Original Article

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Efficacy of Dual Triggering Versus hCG in Consecutive IVF Cycles in Women with Poor Ovarian Response

Düşük Overyan Yanıtı Olan Kadınlarda Art Arda IVF Sikluslarında Dual Tetiklemenin hCG'ye Karşı Etkinliği

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ABSTRACT

Objective: Bolus administration of gonadotrophin-releasing hormone (GnRH) analogs (GnRH-a) mimics physiological ovulation and reduces the risk of ovarian hyperstimulation syndrome. Adding GnRH-a to human chorionic gonadotropin (hCG) (dual triggering) to induce final oocyte maturation stimulates the luteinizing hormone surge and improves in vitro fertilization (IVF) outcomes by decreasing the rates of immature oocytes. The aim of this study was to compare the effects of hCG and dual triggering on cycle outcomes in patients with poor ovarian response (POR) in consecutive IVF cycles.

Methods: This retrospective cohort study included 54 patients with POR who underwent two consecutive IVF treatments within two years at the IVF Unit of Yeditepe University Hospitals. Two different triggering protocols (dual and hCG) were compared in terms of cycle outcomes.

Results: No statistically significant difference was found between the two triggering protocols in different IVF cycles of the same patients in terms of the total retrieved oocyte in the oocyte pick-up (dual: 3.72±2.96 vs hCG: 3.61±2.13, p>0.05), mature oocyte (dual: 2.88±2.40 vs hCG: 2.94±1.95, p>0.05), and normally fertilized oocyte (2 pronuclei) oocyte (dual: 2.83±1.91 vs hCG: 2.81±1.69, p>0.05) counts. No significant results were obtained

ÖZ

Amaç: Gonadotropin salgılatıcı hormon (GnRH) analoglarının (GnRH-a) bolus olarak uygulanması, fizyolojik ovulasyonu taklit eder ve ovaryen hiperstimülasyon sendromu riskini azaltır. Son oosit olgunlaşmasını indüklemek için insan koryonik gonadotropine (hCG) GnRH-a eklenmesi [ikili (dual) tetikleme], luteinize edici hormon (LH) dalgalanmasını uyarıp olgunlaşmamış oosit oranlarını azaltarak in vitro fertilizasyon (IVF) sonuçlarını iyileştirir. Bu çalışmada, düşük ovaryen yanıtı (DOY) olan olgularda hCG ve ikili tetiklemenin siklus sonuçlarına etkisinin hastaların ardışık IVF sikluslarında karşılaştırılması amaçlanmıştır.

Yöntemler: Bu retrospektif kohort çalışmasına, Yeditepe Üniversitesi Hastaneleri IVF Ünitesi'nde iki yıl içinde iki ardışık IVF tedavisi uygulanmış 54 DOY tanılı olgu dahil edilmiştir. İki farklı tetikleme protokolü (dual ve hCG) siklus sonuçları açısından karşılaştırılmıştır.

Bulgular: Aynı hastaların farklı IVF sikluslarında iki farklı tetikleme protokolü arasında oosit toplama işleminde (OTİ) alınan toplam oosit (değerleri: 3.72±2.96 ve hCG: 3.61±2.13, p>0.05), matür oosit (değerleri: 2.88±2.40 ve hCG: 2.94±1.95, p>0.05) ve normal olarak döllenen (2 pronükleus) oosit (dual: 2.83±1.91 ve hCG: 2.81±1.69 vs, p>0.05) sayılarında istatistiksel olarak anlamlı bir fark izlenmemiştir. Farklı tetikleyici grupları arasında pozitif

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ABSTRACT

in terms of positive β-hCG, implantation, clinical pregnancy, ongoing pregnancy, and abortion rates between different trigger groups (p>0.05).

Conclusion: Our findings showed that the different triggering methods did not significantly affect the cycle outcomes.

Keywords: Poor ovarian response, dual triggering, IVF, oocyte maturation, fertilization

ÖZ

β-hCG, implantasyon, klinik gebelik, devam eden gebelik ve abort oranları açısından anlamlı bir fark bulunamamıştır (p>0.05).

Sonuç: Bulgularımız, farklı tetikleme yöntemlerinin IVF siklus sonuçlarını önemli ölçüde etkilemediğini göstermiştir.

