Effect of Coasting Duration on In-vitro Fertilization Cycle Success

Dilek Benk Silfeler¹  Ali Ovayolu²  Ismet Gun³  Kenan Sofuoglu⁴  
Bulent Emre Bilgic⁵  Ilter Yenidede⁴

¹ Dilek Benk Silfeler, Yildirim Beyazit University, Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara/Turkey, drsilfeler@yahoo.com 
² Ali Ovayolu, Cengiz Gokcek Public Hospital, Department of Obstetrics and Gynecology, Gaziantep/Turkey drovayolu@yahoo.com 
³ Ismet Gun, GATA Faculty of Medicine, Department of Obstetrics and Gynecology, Istanbul/Turkey, drsmetgun@yahoo.com 
⁴ Kenan Sofuoglu, Zeynep Kamil Education and research hospital, Department of Obstetrics and Gynecology, Istanbul/Turkey, ksofuoglu@netscape.net 
⁵ Bulent Emre Bilgic, ZeynepKamil Education and research hospital, Department of Embriology, Istanbul/Turkey, bulentemrebilgic@yahoo.com

Corresponding Author: Dilek Benk Silfeler, Yildirim Beyazit University, Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara/Turkey, drsilfeler@yahoo.com 
GSM: +90 (532) 360 56 26 
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Abstract

Objective: Coasting is used in in-vitro fertilization(IVF) cycles to prevent ovarian hyperstimulation syndrome(OHSS). It is thought that increased coasting duration may decrease oocyte count, oocyte quality and implantation ratio. The aim of this study is to evaluate the effect of coasting duration on IVF outcomes and pregnancy rate.

Methods: This study was a single centered and retrospective study. Study population were selected from women applied Zeynep Kamil Research Hospital IVF department between January 2003 and December 2013(n=7850). Patients who were given GnRH agonist or antagonist protocol and performed coasting(n=108) were included in the study. Patients were divided in two groups as: Group-1(n=85) coasting duration 1-3 days and Group-2(n=23) coasting duration 4-5 days. Basal FSH levels, starting gonadotrophin dosage, total gonadotrophin dosage, gonadotrophin induction period, peak estradiol levels before coasting, estradiol level on HCG day, follicle count before oocyte pick-up, M2 oocyte count, fertilized oocyte count, OHSS incidence and pregnancy rate were compared in between two groups.

Results: Basal FSH levels (5.8±1.4 to 6.9±1.5, p=0.001), starting gonadotrophine dosage (246.6±71.7 to 297.7±67.1, p=0.0027), total gonadotrophine dosage(1813.5±870.8 to 2216.1±832.3, p=0.049) were higher and gonadotrophine induction period (9.4±1.8to11.1±2.8, p=0.0003) was longer in Group-2 than Group-1. Although Peak estradiol levels before coasting is higher in Group-2 than Group-1 (7037.2±1405.5vs5784.4±2701.9, respectively p=0.035), estradiol levels on HCG day were not
statistically different between groups (2993.7±1198.1 vs 3553.2±2746, p=0.154). Fertilized oocyte count was similar between groups. Although there were no difference between groups regarding pregnancy rate(%29.4 to %8.7, p=0.056), pregnancy rate in Group-1 was higher with an odd ratio of 3.38 (95 % confidence interval, 0.864-13.244).

**Conclusion:** This study revealed that coasting duration doesn’t affect oocyte quality and fertilization rate. However, coasting duration should not be routinely extended since it may affect pregnancy rate.

**Keywords:** In-Vitro Fertilization, Coasting, Coasting duration

**Introduction**

Ovarian hyperstimulation syndrome (OHSS) is a life threatening complication of assisted reproductive technology. Coasting is an important method to prevent OHSS in in-vitro fertilization (IVF) cycles (1). Coasting refers to withholding exogenous gonadotropine usage and delaying the administration of hCG in high risk cycles until serum estradiol falls into safe levels (typically less than 2500 to 3000pg/mL) (2). There are many advantages of coasting compared to other preventive methods of OHSS. Coasting doesn’t require cycle cancellation and it allows fresh embryo use rather than cryopreservation (3). However, coasting doesn’t completely prevent OHSS incidence. There are many investigations about effect of coasting on IVF success (4). There is no concurrence about when to start coasting, duration of coasting and the exact protocol to be used for coasting (5). Coasting period>4 days was found to be associated lower pregnancy rates in IVF cycles (6). The aim of present study is to compare the results of different coasting periods.

**Materials and Methods**

**Study Design**

This study was a single centered and retrospective study. The study population was selected from infertile women applied Zeynep Kamil Research Hospital IVF department between January 2003 and December 2013 (n= 7850). Inclusion criterion were having normal serum hormone profile, regular menstrual cycle, first or second cycle of IVF and body mass index (BMI) of 23–28 kg/m2. Women having uterine pathology were also excluded. Patients who were given GnRH agonist or antagonist protocol and performed coasting (n=108) were included in study. Patients were divided in two groups as: Group-1 (n=85) coasting duration 1-3 days and Group-2 (n=23) coasting duration 4-5 days.

