SEXUAL MEDICINE REVIEWS

Male Sexual Function and Smoking

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ABSTRACT

Introduction: Erectile dysfunction (ED) is a common disorder that has many potential etiologies, including hormonal imbalances, psychogenic factors, neurologic disorders, vascular insufficiency, and other risk factors. Cigarette smoking has been well established as a risk factor for cardiovascular disease and stroke, but the relation between smoking and ED is less frequently considered.

Aim: To review the current literature that analyzes the association between cigarette smoking and ED.

Methods: The PubMed database was searched using the terms *erectile dysfunction and smoking* and *erectile dysfunction and tobacco* through December 2015.

Main Outcome Measures: Main outcome measures were significant changes in erectile function in relation to smoking status.

Results: Eighty-three studies and articles were reviewed. Multiple human studies, animal studies, case series, cross-sectional, and cohort studies analyzed the relation between smoking or nicotine and ED.

Conclusion: There is substantial evidence showing that cigarette smoking is a risk factor for ED. Multiple human, animal, case series, cross-sectional, and cohort studies support this conclusion. A positive dose-response relation also is suggested such that increased quantity and duration of smoking correlate with a higher risk of ED. Smoking cessation can lead to recovery of erectile function, but only if limited lifetime smoking exposure exists. Smoking contributes to ED in different ways, especially by causing penile vasospasm and increased sympathetic nervous system tone.

Key Words: Erectile Dysfunction; Penile Erection; Smoking; Tobacco; Smoking Cessation

INTRODUCTION

Erectile dysfunction (ED) is defined as the persistent inability of a man to attain and maintain an erection that is adequate for satisfactory sexual performance.[1] It is estimated that 18.4% of U.S. men at least 20 years of age have ED and that the condition affects 18 million men nationwide.[2,3] The Massachusetts Male Aging study found that 25.9 cases of new-onset ED occurred per 1,000 men annually.[4]

The etiology of ED has been attributed to hormonal derangement, psychogenic factors, neurologic disorders, vascular insufficiency, and multiple other factors. Reports of patients with vasculogenic ED have suggested predisposing vasculopathy risk factors that include cigarette smoking, high-fat diets, higher serum lipid levels, hypertension, physical inactivity, and obesity.[5-7] There is growing evidence that tobacco smoke adversely affects sexual health and erectile function.[8-17] However, patient awareness that smoking is a risk factor for ED is low—only 24.2% of surveyed patients in a urology clinic were aware of this association.[18] A major proposed mechanism behind this is that cigarette smoke has a similar atherogenic effect on penile vasculature as on coronary vasculature in increasing heart disease risk.

AIMS

The goal of this review is to analyze current observational, clinical, and experimental data that link cigarette smoking to ED, including the relevant pathophysiologic concepts.

METHODS

This review article is based on a detailed literature search of the National Library of Medicine using the search terms *erectile*

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dysfunction and smoking and *erectile dysfunction and tobacco* through December 2015.[19] Articles in the English language were selected. Eighty-three articles were reviewed.

MAIN OUTCOME MEASURES

Main outcome measures were significant changes in erectile function in relation to smoking status.

RESULTS

Erectile Dysfunction in Smokers

Multiple case series, cross-sectional, and cohort studies have attempted to analyze whether smoking contributes to ED and the prevalence of ED in smokers.

Glina et al[20] measured intracavernous pressures (ICPs) after pharmacologic stimulation of an erection in patients who did not smoke before the experiment at 1 week and then smoked two high-nicotine cigarettes before pharmacologic stimulation the following week. Without smoking, 12 of 12 participants achieved erections, with a mean ICP of 85.83 mmHg. After smoking, only 33% of subjects achieved an erection, with a mean ICP of 53.50 mmHg.

Multiple observational case series have linked cigarette smoking and ED. These studies are limited by not having a true comparison group, but they are included because they are often cited in the literature.

One case series by Wabrek et al[21] in 1983 observed 120 men who were referred to a medical sexology clinic for evaluation of ED. Of these men, 50% were smokers. Another similar study found that 64% of 440 men referred for clinical evaluation of ED were smokers.[22] An additional comparable study looked at 300 men referred to an andrology clinic for impotence. Of the men diagnosed with psychogenic or vasculogenic ED, 62% of them smoked approximately 25 cigarettes daily for at least 20 years.[8]

Condra et al[23] studied 178 men referred for clinical evaluation of ED. The study found that 51.4% of these subjects were current cigarette smokers and 81% were current or former smokers. Tengs and Osgood[24] analyzed 19 clinical studies of ED involving 3,819 men. Across all these studies, the investigators found that 40% of the studied men with ED were current smokers.

