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Might retrigger with human chorionic gonadotropin be a solution for empty follicle syndrome after gonadotropin releasing hormone agonist trigger?

Gonadotropin salgılatıcı hormon agonisti ile tetikleme sonrası karşılaşılan boş folikül sendromu için insan koryonik gonadotropin ile yeniden tetikleme bir çözüm olabilir mi?

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Abstract

Objective: This study aimed to determine whether the use of human chorionic gonadotropin (hCG) as a trigger could offer a potential solution for addressing empty follicle syndrome following the administration of a trigger for gonadotropin-releasing hormone agonist.

Materials and Methods: A retrospective cohort analysis was conducted using data extracted from the hospital database pertaining to 415 patients who underwent in vitro fertilization (IVF) with an antagonist protocol triggered by a gonadotropin-releasing hormone (GnRH) agonist between December 2019 and January 2023 at the Acıbadem Maslak Hospital Assisted Reproductive Technologies Unit. All cases that failed to obtain oocytes and required rescue were analyzed.

Results: This study analyzed 415 women who underwent IVF using GnRH agonist-triggered antagonist protocols. Among them, 6 (1.4%) had empty folicle syndrome (EFS). Patients with EFS had lower luteinizing hormone levels and fewer oocytes, embryos, and blastocysts, resulting in lower oocyte utilization rate. However, pregnancy rates were similar, with no biochemical or ectopic pregnancies observed in the EFS group.

Conclusion: Use of an hCG retrigger in hyperresponders with no oocytes after GnRHa trigger may prevent cycle cancelation. Although the rates of egg utilization may decrease, oocyte maturity remains comparable. Frozen embryo transfer following hCG retrigger administration yields similar positive pregnancy test results and live birth rates.

Keywords: Empty follicle syndrome, rescue hCG trigger, failed agonist trigger

Öz

Amaç: Bu çalışma, gonadotropin salgılatıcı hormon agonisti tetiklemesi sonrası karşılaşılan boş folikül sendromuna potansiyel bir çözüm olarak insan koryonik gonadotropin (hCG) ile yeniden tetiklemenin sonuçlarını değerlendirmeyi amaçlamıştır.

Gereç ve Yöntemler: Bu çalışma, retrospektif bir kohort analizi olarak tasarlanmış olup, Acıbadem Maslak Hastanesi Yardımcı Üreme Teknikleri Birimi'nde Aralık 2019 ile Ocak 2023 tarihleri arasında gonadotropin salgılatıcı hormon (GnRH) agonisti tetiklemesi sonucu tüp bebek (IVF) uygulanan 415 hasta verilerini içermektedir. Oosit elde edilemeyen ve yeniden tetikleme gereken tüm olgular bu çalışmada değerlendirilmiştir.

Bulgular: GnRH agonisti ile tetiklemenin ardından IVF uygulanan 415 hastanın 6'sında (%1,4) boş folikül sendromu (BFS) ile karşılaşılmıştır. BFS'li hastalarda luteinize edici hormon seviyeleri daha düşük, elde edilen oosit, embriyo ve blastokist sayısı da daha azdı, bu da oosit kullanım oranlarının daha düşük olduğunu göstermektedir. Ancak, BFS grubunda biyokimyasal veya ektopik gebelik olmaksızın benzer gebelik oranları elde edilmiştir.

PRECIS: HCG retrigger in hyperresponder patients with no oocytes after GnRHa trigger is a potential strategy, avoiding cycle cancellation and yielding comparable IVF outcomes.

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Sonuç: GnRHa tetiklemesi sonrası oosit elde edilemeyen yüksek yanıtlı hastalarda hCG ile yeniden tetiklemenin siklus iptalini önleyebileceği görülmüştür. Bu yaklaşım oosit kullanım oranının azalmasına rağmen yeterli düzeyde olgun oosit elde edilmesini sağlamıştır. hCG ile yeniden tetiklemeyi takiben dondurulmuş embriyo transferi sonrası benzer pozitif gebelik testi sonuçları ve canlı doğum oranları elde edilebilir.

