HHS Public Access

Author manuscript

Postgrad Med. Author manuscript; available in PMC 2016 April 01.

Published in final edited form as:

Postgrad Med. 2015 April ; 127(3): 338–341. doi:10.1080/00325481.2015.1015928.

The Effects of Cigarette Smoking on Male Fertility

Jason R. Kovac, MD, PhD, FRCSC[1], **Abhinav Khanna, MD**[2], and **Larry I. Lipshultz, MD**[2]

[1]Urology of Indiana, Male Reproductive Endocrinology and Surgery, Carmel, IN

[2]Department of Urology, Baylor College of Medicine, Houston, TX

Abstract

Cigarette smoking, one of the main causes of preventable morbidity and mortality, has a multitude of well-known side effects. The relationship between cigarette smoking and infertility has been studied for decades; however, large-scale, population-wide prospective studies are lacking. The majority of the current literature is in the form of retrospective studies focused on the effects of smoking on semen analyses. This article discusses the results of these studies and reviews the postulated mechanisms. The effects of smoking on assisted reproduction and in vitro fertilization outcomes are noted. The consequences of smoking while pregnant on future fertility as well as the outcomes of second-hand smoke are analyzed. The current evidence suggests that men should be advised to abstain from smoking in order to improve reproductive outcomes.

Keywords

smoking; male infertility; semen parameters; outcomes; zinc; in vitro fertilization

Introduction

It has been estimated that over one third of all men globally smoke some form of tobacco and that 21.6% of American men smoke cigarettes.[1] Smoking has been linked to a myriad of adverse health outcomes, including cardiovascular disease, respiratory disease, and cancer of the lungs, bladder, cervix, esophagus, kidney, pancreas, and stomach.[2] More recently, researchers have begun to explore the relationship between cigarette smoking and reproductive health.

The American Society for Reproductive Medicine defines infertility as the inability to achieve pregnancy following 12 months of regular, unprotected sexual intercourse.[3] It has been estimated that up to 15% of all couples attempting to have children face some form of infertility.[4] Although almost half of all cases of infertility are due exclusively to female

Correspondence: Dr. Jason R. Kovac, MD, PhD, FRCSC, Male Reproductive Endocrinology and Surgery, 12188-A North Meridian Street, Suite 200, Carmel, IN. Tel: 317-564-5100, jkovac@urologyin.com.

Financial and competing interests disclosure

Larry I Lipshultz is a consultant and member of the speakers' bureaus of Auxilium, Lily, and Endo. Jason R Kovac is a National Institutes of Health K12 Scholar supported by a Male Reproductive Health Research Career Development Physician-Scientist Award (HD073917-01) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development Program. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

factors, the male factor is the sole etiology in approximately 30% of couples. An additional 20% of infertile couples have a combination of male and female factors. Thus, male factor infertility plays a significant role in 50% of all couples with infertility.[5] This review examines the literature to elucidate the potential effects of cigarette smoking on male infertility.

Materials and Methods

A PubMed/Medline search was conducted of the literature from 1960 to March 2014. The search was performed using combinations and derivatives of the following terms: smoking, male infertility, outcomes, in vitro fertilization, semen analysis, morphology, prenatal (or) maternal smoking, and *second-hand smoking.* The Related Citations in PubMed link from the U.S. National Library of Medicine was used to screen additional abstracts related to the aforementioned searches. In excess of 1000 manuscripts were screened using title search, related links, and abstract summaries. Applicable studies were read and included in this current review.

Effects of Smoking on Semen Analysis Parameters

Smoking has been shown to have a detrimental effect on various parameters of semen analysis. A cross-sectional analysis of 2542 healthy men from 1987 to 2004 by Ramlau-Hansen et al[6] found that on semen analysis, cigarette smokers had lower semen volumes, sperm counts, and percentage of motile sperm compared to men who did not smoke. Further, it was suggested that the relationship between smoking and sperm concentration was dose-dependent. Indeed, men who smoked > 20 cigarettes per day experienced a 19% reduction in sperm concentration compared with nonsmokers, even after controlling for age, recent fevers, and duration of abstinence as well as diseases in reproductive organs. It was concluded that adult smoking resulted in moderate impairment of semen quality.

