

Conference Paper

Outcomes Comparison of In-Vitro Fertilization (IVF) between GnRH Agonist Trigger and hCG for Final Oocyte Maturation

Ade Permana¹, Budi Wiweko², Andon Hestiantoro²,
and Soegiharto Soebijanto²

¹Obstetrics and Gynaecology, Medical Faculty, Jambi University, Indonesia

²Obstetrics and Gynaecology, Medical Faculty, Indonesian University, Indonesia

Abstract

Introduction. For decades, human chorionic gonadotropin (hCG) has been used for final oocyte maturation. It is proven to have highest life birth rate, comparing to gonadotropin releasing hormone (GnRH) agonist, but unfortunately it can increase the risk of developing ovarian hyper stimulation syndrome (OHSS). There is an ongoing debate over the optimal agent that can trigger final oocyte maturation in antagonist protocol, leading to higher IVF success rate without increasing the risk of OHSS. **Objective.** To compare IVF outcomes in patient using GnRH agonist trigger and hCG for final oocyte maturation. **Method.** A retrospective review of in vitro fertilization patient at Daya Medika Clinic and Yasmin Clinic. **Result.** 76 women were analyzed consist of 38 women using GnRH agonist and 38 women using hCG. We found no significant differences on biochemical pregnancy rate (24.00% and 20.51%) between two group, but there were significant differences on fertilization rate (67.72% and 61.32%), cleavage rate (95.04% and 88.92%) and blastocyst rate (13.90% and 7.38%). There was one patient developed OHSS in hCG group. **Conclusion.** GnRH agonists can be considered for use as a trigger final oocyte maturation in the antagonist protocol because some IVF outcomes data showed that GnRH agonists triggering were better than hCG without increasing the risk of OHSS.

Corresponding Author: Budi
Wiweko; email:
wiwekobudi@yahoo.co.id

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Keywords: GnRH agonist, hCG, oocyte maturation

1. Introduction

According to WHO data in 2012, as many as 50-80 million couples of reproductive age around the world have problems in fertility (infertility) and estimated that each year brings 2 million infertile couples [1]. In Indonesia, 12-15% of the total number of couples of reproductive age have infertility problems [2].

One way to deal with the problem of infertility is using Assisted Reproductive Technology (ART). One commonly method that is used today is In vitro fertilization (IVF).

In doing IVF, we have to consider the likelihood of complications of ovarian hyperstimulation syndrome (OHSS ovarian hyperstimulation-Syndrome) which is an exaggerated response to ovulation induction and is a serious complication that can lead to organ failure [3]. OHSS prevalence ranges from 5% in patients FIV, where one risk

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factor is the administration of hCG to trigger oocyte maturation as well as luteal phase support [4].

Provision of human chorionic gonadotropin (hCG) as a trigger oocyte maturation is now a method that is done, it has been proven that the luteinizing hormone (LH) has an important role in regulating ovarian function and is important to the process of oocyte maturation, as well as for the process of ovulation. Currently, many clinicians still rely only on the activity of LH in triggering final oocyte maturation process, so if we look at the process of folliculogenesis can be said that a surge of follicle stimulating hormone (FSH), which occurred in mid-cycle is not have any function. It becomes a big question, whether it's like that? Most mammalian species in need of a surge of LH and FSH for ovulation, the combination of these two hormones surge required for oocyte nuclear maturation, follicular rupture of initiating and triggering the expression of LH receptors in granulosa cells, this happens on a normal cycle [5].

The use of gonadotropin-releasing hormone (GnRH) agonist as a substitute for hCG to trigger oocyte maturation was first introduced by Gonen et al. There are so many research has been done showing that the use of GnRH agonists to trigger oocyte maturation is the most effective method to prevent OHSS [6]. But does the use of GnRH agonists to trigger oocyte maturation when compared to the use of hCG causes a decrease in the numbers of implantation and increased incidence of significant abortion. Recent publications by Humaidan et al, compared the use of GnRH agonists and hCG to trigger oocyte maturation, the results obtained in the use of GnRH agonists significant increase in the number of metaphase II oocytes [7]. The reactivation process meiosis process regulated by the possibility of LH and FSH, and recent studies state that FSH has a specific function in the process [8]. Based on all that above, it is important for us to see the output of in vitro fertilization in patients with GnRH agonists and hCG triggers, so that we have the data that will be able to support the increasing success of in vitro fertilization techniques that we do.

2. Material and Method

This is a cross sectional study using secondary data which aims to determine the outcome of the technique FIV in patients receiving GnRH agonists and hCG as induction of oocyte maturation and its relationship with the quality of oocytes, the rate of fertilization, the rate of cleavage, the rate of blastocyst, and the pregnancy rate. The study was approved by the institutional review board. Samples are affordable populations who met the study criteria. The samples in this study conducted by consecutive sampling, all medical records, both old patients or new patients or who are or will undergo a procedure FIV get trigger with GnRH agonists or hCG, and meets the selection criteria for inclusion in the study. 76 women were analyzed consist of 38 women using GnRH agonist and 38 women using hCG. Ovarian stimulation was initiated with recombinant FSH from Day 2 or 3 of the cycle and continued until the day of ovulation induction. Cycles were monitored using ultrasound scanning. A GnRH antagonist, was administered when the leading follicle reached a maximum diameter of 14 mm. When at least two follicles had reached a diameter of 17 mm, final oocyte maturation was triggered

	Agonis	hCG
Cases	38	38
Total Oocyte	770	622
Matur Oocyte	660	530
2pn	444	325
cleavage	422	289
blastocyst	62	24
ET	100	102
Pregnancy	24	21
OHSS	-	1

TABLE 1: The number of oocytes.

by administering 0.5 mg buserelin for study group and hCG for control group. Oocyte pick-up was performed 35 h and 30 min after triggering. ICSI was performed in all patients. Embryos were evaluated on the second and third days, and up to embryos were transferred. For luteal phase support, all patients received micronized progesterone vaginally. Biochemical pregnancy was detected by measuring β -hCG levels on Day 12 after embryo transfer. All the data was recorded in medical record.

