

STOPPING SMOKING IMPROVES SEMEN PARAMETERS IN SMOKER INFERTILE MEN

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ABSTRACT

Purpose: Infertility affects up to 15% of the couples, which in 50% of cases, a male factor is involved. Several studies showed that smoking decrease the semen parameters including sperm count, motility and morphology. The aim of this study was to evaluate the effect of stop smoking on the semen parameters in infertile men.

Materials and Methods: Between Sep 2004 to Sep 2011, 716 infertile men were enrolled and history taking and physical examination were performed by experienced urologist with emphasis on the positive history of cigarette smoking. In a case-control study, the patients who were successful in discontinuing cigarette smoking were re-examined after 3 months and the same evaluation including semen analysis were performed.

Results: 238 out of 716 men were excluded and 478 enrolled, which of them 179 men were smoker, who encouraged to stop smoking. Giving up cigarette smoking in 134 patients resulted in 14-26% increase in sperm count as well as 8-27% improvement in sperm motility and 5-20% in sperm morphology. Also, without any accompanied therapeutic interventions, resulted in pregnancy in 35 patients (26.1%) and delivery in 24 patients (18%).

Conclusion: Although not all the mechanisms through which cigarette smoking could affect fertility are well-known, every smoker must be advice to discontinue smoking, especially in reproductive age that pregnancy may be planned.

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INTRODUCTION

Infertility is a common problem affecting about 15% of couples, of then 30% have male factor, which abnormal sperm quality is the majority of causes. [1] Although there are many anti-smoking campaigns around the world, yet cigarette smoking is an important health hazard which is very common especially in young adult men during their reproductive period [2-4] and 46% of smokers are between age of 20 and 39 years old. [5] Many studies have claimed that cigarette smoking is associated with alteration in sperm quality, motility and morphology, but, the exact molecular mechanism of these effects is not well recognized. [6] The male reproductive system is highly sensitive to many drugs and other chemicals and they may lead to many uninvited side effects on male reproductive capacity under certain condition. [7] A report have shown that the mutagenic and carcinogenic components of cigarette smoke may have negative effects on testicular germ cells. [8] The combination of smoking and varicocele cause a higher risk in impairing human semen quality. [2] The incidence of oligozoospermia in smoker patients with varicocele is two times greater than nonsmokers with varicocele and five-times greater than smokers devoid of varicocele. [9-11] It means that

smoking in the presence of varicocele could will highly increase the risk of oligozoospermia in young adult men. Due to many studies that have been performed, we are informed of smoking various effects on different parts of body and reproductive system of animals and humans. [12,13] Therefore, the aims of the present study is to evaluate the effect of quit smoking on semen parameters of smoker infertile men and the role of stop smoking to improve the semen quality.

Materials and methods

Between Sep 2004 to Sep 2011, after a pilot study on 78 smoker men, which showed improvement of the semen quality with stop smoking, we started this study with 716 men referred to our infertility clinic for evaluation of the causes of their infertility. All participants gave written informed consent before enrolment in the study and this protocol was approved by Ethical Committee of Shiraz University of Medical Sciences, Shiraz, Iran. In first phase of this study we aimed to find the men with infertility due to smoking and all referred men were enrolled. Female factor of infertility, azospermia, infertility due to systemic disease, congenital anomalies of external genitalia, high grade (III) varicocele, occupational heat

exposure and positive history of opium addiction were considered as exclusion criteria. Inclusion criteria were age between 20-40 years, infertile couples with a male factor of infertility and heavy smoker male subject. Diagnosis of infertility was confirmed by history of no child bearing, during at least one year of marriage and active intercourse. Heavy smoker was defined as a positive history of cigarette smoking for more than one year and mean of 1.2 packs per year. History taking was performed by experienced urologist, then patients underwent a complete physical examination and semen analysis. The presence of varicocele was determined through physical examination and was confirmed by color Doppler scrotal ultrasonography. Of total 716 patients, 238 patients were excluded from the trial due to other confounding factors (exclusion criteria). These factors were female causes of infertility (112 men), occupational factors (69 men), opium addiction (16 men) and high grade varicocele (41 men). So finally 478 patients were enrolled in the study. With diagnosis of infertility, of them 179 were smoker. All had abnormal semen analysis. In the second phase of our study, we designed a case-control study to evaluate the effects of smoke stopping on the semen fertility. These smoker patients encouraged to quit smoking, which 134 remained smoke free during the study period. Second semen analysis performed three months later. Flow chart of enrollment, exclusion and inclusion criteria and also our experimental setup was presented as Figure 1.

Evaluated parameters included sperm count, sperm motility, and sperm morphology. All data expressed as percentage and analysed using SPSS version 16. The results of semen analysis of the beginning of the study and three months after were compared by paired t- test and p value less than 0.05 was considered as significant.