In another large cohort of 1786 men undergoing infertility workup (655 smokers and 1131 nonsmokers), Kunzle et al[7] demonstrated that smoking was associated with decreases in sperm density (15.3%), total sperm counts (17.5%), and total motile sperm (16.6%) compared with nonsmokers. Furthermore, morphology (percent of normal forms) as well as ejaculate volume was slightly affected by smoking but not to any significant degree. Effects on ejaculate volume were found in a study by Saaranen et al,[8] who noted smokers had lower semen volumes per ejaculate than nonsmokers with a more specific inhibition occurring in men who smoked > 16 cigarettes per day.

Several smaller studies have corroborated the aforementioned findings. Zhang et al[9] studied 362 Chinese men attending an infertility clinic and found that smokers demonstrated decreased semen volumes, sperm concentrations, and rates of forward progression compared with nonsmokers. The authors also examined the physiological basis for these changes by testing seminal plasma levels of superoxide dismutase, which is an enzyme that participates in the oxidative stress pathway and has been previously shown to be lower in the seminal plasma of infertile men.[10,11] Zhang et al found that superoxide dismutase levels were inversely correlated with the amount and duration of cigarette smoking, suggesting a

relationship among smoking, oxidative stress, and infertility. Another study of 200 infertile men found higher rates of reduced sperm motility and abnormal sperm morphology among smokers.[12] Chia et al[13] reported similar results in 618 Chinese men. Within the cohort studied by Chia et al, the lower sperm concentrations and higher rates of abnormal sperm morphology identified in smokers were also found to be dose dependent.

Merino and colleagues,[14] who studied 358 Mexican men stratified into 3 categories based on the number of cigarettes smoked per day, also confirmed this type of dose dependency. The authors confirmed the effects of smoking on reduced sperm density and abnormal morphology, but also extended these findings to note that men who smoked < 10 cigarettes per day experienced significant changes in their semen analysis parameters. Therefore, even "light" smokers appeared to be at risk for adverse effects on fertility.

Interestingly, some studies have failed to establish the relationship between cigarette smoking and adverse effects on semen parameters. The largest of these was a case-control study of > 2000 British men being treated for infertility.[15] Results from this study suggested that smoking was not an independent risk factor for decreased concentrations of motile sperm. However, additional sperm parameters, including sperm morphology, were not assessed. Dikshit et al[16] found that neither cigarette smoking nor chewing tobacco were significant risk factors for impaired semen quality among 626 men presenting to infertility clinics. Hassa and colleagues[17] noted similar results in a cohort of 223 Turkish men. Furthermore, when 889 men presenting for vasectomy were examined, no significant differences in sperm density or motility were observed between smoking and nonsmoking men.[18] Of note, this particular study population was not drawn from patients presenting for an evaluation of male infertility, in contrast to many of the aforementioned studies. Indeed, men presenting for vasectomy can be presumed to be fertile, suggesting variable effects of smoking in men with infertility and those without. While highlighting the importance of patient selection in examining the effects of smoking on fertility, these studies do suggest that men with difficulty conceiving should be counseled to stop smoking in order to optimize their fertility outcomes.

In addition to the observational studies mentioned above, a small number of meta-analyses have also been performed to explore the relationships between cigarette smoking and semen parameters.[19,20] One meta-analysis by Li et al[20] included 57 observational studies and > 29000 men. Findings were applied to infertile as well as fertile men, and cigarette smoking had adverse effects on all sperm parameters, including semen volume, sperm density, total sperm counts, and percentage of sperm with progressive motility. An earlier, second meta-analysis by Vine et al[19] found that smokers had a 13% to 17% lower sperm density than nonsmokers. To summarize, cigarette smoking affects semen analysis outcomes in infertile men. Thus, those men with fertility difficulties should be counseled to stop smoking as soon as possible to optimize their reproductive potential.

Mechanisms by Which Smoking Affects Male Reproductive Outcomes

Some authors have attempted to provide mechanistic explanations for the observed link between cigarette exposure and abnormal semen parameters. In a study of 147 Chinese men,

Liu et al[21] examined the relationship between seminal zinc levels and semen parameters. The authors found that smokers had lower seminal zinc levels than nonsmokers, with associated decreases in sperm concentration, motility, and morphology. Interestingly, smokers with normal seminal zinc concentrations did not experience the same degree of abnormal semen parameters as those smokers with decreased seminal zinc, suggesting that zinc concentrations could play a role.