Several cross-sectional, random surveys of sample populations have been performed to offer more population-based appraisals of the association between smoking and ED.

The Vietnam Experience Study of 1985 through 1986 surveyed 4,462 U.S. Army Vietnam-era veterans 31 to 49 years of age. They found the prevalence of ED to be 2.2% among never smokers, 2.0% among former smokers, and 3.7% among current smokers ($P = .005$). The correlation remained significant for increased ED in current smokers even after adjusting for multiple confounders.[10]

An Italian study by Parazzini et al[25] assessed the prevalence of ED in 2,010 men older than 18 years in 1996 through 1997. After controlling for age, marital status, socioeconomic status, and chronic diseases, they found an increased risk of ED for current smokers (odds ratio [OR] = 1.7, 95% CI = 1.2−2.4, $P < .05$) and former smokers (OR = 1.6, 95% CI = 1.1−2.3, $P < .05$) compared with lifetime non-smokers. The Krimpen Study surveyed 1,688 men in the Netherlands and found that smokers were more likely than non-smokers to report ED (OR = 1.6, 95% CI = 1.1−2.3, $P < .05$).[26] In Spain, Martin-Morales et al[27] found that among 2,476 men, smoking was significantly associated with ED (OR = 2.5, 95% CI = 1.64−3.80, $P < .05$).

Shiri et al[28] observed 1,442 men in Finland who responded to baseline and follow-up questionnaires. The risk for ED from smoking was increased but was not statistically significant (OR = 1.4, 95% CI = 0.9−2.3). They suggested that the non-significance was due to the fact that only a small sample of 203 subjects had newly developed ED after the 5-year follow-up questionnaire. They also found that smokers had lower odds of recovering from ED compared with never smokers (OR = 0.6, 95% CI = 0.2−1.4).

Lam et al[29] surveyed 819 Chinese men 31 to 60 years old to look for an association of smoking with self-reported dissatisfaction with or without erection difficulty during sexual intercourse. The study found that smoking at least 20 cigarettes per day was associated with a 47% increased risk of ED (OR = 1.47, 95% CI = 1.00−2.16, $P < .05$) compared with never smoking. Also, they found that sexual intercourse dissatisfaction was more common in current smokers.

Weber et al[30] surveyed a group of 108,477 men at least 45 years old. The study found that 18.8% of men had moderate ED and 16.7% had complete ED. The risk of moderate or complete ED was higher in current cigarette smokers, with those who smoked at least 20 cigarettes per day (OR = 1.86, 95% CI = 1.69−2.06) having a higher risk than those who smoked fewer than 20 cigarettes per day (OR = 1.48, 95% CI = 1.37−1.59).

Only a few large cohort studies have been performed, but they have provided useful data.

The Health Professionals Follow-Up Study began in 1986 as a prospective cohort study of heart disease and cancer in 51,529 male health professionals in the United States. Bacon et al[31] analyzed 34,282 of these men 53 to 90 years old and found an increased probability of ED in current smokers vs non-smokers (OR = 1.3, 95% CI = 1.1−1.4, $P < .05$). In 2006, Bacon et al[32] studied 22,086 men 40 to 75 years old in the same cohort and found that the risk ratio of developing ED during the 14-year follow-up among smokers was 1.5 (95% CI = 1.3−1.7).

The Massachusetts Male Aging Study surveyed 1,290 men 40 to 70 years old from 1987 through1989 and did not find an independent association between smoking and ED.[33] However, the prospective phase of this study, which extended over a median of

9 years, found the comorbidity-adjusted rate of incident ED to be significantly higher in cigarette smokers (24%) than non-smokers (14%; OR = 1.97, 95% CI = 1.07−3.63, $P = .03$).[34]

A meta-analysis of multiple cohort and case-control studies was performed by Cao et al[35] in 2013. It showed that, across prospective cohort studies, the OR of ED was 1.51 (95% CI = 1.34−1.71) for current smokers and was 1.29 (95% CI = 1.07−1.47) for former smokers.

Dose-Response Relation

Because many studies have shown a link between smoking and ED, other studies sought to determine whether heavier smokers had worse erectile function.

