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Original Article

Comparison of the administration of dual and standard trigger in patients undergoing IVF Treatment

Fatih Yigit[1], Abdullah Karaer[2], Gorkem Tuncay[2]

[1]Clinic of Obstetrics and Gynecology, Malatya Training and Research Hospital, Malatya, Turkey
[2]Department of Obstetrics and Gynecology, Faculty of Medicine, Inonu University, Malatya, Turkey

Abstract

Aim: This study aimed to compare in vitro fertilization (IVF) outcomes in patients who were administered dual trigger due to OHSS risk in the GnRH antagonist protocol with patients who were administered standard trigger.

Materials and Methods: The medical files were retrospectively scanned for all the patients who were admitted to Inonu Unıversity department of obstetrics and gynecology.While the dual trigger group was composed of patients with OHSS risk who were stimulated with GnRH antagonist and received dual trigger(hCG + GnRHa) for final oocyte maturation, the age-matched (20-40) control group consisted of patients who were administered standard trigger (10000 IU uhCG or 500 µgrrhCG and obtained oocyte counts of 500 µgr recombinant hCG). Thetwo groups were compared in terms of the oocyte count, MII oocyte count, and pregnancy and birth outcomes.

Results: There was no statistically significant difference between the two groups in terms of age, weight, height, BMI, duration of marriage, presence of previous pregnancy, number of previous parities, number of pre-existing children, number of previous abortus stories, number of smokers, duration of infertility, LH, E2, prolactin, TSH levels, infertility causes, and hCG dose endometrium thickness. The number of oocytes and MII oocytes obtained was significantly higher in the dual trigger group compared to the control group. There was no statistically significant difference between the two groups in terms of the number of pregnancies and number of deliveries.

Conclusion: Although the number of oocytes and MII oocytes was higher in the dual trigger group compared to the control group, there was no significant difference in terms of the pregnancy ratios and the number of deliveries.

Keywords: Invitro fertilization; dual trigger; standard trigger; OHSS

INTRODUCTION

Infertility is defined as the failure to achieve pregnancy after one year of unprotected intercourse between partners. Infertility affects 10 to 15% of couples at reproductive age (1). There are numerous treatment methods used for infertile couples; in vitro fertilization (IVF) is one of these treatment methods. While generally it could beused after other treatment methods have failed, sometimes it is considered as the first option. Through controlled ovarian stimulation, assisted reproductive therapies enable to develop high numbers of follicles to obtain good quality and high numbers of oocytes from ovaries.

Recently, GnRH antagonist protocols have become more popular. Several studies have shown that GnRHa could be used instead of hCG for triggering before the final oocyte maturation. The concept of "dual trigger" in ART cycles includes the use of GnRHa and low doses of hCG in tandem (2). Although some studies show that the oocyte count is higher in patients who were given GnRHa and hCG in tandem, there is a limited number of randomized controlled studies on this issue.

Patients who are administered the Controlled Ovarian Stimulation (COS) have been administered dual trigger (in combination with GnRH agonist hCG (Human Chorionic Gonadotropin) to achieve final oocyte maturation to decrease OHSS (Over Hyperstimulation Syndrome) risk.

This study main aim to compare the number of live births in patients (who were administered COS and had OHSS risk) who received ovulation induction via dual trigger with patients who were matched in terms of age, BMI (Body Mass Index) and ovary reserve and who underwent standard trigger.

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Corresponding Author: Fatih Yigit, Clinic of Obstetrics and Gynecology, Malatya Training and Research Hospital, Malatya, Turkey
E-mail: dr_fatih87@hotmail.com

MATERIALS and METHODS

Before the study was conducted, ethics committee approval was obtained from the Medical Faculty Ethics Committee of Inonu University (Ethics Committee Approval No: 2016/186). We conducted a case-control study retrospectively. The medical files were retrospectively scanned for all the patients who were admitted to Inonu University Division of Obstetrics and Gynecology Division of the Reproductive Endocrinology and Infertility between April 2014 and March 2017, whose final maturation was performed by using the standard controlled ovarian stimulation (COS) and dual trigger, and then who were administered the ICSI (Intra Cytoplasmic Injection) procedure.

