Does Cigarette Smoking Affect Intracytoplasmic Sperm Injection (ICSI) and Embryo Transfer (ET) Outcomes?

Lale KARAKOÇ SÖKMENSÜER[1,2], İbrahim ESİNLER[2], Gürkan BOZDAĞ[2], Tarık AKSU[2], Serdar GÜNALP[2]
Ankara-Turkey

OBJECTIVE: To investigate the effect of smoking on controlled ovarian stimulation performance and ICSI-ET results.
STUDY DESIGN: 193 ICSI cycles with ejaculated sperm were included. ICSI-ET outcome of smokers (n=54) and non-smokers (n=139) were compared. Only initial cycles stimulated via luteal long leuprolide acetate with recombinant follicle stimulating hormone or oral contraceptive plus luteal long leuprolide acetate with rFSH protocol were included. Patients with confounding factors such as female age >40, the presence of any ovarian surgery, unilateral oophorectomy or advanced endometriosis (stage III or more) were excluded.
RESULTS: The number of retrieved oocyte cumulus complexes (OCC), metaphase-2 oocytes (M2), the fertilization rate, and the total number of the embryos available on day 3 were comparable among the two groups. Mean number of transferred grade 1, grade 2 and total embryos were also comparable between smokers and non-smokers groups. The cycle cancellation rates due to inadequate response to COH were similar among two groups. The clinical pregnancy rates were not statistically different for the two groups.
CONCLUSION: Smoking is a well known poor prognostic factor for spontaneous conception or IVF-ET cycles. However, deleterious effect of smoking may not be directly adapted to the whole ICSI-ET cycles in patients without another risk factor threatening ovarian reserve.
(Gynecol Obstet Reprod Med 2007;13:1 46-48)

Key Words: Cigarette smoking, İnfertility, ICSI, Embryo quality, Pregnancy rate

ICSI outcomes are affected by several factors such as female age, type of infertility, previous ovarian surgery, embryo culture conditions, embryo quality, embryo transfer technique and endometrial receptivity. There are also many unknown factors such as cigarette smoking which may be responsible for the failure of ICSI treatment.

The effect of smoking on female infertility has been investigated for many years. It has been known that cigarette contains many toxic constituents such as nicotine, nicotine metabolites (cotinine), heavy metals such as cadmium, carbon monoxide, radioactive polomine, naphthalene and methylnaphtalene[1]. In a study by Zenzes et al.[2] follicular cotinine level in smokers was higher than passive smokers and nonsmokers. Another study showed that cadmium was detected higher in follicular fluid in smokers than non smokers [3]. It has been concluded that metabolites of cigarette such as cotinine and cadmium may be responsible for the negative effect of smoking on ovarian function [4].

In this retrospective study we aimed to evaluate the effect of smoking on controlled ovarian stimulation performance and ICSI-ET results.

Material and Methods

A total of 193 ICSI cycles with ejaculated sperm were included. Smoking more than five cigarettes per day was included (n=54). Nonsmokers were defined as persons who never consumed cigarettes (n=139). Only initial cycles stimulated via luteal long leuprolide acetate with recombinant follicle stimulating hormone or oral contraceptive plus luteal long leuprolide acetate with rFSH protocol were included. Patients with confounding factors such as female age >40, the presence of any ovarian surgery, unilateral oopherectomy or advanced endometriosis (stage III or more) were excluded. Standard culture conditions with day 3 transfers were employed. Vaginal progesterone was used for luteal phase support in all patients. Values were expressed as mean ±SD, unless stated otherwise. Mann Whitney U test, chi square and fisher exact tests were used. Type 1 error was set at 0.05.

Results

The mean female age (31.3±5.2 vs 31.6±4.9y), the body mass index (24.5±4.0 vs 24.8±3.9 kg/m²), the duration of

[1]*Department of Histology and Embryology,*
[2]*Department of Obstetrics and Gynecology, Unit of Test-Tube Baby Hacettepe University Faculty of Medicine, Ankara, Turkey*

Address of Correspondence *Lale Karakoç Sökmensüer*
Hacettepe Üniversitesi Tıp Fakültesi
Histoloji ve Embriyoloji A.D.
Sıhhiye/Ankara

Submitted for Publication: 19.03.2007
Accepted for Publication: 19.03.2007

stimulation (9.6±1.6 vs 9.7±1.7 d), the total dose of gonadotrophin used (35.2±17.4 vs 36.9±18.3 IU), the antral follicle count (12.5±6.4 vs 11.3±5.4) and maximum estradiol level (2060.8±1120.1 vs 2470±1583.2 pg/ml) were similar among the smokers and nonsmokers groups, respectively ($p>0.05$). The mean early follicular phase FSH serum level (7.2±2.5 vs 5.8±1.6 mIU/L, $p<0.05$) was higher and the number of available follicles with a diameter of 15-17mm on the day of hCG administration was less (3.0±2.4 vs 4.7±5.3, $p<0.001$) in the smokers group when compared with non-smokers. However, the number of retrieved oocyte cumulus complexes (OCC), metaphase-2 (M2) oocytes, the fertilization rate and the total number of embryos available on day 3 were comparable among the two groups. The mean number of transferred grade1 (0.4±0.6; 0.3±0.6), grade 2 (2.5±1.2; 2.1±1.1) and total embryos (2.5±1.0; 2.6±1.0) were also comparable between smokers and non-smokers groups. The cycle cancellation rate due to inadequate response to COH were similar ($p>0.05$). The clinical pregnancy rates among smokers and non-smokers were 47.9% and 46.1%, respectively ($p>0.05$).

