

The Effects of Smoking and Obesity on ICSI Outcomes: A Retrospective Analysis

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Cigarette smoking and obesity are both common health problems in developed and developing countries and are associated with an increased morbidity and mortality. The fecundity rate is found to be decreased by both smoking and obesity in unassisted reproduction in large epidemiologic studies. In the literature, the effects of obesity and smoking on ICSI are demonstrated separately. Our current study aims to reveal the effects of smoking together with obesity on ICSI outcomes. Our result showed that there was no statistically significant difference of outcomes between smokers and nonsmokers in all BMI groups which scheduled to GnRH Agonist ICSI cycle.

Key Words: Smoking, Obesity, GnRH agonist, ICSI

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Introduction

Cigarette smoking and obesity are both common health problem in developed and developing countries and are associated with an increased morbidity and mortality. The fecundity rate is found to be decreased by both smoking and obesity in unassisted reproduction in large epidemiologic studies.¹⁻³ Although the time to natural conception may be delayed in smokers, overall cumulative pregnancy rates have been reported to be remarkably similar.⁴ Toxins in cigarette smoke have been implicated in diminishing ovarian reserve.⁵ Furthermore, smoking by males decreases the success rates of assisted reproduction procedures, not only in IVF, but also in ICSI.⁶

Overweight women are known to be at a higher risk of menstrual dysfunction and anovulation, possibly due to altered secretion of pulsatile GnRH, resulting in altered sex hormone binding globulin (SHBG), ovarian and adrenal androgens and Luteinizing hormone (LH). Weight loss in these women is associated with the return of spontaneous ovulation and a reduced likelihood of requiring induction of ovulation.⁷ The detrimental effect of obesity on reproduction may be due to multiple endocrine and metabolic alterations including steroid metabolism, altered secretion and action of insulin and

other hormones, such as leptin, resistin, ghrelin or adiponectin.⁸⁻⁹ Obese women require higher dose of gonadotrophins and have an increased miscarriage rate in ART cycles.¹⁰ In the literature, the effects of obesity and smoking on ICSI are demonstrated by separately. The isolated obesity seems to have a detrimental effect on ICSI outcomes.¹¹ However, female tobacco smoking has no effect on IVF outcomes.¹² Our current study aims to reveal that what are the effects of smoking together with obesity on ICSI outcomes.

Material and Method

This study was conducted from November 2003 to April 2008 in Baskent University Department of Gynecology and Obstetrics, Division of Reproductive and Endocrinology Unit. A total of 1215 patients undergoing ICSI cycles were enrolled via the computerized IVF database system. Patients who had undergone first ICSI cycle with a long-luteal GnRH agonist protocol were selected in order to get uniform data and to minimize the female factor. Microdose flare and GnRH antagonist protocols were omitted from the study, which patients diagnosed as poor responders (<6 oocytes in the OPU) and potential poor responders (FSH>10 mIU/L and antral follicle count < 6). Freeze-thaw cycles, advanced female age (>40 year-old) were also excluded from the study. Patients were categorized as group 1: normal weight with nonsmoking (BMI:18,5-24,99 kg/m²), group 2: Overweight with nonsmoking (BMI:25-29,99 kg/m²), group 3: Obese with nonsmoking (BMI: 30-35 kg/m²), group 4: Normal weight with smoking, group 5: overweight with smoking and group 6: obese with smoking.

Ovarian down-regulation was initiated with daily leuprolide acetate 1 mg (Lucrin, Abbott, France), beginning on the 21st day of the preceding menstruation. After ovarian suppression was achieved, the dose was reduced to 0.5 mg until the day of hCG. If there were no cysts \geq 2 cm and the E2 was