Several epidemiologic analyses have explored the relation between the amount of smoking exposure and the extent of ED. The Vietnam Experience Study of 1985 through 1986 showed no relation between ED and the number of cigarettes smoked daily or the number of years of smoking.[10] In contrast, an Italian cross-sectional study by Parazzini et al[25] found that the duration of smoking was associated with a higher risk of ED. The OR for ED risk was 1.2 (95% CI = 1.0−7.4) for men who smoked for less than 20 years, whereas the OR was 1.6 (95% CI = 1.1−2.3) for men who smoked longer than 20 years.

One of the first experimental studies to observe the relation between smoking and ED was performed in 1986 by Gilbert et al.[36] Male smokers (n = 42) had polygraphic recordings of their erections while watching erotic videos. They were broken into three groups—one that smoked high-nicotine cigarettes, one that smoked low-nicotine cigarettes, and a control group that ate a mint candy during the session. The results showed that smoking two high-nicotine cigarettes significantly decreased the rate at which the diameter of the penis increased compared with the other two conditions during the session ($P < .001$). High-nicotine cigarettes also caused more vasoconstriction and a higher heart rate.

A 2001 Australian study of sexual and reproductive health had a sample of 8,367 Australian men 16 to 59 years of age who were interviewed from 2001 through 2002. The results showed that smokers were more likely to have ED than non-smokers. The association was stronger for heavier smokers (≥20 cigarettes daily; OR = 1.39, 95% CI = 1.05−1.83, $P < .05$) than for lighter smokers (<20 cigarettes daily; OR = 1.24, 95% CI = 1.0−1.52, $P < .05$).[37]

Polsky et al[11] investigated the associations between several lifestyle and medical factors and ED, including smoking. The case-control study compared men with and without clinically diagnosed ED. The results showed an estimated OR of 2.2 (95% CI = 1.17−3.94, P value not reported) for ED in former smokers compared with non-smokers. The OR for current smokers was not increased, raising the possibility of reverse causation. Subjects with a smoking history of at least 10 pack-years had twice the risk of ED as never smokers. The finding that current smoking was not a risk factor for ED was attributed by the investigators to the possible bias introduced by the potentially higher likelihood of smokers with symptoms of ED to be encouraged and motivated to quit smoking and thus not be included as smokers in this study.

In 2007 He et al[13] studied 7,864 Chinese men, and they reported a significant dose-response relation between the risk of ED and cigarette smoking (OR = 1.41, 95% CI = 1.09−1.81). The number of cigarettes smoked per day also showed a significant dose-response relation with ED (1−10 cigarettes per day, OR = 1.22, 95% CI = 0.88−1.68; 11−20 cigarettes per day, OR, 1.39, 95% CI = 1.05−1.85; >20 cigarettes per day, OR = 1.70, 95% CI = 1.13−2.56).

Kupelian et al[14] used data from the Boston Area Community Health Survey to assess the relation between smoking and ED. The International Index of Erectile Function questionnaire was given to 2,301 men 30 to 79 years old, and after controlling for comorbidities, the study found an association between increased pack-years and greater severity of ED. For 10 to 19 pack-years of smoking, the OR was 1.28 (95% CI = 0.71−2.32), and for at least 20 pack-years of smoking, the OR was 1.68 (95% CI = 1.03−2.30). In 2010, Kupelian et al[15] investigated the relative contributions of modifiable risk factors to ED using the same cohort data. They again found that increased duration and intensity of smoking were associated with greater risk of ED.

Wu et al[38] (2012) examined the results of the Fangchenggang Area Male Health and Examination Survey performed in 2009, which surveyed 2,686 subjects about their smoking habits and erectile function. The results showed that smokers who smoked more than 20 cigarettes daily had a significantly increased risk of ED compared with never smokers (OR = 1.23, 95% CI = 1.03−1.49, $P = .02$).

Cao et al[39] performed a meta-analysis in 2014 and found that for an increase in 10 cigarettes smoked per day, the OR for risk of ED was 1.14 (95% CI = 1.09−1.18). For an increment of 10 years of smoking, the OR for risk of ED was 1.15 (95% CI = 1.10−1.19). This study showed a positive dose-response relation between the amount and duration of smoking and ED.