Results

One hundred seventy nine smoker infertile men, mean age 28 [20-40], mean duration of the marriage 17 months [12-27], with abnormal semen analysis were investigated. They were encouraged to stop smoking. 134 patients cooperated and remained smoke free for at least three months and at in follow up visits in 9 months. Second semen analysis which done after three months stopping smoke revealed improvement in three major parameters including count, motility and morphology in comparison to the first one. Sperm count increased 14-26% (mean: 19%), sperm motility 8-27% (17%), and sperm morphology 5 to 20% (14%), that all were significant ($P < 0.05$). Also, without any accompanied therapeutic interventions, pregnancy occurred in 35 patients (26.1%) which resulted to delivery in 24 (18%) in 14 months follow up.

Discussion

Smoking is a lifestyle hazard for everyone who smokes even if he is a passive smoker. Although there are many scientific documentaries about the effects of carcinogens in tobacco cigarette smoke on the body organs such as urinary bladder and lungs, their effect on fertility status have been less documented. [14] Smoke produced DNA damage, inflammatory, and oxidative stress in humans. [15] However, there are two types which human contact with cigarette smoke, passive and active. Previous study demonstrated that among Danish pregnancy planners, cumulative exposure to active cigarette smoking was associated with delayed conception among current and former smokers. Time since smoking

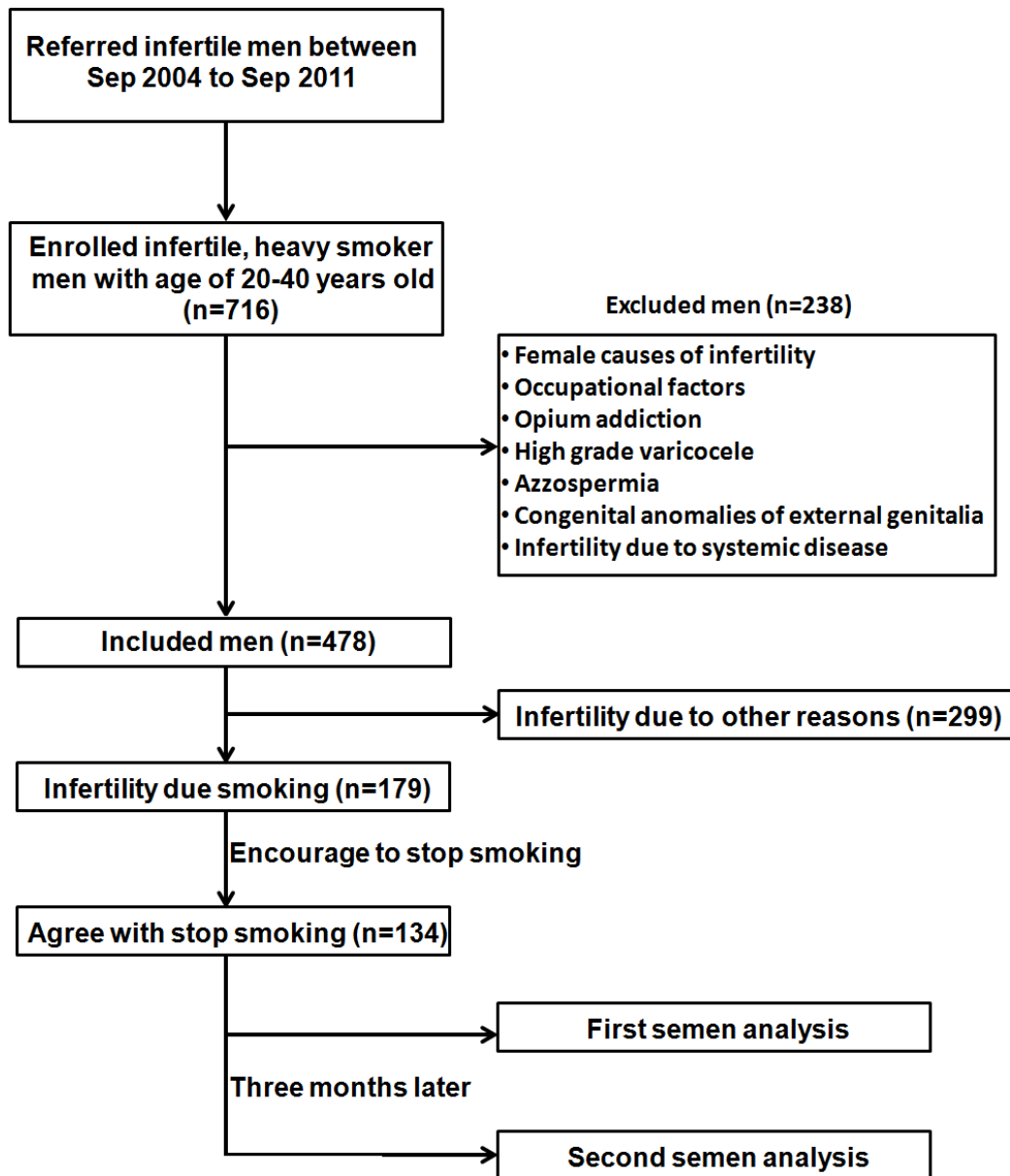
cessation and passive smoking were not appreciably associated with fecundability. [16] Although the power of epidemiological studies is not sufficient to detect specific alterations, the outcome of experimental studies as well as mechanistic considerations suggest that paternal exposure to passive smoke is potentially able to affect the quality of semen. This conclusion adds a further reason of public health concern related to the involuntary exposure to this complex mixture. [17] The mechanism of the noxious effects of cigarette smoke on semen quality is not fully determined. Some of possible causes are: abnormal function of the hypothalamo-pituitary-gonadal axis [6,18,19] or disturbance in the blood circulation of the testes that results in hypoxia, [20] so factors that disturb delivery of oxygen to the testis may have a harmful effect. [21] A more likely mechanism is a direct toxicity of the germinal cells by the toxin containing cigarette smoke. [22,23] Cigarette smoking enhance oxidative stress in seminal fluid which has noxious effect on membrane integrity of human sperm. [4] Hormonal studies have been shown that serum level of FSH, LH, prolactin and estradiol are increased and serum level of testosterone is decreased in smokers compared to non-smokers. [24] Increase in estradiol level has negative effect on spermatogenesis through several mechanisms, including alteration of the hypothalamus-pituitary-gonadal axis, increase in catecholamine level, which in turn could induce ischemia of the seminiferous tubules. [25]