Anahtar Kelimeler: Düşük ovaryen yanıt, ikili tetikleme, IVF, oosit matürasyonu, fertilizasyon

Introduction

For many years, human chorionic gonadotropin (hCG) has been widely used in vitro fertilization (IVF) treatments to stimulate oocyte maturation and ovulation triggering by mimicking reproductive physiology and influencing the natural luteinizing hormone (LH) surge. Luteotropic effects of hCG, with its long half-life, result in an intrauterine environment that is optimal for pregnancy (1,2). The extended half-life of hCG is, however, a key contributor to the increased risk of ovarian hyperstimulation syndrome (OHSS) (3,4). Different medical approaches have been tried to prevent OHSS in oocyte pick-up (OPU) cycles, but no effective treatment method has been proven. To lower the incidence of OHSS, Shapiro et al. (5) put forward the administration of low-dose hCG and gonadotrophin-releasing hormone (GnRH) analogs (GnRH-a) on the same day of oocyte retrieval, so-called dual triggering. Shortly after, it was shown that patients with a history of recurrent empty follicles and immature oocyte rates achieved better results after dual triggering in terms of mature oocytes [metaphase II (MII)]. In another study, Griffin et al. (6) observed that by dual triggering, more mature oocytes were retrieved from the patients who had more than 25% immature oocytes in their previous OPU cycles.

Studies until today aimed to investigate the effects of dual triggering to prevent OHSS in patients who had high, normal, or low responses to controlled ovarian hyperstimulation (COH). Through those studies, the effect of dual triggering on oocyte maturation has been brought to light. While investigating the live birth rates in patients who had normal responses to dual triggering, Lin et al. (7) found a statistically significant increase in the total number of oocytes and the number of mature (MII) oocytes retrieved. Recently, the first prospective, double-blinded, randomized controlled study on normal responders to dual triggering (n=155) demonstrated the increase in oocytes per follicle, MII oocytes, and total oocyte counts, with no reported cases of OHSS (8). However, the effects of different triggering methods on the same poor responder patients' oocytes have not been evaluated and compared before. Our aim in this study is to apply two different triggering methods in consecutive COH cycles to poor responder patients and compare the total, mature (MII), and normally fertilized [2 pronuclei (2PN)] oocyte counts as well as cycle outcomes after each treatment.

Methods

Patient Selection

A total of 54 patients who had two consecutive treatment cycles within two years with different triggering protocols each were included in this single-centered, retrospective cohort study that was conducted at the IVF Unit of Yeditepe University Hospitals, İstanbul, Türkiye, between 2014 and 2021. The Ethical Committee of Yeditepe University approved the study protocol (approval no: 2022/12, date: 17.03.2022). The protocol was consistent with the World Medical Association Declaration of Helsinki's "Ethical Principles for Medical Research Involving Human Subjects". All participants received medical approval from their physicians and gave written, informed consent before they participated in the study. Every patient in this study was categorized as having poor ovarian response (POR) based on the Bologna Criteria, which were created in 2011. For the purposes of this study, patients were deemed to have POR if they met two of the three criteria outlined in the Bologna definition, which offer a precise framework for diagnosing POR.

Women 40 years of age or older meet the first criterion for the diagnosis of POR. Other risk factors that can make people more susceptible to a decreased ovarian reserve were also taken into account. These variables could include a history of radiation, chemotherapy, or ovarian surgery. The second criterion relies on past reproductive history. Specifically, POR is defined as the retrieval of 3 or fewer oocytes after 1 or more cycles of ovarian stimulation based on a conventional stimulation protocol. An inadequate number of oocytes retrieved with adequate stimulation is consistent with a diminished ovarian reserve, with an inability to respond adequately to traditional IVF protocols. Laboratory assessments of ovarian reserve include the third diagnostic criterion. If a patient's anti-Müllerian hormone (AMH) levels were <0.5-1.1 ng/mL or their antral follicle count (AFC) was ≤5-7, they were deemed to fit this condition. Since both AFC and AMH levels are correlated with the number and quality of a woman's remaining oocytes, these indicators are commonly accepted in clinical practice as being suggestive of a reduced ovarian reserve (5).