Endothelial Dysfunction

One suggested mechanism for ED is smoking-induced endothelial dysfunction of the penile vasculature. The vascular endothelium and the lining of the lacunar spaces release vasoactive substances that control the smooth muscle relaxation required for erection.[40,41] Overall, studies have shown that smoking adversely affects penile vascular endothelial function by decreasing the activity of neuronal nitric oxide synthase (NOS), which in turn decreases the NO needed for vasodilation. Smoking also harms vascular medial elastic fibers.

In a study of rats by Xie et al[42] in 1997, there was no difference found in the protein expression of penile tissue endothelial NOS between smoke-exposed and smoke-unexposed rats. However, the study did find that the protein expression of the neuronal form of NOS was significantly decreased in smoke-exposed rats, suggesting

impaired neuronal signaling pathways. Another animal study by Xu et al[43] in 2012 showed that rats undergoing nicotine injections had decreased endogenous carbon monoxide and NOS activity in harvested corpora cavernosa. The effect was more significant in rats that underwent nicotine injections for a longer period.

Huang et al[44] studied 40 rats that were divided into four groups. Group 1 was the control group and exposed to no smoke. Groups 2, 3, and 4 were exposed to cigarette smoke for 4, 12, and 24 weeks, respectively. After 24 weeks, groups 3 and 4 had significantly decreased ICPs and cavernosal smooth muscle and endothelial contents. Group 4 had significantly higher oxidative stress. Mean neuronal NOS expression was significantly lower in smoke-exposed rats, and the levels of apoptosis were significantly higher.

Several other studies have described decreased endothelial-mediated vasodilation owing to decreased endothelial NO production in acute and long-term smoking. A mechanism suggested throughout these studies is that smoke exposure increases adhesion and migration of monocytes across the vascular endothelium, thereby increasing early atherogenesis and decreasing endothelial NO production.[17,45-49] In addition, long-term smoking has been shown to adversely affect vascular medial elastic fibers.[50,51]

In contrast, Saenz de Tejada et al[52] found no alteration of endothelial function from smoke exposure. They studied strips of human corpora cavernosa and found that smoking was not associated with greater impairment of endothelium-mediated relaxation responses. They also showed that the neurogenically mediated relaxation of penile vascular smooth muscle did not differ in smokers and non-smokers.

Effects on Penile Blood Flow

Penile erection is a neurovascular event that depends on proper function of the arterial inflow and venous drainage systems. Multiple studies have assessed the relation between smoking and penile blood flow using techniques such as Doppler ultrasound, arteriography, and the RigiScan (GOTOP Medical, Inc, St Paul, MN, USA). Most studies have suggested that smoking contributes to ED by vasoconstricting penile arteries in the short and long term because of atherosclerosis. A few studies did not find this significant correlation and suggested that venous disease also might play a role.

The penile-brachial index (PBI) is one technique used to assess erectile function. It uses Doppler ultrasound to calculate the ratio of penile to brachial blood pressures. Lower PBI values have been associated with impaired erections.[53] Condra et al[23] reported significantly lower PBI values in smokers than in non-smokers. A larger 314-subject study in 1992 by Hirshkowitz et al[54] confirmed this significantly lower PBI value in smokers. Also, this study found significant correlations between the number of cigarettes smoked per day and the magnitude of these decreases in PBI for the left dorsal artery ($r = -0.14$, $P = .01$) and right cavernosal artery ($r = -0.13$, $P < .03$). When pharmacologically stimulating an erection before Doppler analysis, Shabsigh et al[55] found a marginally significant difference in vascular impairment between smokers and non-smokers.

Vascular morphology also has been analyzed by arteriography. Virag et al[22] found a 67.8% prevalence of arteriographic abnormalities in the four main blood vessels of the penis in patients in whom organic ED had been established, of whom 86% were smokers. Bahren et al[56] found that 82% of their subjects with arteriographically proved peripheral arteriosclerotic lesions were heavy smokers. In a similar study, Rosen et al[57] found smoking to be a significant independent risk factor for atherosclerotic lesions in the internal pudendal and common penile arteries. The study also found that for each 10 pack-years of smoking, the risk ratio of hypogastric-cavernous arterial bed atherosclerosis was 1.31 (95% CI = 1.05−1.64) compared with 1.03 (95% CI = 1.01−1.05) for 1 pack-year of smoking.

Levine and Gerber[58] observed one 38-year-old man with a smoking history before and after smoking two cigarettes using pelvic arteriography. The post-smoking arteriogram showed decreased caliber in the pudendal artery and non-visualization of the deep penile artery, suggesting acute vasoconstriction as the mechanism behind the observed effects.