3. Statistical Analysis

The primary outcome are rate of maturation, fertilization rate, cleavage rate, blastocyst rate and pregnancy rate. Once collected, the data will be conducted verification, editing, and coding. Once the data is entered, then we do statistical analysis using SPSS 17. The p-value is regarded as significant in this study was set at 5% with a confidence interval of 95%. Relationship rate of maturation, fertilization rate, cleavage rate, blastocyst rate and pregnancy rate among patients receiving GnRH agonists and hCG trigger with oocyte quality will be analyzed by Pearson correlation test if the distribution of normal data or Spearman if the data distribution is not normal

4. Results

76 women were analyzed consist of 38 women using GnRH agonist and 38 women using hCG. The results can be seen in table 1 and table 2. After statistical analysis of the relationship between methods of triggering to the fertilization rate, cleavage rate, blastocyst rate and pregnancy rate, its show that no significant differences on biochemical pregnancy rate (24.00% and 20.51%) between two group, but there were significant differences on fertilization rate (67.72% and 61.32%), cleavage rate (95.04% and 88.92%) and blastocyst rate (13.90% and 7.38%). There was one patient developed OHSS in hCG group.

	Agonis	hCG	p
cases	38	38	
Total Oocyte	770	622	
Fertilization rate	67.77%	61.32%	0.03
Cleavage rate	95.04%	88.92%	0.01
Blastocyst rate	13.9%	7.38%	0.04
Pregnancy rate	24.00%	20.51%	0.54

TABLE 2: Comparison of fertility rates, the rate of cleavage, blastocyst and the pregnancy rate.

5. Discussion

HCG to trigger oocyte maturation is currently the most widely used method for ovulation triggering, and pregnancy rate, live birth rate is higher when compared to administration of GnRH agonist as a trigger oocyte maturation, but it is surely due to their interference luteal phase on administration GnRH agonists when compared to administration of hCG [9]. Research conducted by Tanni Borgbo et al comparing gene expression in granulosa cells in the administration of GnRH agonists and hCG to trigger oocyte maturation concluded that the administration of GnRH agonists increased gene expression of the prosteroidogenesi significant than hCG, it explains why the agonist GnRH triggering obtained better oocyte quality [10]. In that study also found a decrease in the expression of genes that can cause OHSS. Provision of GnRH agonist trigger will cause a surge of LH and FSH, which will lead to the continued return meosis process, maturation of the nucleus and cytoplasm of the oocyte, the expansion of cumulus and ovulation [11]. FSH will lead to an increase of the receptor itself and also an increase in LH receptors in granulosa cells that are important in the process of oocyte maturation [12].

From our study it appears that there are significant differences in fertilization rate (67.72% and 61.32%), cleavage rate (95.04% and 88.92%) and blastocyst rate (13.90% and 7.38%) in both groups and none of the patients developed OHSS in hCG group.

One major advantage of the trigger with GnRH agonists that can reduce the incidence of OHSS [13]. GnRH agonists have been used to prevent OHSS in donor oocytes and maintain good pregnancy rate for recipient [14]. On a normal cycle, there are surge of LH and FSH hormones, these hormones surge more helpful in the process of oocyte maturation when compared with the LH surge only in the use of hCG to trigger ovulation, a surge of FSH required to pursue reprocess meosis oocytes [12]. Although, there have been studies that show the pregnancy rate is lower and higher rates of miscarriage in patients induced by a GnRH agonist compared with hCG in a cycle of autologous because of disorders luteal phase and lower revenue endometrium, but we found no significant differences on biochemical pregnancy rate (24.00% and 20.51%) between agonis triggering dan hCG triggering group. We think thatthe concept of oocyte maturation should be distinguished from the conceptof luteal phase support, so we could get a good oocyte quality, good endometrium reception, and minimize the possible complications of OHSS [15, 16].

GnRH is an alternative to HCG to trigger final oocyte maturation. GnRHa triggering a safer, patient friendly and offers several advantages over HCG physiological triggers. Although the most optimal luteal phase support after GnRHa trigger is still being explored, the time has come to question the concept of HCG triggers automatically and to move forward with thoughtful consideration of the needs and comfort of patients, particularly in terms of prevention of OHSS [7, 17].

Although the exact role of midcycle FSH has not been fully explored, it has been shown that FSH, among other actions, promoting nuclear maturation and the return of meiosis [11]. This may explain why some studies have reported more metaphase oocyte retrieval after GnRHa compared with HCG triggers. GnRHa triggering combined with low dose hCG supplementation, administered either on the day of oocyte retrieval or in the form of dual trigger, rescues the luteal phase and provides a reproductive outcome similar to that seen after hCG triggering

33% of IVF cycles have been reported to be associated with mild forms of OHSS, whereas the more severe forms have been reported in 2%–6% of IVF cycles. GnRH agonists significantly reduce the risk of ovarian hyperstimulation [18]. In this study we found one patient developed OHSS in hCG group

Therefore, GnRHa triggering is now a valid alternative to hCG triggering. Moreover, GnRHa triggering offers the possibility to individually tailor the luteal phase support according to the ovarian response to stimulation.

6. Conclusion

GnRH agonists can be considered for use as a trigger final oocyte maturation in the antagonist protocol because some IVF outcomes data showed that GnRH agonists triggering were better than hCG without increasing the risk of OHSS

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