Medical history, gynecologic examination and basic infertility tests had been performed all patients. All patients had venous blood sampling in early follicular period and on the day of HCG to detect FSH and estradiol (E2) levels. Transvaginal ultrasonography (TV USG) had been performed to detect antral follicle count in early follicular phase.

Ovulation induction with a agonist or antagonist protocol, 100 mg aspirine and 400 mcg folic acid had been administered patients. Gonadotropine releasing hormone (GnRH) agonist had been started in 21.day of previous cycle and recombinant (rec) FSH [rec-FSH, Gonal-f® (MerckSerono, Turkey) or Puregon®

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(SheringPloug, Turkey)] had been added on third day of cycle in long agonist protocol. rec-FSH(150 IU, recFSH) had been started on second or third day of cycle and GnRH antagonist had been added on the sixth day of cycle in antagonist protocol. Starting dosage of rec-FSH was made according to patients’ age, BMI, antral follicle count and basal FSH levels. Following, in both protocols recFSH dosage had been arranged according to follicle diameter in TV USG and serum E2 levels. When the leading follicle diameter reached to 18 mm or two follicle diameter were greater than 16 mm, 10,000 IU hCG (Pregnyl®, SheringPloug) intramuscularly or 250 mcg rec-hCG(Ovitrelle; Merck. Serono) subcutenously were enjected. Gonadotropines administration were stopped in women having peak E2 levels greater than 4000.

Oocyte pick-up (OPU) were performed 35.5 hours after HCG administration under intravenous (IV) sedation and with guidance of TV USG. Single dose Cefazolin sodyum (iv, 1 gram) were given all patients during OPU. Doxycycline (100 mg, two times daily, po) and methylprednisolone (16 mg, one daily, po) were given patients for 4 days. Intravaginal 90 mg progesterone (% 8 Crinone gel,Serono) for luteal phase support were started all patients from OPU day.

Oocyte maturation scoring were made according to Veeck’s classification as 0-4 (7). Pronuclear scoring was evaluated 16-18 hours after intracytoplasmic sperm enjection (ICSI). Embryo quality was scored as 1-5 according to morphology of embryo splitting before ET (8).

Single Embryo transfer (ET) were performed via USG guidance after 2-5 days. After 12 days, serum Beta-HCG levels were measured for pregnancy detection. Beta-HCG levels>20 IU/l were named as biochemical pregnancy and fetal cardiac activity observed in USG after 6 weeks of ET was called as clinical pregnancy. Basal FSH levels, starting gonadotrophin dosage, total gonadotrophin dosage, gonadotrophin induction period, estradiol levels before coasting, follicle count before oocyte pick-up, M2 oocyte count, fertilized oocyte count, OHSS incidence and pregnancy rate were compared in between two groups.

Statistical analysis
Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows 15.0 software (SPSS, Chicago, IL., USA). Descriptive statistics were given as mean, standard deviation, frequency and percentage. To compare parametric continuous variables, the Student t test was used; to compare nonparametric continuous variables, the Mann-Whitney U test was used; and to compare categorical variables, the chi-square test was used. P values <.05 were considered to indicate statistical significance.

Results
Study population consisted of 108 patients as 85 patients in Group-1 and 23 patients in Group-2. There are no statistically significant difference between groups regarding age (30.4±4.1 vs 31.7±2.8, respectively, p=0.174). The demographic characteristics of the study
population were described in Table 1. Basal FSH levels (5.8±1.4 vs 6.9±1.5, p=0.001), starting gonadotrophin dosage (246.6±71.7 vs 297.7±67.1, p=0.0027), total gonadotrophine dosage(1813.5±870.8 vs 2216.1±832.3, p=0.049) were higher and gonadotrophine induction period(9.4±1.8 to 11.1±2.8, p=0.0003) was longer in Group-2 than Group-1. Although Peak estradiol levels before coasting is higher in Group-2 than Group-1. Although Peak estradiol levels before coasting is higher in Group-2 than Group-1 (5784.4±2701.9 vs 7037.2±1405.5, respectively p=0.035), estradiol levels on HCG day were not statistically different between groups (2993.7±1198.1 vs 3553.2±2746, p=0.154). No patient in Group-2 had OHSS whereas 2 patients in Group-1 had mild OHSS. Fertilized oocyte count was similar between groups. Although there were no difference between groups regarding pregnancy rate(%29.4to %8.7, p:=0.056)), pregnancy rate in Group-1 was higher with an odd ratio of 3.38 (95% confidence interval, 0.864-13.24).