Among all patients with POR, patients who were treated with hCG mono for ovulation induction in their first COH protocol and who used dual trigger for the next, that is, consecutive

treatment, were included in this study. Patients who had not met the above-given criteria, and identified a genetic mutation regarding the oocyte maturation or had more than two years between those consecutive treatment cycles were excluded from the study.

Treatment Protocol

Patients were evaluated ultrasonographically on the 2nd or 3rd day of their menstrual cycle. COH was initiated to patients who did not have any contraindications for treatment. Appropriate dosage was determined according to the patients' characteristics. Recombinant follicle-stimulating hormone (FSH) (GONAL-f, merck-serono) and/or human menopausal gonadotropin (merional, IBSA) were/was used for COH.

Patients who were scheduled for flexible GnRH-antagonist protocol for pituitary suppression were evaluated ultrasonographically on the 5th or 6th days of their menstrual cycles. GnRH-antagonist (cetrotide, merck-serono or orgalutran, MSD) 0.25 mg subcutaneously daily was administered if at least one follicle was ≥14 mm. Ultrasonography was performed at regular intervals to follow up the follicular developments. When at least two dominant follicles of 17 mm were observed; standard 10.000 IU hCG (pregnyl 10.000 IU, merck or ovitrelle 500 mcg, Merck) or dual triggering was planned. Dual triggering was accomplished by the simultaneous injections of 10.000 IU hCG (pregnyl 10.000 IU, merck or ovitrelle 500 mcg, merck) and 0.2 mg triptorelin acetate (gonapeptyl, ferring). Three of the individuals who met the criteria had their ovulation induction induced by 500 mcg of choriogonadotropin alfa in the hCG mono arm. For the remaining 51 individuals, hCG was administered. To induce ovulation in each patient, 10.000 IU hCG and 0.2 mg triptorelin acetate were administered in successive doses. OPU was performed 36-38 hours after ovulation triggering.

On the second or third day of the menstrual cycle, oral estradiol (E2) (estrofem® 6 mg) was given to prepare the endometrium. When the endometrial thickness surpassed 7 mm on day 12 or 13, 400 mg of intravaginal progesterone (progestan 200 mg) and 50 mg of subcutaneous progesterone (prolutex® 25 mg) were administered daily. A frozen embryo from day five was thawed and transferred on day six of the progesterone regimen. Up to six weeks after conception, luteal-phase support was maintained using oral E2, subcutaneous, and intravaginal progesterone.

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences software (SPSS, version 25, IBM Corp, Armonk, NY, USA). Non-parametric Wilcoxon signed ranks test was used for the comparisons of two different triggering protocols that were applied to the same patients. A chi-square test was performed for the comparisons of IVF results of fresh embryo transfers between two different triggering methods. A p-value of <0.05 was considered statistically significant. The primary outcome was the effect of dual triggering on oocyte maturation, hence on mature oocyte counts.

Results

The comparison of demographics and clinical characteristics of the patients in each treatment is given in Table 1. The vast majority of patients [77.8% (n=42)] had primary infertility and the remaining ones [22.2% (n=12)] had secondary infertility. The average infertility duration of patients was 6.81±4.89 (mean ± standard deviation) years. Other concomitant pathologies to POR were advanced maternal age [44.4% (n=24)], endometrioma [3.7% (n=2)], absolute tubal factor [3.7% (n=2)], and male factor [3.7% (n=2)]. Although a statistically significant difference was observed between the ages of patients in their consecutive IVF cycles (dual vs hCG triggering), it did not have a clinical significance (38.80±3.72 vs 38.17±3.75, p<0.001, respectively). AMH (ng/mL) levels and body mass index (BMI) (kg/m^2) were found similar between dual and hCG triggering groups (AMH: 0.4565±0.30 vs 0.4561±0.30, BMI: 29.86±3.76 vs 29.24±4.23, respectively). Basal FSH and E2 levels were not statistically significant between the two treatment groups (p>0.05). Total gonadotropin doses were higher in dual triggering group than hCG triggering group (3955.56±963.78 vs 3619.81±911.27, p=0.011), however, stimulation days were similar (10.24±1.45 vs 9.98±1.18, respectively). No statistically significant difference was found between the dual triggering protocol and hCG protocol in different assisted reproductive technology cycles of the same patients in terms of total retrieved oocytes (dual: 3.72±2.96 vs hCG: 3.61±2.13, p>0.05) and mature oocytes (dual: 2.88±2.40 vs hCG: 2.94±1.95, p>0.05) (Table 1).

