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Effect of female nargile smoking on in vitro fertilization outcome

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ABSTRACT

Objective: Smoking is a significant health hazard that has been associated with poor reproductive outcome and reduced fertility in reproductive age women. The aim of this study was to assess the effect of nargile smoking on intra-cytoplasmic sperm injection (ICSI) outcome.
Study design: A prospective analysis of the outcomes of 297 women who underwent ICSI treatment at the ART Unit at the American University of Beirut Medical Center between January 1, and December 31, 2006 was done. The patients were divided into 3 groups based on their smoking status: cigarette smokers ($n = 42$), nargile smokers ($n = 51$) and non-smokers ($n = 204$).
Results: The mean age of nargile smokers was significantly lower than the other groups; however, the 3 groups were similar with respect to the cause of infertility, total dose of follicular stimulating hormone (FSH), number of oocytes and embryos obtained, and number and quality of embryos transferred. There was no significant difference in the clinical pregnancy rate between nargile smokers and non-smokers (51.0% vs 43.6%). However, cigarette smokers had a significantly lower clinical pregnancy rate compared to non-smokers (23.8% vs 43.6%, $p = 0.0238$). On multiple logistic regression analysis, factors that decreased the clinical pregnancy rates were cigarette smoking and maternal age.
Conclusion: Although this study did not find a deleterious effect of nargile smoking on ICSI outcome, the results need to be confirmed in prospective studies that would include larger number of women with more objective measures of nargile smoke exposure.

1. Introduction

Tobacco use is widely recognized as a significant health hazard, and smoking, in reproductive age women, has been associated with poor reproductive outcome and reduced fertility [1–3]. Epidemiological studies of spontaneous conception confirm that 38% of non-smokers conceive in their first cycle compared with 28% of smokers, who are 3.4 times more likely to have a 1-year delay to conceive [2]. This impaired fertility is postulated to result from interference with gametogenesis, fertilization, failure of implantation and subclinical loss after implantation [2,4]. Smoking is also associated with an earlier age of onset of menopause possibly through exacerbating the steady decrease in ovarian reserve that occurs with advancing age [5–7].

Studies evaluating the effect of smoking on the outcome of assisted reproductive techniques have produced conflicting results. Some have shown that maternal smoking is associated with decreased fertilization rates [8–10], decreased numbers of oocytes [11], decreased pregnancy rates [3,11–14], and increased miscarriage rates [15]. In contrast, other studies reported no effect of smoking on fertilization [15–17] and pregnancy rates [7,16–18].

While extensive research has been conducted on the effect of cigarette smoking on reproductive outcomes, little is known about nargile, hubble-bubble or water pipe smoking. Nargile smoking is another form of tobacco consumption that originated more than 400 years ago in Turkey, India, and Iran but whose use has spread rapidly worldwide, thus constituting a major part of the global tobacco use epidemic [19]. It involves the burning of a dark tobacco paste of the *Nicotiana tabacum* family (containing 2–4% nicotine and 1.5–2% protein nitrogen) that is usually lit by charcoal embers underneath a metallic tray connected to a water container through a metallic tube. Tobacco smoke is inhaled through a long, flexible tube that is connected to the water container.

Nargile smoke has harmful components similar to those found in cigarette smoke, namely carbon monoxide, heavy metals, potentially cancerous tar fractions, and nicotine [20]. In the few published studies, nargile smoking has been associated with oral cavity and lung cancers, coronary heart disease, reduced ventilator capacity, bronchitis, emphysema, obstructive airway diseases, and low birth weight [21,22]. Data on the effect of nargile smoking on female fertility and assisted reproductive techniques (ART) outcome is not available. Only one study showed that Egyptian

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men who are regular nargile smokers were at 2.5 times increased risk of male infertility as opposed to non-smokers [23].

With the increasing habit of nargile smoking (exact prevalence is undetermined), especially among women in our society, this study was performed to assess the effect of female nargile smoking on the outcome of intra-cytoplasmic sperm injection (ICSI) procedures.

2. Materials and methods

A prospective analysis of the outcomes of 297 ICSI treatment cycles, performed at the ART Unit of the American University of Beirut Medical Center, between January 1, and December 31, 2006, was performed after obtaining Institutional Review Board approval. Indications for ART (ICSI procedures are performed for almost all cases in our IVF center) were male factor, unexplained infertility, tubal factor, endometriosis, and old age. Smoking status was obtained from detailed questionnaires completed by the woman on the day of oocyte retrieval. Smoking was categorized as cigarette smoking (defined as cigarette smoking alone or smoking cigarette and nargile) versus exclusive nargile smoking within 6 months before the IVF cycle and up to the day of egg retrieval [24]. The dose of smoking was recorded as the number of cigarettes or nargiles smoked per day. Less than one nargile per day refers to instances when the episode of smoking lasted for periods less than the average duration of nargile smoking (10–30 min) or when the woman described smoking only a few puffs of the nargile. Occasional social smokers, whether smoking cigarettes or nargile, were excluded from the study. Former smokers (ceased smoking >6 months prior to treatment) were considered non-smokers since several studies have shown that the fertility of ex-smokers is comparable with that of non-smokers, rather than that of current smokers [2]. Non-smokers whose husbands were heavy smokers at home were excluded from the study. All patients were instructed by their treating physicians to quit smoking on the day of oocyte retrieval and thereafter especially with a successful pregnancy outcome. Also husbands who smoke were advised to quit smoking or at least to avoid smoking near their wives.