There is also evidence to suggest that the adverse effects of smoking may not be due exclusively to the toxins found in cigarette smoke. Indeed, a study examining the effects of oral nicotine on male rats found that rats exposed to oral nicotine experienced significant decreases in sperm motility and sperm count.[22] Thus, nicotine may also play an important role in the adverse effects of smoking on fertility, independent of the toxins found in the smoke. Interestingly, parameters affected by oral nicotine were improved following 30 days of cessation, suggesting a component of reversibility to these effects. Furthermore, a study of 210 men suggested that men with higher cotinine concentrations in the seminal plasma also had a greater percentage of abnormal sperm morphology.[23] Because cotinine is a metabolite of nicotine, these findings further the theory that nicotine itself may be a possible driver of the adverse effects of smoking on fertility. Further studies are needed to determine the exact role of nicotine in the pathogenesis of semen analysis and morphology changes.

Smoking and Assisted Reproduction

Not only can smoking have unfavorable effects on male semen parameters, it may also reduce the success of assisted reproduction techniques, such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Paternal smoking has been suggested to contribute to decreased IVF success rates. Indeed, a study of 166 couples undergoing assisted reproduction techniques demonstrated that couples in which the male partner recently smoked had a significantly lower live birth rate with IVF or ICSI (7.8% vs 21.1% in nonsmoking males).[24] Furthermore, a significant association was identified between recent female smoking and the decreased ability to retrieve ova during IVF.[24] A second study examined 221 couples undergoing IVF (aged > 20 years) and found that in couples in which either member had a positive smoking history, an increased relative risk (2.41) of not achieving a pregnancy was present (compared with nonsmoking couples).[25] This relative risk was even higher (4.27) among couples that had smoked for > 5 years. This trend extended to women who had smoked at some point in their lives (adjusted risk of 2.71 for not achieving a pregnancy).

Joesbury et al[26] performed a study on 498 couples undergoing IVF in which the male partner's smoking resulted in a significantly lower chance of achieving a 12-week pregnancy. These odds of pregnancy were decreased by 2.4% for each additional year of male age, suggesting that smoking and increasing male age acted in concert to affect fertility potential. A study of 301 German couples demonstrated that paternal smoking was associated with significantly reduced success rates for IVF (18% vs 32% in nonsmokers) and ICSI (22% vs 38% in nonsmokers).[27] In fact, logistic regression analyses found that paternal smoking was a significant risk factor for IVF and ICSI failure, whereas maternal

smoking was a risk factor only for IVF failure. Thus, paternal smoking may play at least as great a role in the success of assisted reproduction techniques as maternal smoking.

Prenatal Smoking Exposure and Future Fertility

In addition to the effects of cigarette smoking on a man's semen parameters, exposure to cigarettes in utero may have an impact on a man's ultimate fertility in the future. Although the studies in this area are limited, given the long-duration follow-up that is required, several important pieces of data are known.

A retrospective study of 1770 male European military recruits demonstrated that men who had prenatal exposure to smoking had a 20.1% lower sperm density as adults than those recruits without such exposure.[28] Men with intrauterine smoking exposure also had modest but statistically significant reductions in sperm motility and testis size. A more focused study on 945 Danish men suggested a trend toward decreasing sperm concentration in adult men with prenatal exposure to maternal smoking, although the results did not achieve statistical significance.[29] However, the cohort did demonstrate a significantly increased risk for oligospermia among men whose mothers smoked > 10 cigarettes per day during pregnancy. Unfortunately, the degree to which this oligospermia translates to male fertility potential is not known.

A further study by Storgaard et al[30] observed that men whose mothers were classified as high level smokers (i.e. > 10 cigarettes per day) during pregnancy had a 48% lower sperm density than men who were not exposed to cigarettes in utero. Of note, this association was not significant in the subset of men whose mothers were in the lower smoking category (i.e. <10 cigarettes per day during pregnancy), suggesting dose dependence in the relationship between in utero cigarette exposure and subsequent semen abnormalities.

Second-Hand Smoke and the Effects on Fertility

Smoking is not a risk factor but can still be considered in isolation. Paternal first-hand smoking often results in maternal second-hand smoke exposure, which can have further detrimental effects on female fertility. One retrospective study of 225 women undergoing IVF/ICSI found that women exposed to second-hand smoke had implantation rates that were comparable to those of women who directly smoked (12.0% vs 12.6%) and were significantly lower than the implantation rates of unexposed women (25.0%).[31] Similarly, women exposed to second-hand smoke experienced a significantly lower pregnancy rate than women not exposed to cigarette smoke (20.0% vs 48.3%).[31] Although data examining the direct effect of second-hand smoke on females attempting to conceive naturally is limited, this exposure may decrease the likelihood of achieving pregnancy by adversely affecting both male and female factors.