Power analysis is applied to all studies before being evaluated by the ethics committee by statistician. A sample size calculation was performed with a significance level (alpha) of 0.05 and power (% chance of detecting) of 80% using MedCalc statistical software.

While the dual trigger group (n=40 patients) included patients who received ovulation induction via dual trigger due to OHSS risk, the control group (n=80 patients) included patients who were matched in terms of age, BMI and number of oocytes obtained and who received standard trigger (10000 IU uhCG or 500µgr rhCG (Recombinant Human Chorionic Gonadotropin).

To reduce pre-trial bias: We selected patients using rigorous criteria to avoid confounding results. Case and controls originate from same general population. To reduce trial bias: Case and control groups were selected from patients treated within a similar chronological range. Treatment procedures were carried out by same experienced reproductive endocrinologist (G.T).To reduce post-trail bias: we matched cases and controls in terms of age, BMI and number of oocytes obtained to reduce the confounding factors.

The search included the following data of the patients: age, duration of infertility, height, weight and BMI, FSH (Follicle StimulatingHormone) on the third day of menstruation, E2 (Estradiol), LH (Luteinizinghormone) levels, total FSH stimulation duration, and total RFSH (Recombinant FSH) doses, follicle count obtained, E2 levels on the day of hCG administration, endometrial thickness measured on the day of hCG, total oocyte count, MII oocyte count, fertilized oocyte count, total embryo count obtained, number of transferred embryos, chemical pregnancy, presence of clinical pregnancy, and the number of babies taken home.A clinical pregnancy is defined as the TVUSG (Transvaginal ultrasound) confirmation of the gestational sac in the uterus (independently of the presence of fetal cardiac activity) at least once. All the patients in this study were administered the GnRH (Gonadotropin-releasing hormone) antagonist protocol. Forthe GnRH antagonist protocol, two GnRH antagonists (cetrorelix or ganirelix) with equal efficiency and potentials were utilized. The GnRH antagonists were started on the 6th day of the menstrual cycle. The treatment continued until the hCG day. The gonadotropin dose was identified according to the patient's age, weight, basal E2, FSH level, antral follicle count, and response to previous ovulation induction, if any (150 IU/day). The patientswere described how to use the determined dose and the medicine, and regular use was confirmed in each follow-up. After it is applied every day at the same time for six days, the patients were called for a follow-up visit to check their follicle development and serum E2 levels. According to the patient's follicular growth response, the gonadotropin dose was rearranged or the same dose was continued. After the serial USG (Ultrasonography) and serum E2 were checked, the patients who were found to develop at least two-three follicles≥18mm were planned to have the oocyte collection procedure. Intramuscular urinary hCG or rhCG (recombinant human chorionic gonadotropin) was administered. While the standard trigger administration was performed by using urinary or recombinant hCG (Ovitrelle®, Merck Inc., İstanbul, TR, 250 µg or Pregnyl®, Merck Sharp&DohmeInc, İstanbul, TR, 10000IU) GnRH agonist (triptorelin acetate- Gonapeptyl®, FerringInc, İstanbul, TR, 0.1mg/ml), the dual trigger was performed using one of hCG+GnRHa (Gonadotropin-releasing hormone agonist)urinary or recombinant hCG (Ovitrelle®, Merck Inc, İstanbul, TR, 250 µg or Pregnyl®, Merck Sharp & Dohme Inc., İstanbul, TR, 10000 IU) and one of (triptorelin acetate - Gonapeptyl®, Ferring Inc., İstanbul, TR, 0.1mg/ml). After 34 to 36 hours, (oocyte pick up (OPU)) was performed administered. Oocytes are classified as GV (Germinal vesicle), MI, and MII according to their development. MII oocytes were prepared for ICSI. The oocytes prepared forthe ICSI were left to incubation in the same medium for 30-60 minutes at 37°C and in an environment containing 5% CO2. Meanwhile, the semen taken from the male partner was processed by the swim-up method. After 2 to 6 days of sexual abstinence, male partners gave semen by masturbating.

