Impact of passive smoking on the results of assisted fertilization

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Summary: The hazardous effect of cigarette smoking on sperm fertilizing potential and oocyte quality have been well documented in active male and female smokers respectively. The concept of passive smoking, however, in a country where the population of male smokers is grossly in excess of female smokers, has significant implications with respect to the reproductive outcome. The aim of the study, was to evaluate the impact of male smoking on the outcome of In vitro fertilization-embryo transfer (I.V.F-E.T). The number of oocytes retrieved per cycle, fertilization rates number of embryo-transferred, the clinical and ongoing pregnancy rates were decreased in passive women smokers when compared to non-smokers. The low fertilization and pregnancy rates may be explained in terms of sperm defects, oocyte defects possibly due to passive inhalation of toxic chemicals, or both. The poor oocyte retrieval rates, however suggest a causal relationship between passive smoking and decreased fecundity.

Introduction

The sequelae leading to conception is orchestrated by a complex co-ordination between gamete interaction, embryo implantation, and an optimum hormonal milieu for the establishment of a pregnancy. Reproductive dysfunction in either of the parents may significantly influence the outcome of a pregnancy. Failure to conceive, may be regarded as a problem of gamete quality and interaction (Welner et al 1988), embryo quality and transportation in the pre-implantation stages (Navot et al 1988), or implantation and subsequent development (Lipitz et al 1993). Several factors may be instrumental in the establishment of a pregnancy and its outcome, smoking among the life style factors having one of the most profound impacts on the reproductive status. Apparently, normal fertilization and cleavage does not exclude subtle gamete defectivities which can interfere with implantation and/ or subsequent risk of abortion (Raziel et al 1997).

It is estimated that among the 400 million individuals aged 15 years and above in India, 47% use tobacco in one form or another, of whom 12% roughly equivalent to 48 million smoke cigarettes. Cigarette smoking not only impairs spermatogenesis (Vine 1996), sperm motility, and normal sperm morphology (Chia et al 1994), but also compromises sperm fertilizing capacity as is evidenced by a decreased ability to undergo the acrosome reaction (Sofikitis et al 1994; El Mulla et al 1995). Reports of an increased percentage of sperm with fragmented DNA (Sun et al 1997) and an increased proportion of sperm with single stranded DNA which show poor fertilizing capacity (Sofikitis et al 1994) further substantiate the deleterious effects of smoking on sperm quality.

There is epidemiological evidence that women who smoke may experience delay in conception (Zenzes 1995a) and increased rates of pregnancy loss (Walsh 1994). Contaminants of cigarette smoke can affect the meiotic process of oocytes (Zenzes et al 1995b). Cotinine, a metabolite of the highly toxic alkaloid, nicotine in cigarette smoke incorporates into the ovarian cells and interacts directly (Zenzes et al 1997a). Cadmium, a heavy metal in cigarette tobacco, has been detected in follicular fluid samples, access to which may compromise the quality of oocytes thus posing significant risk (Zenzes et al 1995c).

Though the hazardous effects of cigarette smoking on gamete quality have been independently proven in male, and female smokers, there has been little emphasis on the influence of passive smoking on the outcome of a pregnancy. Owing to the numerous toxins that are present within cigarette smoke, this study was designed to evaluate the outcome of in vitro fertilization in couples whose male partners were smokers.

Materials and Methods

One hundred & sixty cycles of I.V.F-E.T were conducted in 100 infertile couples (50 male smokers and 50 male non-smokers) who attended the Assisted Conception

Services Unit, Mahavir Hospital and Research Centre, Hyderabad. Non-smokers were defined as couples who neither smoked nor were exposed to cigarette smoke inhalation. Passive smokers were defined as non-smoking women with smoking male partners.

Criteria for the selection of patients

i) Male factor infertility with oligospermia (count<20 mill/ml) as the only problem
ii) No semen infection (ruled out by semen culture and sensitivity)
iii) No history of medical problem such as diabetes mellitus, hypertension, etc.
iv) No history of varicocoele.
v) Female age<30 years. FSH<10mIU/ml. The reason for restricting the female age was to eliminate age related bias as to the oocyte quality, and because number and quality of embryos transferred decrease with age.

Patients were down-regulated with LHRH analogue (Busereline acetatae) until the day of hCG administration. When estradiol (E2) levels as measured by radioimmunoassay fell to below 50pg/L, patients were stimulated with FSH (Metrodin, Laboratories Serono). Follicular development was monitored daily by E2 assays and ultrasound (US) measurements. When 3-4 follicles with a mean diameter of 18mm were obtained and the serum E_2 level was equivalent to 1000 pg/L, 10000 IU of hCG (Profassi, Laboratories Serono) were administered. Transvaginal oocyte recovery was performed under ultrasound guidance 34 hours post hCG administration. Uterine embryo transfer was performed two days later. 50 mg of uniprogestin was given intramuscularly as luteal phase support to all the patients beginning on the day of embryo transfer. A clinical pregnancy was defined as the presence of a gestational sac as documented by USG.

Results:

The results are given in Table 1. There was a significant reduction in the number of oocytes retrieved/ cycle, number of oocytes fertilized/ cycle, embryos transferred/ cycle, and the clinical and ongoing pregnancy rates in passive smokers when compared to non-smokers.

Table-1
The outcome of IV-ET in passive smokers and non-smokers

Characteristics	Passive Smokers	Non-Smokers
No. of patients	50	50
No. of cycles	85	75
Oocytes retrieved / cycle	2.2 ± 0.87	3.3 ± 1.13*
Oocytes fertilized / cycle	1.2 ± 0.73	2.1 ± 1.19*
Embryos transferred / cycle	1.01 ± 0.64	1.87 ± 0.878*
Clinical pregnancy rate (%)	14	26
Ongoing pregnancy rate (%)	5	9

Values represent mean ± sd
**p < 0.001*

Discussion

It is clearly evident from the results that passive smokers adjusted for confounding variables like age, one of the most important predictors of the outcome of IVF-ET, were significant targets of reproductive insult possibly caused by exposure to cigarette smoke. Observations of the accumulation of toxic constituents of cigarette smoke in the follicular fluid of passive smokers in earlier studies lend support to the hypothesis that access to such chemicals may be a causative factor in compromising oocyte quality, fertilization, and pregnancy rates.

Women who smoke have an accelerated development of clinically detectable diminished ovarian reserve which may be a principal mechanism reducing fecundity (Sharara et al 1994). Moreover, smoking has been shown to have further reduced the number of mature oocytes in older women, therefore risking a negative IVF-ET outcome (Zenzes et al 1997b). Simulation of similar conditions in passive smokers but to a milder extent have shown similar results in this study.

Chromosomal abnormalities in women with no fertilized oocytes was significantly higher compared to those with at least one fertilized oocyte. A high frequency of chromosomal abnormalities in unfertilized oocytes suggests that natural selection against the oocyte may have occurred even prior to fertilization (Ma et al 1994). Documentation of the deleterious effects of cigarette smoking on the sperm at the chromosomal level may account for the low pregnancy rates in passive smokers when compared to non-smokers, but cannot offer an explanation for the low oocyte retrieval rates in passive smokers.

The low fertilization rates in passive smokers may be attributed to defects in sperm fertilizing capacity, oocyte defects possibly due to exposure to harmful substances in cigarette smoke, or both. Further research on the oocyte reserve and quality in passive smokers will help strengthen the conclusions.

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