Anahtar Kelimeler: Boş folikül sendromu, hCG ile kurtarıcı tetikleme, başarısız agonist tetikleme

Introduction

In vitro fertilization (IVF) steps follow the same modalities that occur during normal menstrual cycles. During a normal menstrual cycle, preovulatory follicles grow to an adequate size and secrete estradiol (E2) through granulosa cells. When E2 levels rise, luteinizing hormone (LH) levels also increase, and once the LH level reaches a specific threshold, LH is triggered. This triggers a series of reactions, including loss of gap junction connections between oocytes and cumulus cells, expansion of cumulus cells, disintegration of the germinal vesicle, resumption of meiosis, and luteinization of granulosa cells[1]. During controlled ovarian stimulation in IVF treatment, human chorionic gonadotropin (hCG), which is similar to LH in terms of physiological activity, has been used to mimic the effects of LH trigger. From this perspective, hCG is the most common method for stimulating and luteinizing granulosa cells, final maturation of the oocyte before egg retrieval, and resumption of meiosis[2].

Women with multiple follicles, such as those with polycystic ovary syndrome, might be at increased risk of ovarian hyperstimulation syndrome (OHSS) following the administration of hCG for final maturation after ovarian stimulation[3]. OHSS during controlled ovarian stimulation is a rare but potentially life-threatening complication[4]. In recent years, the use of gonadotropin-releasing hormone agonist (GnRH-a) for oocyte maturation has gained popularity as a safer alternative to hCG, particularly in patients at risk of OHSS[3,5]. Triggering with GnRH-a to induce oocyte maturation is the most effective method for reducing the risk of OHSS[6]. GnRH-a can trigger oocyte maturation and ovulation by inducing the release of LH, and its activation effect called "flare-up".

The most common complication preventing the widespread adoption of this treatment protocol is that some patients may not adequately respond to GnRH agonists. There are reports in the literature on failed GnRH agonist trigger in which no oocytes were obtained from patients despite multiple appropriate follicle aspirations[7-9]. This condition, known as empty follicle syndrome (EFS), is extremely challenging for both clinicians and couples. The exact etiology of EFS is not clear, and its incidence has been reported to be approximately 1-3.5%[10,11]. EFS is characterized by the inability to retrieve oocytes from the follicles aspirated during the egg retrieval procedure, despite hCG or GnRH-a triggering, even when normal follicles develop during controlled ovarian stimulation with increasing serum E2 levels[8]. Two types of EFS have been defined in the literature. Genuine EFS is an inadequate response to hCG or GnRH-a and is probably related to intrinsic ovarian factors. Pseudo-EFS occurs mostly because of problems related to the structure of the medication or administration methods. Several hypotheses have been proposed regarding the causes of EFS after hCG stimulation. These include early oocyte atresia in functional folliculogenesis despite an apparently normal hormonal response[12], a biological abnormality of mature oocytes to be retrieved despite normal bioavailability[13], genetic factors such as LH/hCG receptor mutations[14], abnormalities in the *in vivo* biological activity of some commercially available batches of hCG or GnRHa[15], rapid clearance of hCG by the liver[15], pharmacological issues, and patient-related administration errors[13].

The aim of this study was to investigate whether retriggering with hCG might be a solution for EFS after triggering a gonadotropin-releasing hormone agonist.

Materials and Methods

Study Design

This study enrolled patients aged 20-42 years diagnosed with polycystic ovarian syndrome and underwent IVF treatment at the Acıbadem Maslak Hospital Assisted Reproductive Technologies Unit between December 2019 and January 2023. All patients were treated using the GnRH antagonist protocol, with the final follicular maturation being induced by GnRH-a. Additionally, patients who were unable to retrieve oocytes after aspirating up to four follicles during egg retrieval and who required rescue triggers were also included in the study. Patients with severe male factor infertility, those diagnosed with malignancy, those with endometriomas, and those diagnosed with hypogonadotropic hypogonadism were excluded from this study.

