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Original Article

Do Cigarette Smoking and Obesity Affect Semen Abnormality in Idiopathic Infertile Males?

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Purpose: This study was conducted to find the relative risk of semen abnormality with respect to smoking history and obesity.
Materials and Methods: Subfertile or infertile men were enrolled in this study from July 2010 to June 2011. All participants provided their cigarette use information, self-reported weight, height, semen analysis, physical examination, and sexually transmitted disease status. None of the enrolled patients had any specific pathological reason for infertility. Semen abnormality was defined as a condition in which one or more parameters did not satisfy the World Health Organization's criteria.
Results: A total of 1,073 male patients were considered for this study. After the application of the inclusion criteria, 193 patients were finally analyzed. These patients were divided into two groups according to semen abnormality: the normal semen group (n = 72) and the abnormal semen group (n = 121). Baseline characteristics, except age and smoking history, were not significantly different between the two groups. Smoking history and age were risk factors for the semen abnormality of idiopathic infertile male patients.
Conclusions: Smoking and old age were risk factors for semen abnormality. However, obesity did not affect the semen abnormality. Smoking affected semen quality and is therefore expected to play a negative role in conception.

Key Words: Infertility, male; Semen; Smoking; Obesity

INTRODUCTION

Cigarette smoking is a recognized health hazard and a major cause of various malignant diseases. In the case of women of reproductive age, cigarette smoking has a dose-related effect that can delay the time to conception [1]. In the case of male infertility, cigarette smoking has been reported to have a negative impact on sperm parameters [2]. Semen quality measures were significantly associated with the pregnancy rate, with the percentage of morphologically normal sperm, and with the total number of sperm showing a particularly strong association [3]. Smokers inhale a host of toxins, such as nicotine, carbon monoxide, cadmium, and other mutagenic compounds [4]. Smoking cigarettes may be associated with infertility in men and may damage the chromatin structure and pro-

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duce endogenous DNA strand breaks in human sperm [5]. Cigarette smoking has been associated with adverse effects on semen quality, such as those on semen density, motility, and morphology [6,7]. Previous studies have suggested that semen quality may be greatly impacted by smoking [6-9].

In recent decades, the prevalence of obesity has doubled in the Western and the westernizing countries. In South Korea, according to the Korean National Health and Nutrition Examination Survey IV (KNHANES IV), obesity has increased gradually. There have been several studies on the relationship between obesity and male infertility. In a sperm function test, the hyaluronan binding of sperm and a high body mass index (BMI) had a negative effect on sperm quality and function [10]. Moreover, overweight men have a markedly changed sex hormone profile in serum, as well as a degradation of semen quality [11].

The aim of this study was to find the risk factors for semen abnormality. Further, we aimed to document semen abnormality depending on the smoking frequency and BMI.

MATERIALS AND METHODS

A retrospective medical record study was conducted. Men visiting the hospital between July 2010 and June 2011 for subfertility or infertility were enrolled in this study. The Cheil General Hospital & Women's Healthcare Center Institutional Review Board approved the study. All participants provided their cigarette use information, self-reported weight and height to calculate their BMI, semen analysis and physical examination results, and history of sexually transmitted diseases. Semen samples were collected by masturbation following more than three days of abstinence. After liquefaction, a seminal analysis was performed according to the standard World Health Organization (WHO) criteria, a sperm concentration of $>15\times 10^6$/mL, >4% morphologically normal cells, >40% motile sperm (categories 'a,' 'b,' and 'c'), and >58% alive sperm [12], and the sperm morphology was evaluated using Kruger's morphology criteria. If any single parameter did not satisfy these WHO criteria, we defined the case as an abnormality. The status of sexually transmitted diseases was evaluated via a polymerase chain reaction examination. Patients with infection, varicocele upon physical examination, or azoospermia, or those who submitted an incomplete questionnaire were excluded. None of the enrolled patients had any specific pathological reason for infertility. The questionnaire helped define the smoking amount per day and the smoking duration for the participants. Individuals were divided into two groups: the normal semen group and the abnormal semen group.

Patient characteristics are reported as mean±standard deviation unless otherwise indicated. A statistical analysis was performed with a paired t-test for normally distributed data and a Mann-Whitney U test for skewed data in order to evaluate the baseline characteristics. The correlation between two factors was analyzed by Pearson's or Spearman's rank correlation. The predictive risk factors were identified using binary logistic regression, odds ratio, and 95% confidence interval. A value of $p<0.05$ was considered statistically significant. For the statistical analysis, PASW Statistics version 18.0 (IBM Co., Armonk, NY, USA) was used.

RESULTS

A total of 1,073 male patients were enrolled in this study. After the application of the inclusion criteria, 193 medical records of idiopathic infertile male patients were analyzed. Patients were divided into two groups according to semen abnormality: the normal semen group (n=72) and the abnormal semen group (n=121). Baseline characteristics, including testicular sizes and BMI, were not significantly different between the two groups, except smoking history (Table 1). Smoking and BMI did not statistically affect the semen parameters in the correlation test. Semen volume, sperm count, motility, viability, and morphology of all the subjects did not correlate with the smoking history or BMI. Table 2 shows the results of the analyses for the semen abnormality risk factors. Age and smoking history were found to be the risk factors for semen abnormality. Further, it was found that BMI did not significantly affect semen abnormality.