Prezioso et al[59] used penile cavernosal artery intima-media thickness to assess erectile function. The study found that subjects with vasculogenic ED had greater intima-media thickness. This method could help in future studies of the association between ED and smoking.

Several animal studies also have attempted to investigate the association of smoking and ED. In 1987, Juenemann et al[9] used a canine model to monitor arterial inflow, venous outflow, and ICP of the penis during cavernosal nerve stimulation before and after cigarette smoke inhalation. After smoking, peak arterial inflow was significantly decreased, peak ICP was significantly decreased and could not be maintained, and venous outflow was not significantly restricted.

Several contrasting studies have found no significant association between smoking and decreased penile blood flow. Two of these studies, by Wabrek et al[21] and Virag et al,[22] found no correlation using the PBI technique. However, the study by Virag et al did find a synergistic effect of smoking on PBI when combined with other arterial risk factors, such as diabetes and hypertension. Elhanbly et al[60] studied 109 patients with ED (71 smokers and 38 non-smokers) with the RigiScan, to assess for nocturnal penile tumescence (NPT) and rigidity, and duplex ultrasonography. NPT and rigidity results were abnormal for 86% of smokers and 55% of non-smokers ($P = .02$), but the difference in the peak systolic velocity of the cavernosal artery between smokers and non-smokers was not significant. In 2013, Goksu et al[61] analyzed cavernosal artery blood flow and carotid and femoral artery intima-media thickness. Of 102 patients with ED, 42.2% had arterial ED (according to Doppler ultrasound).

Of the arterial ED group, 53.5% of subjects were smokers, which showed a non-significant association between arterial ED and smoking. These contrasting studies could suggest that ED vascular pathology is due in part to veno-occlusive disease and other factors and not purely to arterial insufficiency.

Autonomic Nervous System Dysfunction

Penile erection is mediated by the parasympathetic nervous system. Acute nicotine exposure increases sympathetic nervous system tone, which could be another contributing factor to smoking-related ED.

In a 2008 randomized, double-blinded, placebo-controlled trial by Harte and Meston,[16] the acute effects of nicotine exposure were studied. In 28 men, the study found a 23% decrease in physiologic sexual arousal with acute nicotine exposure. The investigators suggested this occurrence was due to the sympathomimetic effects of nicotine, causing vasoconstriction by norepinephrine and epinephrine release. However, the subjects' self-reports did not show a decreased sexual arousal after nicotine.

Heart rate variability (HRV) is another method being used to study the effects of smoking. HRV analyzes the changing interval between consecutive heartbeats and is used as an indicator of sympathetic-parasympathetic balance. Low HRV signals sympathetic nervous system dominance, and high HRV signals suggest parasympathetic dominance. One study by Harte[62] in 2014 compared 64 smokers with 55 non-smokers and found that current long-term cigarette smokers had sympathetic dominance (low HRV) and decreased magnitude of erectile tumescence. Harte[63] also analyzed HRV after acute nicotine exposure by comparing subjects given nicotine gum vs placebo gum. This study showed low HRV after nicotine exposure and decreased penile tumescence as measured by penile plethysmography. These studies show that smoking might contribute to ED in part by increasing sympathetic tone, which decreases parasympathetic-mediated erections.

Histopathology

Smoking also has been found to alter the histologic makeup of erectile tissue. Overall, it decreases smooth muscle and increases collagen density.

A histopathologic study of erectile tissue by Mersdorf et al[64] found that smokers had degenerative changes, including decreases in smooth muscle content, sinusoidal endothelium, nerve fibers, and capillaries, and an increase in collagen density.

Park et al[65] examined the corpora of smoke-exposed rats and showed increased collagen fibers with decreased smooth muscle.

Chemical Effects of Smoking

Smoking also can increase ED by lowering testosterone levels and increasing superoxide free radicals.

Park et al[65] studied the effects of smoking on erectile function in rats. Rats with long-term exposure to smoke showed higher blood levels of thiocyanate (a good indicator of smoke exposure), lower testosterone levels, and lower corpora filling rates than the control group. High thiocyanate and low testosterone were significantly associated with erectile function in the group with long-term smoke exposure. Smoking-induced lower testosterone levels might be another way in which smoking decreases erectile function.

