oocytes were more than in different protocol groups which means that however there was no statistical difference in M2 rate but the difference between the same group and different group was noticeable in our study (9 M2 in opposite 5.5 M2). Big data indicates that a higher number of oocytes has better CLBR per started cycles and it is the core stone for the novel POSEIDON (Patient-Oriented Strategies Encompassing Individualized Oocyte Number) criteria for "low prognosis" patients undergoing ART in recent years which suggests a prognostic plan to estimate the CLBR per started cycle based on female age and oocyte

number (19). Regarding this new manner, it seems better not to change the protocols in repeated IVF cycles however a greater number of patients in a larger study can make a more definitive result not only about M2 rate, but also on pregnancy rates. In another study, Lai et al. retrospectively compared the efficacy of GnRH agonist and antagonist protocols on the same patients in IVF. Each of the patients had at least one agonist long protocol and one antagonist protocol. They found that using antagonist protocol significantly increases the rates of implantation and clinical pregnancy, and concluded that GnRH antagonists are more likely to improve the pregnancy outcomes of IVF in patients with multiple previous failures (18). In our study, the main question was not the priority of one protocol over another but whether it was the changing protocols inter cycles or not. Given the fact that our dataset only contained a limited number of patients, future studies with more subjects and stimulation cycles specially randomized controlled trials (RCTs), would be necessary to further confirm those observations.

Conclusions

This study, found that there is no statistical difference in number of M2 oocytes,number of transferred embryos, chemical pregnancy rate, clinical pregnancy rate and live birth rate between "changing" the ovarian stimulation protocol (from agonist to antagonist or vice versa) or "not to change" in two consecutive IVF cycles.

Authors' Contribution

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Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The protocol of the current study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS.MEDICAL.REC.1400.124).

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References

1. Wald K, Hariton E, Morris JR, et al. Changing stimulation protocol on repeat conventional ovarian stimulation cycles does not lead to improved laboratory outcomes. Fertil Steril. 2021;116(3):757-765. doi:10.1016/j.fertnstert.2021.04.030
2. Hanevik HI, Hessen DO. IVF and human evolution. Hum Reprod Update. 2022;28(4):457-479. doi:10.1093/humupd/dmac014
3. Cao X, Chang HY, Xu JY, et al. The effectiveness of different down-regulating protocols on in vitro fertilization-embryo transfer in endometriosis: a meta-analysis. Reprod Biol Endocrinol. 2020;18(1):16. doi:10.1186/s12958-020-00571-6
4. Del Gadillo JC, Siebzehnrübl E, Dittrich R, Wildt L, Lang N. Comparison of GnRH agonists and antagonists in unselected IVF/ICSI patients treated with different controlled ovarian hyperstimulation protocols: a matched study. Eur J Obstet Gynecol Reprod Biol. 2002;102(2):179-183. doi:10.1016/s0301-2115(01)00580-2
5. Depalo R, Jayakrishan K, Garruti G, et al. GnRH agonist versus GnRH antagonist in in vitro fertilization and embryo transfer (IVF/ET). Reprod Biol Endocrinol. 2012;10:26. doi:10.1186/1477-7827-10-26
6. Rizk B, Smitz J. Ovarian hyperstimulation syndrome after superovulation using GnRH agonists for IVF and related procedures. Hum Reprod. 1992;7(3):320-327. doi:10.1093/oxfordjournals.humrep.a137642
7. Cheung LP, Lam PM, Lok IH, et al. GnRH antagonist versus long GnRH agonist protocol in poor responders undergoing IVF: a randomized controlled trial. Hum Reprod. 2005;20(3):616-621. doi:10.1093/humrep/deh668
8. Huirne JA, Homburg R, Lambalk CB. Are GnRH antagonists comparable to agonists for use in IVF? Hum Reprod. 2007;22(11):2805-2813. doi:10.1093/humrep/dem270
9. Xu Y, Zhang YS, Zhu DY, Zhai XH, Wu FX, Wang AC. Influence of GnRH antagonist in reproductive women on in vitro fertilization and embryo transfer in fresh cycles. Biomed Rep. 2019;10(2):113-118. doi:10.3892/br.2018.1176
10. Wang R, Lin S, Wang Y, Qian W, Zhou L. Comparisons of GnRH antagonist protocol versus GnRH agonist long protocol in patients with normal ovarian reserve: a systematic review and meta-analysis. PLoS One. 2017;12(4):e0175985. doi:10.1371/journal.pone.0175985
11. Yang J, Zhang X, Ding X, Wang Y, Huang G, Ye H. Cumulative live birth rates between GnRH-agonist long and GnRH-antagonist protocol in one ART cycle when all embryos transferred: real-word data of 18,853 women from China. Reprod Biol Endocrinol. 2021;19(1):124. doi:10.1186/s12958-021-00814-0
12. Al-Inany HG, Youssef MA, Aboulghar M, et al. Gonadotrophin-releasing hormone antagonists for assisted reproductive technology. Cochrane Database Syst Rev. 2011(5):CD001750. doi:10.1002/14651858.CD001750.pub3
13. Kolibianakis EM, Collins J, Tarlatzis BC, Devroey P, Diedrich K, Griesinger G. Among patients treated for IVF with gonadotrophins and GnRH analogues, is the probability of live birth dependent on the type of analogue used? A systematic review and meta-analysis. Hum Reprod Update. 2006;12(6):651-671. doi:10.1093/humupd/dml038
14. Johnston-MacAnanny EB, DiLuigi AJ, Engmann LL, Maier DB, Benadiva CA, Nulsen JC. Selection of first in vitro fertilization cycle stimulation protocol for good prognosis patients: gonadotropin releasing hormone antagonist versus agonist protocols. J Reprod Med. 2011;56(1-2):12-16.
15. Stimpfel M, Vrtacnik-Bokal E, Pozlep B, Virant-Klun I. Comparison of GnRH agonist, GnRH antagonist, and GnRH antagonist mild protocol of controlled ovarian hyperstimulation

in good prognosis patients. Int J Endocrinol. 2015;2015:385049. doi:10.1155/2015/385049
16. Griesinger G, Felberbaum R, Diedrich K. GnRH antagonists in ovarian stimulation: a treatment regimen of clinicians' second choice? Data from the German national IVF registry. Hum Reprod. 2005;20(9):2373-2375. doi:10.1093/humrep/dei086
17. Engel JB, Griesinger G, Schultze-Mosgau A, Felberbaum R, Diedrich K. GnRH agonists and antagonists in assisted reproduction: pregnancy rate. Reprod Biomed Online. 2006;13(1):84-87. doi:10.1016/s1472-6483(10)62019-6
18. Lai Q, Zhang H, Zhu G, et al. Comparison of the GnRH agonist and antagonist protocol on the same patients in assisted reproduction during controlled ovarian stimulation cycles. Int J Clin Exp Pathol. 2013;6(9):1903-1910.
19. Esteves SC, Alviggi C, Humaidan P, et al. The POSEIDON criteria and its measure of success through the eyes of clinicians and embryologists. Front Endocrinol (Lausanne). 2019;10:814. doi:10.3389/fendo.2019.00814