Of 108 COH cycles (54 cases in each group), no oocyte was obtained in six (5.5%) [hCG: 1 (1.9%), dual: 5 (9.3%)], no MII oocyte was obtained in two (1.9%) (both patients were in hCG group), no 2PN was observed in three (2.8%) [hCG:1 (1.9%), dual: 2 (3.7%)], oocyte vitrification was performed in six (5.5%) [3 (5.5%) in each group], cleavage arrest occurred in sixteen (15.2%) [8 (14.8%) in each group], total embryo freezing was applied in forty-one (38%) [hCG:21 (38.9%), dual: 20 (37%)] and embryos transfer was applied in forty-three (39.8%) [hCG: 23 (42.6%), dual: 20 (37%)] cases.

Regarding the normal fertilization, no statistical significance was observed in terms of 2PN oocyte count between two trigger methods in the COH cycles of 47 patients (hCG: 2.81±1.69 vs dual: 2.83±1.91, p>0.05) (Table 1).

When we evaluated the fresh embryo transfer results according to different trigger methods, rates of positive β-hCG, implantation, clinical pregnancy, and ongoing pregnancy were higher, while biochemical and clinical miscarriage rates were lower in the dual trigger group than hCG group. However, the differences were not found statistically significant (p>0.05). Similarly, the day of transfers and number of transferred embryos were not found statistically significant (p>0.05) (Table 2). Of 54 patients only eight patients (14.8%) had embryo transfers in both IVF cycles with different trigger methods. In the hCG triggering group, only two of them had positive β-hCG (25%). The implantation rate of 15 embryos that were transferred was 13.3%. However,

Table 1. The comparison of demographics, clinical characteristics and cycle outcomes of the patients in their COH cycles with dual vs hCG trigger

(n=54)	Dual triggering	hCG triggering	p-value
Age (years)	38.80±3.72	38.17±3.75	**<0.001**
AMH (ng/mL)	0.4561±0.30	0.4565±0.30	NS
BMI (kg/m²)	29.86±3.76	29.24±4.23	NS
Basal FSH (mIU/mL)	10.74±4.10	9.71±3.85	NS
Basal E2 (pg/mL)	36.76±17.64	43.06±19.52	NS
Total gonadotropin dose (units)	3955.56±963.78	3619.81±911.27	**0.011**
Duration of stimulation (days)	10.24±1.45	9.98±1.18	NS
Total retrieved oocytes (n)	3.72±2.96	3.61±2.13	NS
MII oocyte (n) (%)	2.88±2.40 (77.4%)	2.94±1.95 (81.4%)	NS
2PN oocyte (n)	2.83±1.91	2.81±1.69	NS

Values were given as mean ± standard deviation (SD)
Wilcoxon signed rank test was applied for the two related sample comparisons. Bold values are statistically significant (p<0.05)
COH: Controlled ovarian hyperstimulation, hCG: Human chorionic gonadotropin, AMH: Anti-Mullerian hormone, BMI: Body mass index, FSH: Follicle-stimulating hormone, E2: Estradiol hormone, MII: Metaphase II, NS: Statistically non-significant, n: Number, 2PN: 2 pronuclei

Table 2. Comparing the fresh embryo transfer results between hCG and dual triggering protocols

	Dual triggering (n=20)	hCG triggering (n=23)	p-value
β-hCG positive %	8/20 (40%)	7/23 (30.4%)	NS
Implantation %	6/32 (18.8%)	6/40 (15.0%)	NS
Clinical pregnancy %	8/20 (40%)	6/23 (26.1%)	NS
Biochemical miscarriage %	0/8	1/7 (14.3%)	-
Clinical miscarriage %	4/8 (50%)	5/6 (71.4%)	NS
Ongoing pregnancy %	4/20 (20%)	1/23 (4.3%)	NS
Day of transfer (n)			
Day 2/3	14	18	NS
Day 4	-	2	
Day 5	6	3	
Number of the embryos transferred	1.60±0.50	1.73±0.44	NS

Chi-square test was used for the comparisons. p<0.05 was accepted as statistical significance
NS: Non-significant, hCG: Human chorionic gonadotropin

all these pregnancies resulted with clinical miscarriage. In the dual triggering group, four patients had positive β-hCG (50%). The implantation rate was calculated as 30.8% with a total number of 13 embryos that were transferred. Only one of the four pregnancies was ongoing (12.5%), remaining three resulted with clinical miscarriage.