Ovarian Stimulation

Controlled Ovarian Hyperstimulation was initiated on the second to third days of the menstrual cycle, with the dose of recombinant FSH *(Gonal F; Merck or Fostimon; IBSA)* adjusted between 150 and 300 IU according to individual patient characteristics. When the dominant follicle reached 14 mm, Cetrorelix at a dosage of 0.25 mg per day subcutaneously (Cetrotide from Merck) was administered, and follicle maturation was triggered with triptorelin acetate at a concentration of 0.2 mg/mL (Gonapeptyl 0.1 mg/mL from Ferring) once the leading follicle reached 18 mm. Serum E2 and progesterone (P4) concentrations were measured on the day of trigger.

Oocyte pick-up was performed 36 hours after trigger injection under intravenous sedation. In cases in which no oocytes were retrieved from the initial follicles aspirated, the retrieval procedure was terminated, assuming that follicle maturation had failed. The retrieval attempt was terminated after aspirating

four follicles, with two follicles from each ovary. No oocytes were retrieved despite extensive aspiration and flushing of a minimum of four follicles with a diameter ≥17 mm, which was considered indicative of empty follicle syndrome. As a rescue procedure, 250 mcg recombinant hCG (rhCG) (250 µg/0.5 mL *Ovitrelle from Merck)* was administered subcutaneously. The second oocyte retrieval was scheduled 36 hours after hCG administration.

Retrieved oocytes were fertilized using intracytoplasmic sperm injection and subsequently cryopreserved at the blastocyst stage. Frozen-thawed embryo transfer was performed in hormonally primed cycles. For patients undergoing frozen-thawed embryo transfer, oral contraceptives were initiated on the 2-5th day of the preceding menstrual cycle. Following a 3.75 mg leuprolide acetate depot *(Lucrin; Abbott)* injection subcutaneously during the midluteal phase. Endometrial priming was initiated on the second day of the subsequent menstrual cycle. E2 (2 mg, *Estrofem; Novo Nordisk*) was administered orally, starting at 4 mg for 5 days and then sequentially increasing to 6 mg for an additional 4 days and to 8 mg for a subsequent 5 days. Fourteen days after E2 administration, the endometrium was assessed via transvaginal ultrasound, along with E2 and P4 level measurements. If the endometrial thickness exceeded 8 mm and the P4 level was less than 1.5 ng/mL, vaginal P4 (*Crinone* gel 8% *BID; Merck*) was administered twice daily, and frozen-thawed embryo transfer was scheduled. If the endometrial thickness remained below 8 mm, a 7.8 mg transdermal E2 patch (*Climara; Bayer*) was applied, and the cycle was reassessed 4 days later. If the thickness did not reach 8 mm, the cycle was canceled.

The oocyte utilization rate was calculated as the number of oocytes/number of follicles on the second egg retrieval after the hCG trigger for EFS and the number of oocytes/number of follicles on the first egg retrieval after the GnRHa trigger for non-EFS cases. The oocyte maturity index was calculated as the number of metaphase II (MII) oocytes/number of oocytes collected on the second egg retrieval after the hCG trigger for EFS and the number of MII oocytes/number of oocytes collected on the first egg retrieval after the GnRHa trigger for non-EFS cases. Clinical pregnancy was confirmed by elevated serum ß-hCG levels 12-14 days after embryo transfer, in conjunction with ultrasound verification of the gestational sac or fetal pole. Sustained implantation was defined as discharge from care at 12 weeks of pregnancy with a detectable fetal heartbeat.