The embryo classification was analyzed according to David K. Gardner (3).

Grade 1 Embryo: These embryos have equal size and symmetricalblastomeres, and with no fragmentation.

Grade 2 Embryo: They contain non-equal sizes of blastomeresand low amounts of fragmentation (<10%)

Grade 3 Embryo: They do not have equal blastomeres, and they have high fragmentation (10-50%).

Grade 4 Embryo: Their blastomeres are not equal, and their fragmentation is more than 50%.

Grade 1 embryos were used if the patients had any Grade 1 embryos. ET (embryotransfer) was applied on the second or third day from the oocyte collection. The embryo transfer was administered in line with the guidance of transabdominal ultrasonography. The duration, time, and difficulty of the transfer, embryocount given, and the Grade 1 embryo count transferred were recorded. All patients

were advised to have a rest for 60 minutes. β-hCG was analyzed 15 days after the OPU (oocyte pick-up) date. The luteal phase support was given to the patients vaginally via micronized progesterone (Progestan® capsule, KoçakInc, İstanbul, TR, 100 mg). The luteal phase support was started one day after the oocyte pick-up. It was continued according to the β-hCG result. The treatment was ceased if β-hCG was negative, and the progesterone support was continued until the 10th gestational week if it was positive. If a pregnancy was achieved, the patients were invited for TVUSG and fetal pole and heartbeat evaluations in the 7th week according to the last menstrualperiod.

Statistical Analysis

The statistical analyses were performed in SPSS 18.0 package program. While the categorical variables were presented using numbers and percentages, continuous variables were presented using means and standard deviations (medians and minimum-maximum where necessary). Comparison of the categorical measurements between the groups was done using Pearson Chi-Square Analysis and Fisher's Exact Chi-Square analysis. Whether continuous measurements met the normal distribution was determined using the Kolmogorov Smirnov test. Comparison of the measurements between the groups was done using independent groups t-test when the assumptions were met and the Mann Whitney U test when the assumptions were not met. Statistical significance was taken p<0.05 for all tests.

RESULTS

The patient groups were compared in terms of demographic data. The mean age of the women was 30.40 ± 4.5 in the dual trigger group, and it was 30.20 ± 4.03 in the control group, indicating no significant differences between the groups (p=0.52). The average age of the men was 34.05 ± 4.3 in the dual trigger group, and it was 33.7 ± 4.3 in the control group, indicating a significantly higher value in the dual trigger group in comparison to the control group (p=<0.001). While the BMI was 25.05 (23.1-28.6)in the dual trigger group, it was 24.9 (23.1-27.5) in the control group, indicating no statistically significant differences between the groups (p=0.54). The duration of infertility was found 6 years on the average in the dual trigger group; and itwas 6 years as a mean in the control group as well. The groups demonstrated no significant differences in terms of the infertility duration (p=0.79). While the number of patients who had a live birth was 1 in the dual trigger group, it was found 1 in the control group as well. The groups demonstrated no significant differences in terms of the number of live births (p>0.999). While the number of patients with abortus history was 6 in the dual trigger group (15%), the number of patients without abortus history was 34 (85%) in the control group. As to the control group, while the number of patients who had abortions previouslywas 16 (20%), the number of patients who had not abortions previously was 64 (80%).The groups demonstrated no significant differences in terms of the number of patients with an abortus history (p=0.51). While the number of patients with previous pregnancy was 9 (22.5%) in the dual trigger group, it was found 19 (24%) in the control group. No significant differences were detected between the groups in terms of the number of patients with a previous pregnancy(p=0.88). No statistically significant differences were detected between the groups in terms of the number of smoking women, the number of patients with previous parity, and the number of patients who received IVF treatment (p=0.79, p=0.78, p=0.39, p=0.79 respectively) (Table 1).