DISCUSSION

Various environmental materials may affect spermatogenesis, including toxins and medications. Numerous and widespread environmental chemicals may interfere with

Table 1. Baseline characteristics of both groups divided according to semen abnormality

	Normal semen group (n=72)	Abnormal semen group (n=121)	p value
Age (yr)	35.15±3.90	36.82±4.34	0.657
Testis volume (mL)			
Right	19.63±3.89	19.47±3.61	0.989
Left	19.63±3.88	19.33±4.47	0.425
Smoking (pack/year)	3.54±5.81	6.16±7.48	0.018
Height (cm)	174.11±4.93	173.99±4.94	0.780
Weight (kg)	73.84±9.07	76.10±14.24	0.371
Body mass index (kg/m^2)	24.32±2.49	25.09±4.14	0.260

Values are presented as mean±standard deviation.

Table 2. Predictive factors for semen abnormality of idiopathic male infertility using binary logistic regression

	Univariate			Multivariate		
	Odds ratio	p value	95% confidence interval	Odds ratio	p value	95% confidence interval
Age	0.906	0.009	0.841~0.976	0.915	0.022	0.849~0.988
Testis volume						
Right	1.011	0.780	0.935~1.094	-	-	-
Left	1.017	0.636	0.950~1.088	-	-	-
Smoking history	0.943	0.013	0.900~0.988	0.945	0.023	0.900~0.992
Body mass index	0.934	0.158	0.849~1.027	0.929	0.154	0.839~1.028

-: not available.

sexual hormone signaling *in vitro* and *in vivo* [13]. Cigarette smoke is known to be a somatic cell mutagen and a carcinogen. Toxic substances such as nicotine, carbon monoxide, benzo(a)pyrene, mutagenic pyrolysis-derived compounds, and cadmium can be absorbed during the inhalation of cigarette smoke. Toxic metabolites of cigarette smoke may impair spermatogenesis, resulting in the production of defective spermatozoa. Further, cigarette smoking is correlated with increased levels of seminal oxidative stress [14]. It appears that smoking is more likely to be associated with decreased semen quality in studies of healthy men. Among normal healthy men, smokers had about 24% lower sperm concentration than non-smokers. However, in a study of infertile male patients, smoking was not as closely associated with decreased semen quality [15].

Smoking is associated with sperm morphology, motility, and concentration. The average percentage reduction in the mean sperm concentration of smokers as compared to non-smokers was 13%. However, another study showed a different result. In healthy males, semen quality is more affected by smoking, and couples experiencing female factor infertility may be more affected by smoking than couples with only an infertile male. Among infertile male patients with poor semen quality, quitting smoking may improve the semen quality [15].

In this study, cigarette smoking was shown to be related to semen abnormality in idiopathic infertile male patients. However, there was no statistically significant correlation between smoking history and semen parameters. Moreover, age was a risk factor for semen abnormality. The sperm concentration of those smoking more than 20 cigarettes per day was lower than that of non-smokers [16]. Some studies have shown no significant difference in sperm concentration due to cigarette smoking. In fertile men and subfertile asthenozoospermic patients, there was no significant difference in the semen parameters [17]. In the case of semen morphology, some reports have shown that semen morphology correlated with smoking, while others have not. Although semen morphology was shown to be an important parameter related to pregnancy [3], the

definition of abnormal sperm morphology was not consistent. In this study, all enrolled subjects had idiopathic infertility; this result does not agree to that of a previous study that compared fertile and infertile male patients.

A prior longitudinal study regarding the correlation of semen parameters and the pregnancy rate showed that morphologically normal sperm and sperm concentration affected the pregnancy rate [3]. In the present study, smokers represented only 6.0% of the study population, which did not effectively contribute to the overall analysis.

In South Korea, according to KNHANES IV data, the number of adult patients with severe obesity increased by about 1.5 times from 2.4% in 1998 to 3.9% in 2007～2009. Obesity affects gonadotropin-releasing hormone, which may impair Leydig and Sertoli cell functioning [18]. The conversion of androgens into estrogens in the adipose tissue may augment leptin production and depress pituitary gland function [19,20]. Moreover, being overweight was dose-dependently related to hormonal changes such as changes in the levels of testosterone and the sex hormone-binding globulin [11]. Overweight men had a slightly lower sperm concentration and total sperm count than normal-weight men [11,21]. However, in this study, BMI did not affect the abnormality of semen parameters.

In this study, there were a few limitations. In several previous studies, many confounders, which may affect semen parameters, were considered. However, in this retrospective study, other confounders were not considered. In addition, the hormonal status may differ according to body weight; we did not check the hormonal status of the patients. To overcome these limitations, we plan to conduct a well-designed prospective study in the near future.

CONCLUSIONS

In idiopathic infertile male patients, smoking and age may be the risk factors for semen abnormality. However, smoking and BMI did not correlate with semen parameters. Obesity did not affect the semen abnormality. Smoking adversely affects the semen quality and may play a negative role in conception. A more prospective and well-designed study is needed for establishing an accurate relationship between smoking and semen quality.

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