Statistical Analysis

All data were analyzed using SPSS (SPSS-IBM 2.3, Inc., Chicago, IL, USA). Shapiro-Wilk test was used to assess data normality. Continuous variables were presented as mean values with accompanying standard deviations, whereas categorical variables were expressed as counts and percentages for both the EFS and non-EFS groups. Statistical significance between mean values was assessed using Student's t-test, and for categorical variables, the chi-squared test was employed. A significance level of $p<0.05$ was considered statistically significant.

Results

A total of 415 women [mean age ± standard deviation (minimum-maximum): 29.9±3.7 (25-42)] were analyzed in the study. Among the GnRHa trigger, the data of 6 (1.4% of total) women diagnosed with EFS were compared with 409 age-follicle number-matched women. Age, duration of infertility, body mass index (BMI), and serum follicle stimulating hormone (FSH) levels were similar between the groups (Table 1). Serum LH levels were compared between the groups and revealed a significantly lower value in the EFS group (6.5±0.9 vs. 8.7±2.2; p=0.02). Serum anti-Müllerian hormone (AMH) levels were also compared between the groups and revealed a significantly higher value in the non-EFS group (3.38±0.68 vs. 4.01±0.72; p=0.04).

The IVF stimulation cycles and laboratory outcomes were also compared between the two groups (Table 2). Variables affecting the oocyte output rate were also compared between the two groups. Among these factors, the duration of stimulation, gonadotrophin dose, number of antral follicles at the start of the cycle, on the trigger day, and the number of follicles ≥14 mm on the trigger day showed similar results between the two groups. Serum E2 and P4 levels were also similar on the trigger day among the two groups. The numbers of oocytes,

Table 1. Sociodemographic characteristics and basal hormonal levels of the patients compared in between the groups

Variables	EFS (n=6)	Non-EFS (n=409)	p
Age (years)	30.8±3.8	29.9±3.7	0.55
Infertility duration (years)	37.7±23.6	40.9±10.1	0.45
BMI	26.4±4.9	26.3±3.5	0.97
FSH (IU/mL)	7.5±1.2	7.4±1.3	0.94
LH (IU/mL)	6.5±0.9	8.7±2.2	0.02*
AMH (ng/mL)	3.38±0.68	4.01±0.72	0.04*

EFS: Empty follicle syndrome, BMI: Body mass index, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, AMH: Anti-Müllerian hormone

MII oocytes, 2 pronuclei (2 pn) embryos, cleavage stage embryos, and blastocysts were significantly lower in the EFS group than in the non-EFS group. The oocyte utilization rate was compared between the groups, and the analysis revealed a statistically significantly lower rate in the EFS group compared with the non-EFS group (62.6±8.4 vs. 80.4±11.6; p<0.01). In contrast to the oocyte utilization rate, the oocyte maturity index was not significantly different between the groups (81.1±7.8 vs. 85.9±10.5; p=0.27).

The data of the six patients diagnosed with EFS are presented in Table 3. The mean age of the patients was 30.8±3.8 (minimum-maximum: 26-37). The mean serum FSH, LH, and AMH levels were 7.5±1.2, 6.5±0.9 and 3.4±0.7 (minimum-maximum: 5.5-9.1; 5.8-8.1; and 2.3-4.1, respectively). The mean serum E2 and P4 levels on the trigger day were 5641±1293 and 0.7±0.1 (minimum-maximum: 4370-7133; and 0.5-0.9, respectively). Analysis of antral follicle count and number of follicles on the trigger day revealed mean numbers of 36.8±8.4 and 30.5±7.2 (minimum-maximum: 26-50 and 24-42, respectively). Analysis of the number of follicles on the second egg retrieval day and the egg utilization rate revealed a mean number of 22.0±7.0 and 62.6±8.4% (minimum-maximum: 16-33; and 50.0-70.6%, respectively). The mean numbers of oocytes, MII oocytes, 2pn embryos, cleavage stage embryos, and number of blastocysts have been reported as 13.3±2.7, 10.8±2.5, 9.2±2.0, 6.5±0.5, and 3.3±0.8 respectively (minimum-maximum: 11-18, 8-15, 7-12, 6-7, and 2-4). Frozen embryo transfer was performed in all patients using hormone replacement therapy as part of the endometrial preparation protocol. Positive pregnancy test and live birth rates among the two groups revealed similar pregnancy test results between the two groups (50.0% vs. 58.4%; p=0.49; 33.3% vs. 49.4%; p=0.69). In the non-EFS group, while 14 patients (3.4%) had a biochemical pregnancy, 2 patients (0.5%) had an ectopic pregnancy, and none of the patients in the EFS group had either a biochemical or ectopic pregnancy. Among the 239 patients with a positive pregnancy test result, 21 (5.1%) experienced miscarriage. Among the three pregnant patients in the EFS group, one had a miscarriage at the 7th gestational week, and two had live births at the 38th and 39th gestational weeks. The mode of delivery was C-section in both patients, with healthy live births of 3460 and 3720 g.