Table 1. Characteristics of the dual trigger group and the control group

	Dual Trigger Group	Standard Trigger (Control Group)	P
Women's year	30.40 ± 4.5	30.20 ± 4.03	0.52
Men's year	34.05 ± 4.3	33.7 ± 4.3	<0.001
Weight(kg)	64.0 (58. 25-72.5)	63.0(57. 0-71.0)	0.35
Height(cm)	160(155-164)	159 (155-163)	0.44
BMI (kg/m²)	25.05 (23.1-28.6)	24.9 (23. 1-27.5)	0.54
Duration of marriage(year)	7(4-9)	7 (4-9)	0.61
Duration of infertility (year)	6(3.5-8)	6(3-8)	0.79
Number of Smoking Women	6 (15%)	10 (12.5%)	0.78
Presence of Previous Pregnancy	9 (22.5%)	19 (24%)	0.88
Previous Parity	3 (7.5%)	3 (3.75%)	0.39
Previous Live Births	1 (2.5%)	1 (1.25%)	1
Previous Abortus History	6 (15%)	16 (20%)	0.51
Presence of Previous IVF treatment	18 (45%)	34 (42. 5%)	0.79

The patient groups were also compared in terms of hormone levels. The FSH level was reported to be 5.3 mIU/ml (4.8-6.6 mIU/ml) in the dual trigger group and 6.85 mIU/ml (5.77-7.95 mIU/ml) in the control group. The control group's FSH level was found to be significantly higher (p<0.001). No statistically significant differences were detected between the groups in terms of their LH, E2, Prolactin, and TSH (Thyroid Stimulant Hormone) levels (p=0.40, p=0.14, p=0.60, p=0.67 respectively) (Table 2). Infertility factors in the dual trigger group included male factor for 18 (45%) patients, unexplained fertility for 21 (52.5%) patients, and female factor for 1 (2.5%) patient. As to the control group, the infertility factors includedmale factor for 38 (47.5%) patients, unexplained infertility for 38 (47.5%) patients, and female factor for 4 (5%) patients. No significant differences were detected between the groups (p=0.75), (Table 3).

The E2 level of the cycle on the hCG day was found 2687 pg/ml (1586-4092 pg/ml) in the dual trigger group, and it was found 2142 pg/ml (1299-2782 pg/ml) in the control group. The E2 level on the hCG day was found to be significantly higher in the dual trigger group. total dose of gonadotropin used was found 1650 (1275-1950) in the dual trigger group and 1687.5 (1322-2475) in control group. The comparison of two groups indicated no significant differences in terms of the total gonadotropin (p=0.11). Antral follicle count was calculated as 21 (15-24) in the dual trigger group and it was found 14 (10-21) in control group. In comparison to the control group, the antral follicle count was significantly higher in the dual trigger group (p=0.001). Follicle count, which was 14 and over on the hCG day was found to be 11 (9-13) in the dual trigger group due to OHSS risk, and it was found 8 (6-10) in the control group. Follicle count of 14 and over was found to be higher in the dual trigger group in comparison to the control group (p<0.001), (Table 4).

The number of oocytes among groups was found 13 (10-16) in the dual trigger group, and it was found 10 (7-12) in the control group. The oocyte count was found to be significantly higher in the dual trigger group in comparison to the control group (p=0.001). MII oocyte count was found 9 (7-12) in the dual trigger group, and it was found (5.0-9.75) in the control group. Number of oocytes in the dual trigger group was found to be significantly higher in comparison to the control group(p=0.001). number of embryos developed on the second day was detected 5 (4-7) in the dual trigger group, and it was found 4 (2-5) in the control group. In comparison to control group, number of embryos developed on the second day was found to be significantly higher in the dual trigger group (p=0.008). No significant differences were found between the groups in terms of the number of patients who received embryo transfer and who did not, number of MI oocytes among groups and who did not, and the number of patients who had MI oocyte and who did not (p=0.33, p=0.39, p=0.25 respectively) (Table 5).