Discussion

GnRH-a have shown promise in reducing the risk of OHSS associated with hCG triggering. The concept of dual triggering, combining GnRH-a and hCG, has gained attention for its potential to enhance IVF outcomes, especially in cases of POR.

While previous studies have indicated positive effects of dual triggering on oocyte maturation and overall IVF success, the current study underscores that such benefits might not extend uniformly to patients with POR.

As the landscape of IVF continues to evolve, further investigation is warranted to fully understand the nuances of triggering methods in different patient populations. By shedding light on the specific circumstances of poor responder patients, this study contributes to the broader dialogue surrounding IVF protocols and the optimization of outcomes. However, it is important to note that this study mainly focused on oocyte-related outcomes due to the limited number of embryo transfers in our study groups (hCG: 23, dual: 20 embryo transfers). On the other hand, the potential impact on implantation, ongoing pregnancies, and live birth rates warrants additional exploration, especially considering the potential effects of GnRH-a triggering on luteal phase support and endometrial receptivity.

In Shapiro's research, the study group consisted of high-responder patients. In ovulation induction, the lowest doses of hCG paired with GnRH agonists were modified for each patient based on their weight and the probability of developing OHSS. In the study, there is no uniform dose application. There is no other group or treatment approach that can be used to compare the total number of oocytes collected, the number of mature oocytes, or fertilization rates (5).

Gonen et al. (9) demonstrated the physiological effects of GnRH-a on follicle maturation and oocyte triggering. Since the LH surge occurred within natural limits, the risk of OHSS was shown to be lower with GnRH-a triggering. Later studies demonstrated that endogenous LH surge and the following increase in FSH due to GnRH-a triggering also resulted in increased numbers of MII oocytes (10,11). However, due to inadequate corpus luteum formation, GnRH-a triggering is known to be associated with luteal phase deficiencies. Progesterone support and endometrial stabilization cannot be provided which may result in poor implantation rates and early pregnancy losses in fresh embryo transfers (10,12-14). In a systematic review, it was demonstrated that the administration of GnRH-a as a single triggering agent had negative effects on implantation rates, ongoing pregnancy rates, and live birth rates (15). Adding hCG or E2 and progesterone combinations to the treatment are some of the preventive measures that have been tried over the past years to solve this problem. Freezing all embryos and postponing embryo transfers are some of the common approaches in GnRH-a triggered cycles.

In a study conducted by Griffin (16), in 2012, he divided the patients into two groups and used GnRH agonist (1 mg leuprolide acetate) alone for ovulation induction in one group and GnRH agonist (1 mg leuprolide acetate and 1000 IU hCG) in combination with low dose hCG for ovulation induction in the other. The effects of GnRH-a triggering of high-responder patients, in contrast, showed a positive relationship of GnRH-a triggering with ongoing pregnancy rates and live birth rates without any OHSS case.

Schachter et al. (17) also proved a similar positive relationship between GnRH-a triggering and ongoing pregnancy rates in the normoresponder group. In Lin et al.'s (7) research published in 2013, the study population was normoresponders and the contribution of dual trigger ovulation induction to live birth rates was questioned as the main outcome. Apart from this, the clinical pregnancy rate, the implantation rate, the OHSS incidence, and the blastocyst progression rate were also calculated. In the study, standard doses of hCG (6500 IU of recombinant hCG) and dual trigger (0.2 mg of triptorelin and 6500 IU of recombinant hCG) were applied to two different normoresponder patient population groups. As a result, the total number of retrieved oocytes and the number of mature oocytes in the dual trigger applied group were statistically significantly higher than the hCG group. In the study, all embryo transfers were made as fresh cycles, and implantation rates, clinical pregnancy rates, and live birth rates were found to be statistically significantly higher (7). Dual triggering was associated with a considerably higher number of retrieved oocytes, mature oocytes, pregnancy rate, and live birth rate than the standard hCG trigger, according to the current meta-analysis (18).