Table 2. IVF outcomes and obstetrics results of the patients compared in between the groups

Variables	EFS (n=6)	Non-EFS (n=409)	p
Duration of stimulation (days)	10.0±1.3	9.1±1.2	0.56
Gonadotrophin dose (IU)	1858.3±205.9	2082.6±420.9	0.19
Antral follicle count	36.8±8.4	39.7±13.1	0.59
# Follicles on the trigger day	30.5±7.2	32.9±12.0	0.62
# Follicles ≥14 mm on the trigger day	25.2±5.9	30.9±11.1	0.21
E2 level on the trigger day (pg/mL)	5641.8±1293.3	5771.8±1756.7	0.86
P4 level on the trigger day (ng/mL)	0.69±0.13	0.77±0.15	0.23
# Oocyte	13.3±2.7	26.2±9.8	<0.01*
Oocyte utilization rate (%)[a]	62.6±8.4	80.4±11.6	<0.01*
# MII oocytes	10.8±2.5	22.9±9.7	<0.01*
Oocyte maturity index (%)[b]	81.1±7.8	85.9±10.5	0.27
# 2pn embryos	9.2±2.0	18.7±8.7	<0.01*
Cleavage embryos	6.5±0.5	17.4±8.1	<0.01*
# Blastocyst	3.3±0.8	5.3±1.4	<0.01*
Positive pregnancy test result (n)	50.0 (3)	58.4 (239)	0.49
Livebirth	33.3 (2)	49.4 (202)	0.69

*: Statistically significant
[a]Oocyte utilization rate: For EFS, number of oocytes/follicle on the second egg retrieval after hCG trigger and for non-EFS, number of oocytes/follicle on the first egg retrieval after GnRHa trigger.
[b]Oocyte maturity index: For EFS, #: MII oocytes/oocytes collected on the second egg retrieval after hCG trigger and for non-EFS, #: MII oocytes/oocytes collected on the first egg retrieval after GnRHa trigger.
Mean ± SD and percentage where appropriate
SD: Standard deviation, EFS: Empty follicle syndrome, MII: Metaphase II, GnRHa: Agonists gonadotropin-releasing hormone, hCG: Human chorionic gonadotropin, IVF: In vitro fertilization, E2: Estradiol, P4: Progesterone

Table 3. Sociodemographic characteristics, basal hormonal levels, IVF outcomes, and obstetrics results of the patients compared in between the groups