Table 2. Basal hormone levels of the dual trigger group and the control group

	Dual Trigger Group	Standard Trigger	
(Control Group)	P	0	20
FSH (IU/L)	5.3 (4.8-6.6)	6.85 (5.77-7.95)	<0.001
LH (IU/L)	5.5 (4. 03-7.43)	5.1 (3.87-6.5)	0.40
E2 (pg/ml)	45.5 (36.4-54.6)	46.6 (33.2-63.5)	0.14
PROLACTIN (ng/ml)	13.5 (10.5-18.1)	14.6 (10.3-18.7)	0.60
TSH (mIU/L)	1.5 (0.98-18.7)	1.66 (1.1-2.45)	0.67

Table 3. Infertility causes of the dual trigger group and the control group

	Dual Trigger Group	Standard Trigger (Control Group)	p
	Male Factor 18 (45%)	Male Factor 38 (47.5%)	
Cause of Infertility	Unexplained 21 (52.5%)	Unexplained 38 (47.5%)	0.75
	Female Factor1 (2.5%)	Female Factor 4 (5%)	

Table 4. Comparison of the ovarian stimulation characteristics of the dual trigger group and the control group			
	Dual Trigger Group	**Standard Trigger (Control Group)**	**P**
E2 LEVEL On hCGDAY (Pg/Ml)	2687 (1586-4092)	2142 (1299-2782)	0.04
Total Gonadotropins Used (IU)	1650 (1275-1950)	1687.5 (1322-2475)	0.11
Duration of Induction (days)	9 (9-11)	9 (8-10)	0.07
Endometrium Thickness on the hCG Day (mm)	10.7 (9.8-12)	10.8 (9.1-10.1)	0.51
D3 Antral Follicle Count	21 (15-24)	14 (10-21)	<0.001
Coasting administered	2 (5%)	4 (5%)	1
No Coasting	38 (95%)	76 (95%)	
Follicle Count of 14 and over on the hCG Day	11 (9-13)	8 (6-10)	<0.001
hCG dose	uhCG+GnRHa: 24 (60%) rhCG+ GnRHa:16 (40%)	uhCG: 53 (61%) rhCG:34 (39%)	0.92
rFSH	20 (50%)	31 (38.75%)	0.02
rFSH+hMG (Human Menopozal Gonadotropin)	20 (50%)	49 (61.25%)	

Table 5. Comparison of the oocyte count and embryo count obtained from the dual trigger group and the control group			
Oocyte Count	**13 (10-16)**	**10 (7-12)**	**P**
MII Oocyte Count	9 (7-12)	7 (5.0-9.75)	0. 001
GV Oocyte Detected	31 (77.5%)	56 (70%)	<0. 001
MII Oocyte Detected	5 (12.5%)	20 (25%)	0.39
Empty Oocyte Detected	14 (35%)	20 (25%)	0.25
Degenerated Oocyte Detected	10 (25%)	17 (21%)	0.25
Embryo count developed on the second day	5 (4-7)	4 (2-5)	0.64
Embryo count developed on the third day	5 (3-6.7)	4 (3-5)	0.008
Embryo transfer detected	37 (92.5%)	78 (97.5%)	0.07
Day of Transfer			
2nd day	9 (24.3%)	18 (23%)	0.33
3rd day	21 (56.7%)	46 (59%)	
5th day	7 (19%)	14 (18%)	
1 Embryo Transferred	26 (70%)	59 (76%)	0.54
2 Embryo Transferred	11 (30%)	19 (24%)	

The number of achieved pregnancy outcomes was 18 (45%) and the number of failed pregnancy outcomes was 22 (45%) in the dual trigger group. As to the control group, while the number of pregnancy outcomes was 26 (32.5%), the number of failed pregnancy outcomes was 54 (67.5%). The difference between the groups was not statistically significant (p=0.18). The number of biochemical pregnancy count was 4 (10%), and the number of patients with failed biochemical pregnancy was 36 (90%) in the dual trigger group. Regarding the control group, while the number of achieved biochemical pregnancies was 4 (5%), the number of failed biochemical pregnancies was 76 (95%). No significant differences were detected between the groups (p=0.43). The number of clinical pregnancies was 13 (42.5%) and the number of failed clinical pregnancies was 27 (57.5%) in the dual trigger group. Regarding the control group, while the number of achieved clinical pregnancies was 22 (27.5%), the number of failed clinical pregnancies was 58 (77.5%). The groups demonstrated no significant differences in terms of the clinical pregnancy rates (p=0.57).