2.1. Controlled ovarian stimulation and ICSI procedures

Controlled ovarian hyperstimulation was performed by a long standard protocol with GnRH agonist (GnRH-a; Decapeptyl, Beaufour Ipsen Pharma, France), and recombinant FSH (rec-FSH; Puregon, Organon, The Netherlands). GnRH-a was started in the mid-luteal phase at a daily dose of 0.05 mg until the day of human chorionic gonadotropin (hCG) injection (Pregnyl, Organon, The Netherlands). Rec-FSH 200 U/day was started on the 3rd day of the cycle. Follicular development was assessed by transvaginal ultrasonography. When at least two dominant follicles were ≥18 mm, 10,000 IU of hCG was administered. Oocyte retrieval under transvaginal ultrasonographic guidance was performed approximately 36 h after the hCG administration. The embryo transfer (ET) was performed with Wallace transfer catheter (Smiths Medical, UK) 3 days after oocyte recovery under ultrasound guidance. The embryos were scored according to a previously published grading system [25]. All women received vaginal micronized progesterone 200 mg every 8 h starting the afternoon of the oocyte pickup and continuing up to the day of β-HCG measurement and throughout the first trimester if the β-HCG was positive.

The clinical pregnancy rate was defined as the presence of a positive fetal cardiac activity detected by vaginal ultrasound performed 20 days following a positive pregnancy test. Multiple pregnancy was defined as the presence of two or more gestational sacs with positive fetal heart rates. Fertilization rate was defined as the number of embryos obtained per the number of mature oocytes injected via ICSI. Chemical pregnancy was defined as the initial increase in β-HCG levels followed by a decrease in levels with the absence of gestational sac in the uterine cavity.

2.2. Statistical analysis

Statistical analysis was carried out using SPSS 14 statistical package (SPSS software for windows XP version 14, Chicago, IL). The Mann–Whitney test was used for non-parametric variables. For discrete variables, the Chi-squared test was used and the Fisher-exact test if the expected number in a cell was less than 5. Multiple logistic regression analysis was used to study the effect of smoking on clinical pregnancy rates after controlling for potential confounding variables. Factors entered in the model were maternal age, cause of infertility, and number of embryos transferred (1–3 vs >3).

3. Results

A total of 297 women were studied; 204 (68.7%) non-smokers, 51 (17.2%) nargile smokers and 42 (14.1%) cigarette smokers. Of those who smoked cigarettes, 24 women (57.1%) reported smoking ≥11 cigarettes per day. Of those who smoked nargile, 20 (60.8%) smoked >1 nargile/day.

Table 1 summarizes the characteristics and the outcome of cycles among the three groups. Nargile smokers were significantly younger than non-smokers whereas cigarette smokers were older than non-smokers but the difference did not reach statistical significance. The fertilization rate was significantly higher in the nargile group compared to the other two groups.

Pregnancy outcomes are summarized in Table 2. Cigarette smoking significantly decreased the overall pregnancy rate and the clinical pregnancy rate but had no significant effect on the

Table 1
Patients' characteristics.

	Non-smokers ($n=204$)	Nargile ($n=51$)	Cigarette ($n=42$)
Age (years)	33.6 ± 5.778^a	30.8 ± 6.327^b	35.4 ± 5.28
Dose of FSH (IU)	2731.3 ± 969.5	2596.6 ± 955.5	2867.9 ± 1037.6
No. of oocytes	11.9 ± 6.9	11.9 ± 6.4	11.3 ± 6.8
No. of embryos	6.0 ± 3.9	7.0 ± 4.1	5.9 ± 3.2
Total embryos/total eggs	1224/1820	357/455	248/356
Fertilization rate	$(67.3\%)^c$	$(82.9\%)^d$	(69.7%)
No. of grade A embryos	4.0 ± 2.4	4.2 ± 2.6	3.7 ± 2.6
No.of embryos transferred	3.2 ± 0.9	3.2 ± 0.7	3.3 ± 0.9
No. of grade A embryos transferred	2.8 ± 1.0	2.9 ± 0.9	2.6 ± 1.2

Data presented as mean ± standard deviation; FSH = follicular stimulating hormone; a and c: non-smoker vs nargile; b and d: nargile vs cigarette. p-Values: $a = 0.0026$; $b = 0.0003$; $c = <0.0001$; $d = 0.0045$.
Medians were compared using the Mann–Whitney and percentages were compared using the X^2-test or Fisher-exact tests.