

CLINICAL ASSISTED REPRODUCTION

Cigarette Smoking at Time of *in Vitro* Fertilization Cycle Initiation Has Negative Effect on *in Vitro* Fertilization–Embryo Transfer Success Rate¹

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Submitted: December 15, 1994

Accepted: January 19, 1995

Purpose: To assess cigarette smoking of female patients prior to starting *in vitro* fertilization cycle and possible affect on subsequent *in vitro* fertilization–embryo transfer outcome.

Methods: Retrospective study involving 340 consecutive patient questionnaires filled out at time of *in vitro* fertilization program entry. Only cycles resulting in embryo transfer after transvaginal ultrasound directed ovum retrieval ($n = 253$) were considered. The three patient pregnancy outcomes of not pregnant, spontaneous abortion, and live birth, were cross-referenced with smoking and nonsmoking patients.

Results: No significant difference found in overall pregnancy rate per embryo transfer for smokers (35%) vs nonsmokers (31%). However, the abortion rate was significantly higher for the smokers (73%) vs nonsmokers (24%) with a P value < 0.001 .

Conclusions: Results suggest preentry *in vitro* fertilization cycle cigarette smoking has adverse affect on potential pregnancy outcome by increasing spontaneous abortion. Preconception health consultation concerning adverse cigarette smoking effects should be implemented prior to program entry.

KEY WORDS: smoking; spontaneous abortion; *in vitro* fertilization.

¹ Presented at the 50th Annual Meeting of the American Fertility Society, San Antonio, Texas, November 5–10, 1994.

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INTRODUCTION

Epidemiological studies have suggested an association between reduced fertility and cigarette smoking in women (Pettersson (1), Kline *et al.* (2), Olsen *et al.* (3), Baird and Wilcox (4), Howe *et al.* (5), Stillman *et al.* (6), Phipps *et al.* (7), Rosevear *et al.* (8), Windham *et al.* (9), Sharara (10)). Even though this would seem to be a “commonsense” association, there is only limited data involving *in vitro* fertilization–embryo transfer (IVF-ET) success rate and smoking in female patients. This study is to assess cigarette smoking of female patients at the time of starting the *in vitro* fertilization cycle and to correlate possible effects on subsequent IVF-ET outcome.

MATERIALS AND METHODS

The study design is a retrospective review of patient questionnaires which were filled out at time of IVF program entry. Questions concerning female patient cigarette smoking and packs smoked per day were typically confirmed prospectively at the initial IVF interview. No counseling was instigated to alter patient smoking habits. There were 340 consecutive patient entries into the William Beaumont IVF program between January 2, 1992 and September 1, 1993 which were reviewed. Only cycles meeting all the following criteria were considered for retrospective review of cigarette smoking history (253

patients): (1) luteal phase gonadotropin releasing hormone agonist (GnRH-a) suppression with human menopausal gonadotropin (hMG) stimulation; (2) transvaginal ultrasound directed ovum retrieval (TUDOR); (3) cycles resulting in ET after TUDOR. Treatment cycle outcomes were divided into three groups: not pregnant, spontaneous abortion, live birth. These three groups were cross-referenced by smoking and nonsmoking patients. Outcomes were analyzed on contingency tables with Yates's chi-squared analysis or Fisher's exact test.

RESULTS

There was no significant difference in the overall pregnancy rate per ET for smokers (35%) vs nonsmokers (31%) as seen in Table I.

However, the abortion rate was significantly higher for the smokers (73%) vs nonsmokers (24%), with a P value < 0.001 as seen in Table II.

Multiple factors analyzed that showed no significant differences for the smokers vs nonsmokers included mean age of patient (\pm std. dev. being 36.3 ± 4.5 years for smokers vs 35.5 ± 4.4 years for nonsmokers), etiology for entry into IVF, prelupron initiation serum progesterone level, number of ampules of hMG used, day of human chorionic gonadotropin (hCG) shot, serum estradiol level on day of hCG shot, serum progesterone level on day of hCG shot, in number of embryos transferred, quality of embryos at the time of ET, number of hours to ET, uterine depth of ET, ultrasound derived endometrial thickness or pattern at TUDOR, presence of blood at ET, difficulty of ET, type or amount of luteal progesterone support.

No significant difference was found concerning number of cigarettes smoked by women who aborted vs women who smoked and had live births (mean 15 cigarettes per day, range 5–40). Also no significant difference was found concerning number of weeks of the pregnancy when spontaneous abortion occurred in smoking women (mean 7.1 weeks,

Table I. Overall Pregnancy Rate per Embryo Transfer

Patient group	Nonpregnant ($n = 173$)	Pregnant ($n = 80$)	Pregnancy rate (%) ^a
Nonsmokers	145	65	31
Smokers	28	15	35

^a P value n.s.; $P > 0.02$.

Table II. Spontaneous Abortion Versus Ongoing Pregnancy

Patient group	Abortion ($n = 27$)	Ongoing pregnancy ($n = 53$)	Abortion rate ^a
Nonsmokers	16	49	24% (16/65)
Smokers	11	4	73% (11/15)

^a P value < 0.001 .

range 5.5–11) vs nonsmoking women (mean 8 weeks, range 5.5–13 weeks).

DISCUSSION

This study suggests that patients who conceive through IVF-ET while continuing to smoke cigarettes have a lower live birth rate, compared to nonsmoking patients. This difference is due to increased spontaneous abortion rate in the smoking women. This supports earlier studies. Pattinson *et al.* (11) showed an increased spontaneous abortion rate in smokers, 42% (8/19), vs nonsmokers, 20% (10/50). Harrison *et al.* (12) showed smokers, 55%, vs nonsmokers, 20%, spontaneous abortion rates. Elenbogen *et al.* (13) found only one pregnancy in a small group of smokers ($n = 22$) vs four pregnancies in the nonsmokers ($n = 21$), and that was an ectopic pregnancy. However, Hughes *et al.* (14,15) had no significant difference in clinical outcome after ET in smokers vs nonsmokers.

A fault with this study is that there is no follow-up smoking habit questionnaire. Even though no intervention to change smoking habits was instigated, there are no data to confirm this assumption. There could have been a decrease in smoking from unidentified outside influences. However, there could also be an increase in smoking due to physical, emotional and financial stresses, as shown by Trapp *et al.* (16).

The evaluation of smoking effects on IVF-ET may still be unresolved. This study suggests removing variables, such as smoking, to be in the couples best interest for achieving IVF-ET, live birth outcome.

CONCLUSIONS

Our results suggest female patient cigarette smoking at the time of starting an IVF cycle has an adverse affect on IVF-ET pregnancy outcome by in-

creasing spontaneous abortion rate, thereby decreasing live delivery rate. These results therefore suggest preconception health consultations concerning potential adverse effects of cigarette smoking should be implemented prior to IVF program entry.

ACKNOWLEDGMENTS

The authors thank Nancy Vincent, RN and Marianne Allen, RN for data retrieval. The authors thank Jane Maximovich for assistance in manuscript preparation.

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