The number of patients who gave birth was 11 (27.5%) and the number of patients who did not give birth was 29 (77.5%) in the dual trigger group. As to the control group, the number of patients who gavebirth was 19 (23.75%), and the number of patients who did not give birth was 61 (76.25%). The groups indicated no significant differences in terms of the number of patients who gave birth (p=0.65) (Table 6).

Table 6. Comparison of the pregnancy and birth outcomes of the dual trigger group and the control group

	Dual Trigger Group	Standard Trigger (Control Group)	p
Pregnancy			
Yes	18 (45%)	26 (32.5%)	0.18
Clinical Pregnancy	13 (42. 5%)	22(27.5%)	0.57
Biochemical Abortus Developed	4 (10%)	4 (5%)	0.43
Had Birth	11 (27.5%)	19 (23.75%)	0.65

DISCUSSION

The results of our study showed that in comparison to the trigger done with standard-dose hCG, the dual trigger administered with GnRHa demonstrated improvements in terms of the oocyte count obtained, quality count obtained and embryocount obtained in patients with OHSS risk who were administered normal response GnRH antagonist cycle. FSH and LH have a peak in the midcycle period in spontaneous cycles. Although the FSH and LH concentrations do not increase in patients who were administered hCG as the trigger for the final oocyte maturation, oocyte maturation is totally associated with the LH activity of hCG. On the other hand, GnRHa trigger imitates the natural release of gonadotropins for the final oocyte maturation. This strategy initiates flare-up in both FSH and LH. The significantly high oocyte count in the dual trigger procedure in this study could be explained by the more convenient nature of hormonal mechanisms for biological gonadotropin release. Unlike the present study, in their randomized controlled study that compared the patients who were administered hCG trigger and GnRHa (triptorelin) in combination with hCG in GnRH antagonist cycles, Schachter et al. found no significant differences between the basal FSH, peak serum E2 levels on the hCG day, and the oocyte count obtained (4). In their randomized control study in which they investigated different forms of triggering in 120 patients who received ICSI, Decleer et al. showed that dual trigger administration was associated with obtaining high-quality embryo (5). Another study conducted with 427 patients, Elias at al. found that the combined trigger group had higher oocyte maturity higher clinical pregnancy and higher live birth compared to the hCG trigger group (6). In their randomized controlled study 527 patients were included, Nan Ding et al. found that the oocyte count was lower in the dual trigger group in comparison to the single trigger group, which is different from the findings of the present study (7). Another study conducted with 156 patients, Seval et al. found that the administration of dual trigger for oocyte maturation increased the grade-e number of MII oocytes and embryos in the antagonist cycle who underwent IVF treatment (8). Other study including 226 patients, Li at al. demonstrated that dual trigger is capable of preventing severe OHSS while still maintaining excellent high quality embryo rate in in high ovarian responders of GnRH-antagonist protocols (9).

Another study in 137 patients has reported co-administration of GnRH agonist and hCG for final oocyte maturation substantially increased the oocyte maturation rate in patients with low oocyte maturation rate in their hCG triggered cycle (10).

Fanchin et al. reported that the trigger combination of hCG and GnRH agonist, since it has beneficial effects on the embryo morphology, could be an opportunity for patients with recurrent low graded embryo in final oocyte maturation for this strategy; they also stated that this assumption should be confirmed through studies to be conducted with larger groups (11).