	Age	FSH	LH	AMH	E2	P4	AFC	First trigger	Rescue trigger	# Follicles on trigger day	# Follicles on 2nd egg retrieval day	# Oocytes	Oocyte utilization rate (%)	# MII oocytes	Oocyte maturity index (%)	#2pn embryos	- Clevage stage embryos	# Blastocysts	Outcome
1	28	7.2	6.3	3.8	7133	0.89	42	GnRHa	rhCG	32	21	14	66.7	12	85.7	11	7	4	Positive
2	32	7.2	5.8	2.9	6647	0.72	33	DCP	hCG	24	17	11	64.7	9	81.8	7	6	3	Negative
3	31	7.9	6.1	2.3	4491	0.68	50	DCP	hCG	42	33	18	54.5	15	83.3	12	7	3	Negative
4	26	9.1	6.9	4.1	6650	0.54	38	DCP	hCG	35	28	14	50	10	71.4	9	7	4	Negative
5	37	5.5	8.1	3.3	4370	0.78	26	DCP	hCG	24	17	12	70.6	11	91.7	9	6	2	Positive
6	31	8.0	6.0	3.9	4560	0.56	32	DCP	hCG	26	16	11	68.9	8	72.7	7	6	4	Positive

IVF: In vitro fertilization, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, AMH: Anti-Müllerian hormone, GnRHa:: Gonadotropin-releasing hormone agonist, 0.2 mg; rhCG: recombinant hCG, 250 g, hCG: Human chorionic gonadotropin, E2: Estradiol, P4: Progesterone, AFC: Antral follicle count, MII: Metaphase II

Discussion

The introduction of the GnRH antagonist protocol enabled the use of GnRH agonists for oocyte maturation, dramatically reducing the risk of OHSS. However, GnRHa acts directly at the pituitary level; therefore, in cases of transient or permanent pituitary dysfunction, an increase in LH induced by the GnRHa trigger may be insufficient. This condition can lead to suboptimal maturation or empty follicle syndrome[16]. EFS is a rare but frustrating complication that can lead to cycle cancelation. Two types of EFS have been described in the literature. Genuine EFS is due to intrinsic factors, and false EFS is due to pharmacologic factors or patient practice[8]. According to a systematic review, 67% of EFS cases were false, that is, due to administration errors or pharmacological problems[17]. In this study, we analyzed data from 415 high-responder women. Our analysis revealed an incidence of 1.4% EFS among patients with no oocytes during the first egg retrieval after GnRHa trigger and a high utilization rate of oocytes within 36 hours after a second trigger (almost 72 hours after the first trigger).

Significant differences exist between the LH peak induced by GnRHa, the LH peak in the natural cycle, and continuous LH stimulation by hCG injection. The LH peak in the natural cycle is characterized by three phases with a total duration of 48 h[18]. The GnRHa-induced LH peak is characterized by a 2-phase rise lasting 28-32 hours[18,19]. However, with a long half-life, hCG produces LH-like activity that persists for 9-10 days[20,21]. Therefore, EFS caused by hCG and GnRH may not reflect the same pathology. The response to GnRH is independent of age, type of COS, and ovarian response[8]. In our study, there was no significant age difference among patients. Furthermore, the stimulation protocol was the same for all patients.

Retriggering with hCG is an option in patients who do not respond to GnRHa trigger. Chang et al.[22] reported one of the largest cohorts of patients, comprising 1.878 cycles using a GnRH agonist trigger. Within this cohort, 16 cycles exhibited inadequate response. These patients were subsequently triggered with hCG, leading to comparable outcomes in terms of the number of retrieved oocytes, number of normally fertilized (2pn) oocytes, pregnancy rates, and birth rates resulting from the first embryo transfer procedure. Additionally, the cumulative pregnancy and birth rates from all fresh and cryopreserved embryo transfers were similar[22]. In another report analyzing the use of hCG in poor responders to GnRH agonist trigger, the authors concluded that retriggering solely due to insufficient oocyte retrieval during the initial aspiration attempt might result in oocyte oversaturation, subsequently elevating the risk of abnormal fertilization[23]. Our study showed that after hCG trigger, >70% of the follicles persisted during the second egg retrieval. Although the oocyte utilization rate was lower in the EFS group than in the non-EFS group (almost 60% vs. 80%), the oocyte maturity index was similar between the two groups (80%). In addition, cleavage stage embryos and blastulation rates were statistically significantly lower in the EFS group, whereas positive pregnancy test results and miscarriage rates were not statistically significantly different (50% vs. 58% and 33.3% vs. 49.4%, respectively). In addition, no severe OHSS cases were reported after the second trigger with hCG, even though it has been reported as 0.5-5% in the literature[10].