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<50 pg/mL, gonadotropin stimulation with 150-300 IU of gonadotropins (Gonal-f, Serono, Randolph, MA, USA) was performed, with E2 monitoring commencing on the morning of stimulation day 5. Ultrasound and blood E2 monitoring continued until hCG administration criteria were met with at least three follicles having a maximum diameter of >17 mm. Transvaginal ultrasound-guided oocyte retrieval was performed 35-36 hours after the hCG injection. An oocyte pick-up was performed with a 17-gauge needle for oocyte retrieval under sedation with propofol (propofol 1% Fresenius Kabi, Germany). The oocyte-corona complexes (OOC) were denuded, and ICSI was performed after 2 hours of incubation and the embryos were transferred on day 3. The embryo transfer policy depends on the number and quality of embryos developed. The transfer protocol was individualized for poor grade embryos up to 4 embryos. All patients received luteal support with 90 mg progesterone intravaginally (Crinone 8% gel, Serono, Randolph, MA, USA) daily after embryo transfer. Clinical pregnancy was defined as the presence of at least one

gestational sac with detectable fetal cardiac activity by transvaginal ultrasonography. Live birth was defined as delivery time after 27 weeks of gestation with at least one live baby.

Embryos were graded on day 3 according to a 1 to 4 scoring system (with 1 being the best), which was based on fragmentation, cell symmetry and blastomere number.¹³

Results

In our study group 24.52 % of women scheduled to ICSI program were smoker. ICSI cycle characteristics are shown in table 1. There was no statistically significant difference between smokers and nonsmokers in all BMI groups. Total gonadotropin use is significantly higher in obese patients in both groups and grade 2 embryos are higher in smoker groups ($p<0,05$) (table 1). Although live birth rates of obese smoker group seemed to be lower than the others, the difference did not reach statistical significance. Abortion and cancellation rates were similar in all groups (table 2).

Table 1: Basal Characteristics of Study Group

BMI	Non-smokers			Smokers			P
	18,5-25 kg/m ²	25-30 kg/m ²	30-35 kg/m ²	18,5-25 kg/m ²	25-30 kg/m ²	30-35 kg/m ²	
Age (years)	30,08±5,11	32,45±4,85	32,11±4,66	30,54±4,63	31,7±4,87	31,11±5,08	NS
Duration of Infertility	6,11±4,43	8,86±4,49	9,19±4,56	6,11±4,15	8,62±4,80	8,50±3,86	NS
FSH	6,46±2,73	6,52±2,86	6,00±1,86	6,71±4,59	6,34±1,97	6,37±3,86	NS
Total Gonadotropin Dose	2358*±1086	2685±1120	2761*±877	2405*±1147	2650±1153	2751±986*	0,01
E2 on hCG day	2273±1286	1997±1152	1950±1366	2111±1306	1934±2035	1880±1670	NS
Endometrial Thickness on hCG day	11,44±2,3	11,63±2,53	11,65±2,41	11,15±2,45	11,51±2,48	11,02±2,07	NS
M2 Oocyte number	11,79±5,94	11,55±8,17	11,03±5,77	12,01±6,44	11,11±6,69	11,25±5,55	NS
Fertilization Rate (%)	67,92±22,66	66,77±23,11	65,71±22,74	67,89±22,11	66,39±21,19	76,86±16,95	NS
Total embryo numbers	7,80±4,76	7,27±4,48	7,24±4,77	7,89±4,9	6,87±4,47	7,86±4,08	NS
Transferred embryo numbers	2,83±1,24	2,75±1,36	2,75±1,13	2,87±1,24	2,85±1,41	2,90±1,27	NS
Cryopreserved embryo numbers	7,20±2,81	6,08±2,70	8,92±2,92	7,62±3,62	5,50±1,83	6,16±1,94	NS
Grade 1 embryo numbers	1,40±1,22	1,57±1,27	1,43±1,29	1,32±1,17	1,13±1,23	1,28±1,21	NS
Grade 2 embryo numbers	1,67±1,30	1,51±1,32	1,49±1,24	1,82 ±,31	1,94±1,33	1,96±1,47	0,01