When it was compared with the trigger performed via standard dose hCG, the dual trigger in combination with GnRHa was foundto improve the outcomes in terms of the embryo count obtained in the patients with OHSS risk who were administered the GnRH antagonist cycle with a normal response. However, no significant differences were detected between thecase and control groups in terms of the pregnancy outcomes. Unlike the present study, Schachter et al. reported that the use of triptorelin (0.2 mg) in combination with hCG in GnRH antagonist cycles significantly increased the continuing pregnancy ratios in the completed cycles. On the other hand, they also reported that this effect was not detected in all the cycles initiated. The researchers put forward that this effect happened with the endometrial GnRH receptor effect (4). In their a retrospective cohort study conducted with 376 patients, by Lin et al. investigated the effects of dual triggering in comparison to standard hCG administration in normal responders in GnRH-antagonist cycleon the pregnancy outcomes; unlike the present study, they found that implantation, clinical pregnancy and live birth rates demonstrated significant improvements in patients who were administered dual trigger (12).Different pregnancy outcomes in the dual trigger administration could be associated with the administration of dual triggering only to the patients with OHSS risk. In their prospective randomized study including 120 patients, Decleer et al. investigated the effects of different forms of triggering in patients who received ICSI and found that although the dual trigger was associated with obtaining high-quality embryo, they were reported to cause no significant differences in the clinical pregnancy rates (5). They also obtained similar results to our study. In their retrospective cohort study, Griffin et al. reported an effective strategy in patients who had peak E2<4000pg/ml value and the risk for OHSS development to increase the pregnancy and live birth rates after the GnRHa trigger. In comparison to the patients who were administered only GnRHa for oocyte maturation, the patients who were administered dual trigger through GnRHa and low-dose hCG for oocyte maturation were found to demonstrate significant improvements in implantation, clinical pregnancy, and live birth rates (without increasing the OHSS risk) (13). Similarly, the group that was administered dual trigger in this study was also composed of patients who had OHSS risk. However, unlike the present study, Griffin et al. reported that they had significantly higher pregnancy and birth rates in the group that was administered dual trigger. There is a need for more clinical research to compare and interpret the findings obtained in this study. A study conducted by Shapiro et al. reported that the pregnancy rates were higher in patients who were administered dual trigger for GnRHa and low dose hCG for oocyte maturation in comparison to the patients who did not receive intensive luteal support and triggered via only GnRHa for oocyte maturation (57.7%vs 25.3% p<0.001) (14).In their randomized controlled study conducted with 527 patients, Nan Ding et al. reported that the pregnancy outcomes, unlike the present study, were significantly higher in the dual trigger patient group in comparison to the single trigger patient group (7). In their study conducted with 156 patients, Seval et al. reported that the administration of dual trigger for oocyte maturation in the antagonist cycle administered IVF improved the pregnancy rates significantly (8). In our study, although the patients who were administered dual trigger had higher values of MII oocyte count andhigher embryo quality, no changes were found in the clinical pregnancy rates. Different pregnancy outcomes in the dual trigger administration could be associated with the fact that only the patients who had OHSS risk were administered dual trigger. There is a need for more prospective randomized studies to interpret this finding.

Neither the patients in the dual trigger group nor the patients in the control group were found to develop OHSS in this study. A study conducted by Humaidan. also showed that neither the dual trigger group nor the control group that was administered single trigger developed OHSS. This finding is notable particularlyfor the dual trigger group because several studies on GnRH trigger reported to add only a low dose of hCG (1500IU) following oocyte retrieval to avoid OHSS (15). In their retrospective cohort study conducted with patients with a potential OHSS development risk, Griffin et al. found that in comparison to the patients who received only GnRHa for oocyte maturation, the patients who received dual trigger with GnRHa and low-dose hCG for oocyte maturation demonstrated significant improvement in terms of implantation, clinical pregnancy, and live birth rates (without increasing the OHSS risk). This study also detected no increase in the OHSS risk (13). The dual trigger group in this study demonstrated no OHSS development, so it can beconcluded that dual trigger decreased the OHSS risk.

Only a limited number of studies have investigated the simultaneous triggering of hCG and GnRHas for the final maturation of the oocytes (4,12). Therefore, there is a need for prospective studies with larger patient series to confirm these data.

CONCLUSION

This study found that the oocyte count and MII oocyte count obtained in the dual trigger group were significantly higher in comparison to the control group. The number of pregnancies and the number of births indicated no significant differences between the dual trigger group and the control group. No patients who were administered dual trigger due to OHSS risk developed OHSS. There is a need for prospective studies with larger patient groups to

confirm the beneficial role of the dual trigger.

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

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Ethical approval: Before the study was conducted, ethics committee approval was obtained from the Medical Faculty Ethics Committee of Inonu University (Ethics Committee Approval No: 2016/186).

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