Limitations and Future Directions

The previously published data on the effects of smoking on infertility are not without limitations. First, much of the data presented herein is retrospective in nature and, as such, there is a dearth of longitudinal prospective literature examining the relationship between

smoking and infertility. Second, the setting in which patients are selected for the studies are critical. For example, examination of the effects of smoking on fertility among men with infertility and those undergoing vasectomy reversal yields different results, as detailed above. This dichotomy lends itself to diverse and sometimes conflicting study results. Nonetheless, evidence supporting an adverse effect of smoking on several key semen parameters is strong, irrespective of study design. Future studies should attempt to further elucidate the possible mechanisms in this relationship. Third, many of the studies reviewed utilize semen analysis parameters as primary end points. Future studies should also prospectively analyze the impact of smoking on fertility while incorporating successful pregnancy rates as main outcome measures.

Conclusion

Although a large volume of retrospective data exists examining smoking and the effects on semen analysis parameters and IVF outcomes, large-scale, population-wide studies on the effects of smoking on natural pregnancies are lacking. Nevertheless, the majority of the evidence points to the fact that men with infertility, or those having difficulty conceiving, should quit smoking to optimize their chances for successful conception.

References

1. Centers for Disease Control and Prevention. Current cigarette smoking among adults—United States, 2011. MMWR. 2012; 61(44):889–894. [PubMed: 23134971]
2. The Health Consequences of Smoking: A Report of the Surgeon General. Office of the Surgeon General; Atlanta, GA: 2004.
3. Practice Committee of American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril. 2013; 99(1):63. [PubMed: 23095139]
4. Thoma ME, McLain AC, Louis JF, et al. Prevalence of infertility in the United States as estimated by the current duration approach and a traditional constructed approach. Fertil Steril. 2013; 99(5): 1324–1331. e1321. [PubMed: 23290741]
5. Kovac JR, Pastuszak AW, Lamb DJ. The use of genomics, proteomics, and metabolomics in identifying biomarkers of male infertility. Fertil Steril. 2013; 99(4):998–998. [PubMed: 23415969]
6. Ramlau-Hansen CH, Thulstrup AM, Aggerholm AS, Jensen MS, Toft G, Bonde JP. Is smoking a risk factor for decreased semen quality? A cross-sectional analysis. Hum Reprod. 2007; 22(1):188–188. [PubMed: 16966350]
7. Kunzle R, Mueller MD, Hanggi W, Birkhauser MH, Drescher H, Bersinger NA. Semen quality of male smokers and nonsmokers in infertile couples. Fertil Steril. 2003; 79(2):287–287. [PubMed: 12568836]
8. Saaranen M, Suonio S, Kauhanen O, Saarikoski S. Cigarette smoking and semen quality in men of reproductive age. Andrologia. 1987; 19(6):670–670. [PubMed: 3434857]
9. Zhang JP, Meng QY, Wang Q, Zhang LJ, Mao YL, Sun ZX. Effect of smoking on semen quality of infertile men in Shandong, China. Asian J Androl. 2000; 2(2):143–143. [PubMed: 11232793]
10. Murawski M, Saczko J, Marcinkowska A, Chwilkowska A, Grybos M, Banas T. Evaluation of superoxide dismutase activity and its impact on semen quality parameters of infertile men. Folia Histochem Cytobiol. 2007; 45(Suppl 1):S123–126. [PubMed: 18292819]
11. Sanocka D, Miesel R, Jedrzejczak P, Kurpisz MK. Oxidative stress and male infertility. J Androl. 1996; 17(4):449–449. [PubMed: 8889709]
12. Gaur DS, Talekar M, Pathak VP. Effect of cigarette smoking on semen quality of infertile men. Singapore Med J. 2007; 48(2):119–119. [PubMed: 17304390]