In Shapiro et al. (19) retrospective cohort study published in 2021, clinical pregnancy rates and live birth rates were investigated as the main outcome in the hCG mono (10.000 IU hCG / 250-500 mcg ovidrel) and GnRH-a trigger combined with low dose hCG (1000 IU hCG +2 mg GnRH-a) groups (19). Although the number of retrieved oocytes and fertilization rates were higher in the dual triggering group, clinical pregnancy, and live birth outcomes were found to be statistically significantly lower.

Our initial aim in this study was to apply both hCG and dual triggering to poor responder patients in their consecutive COH cycles to compare the total and mature oocyte counts, that were obtained after each triggering method. Previous studies compared the effects of hCG and dual triggering in consecutive cycles of different patient populations. However, retrieved oocytes and MII/total oocyte counts of the different triggering protocols that were applied to the same patients with POR were compared for the first time. Although some publications demonstrate the increased total oocyte counts and MII oocyte rates after dual triggering in different patient groups; we found that the triggering method did not significantly affect the results in patients with POR.

Previous studies demonstrated the different effects of GnRH-a triggering on implantation rates, ongoing pregnancy rates, and live birth rates of high-responders and normal-responders. When we evaluated the cycle outcomes in the limited number of cases that had fresh embryo transfers (hCG: 23, dual: 20), positive β-hCG, implantation, clinical pregnancy, and ongoing pregnancy rates were higher, on the other hand, biochemical and clinical miscarriage rates were lower in Dual group than hCG group. However, the differences were not found statistically significant ($p>0.05$) (Table 2). Although there is a tendency that dual trigger could decrease clinical miscarriage, our results might

have increased statistical error due to the low number of patients. We could not compare the results of different trigger methods in the same patients since only eight patients had embryo transfers in their both IVF cycles. In the hCG triggering group, only two of them had positive β-hCG (25%) while it was four (50%) in the dual triggering group. The implantation rate was 13.3% for hCG and 30.8% for dual triggering. Only one of the four pregnancies was ongoing (12.5%) in the dual group, remaining ones and all two pregnancies in the hCG group resulted with clinical miscarriage.

Study Limitations

The major limitation of the study is that it was conducted with a small number of cases due to the difficulty of finding patients with two consecutive IVF treatments within two years with different triggering protocols in the same center. Our results should be confirmed in further large-scale studies due to the possibility of statistical errors that may arise from the small sample size.

Conclusion

Our results demonstrated that the choice of triggering method, whether hCG or dual triggering, did not significantly influence either the retrieved / mature / 2PN oocyte counts or clinical IVF outcomes in patients with POR. Our findings emphasize the complexity of IVF treatment and the need for tailored approaches to trigger methods based on individual patient characteristics. While the present investigation adds valuable insights to the field, further research is needed to comprehensively address the multifaceted aspects of triggering methods and their influence on diverse patient cohorts undergoing IVF.

Ethics

Ethics Committee Approval: The Ethical Committee of Yeditepe University approved the study protocol (approval no: 2022/12, date: 17.03.2022).

Informed Consent: All participants received medical approval from their physicians and gave written, informed consent before they participated in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.G.K.Y., M.Y., E.A., Concept: M.G.K.Y., G.Ö., M.Y., E.G.Ç., O.A., E.A., Design: M.G.K.Y., G.Ö., M.Y., E.G.Ç., O.A., E.A., Data Collection or Processing: M.G.K.Y., G.Ö., M.Y., E.G.Ç., O.A., E.A., Analysis or Interpretation: M.G.K.Y., G.Ö., M.Y., E.G.Ç., O.A., E.A., Literature Search: M.G.K.Y., G.Ö., M.Y., E.G.Ç., Writing: M.G.K.Y., G.Ö.