Different potential factors that might increase the likelihood of a failed trigger with a GnRH agonist were examined, with a specific focus on the hypothesis that a lower BMI and baseline LH concentrations at the beginning of the cycle could be linked to a greater risk of GnRH failure[22]. In our study, the dose of GnRH was standard (0.2 mg independent of the BMI), which limits the effect of inadequate dosage of GnRHa administration. LH levels at the start of the cycle were statistically significantly lower in the EFS group than in the non-EFS group. Kitasaka et al.[23] showed that LH levels ≤0.35 IU/L at the start of the cycle might be attributed to an increased risk of EFS. However, the low LH level (6.5±0.9) was above the level of hypophysial hypogonadotrophism; therefore, the reason might not be attributed to hypo-hypo status. In addition, posttrigger LH levels have been suggested as a risk factor for EFS[24]. First, it is difficult to determine a cutoff level for the posttrigger LH threshold. LH reaches a peak level approximately 4 hours after the trigger and decreases gradually within 24 hours. In addition, since the LH has a pulsatile pattern, the measurement of one LH level might be higher than its exact level[25,26]. Kummer et al.[26] showed that LH level <15IU/L might be associated with an 18.8% increased risk of EFS. However, the optimal GnRHa dose might be affected by BMI, endogenous LH molecule, or LH receptor structure and should be investigated in future research. In a case series of 8 patients with failed GnRH agonist triggering following rescue hCG triggering, it was reported that seven patients successfully achieved ongoing pregnancies and delivered after frozen embryo transfer[9]. The first pregnancy after fresh embryo transfer following retriggeration with hCG was reported in 2015[10]. In our study, among the six frozen embryo transfer cycles, pregnancy was achieved in 3 patients with a similar pregnancy rate to the control group. Among the three pregnancies, one resulted in miscarriage at the 7th week of gestation. The other two patients had live births, reaching term (33% of total). From this point of view, we can say that hCG retrigger after GnRHa trigger might also have pregnancy and live birth results comparable to those of the control group.

Study Limitations

The strength of this study was that it showed comparable IVF outcomes in terms of oocytes and embryos, as well as pregnancy outcomes, to controls. A weakness of our study might be its retrospective nature and lack of serum LH levels at the first egg retrieval time with no oocytes. As an opportunity, this study will maintain data regarding a management modality in the case of no oocytes due to different etiologic factors.

Conclusion

Retrigger with hCG in hyperresponder patients with no oocytes after GnRHa trigger may be an alternative strategy without cycle cancelation. Although egg utilization rates might have been lower in the second procedure than in the controls, the oocyte maturity index might have been comparable to that of the controls. Fresh embryo transfer might be debatable, but frozen embryo transfer might result in comparable positive pregnancy test results and live birth rates with the hCG retrigger policy.

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Ethics

Ethics Committee Approval: Ethical approval was waived by the Acıbadem Mehmet Ali Aydınlar University Ethics Committee (ATADEK- 2023-07/231) in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Z.E.U.K., A.Y., Ö.K., Y.Ç., B.T., Concept: Z.E.U.K., A.Y., Ö.K., Y.Ç., B.T., Design: Z.E.U.K., Y.Ç., B.T., Data Collection or Processing: Z.E.U.K., A.Y., Ö.K., Y.Ç., B.T., Analysis or Interpretation: Z.E.U.K., Y.Ç., B.T, Literature Search: Z.E.U.K., Y.Ç., Writing: Z.E.U.K., Y.Ç., B.T.

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