The results of many studies have suggested negative impact of cigarette smoking on sperm production, progressive sperm motility and morphology. [3,26] A review of trials on association between cigarette smoking and quality of semen, a mean reduction of 13% in sperm concentration, 10% in sperm motility and 3% in morphologically normal sperm were reported in cigarette smokers. [27] Gaur et al showed that smoking causes deterioration in sperm quality in direct proportion to the number of cigarette smoked. [14] Rajpurker et al in two studies evaluated the effects of smoking on the testicular tissue and shown reduction in the number of germ cells, decrease in the height of germinal epithelium, diameter of the tubules and induced apoptosis in the germinal cells of the testis. [12] Karamed et al showed a significant decrease in volume of semen in smokers and more round cells and leukocytes in the ejaculate of smokers. [27] Many animal studies evaluated the effects of smoking on the genital system of rats. Ahmadnia et al, showed that in rats exposed to cigarette smoke, a concurrent reduction in the number of germ cells and sertoli cells was seen. [12] Deficiency in sperm maturation and a secretary deficit of leydig and sertoli cells in rat exposed to cigarette smoke have been shown. [2] Oyeyipo et al showed the dangerous effects of the nicotine on the male rats germ cell reproduction, [28] but some researchers reported opposite results. [3] Their studies revealed that smoking did not change semen parameters. Moreover, Ozgur et al reported that heavy smokers have better motility of the sperms in comparison to light smokers. [29] Hassa et al showed that number of cigarette that smoked daily has not correlation with any of semen parameters. [26] However, Collodel et al reported that however in the patients with idiopathic infertility, cigarette smoking has not significant effect on the semen quality, patients with more smoking will have lower sperm count. [2]

Although different studies have shown the relationship between smoking and semen quality but a few studies have assessed the effect of quit smoking on the semen parameters. Dorfman reported that males of the reduced fecundity associated with smoking could be

reversed within a year of cessation. [2] Taymour propounded that males with marginal semen quality may benefit from quitting smoking. [30] So we design this study in order to assess the effect of quit smoking on the semen parameters.

Figure 1. Flow diagram of enrolling, inclusion and exclusion criteria and also experimental setup.



Summary and conclusion

Our study showed that discontinuation of cigarette smoking related in amelioration of semen parameters as sperm count, motility and morphology. Nowadays cigarette smoking is known as an important cell mutant and carcinogen factor and have many adverse effects on male fertility, so every smoker should be encouraged to quit smoking, particularly if pregnancy is planned. Also smokers should stop smoking for the amenability for their futurity as cigarette smoke contain many mutagenic substances. However, there are no studies that discusses about the reversibility of smoke harm effects on the semen quality. It is highly recommended that future studies focused on this topic and evaluate the needed time for this reversibility if it is occurred.

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