Discussion

The earlier onset of menopause and a diminished fertility among smokers in comparison with non-smokers were reported by Jick et al[5]. El-Nemr et al [6] concluded that young women smokers had reduced the ovarian reserve and poor response to ovarian stimulation in their retrospective study. They examined 173 consecutive women undergoing IVF and ET treatment and reported higher mean serum FSH concentration and higher mean dosage of gonadotrophins for ovarian stimulation in smokers. A lower mean number of oocytes, higher cycle cancellation rate and total fertilization failure were observed in smokers. In another study adverse effects of smoking on in vitro fertilization-embryo transfer results were reported by Elenbogen et al.[7]. The follicular fluid estradiol level and fertilization rate were lower in smokers group in their study. Another group showed that serum estradiol concentrations, oocyte number and embryo number were found significantly lower in smoker group[8]. It has been demonstrated that serum testosterone levels was higher in smoker women undergoing in vitro fertilization [9]. Shiloh et al. have shown that increased zona thickness of oocytes and embryos in active and passive smokers[10]. In another study it has been reported that the number of fertilized oocytes was significantly lower in smoking women[11].

In contrast, some other studies concluded that female smoking had no negative effect on IVF outcome. In their prospective study Trap et al. concluded that smoking had no affect on fertilization and pregnancy rate of IVF patients[12]. Sterzik et al. reported that smokers had lower serum estradiol levels, but no differences in fertilization and pregnancy rates were found between two groups[13]. Similar results were reported by Hughes et al., they concluded that no difference in fertilization, pregnancy and abortion rate among two groups[14].

Our data showed that the number of retrieved oocyte cumulus complexes, metaphase-2 oocytes, the fertilization rate and the total number of embryos available on day 3 were comparable among the smokers and non-smokers groups. The mean number of transferred grade 1, grade 2 and total embryos were also comparable between smokers and non-smokers groups. The cycle cancellation rate due to inadequate response to COH and the clinical pregnancy rates among smokers and non-smokers were also similar.

In conclusion, our results suggest that although the well known toxic effects of smoking, it has no deleterious effect on ICSI results. Further studies are needed to elucidate these conflict results of cigarette smoking on infertility treatment.

References

1. Stillman RJ, Rosenberg MJ and Sacks BP. (1986) Smoking and reproduction . Fertil Steril, 46, 545-566.
2. Zenzes MT, Reed TE, Wang P, Klein J. (1996) Cotinine, a major metabolite of nicotine, is detectable in follicular fluids of passive smokers in in vitro fertilization therapy. Fertil Steril, Oct; 66(4): 614-9.
3. Zenzes MT, Krishnan S, Krishnan B, Zhang H, Casper RF. (1995) Cadmium accumulation in follicular fluid of women in in vitro fertilization-embryo transfer is higher in smokers. Fertil Steril, Sep; 64(3): 599-603.
4. Zenzes MT, Reed TE, Casper RF. (1997) Effects of cigarette smoking and age on the maturation of human oocytes. Hum Reprod, 12, 1736-1741.
5. Jick H., Porter J. and Morrison AS. (1977) Relation between smoking and age of natural menapause. Lancet, 1, 1354-1355.
6. El-Nemr A, Shawaf T, Sabatini L, Wilson C, Lower AM and Grudzinskas JG. (1998) Effect of smoking on ovarian reserve and ovarian stimulation in in-vitro fertilization and embryo transfer. Hum Reprod 13, 2192-2198.
7. Elenbogen A, Lipitz S, Mashiach S, Dor J, Lebran D and Ben-Rafael Z. (1991) The effect of smoking on the outcome of in-vitro fertilization-embryo transfer. Hum Reprod 6, 242-244.
8. Voorhis BJ, Dawson JD, Stovall DW, Sparks AE, Syrop CH. (1996) The effects of smoking on ovarian function and fertility during assisted reproduction cycles. Obstet Gynecol Nov; 88(5):785-91.
9. Barbieri RL, Slus PM, Powers RD, McShane PM, Vitonis A, Ginsburg E, Cramer D. (2005) Association of body mass index, age and cigarette smoking with serum testes-

terone levels in cycling women undergoingbin vitro fertilization. Fertil Steril Feb 83(2); 302-308.

10. Shiloh H, LahavBaratz, Koifman M, Ishai D, Bidder D, Weiner-Meganzi Z, Dirnfeld M. (2004) The impact of cigarette smoking on zona pellucida thickness of oocytes and embryos prior to transfer into the uterine cavity. Hum Reprod 19, 157-159.
11. Crha I, Hruba D, Fiala J, Ventruba P, Zakova J and Petrenko M. (2001) The outcome of infertility treatment by in-vitro fertilization in smoking and non-smoking women. Cent Eur J Publ Hlth 9, 64-68.
12. Trapp M, Kemeter P and Feichtinger W. (1986) Smoking and in-vitro fertilization. Human Reprod 1, 357-358.
13. Sterzik K, Strehler E, De Santo M, Trumpp N, Abt M, Rosenbusch B and Schneider A. (1996) İnfluence of smoking on fertility in women attending an in vitro fertilization program. Ferti Steril 65, 810-830.
14. Hughes E, Yeo J, Claman P, Younglai EV, Sagle MA, Daya S and Collins JA. (1994) Cigarette smoking and the outcomes of in vitro fertilization: measurement of effect size and levels of action. Fertil Steril 62, 807-814.