* $p<0,05$ • NS: Not Significant

Table 2: ICSI Outcomes

BMI for Non-smokers	Cycles Numbers	Clinical Pregnancy Rate %	Implantation Rate (%)	Abortion (%)	Live Birth Rate (%)	Cancellation Rate (%)
18,5-25 kg/m ²	493	41,3	26,4	8,0	35,0	11,0 (54/493)
25-30 kg/m ²	303	39,7	25,6	9,4	35,0	14,2 (43/303)
30-35 kg/m ²	121	43,1	28,5	10,1	34,5	10,7 (13/121)
BMI for Smokers						
18,5-25 kg/m ²	186	43,1	29,2	5,7	37,5	10,8 (20/186)
25-30 kg/m ²	78	30,0	24,1	12,2	25,9	11,5 (9/78)
30-35 kg/m ²	34	28,9	20,2	10,5	20,6	17,6 (6/34)
p		NS	NS	NS	NS	NS

NS; Not significant

Discussion

Current study provides that neither obesity nor smoking adversely affect ICSI outcomes in ICSI cycles with GnRH agonist protocol. Instead, we have had expected to be lower live birth rate in obese and smoker group. Although many authors and organizations accuse smoking and obesity for reproductive health, our data did not show a deleterious impact on ICSI outcomes which did not mean to encourage for smoking and obesity. Obesity causes to the use of higher amount gonadotropins in ART cycles which lead to increase to the total cost of cycle. The current study also confirmed that the requirement of gonadotropins increases with the increase of BMI.

This is the first study comparing to the effects of both smoking and obesity on ICSI outcomes. There are several large studies, including ours, fail to show an unfavorable effect of smoking and obesity on IVF/ICSI outcomes, separately. This might be an opportunity of assisted reproductive technology for selection of high quality embryos. One can suspect that obesity and smoking both might lead to the development of poor quality embryos. We could not show poorer embryo quality in obese smoker group. However, Neal MS et al. found that despite similar embryo quality there was a striking difference in implantation and pregnancy rates of mainstream and sidestream smokers when compared with non-smokers.¹⁴ We found similar numbers of grade 1 embryos in all groups that did confirm Neal et al., whereas our live birth rates were similar in terms of smoking and obesity.

Fedorcsak et al has shown that higher BMI was associated with increased incidence of early pregnancy loss (before week 6 of gestation) and cumulative pregnancy rates of 3 cycles were lower in obese group. In that study, there was no difference in live birth rates between obese group and others considering first ICSI cycles.¹⁵ We selected a special group which consisted of almost first ICSI cycles and GnRH agonist protocol however, we could not find a detrimental effect of obesity on ICSI outcomes considering for abortion rates and live birth rates, especially nonsmokers group. Although 15 percent differences of live birth rates between obese smokers and normal weight non-smokers did not reach statistical significance, this difference makes sense considering to the emotional status of infertile couples. Esinler et al. found that cryopreserved embryo numbers were decreased and cancellation rates were increased in isolated obese (BMI > 30 kg/m²) group. However, authors found similar ongoing pregnancy rates in all groups.¹¹ The current study showed that both cancellation rate and cryopreserved embryo number were also similar in all groups even in all smokers.

Sigara ve Obezitenin ICSİ Sonuçlarına Etkileri: Retrospektif Analiz

Sigara ve obezite gelişmiş ve gelişmekte olan ülkelerde artmış mortalite ve morbidite ile ilişkili yaygın bir sağlık problemidir. Geniş epidemiyolojik çalışmalarda sigara ve obezitenin yardımcı üreme tekniği olmayanlarda fekundite oranlarını azalttığı bulunmuştur. Literatürde sigara ve obezitenin ICSI üzerine etkileri ayrı, ayrı gösterilmiştir. Çalışmamız sigara ve obezitenin ICSI üzerine etkilerinin birlikte değerlendirilmesini amaçlamaktadır. GnRH agonist siklus programına alınan hastalarda sigara içen ve içmeyen tüm Vücut Kitle İndeksi (VKİ) gruplarında sonuçlarımız istatistiksel anlamlı fark olmadığını göstermiştir.

Anahtar Kelimeler: Sigara, Obezite, GnRH Agonist, ICSI.

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