13. Chia SE, Ong CN, Tsakok FM. Effects of cigarette smoking on human semen quality. Arch Androl. 1994; 33(3):163–163. [PubMed: 7857167]
14. Merino G, Lira SC, Martinez-Chequer JC. Effects of cigarette smoking on semen characteristics of a population in Mexico. Arch Androl. 1998; 41(1):11–11. [PubMed: 9642454]
15. Povey AC, Clyma JA, McNamee R, et al. Modifiable and non-modifiable risk factors for poor semen quality: a case-referent study. Hum Reprod. 2012; 27(9):2799–2799. [PubMed: 22695289]
16. Dikshit RK, Buch JG, Mansuri SM. Effect of tobacco consumption on semen quality of a population of hypofertile males. Fertil Steril. 1987; 48(2):334–334. [PubMed: 3609347]
17. Hassa H, Yildirim A, Can C, et al. Effect of smoking on semen parameters of men attending an infertility clinic. Clin Exp Obstet Gynecol. 2006; 33(1):19–19. [PubMed: 16761532]
18. Pasqualotto FF, Sobreiro BP, Hallak J, Pasqualotto EB, Lucon AM. Cigarette smoking is related to a decrease in semen volume in a population of fertile men. BJU Int. 2006; 97(2):324–324. [PubMed: 16430638]
19. Vine MF, Margolin BH, Morrison HI, Hulka BS. Cigarette smoking and sperm density: a meta-analysis. Fertil Steril. 1994; 61(1):35–35. [PubMed: 8293842]
20. Li Y, Lin H, Li Y, Cao J. Association between socio-psycho-behavioral factors and male semen quality: systematic review and meta-analyses. Fertil Steril. 2011; 95(1):116–116. [PubMed: 20674912]
21. Liu RZ, Gao JC, Zhang HG, Wang RX, Zhang ZH, Liu XY. Seminal plasma zinc level may be associated with the effect of cigarette smoking on sperm parameters. J Int Med Res. 2010; 38(3): 923–923. [PubMed: 20819428]
22. Oyeyipo IP, Raji Y, Emikpe BO, Bolarinwa AF. Effects of nicotine on sperm characteristics and fertility profile in adult male rats: a possible role of cessation. J Reprod Infertil. 2011; 12(3):201–201. [PubMed: 23926503]
23. Wong WY, Thomas CM, Merkus HM, Zielhuis GA, Doesburg WH, Steegers-Theunissen RP. Cigarette smoking and the risk of male factor subfertility: minor association between cotinine in seminal plasma and semen morphology. Fertil Steril. 2000; 74(5):930–930. [PubMed: 11056235]
24. Fuentes A, Munoz A, Barnhart K, Arguello B, Diaz M, Pommer R. Recent cigarette smoking and assisted reproductive technologies outcome. Fertil Steril. 2010; 93(1):89–89. [PubMed: 18973890]
25. Klonoff-Cohen H, Natarajan L, Marrs R, Yee B. Effects of female and male smoking on success rates of IVF and gamete intra-fallopian transfer. Hum Reprod. 2001; 16(7):1382–1382. [PubMed: 11425817]
26. Joesbury KA, Edirisinghe WR, Phillips MR, Yovich JL. Evidence that male smoking affects the likelihood of a pregnancy following IVF treatment: application of the modified cumulative embryo score. Hum Reprod. 1998; 13(6):1506–1506. [PubMed: 9688383]
27. Zitzmann M, Rolf C, Nordhoff V, et al. Male smokers have a decreased success rate for in vitro fertilization and intracytoplasmic sperm injection. Fertil Steril. 2003; 79(Suppl 3):1550–1554. [PubMed: 12801558]
28. Jensen TK, Jorgensen N, Punab M, et al. Association of in utero exposure to maternal smoking with reduced semen quality and testis size in adulthood: a cross-sectional study of 1,770 young men from the general population in five European countries. Am J Epidemiol. 2004; 159(1):49–49. [PubMed: 14693659]
29. Jensen MS, Mabeck LM, Toft G, Thulstrup AM, Bonde JP. Lower sperm counts following prenatal tobacco exposure. Hum Reprod. 2005; 20(9):2559–2559. [PubMed: 15919771]
30. Storgaard L, Bonde JP, Ernst E, et al. Does smoking during pregnancy affect sons' sperm counts? Epidemiology. 2003; 14(3):278–278. [PubMed: 12859027]
31. Neal MS, Hughes EG, Holloway AC, Foster WG. Sidestream smoking is equally as damaging as mainstream smoking on IVF outcomes. Hum Reprod. 2005; 20(9):2531–2531. [PubMed: 15919779]