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References

1. Srisuparp S, Strakova Z, Fazleabas AT. The role of chorionic gonadotropin (CG) in blastocyst implantation. Arch Med Res. 2001;32:627-34.
2. Jones EE. hCG in assisted reproduction. In: Cole LA, Butler SA editors. Human Chorionic Gonadotropin (hCG). London-London, Burlington: Elsevier; 2003:201-12.
3. Delvigne A, Rozenberg S. Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review. Hum Reprod Update. 2002;8:559-77.
4. Practice Committee of American Society for Reproductive Medicine. Ovarian hyperstimulation syndrome. Fertil Steril. 2008;90:S188-93.
5. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Thomas S. Gonadotropin-releasing hormone agonist combined with a reduced dose of human chorionic gonadotropin for final oocyte maturation in fresh autologous cycles of in vitro fertilization. Fertil Steril. 2008;90:231-3.
6. Griffin D, Feinn R, Engmann L, Nulsen J, Budinetz T, Benadiva C. Dual trigger with gonadotropin-releasing hormone agonist and standard dose human chorionic gonadotropin to improve oocyte maturity rates. Fertil Steril. 2014;102:405-9.
7. Lin MH, Wu FS, Lee RK, Li SH, Lin SY, Hwu YM. Dual trigger with combination of gonadotropin-releasing hormone agonist and human chorionic gonadotropin significantly improves the live-birth rate for normal responders in GnRH-antagonist cycles. Fertil Steril. 2013;100:1296-302.
8. Haas J, Bassil R, Samara N, Zilberberg E, Mehta C, Orvieto R, et al. GnRH agonist and hCG (dual trigger) versus hCG trigger for final follicular maturation: a double-blinded, randomized controlled study. Hum Reprod. 2020;35:1648-54.
9. Gonen Y, Balakier H, Powell W, Casper RF. Use of gonadotropin-releasing hormone agonist to trigger follicular maturation for in vitro fertilization. J Clin Endocrinol Metab. 1990;71:918-22.
10. Humaidan P, Bredkjaer HE, Bungum L, Bungum M, Grøndahl ML, Westergaard L, et al. GnRH agonist (buserelin) or hCG for ovulation induction in GnRH antagonist IVF/ICSI cycles: a prospective randomized study. Hum Reprod. 2005;20:1213-20.
11. Imoedemhe DA, Sigue AB, Pacpaco EL, Olazo AB. Stimulation of endogenous surge of luteinizing hormone with gonadotropin-releasing hormone analog after ovarian stimulation for in vitro fertilization. Fertil Steril. 1991;55:328-32.
12. Kolibianakis EM, Tarlatzis B, Devroey P. GnRH antagonists in IVF. Reprod Biomed Online. 2005;10:705-12.
13. Humaidan P, Polyzos NP, Alsbjerg B, Erb K, Mikkelsen AL, Elbaek HO, et al. GnRHa trigger and individualized luteal phase hCG support according to ovarian response to stimulation: two prospective randomized controlled multi-centre studies in IVF patients. Hum Reprod. 2013;28:2511-21.
14. Griesinger G, Kolibianakis EM, Papanikolaou EG, Diedrich K, Van Steirteghem A, Devroey P, et al. Triggering of final oocyte maturation with gonadotropin-releasing hormone agonist or human chorionic gonadotropin. Live birth after frozen-thawed embryo replacement cycles. Fertil Steril. 2007;88:616-21.

15. Youssef MA, Van der Veen F, Al-Inany HG, Mochtar MH, Griesinger G, Nagi Mohesen M, et al. Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist assisted reproductive technology cycles. Cochrane Database Syst Rev. 2014;CD008046.
16. Griffin D, Benadiva C, Kummer N, Budinetz T, Nulsen J, Engmann L. Dual trigger of oocyte maturation with gonadotropin-releasing hormone agonist and low-dose human chorionic gonadotropin to optimize live birth rates in high responders. Fertil Steril. 2012;97:1316-20.
17. Schachter M, Friedler S, Ron-El R, Zimmerman AL, Strassburger D, Bern O, et al. Can pregnancy rate be improved in gonadotropin-releasing hormone (GnRH) antagonist cycles by administering GnRH agonist before oocyte retrieval? A prospective, randomized study. Fertil Steril. 2008;90:1087-93.
18. Hsia LH, Lee TH, Lin YH, Huang YY, Chang HJ, Liu YL. Dual trigger improves the pregnancy rate in fresh in vitro fertilization (IVF) cycles compared with the human chorionic gonadotropin (hCG) trigger: a systematic review and meta-analysis of randomized trials. J Assist Reprod Genet. 2003;40:2063-77.
19. Shapiro M, Romanski P, Thomas A, Lanes A, Yanushpolsky E. Low dose hCG supplementation in a Gn-RH-agonist trigger protocol is associated with worse pregnancy outcomes: a retrospective cohort study. Fertil Res Pract. 2021;7:1-8.