Table1. Comparison of groups regarding basal Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>Group-1 (n=85)</th>
<th>Group-2 (n=23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>30.4±4.1</td>
<td>31.7±2.8</td>
<td>0.174a</td>
</tr>
<tr>
<td>Basal FSH, IU</td>
<td>5.8±1.4</td>
<td>6.9±1.5</td>
<td>0.001a</td>
</tr>
<tr>
<td>Infertility duration, year</td>
<td>7.3±3.9</td>
<td>8.8±4.3</td>
<td>0.123a</td>
</tr>
<tr>
<td>Induction duration, day</td>
<td>9.4±1.8</td>
<td>11.1±2.8</td>
<td>0.003a</td>
</tr>
<tr>
<td>Starting gonadotrophine dosage, IU</td>
<td>246.6±71.7</td>
<td>297.7±67.1</td>
<td>0.0027a</td>
</tr>
<tr>
<td>Total gonadotrophine dosage, IU</td>
<td>1813.5±870.8</td>
<td>2216.1±832.3</td>
<td>0.049a</td>
</tr>
<tr>
<td>Peak Estradiol level, pg/mL</td>
<td>5784.4±2701.9</td>
<td>7037.2±1405.5</td>
<td>0.035a</td>
</tr>
<tr>
<td>Estradiol level on HCG day, pg/mL</td>
<td>2993.7±1198.1</td>
<td>3553.2±2746</td>
<td>0.154a</td>
</tr>
<tr>
<td>Follicle count before oocyte pick-up, n</td>
<td>13.8±6.2</td>
<td>11.1±6.5</td>
<td>0.09a</td>
</tr>
<tr>
<td>Total M2 oocyte count, n</td>
<td>10.3±4.9</td>
<td>8.5±6.7</td>
<td>0.174a</td>
</tr>
<tr>
<td>Fertilization rate, n</td>
<td>6.2±3.4</td>
<td>5.1±5.3</td>
<td>0.405a</td>
</tr>
<tr>
<td>Pregnancy rate, n (%)</td>
<td>25/85 (%29.4)</td>
<td>2/23 (%8.7)</td>
<td>0.0562b</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD and number (percent).

*aStudent t test.

bχ2 test.
Discussion

Our study results shown that coasting duration in IVF cycles does not affect oocyte quality, fertilization rate and pregnancy rate. Although there were no difference between groups regarding pregnancy rate, short coasted group had higher pregnancy rate than long coasted group with an odd ratio of 3.38. We think that long coasting time may decrease endometrial receptivity because oocyte quality and fertilization rate were not changed in between groups in our study.

Coasting is a frequently applied method for prevention of OHSS in IVF cycles which have high estradiol levels before adequate follicle development(9). Coasting lead to controlled follicle atresia in this situation. Cessation of gonadotrophines and continuation of GnRH analogs result in continued leading follicle grow than decrease in E2 levels to safer levels (<3500 pg/ml). After E2 levels decrease to safe levels, ovulation induction and follicle aspiration are performed. Long coasting duration might increase atretic follicle count and as a result peaked oocyte count decreases. Prolongation of coating might decrease E2 levels to very low levels (10,11).

Mature oocyte number, fertilization rate and pregnancy rate were not different between groups in our study. Izaa et al. stated that prolongation of coasting duration beyond 4 days decreases pregnancy rate in IVF cycles with donor egg (12). Since donor egg IVF cycles eliminated endometrial factor, decrease in pregnancy rate was thought to depend on decreased quality of oocyte and embryo(12). Similarly, Garsia-Velasco et al. found that prolongation coasting duration beyond 4 days decreases clinical pregnancy and implantation rate (13-14). Furthermore, Morenol et al. stated that while 4 days of coasting had implantation rate of 21.9%, 5 days of coasting decreased implantation rate to %14.3 (15). Nardoet et al. found that there were no difference in oocyte maturity, fertilization and embryo cleavage rate between 2 cycles as coasted 1-3 days and 4-5 days (16). However patients coasted for ≥4 days had significantly decreased retrieved oocyte counts and implantation rates (P < 0.05). Pregnancy rate/embryo transfer and livebirth rate were not different between groups. They stated that coasting decreases the risk of OHSS without compromising the IVF cycle pregnancy outcome. Reduced implantation rate in patients coasted for ≥4 days was thought due to the deleterious effects on the endometrium rather than the oocytes (16).

Most studies revealed that prolonged coasting time decreases retrieved oocyte number significantly(16-20). Reduced oocyte retrieval after prolonged coasting may be due to poor follicular response (lack of LH receptor up regulation) to the exogenous hCG which lead to failure of final oocyte maturation. The oocytes that fail to undergo final maturation can not be retrieved because they may stick to the follicular wall. As a result many follicles in appropriate size may not yield any oocytes(6,17). However oocyte retrieval were similar between groups in our study. Although statistisically non- significant, Group-1 had higher pregnancy rate than Group-2 with an odd ratio of 3,38(95 % confidence interval 0.864-13.244,p=0,056). We think that coasting time does not affect oocyte
quality and fertilization rate but it has possible deleterious effect on endometrial receptivity.

In conclusion, coasting is a preferred method to prevent OHSS incidence. Our study result revealed that coating duration does not affect oocyte quality and fertilization rate. However coating duration should not be routinely extended since it may affect pregnancy rate. In high risk patients for OHSS, estradiol levels should be decreased regarding follicle size by step-down protocol firstly. After that if high estradiol levels persist, coasting may be preferred.

References