Smoking also can cause oxidative stress by superoxide free radicals released from the cavernosal smooth muscle. Multiple mechanisms of how these free radicals contribute to vasculogenic ED have been suggested.[17,66-72]

Interaction of Smoking With Other Factors

Several studies have looked at the combined effects of smoking and other risk factors in the development of ED.

Goldstein et al[73] examined 19 patients who underwent pelvic irradiation for prostate cancer. Fourteen of 15 patients who had early decreased tumescence were smokers. Only one of the four subjects with preserved erectile capacity was a smoker. The investigators suggested a possible synergistic effect of radiation and smoking in causing ED.

Feldman et al[33] found that cigarette smoking was not an independent risk factor for ED. However, they found that several risk factors associated with ED greatly increased if smoking also was present. These risk factors included being treated for heart disease (from 21% for non-smokers to 56% for current smokers), treated for hypertension (from 8.5% to 20%), and not treated for arthritis (from 9.4% to 20%). Medications that produced this synergistic effect with smoking were cardiac drugs (from 14% to 41%), antihypertensives (from 7.5% to 21%), and vasodilators (from 21% to 52%).

Similarly, in an Italian cross-sectional study, smoking increased the likelihood of ED associated with diabetes by 13% and with hypertension by 39%.[25]

Gades et al[74] studied 1,329 men 40 to 79 years old and found that among smokers, the OR for ED decreased with increasing age. Compared with never smokers and former smokers in the same age groups, current smokers in their 40s had the highest odds of ED (OR = 2.74, 95% CI = 0.44−16.89), followed by smokers in their 60s (OR = 1.70, 95% CI = 0.82−3.51), 50s (OR = 1.38, 95% CI = 0.51−3.74), and 70s (OR = 0.77, 95% CI = 0.27−2.21). The declining effect with increasing age could reflect the increasing prevalence of risk factors for ED other than smoking at older ages.

Shiri et al[12] investigated the role of vascular disease in causing smoking-related ED. A study of 2,510 men followed over 10 years found that the risk of developing ED was three times higher (adjusted incidence density ratio = 3.1, 95% CI = 1.3−7.5) in men who smoked and developed vascular disease during the study period compared with men who never smoked and did not

develop vascular disease. Smokers who did not develop vascular disease did not show an increased risk of ED (adjusted incidence density ratio = 1.0, 95% CI = 0.5−1.8). The investigators concluded that smoking might cause ED because it can cause vascular disease. Therefore, ED could serve as a good silent marker of vascular disease in smokers.

Capogrosso et al[75] attempted to analyze risk factors for ED in men younger than 40 years. Of 439 men younger than 40 who were surveyed, 26% were found to have ED. Of those younger than 40, fewer comorbid conditions were present compared with those older than 40, but an increased frequency of cigarette smoking and illicit drug use was reported. This might suggest that smoking and drug use are contributors to the increasing prevalence of ED in young men.

Smoking Cessation

If smoking contributes to ED, an important clinical question is whether smoking cessation will improve previously diminished erectile function.

Monitoring NPT during REM sleep is a non-invasive way to quantify the physiology of an erection. Elist et al[76] used NPT monitoring in 20 smokers with ED and found 35% had normal NPT after 6 weeks of not smoking.

Forsberg et al[77] presented case reports of 20- and 27-year-old smokers. They had improved penile vascular test results and resolution of ED after smoking cessation. The Vietnam Experience Study of 1985 through 1986 showed that the prevalence of ED was comparable between former smokers and non-smokers, and the prevalence of ED among current smokers was much higher.[10] The longitudinal phase of the Massachusetts Male Aging Study similarly determined that ED was more common among current smokers than non-smokers and former smokers.[34]

A study of smoking cessation by Guay et al[78] in 1998 observed 10 men with a smoking history of at least 30 pack-years. The men used the RigiScan at home to monitor NPT after a day of smoking and then after a 24-hour smoke-free period. Erectile parameters improved significantly in the men who had stopped smoking for 24 hours. In addition, four of these men quit smoking for 1 month (using a nicotine patch during that month) and were found to have even greater improvements in erectile function. This suggests nicotine is not the only chemical in a cigarette that contributes to the damaging effects of smoking on penile tumescence.

Sighinolfi et al[79] also evaluated acute effects of smoking cessation on penile hemodynamics. They assessed 20 active smokers with ED using the International Index of Erectile Function questionnaire. They underwent penile color Doppler ultrasonography after pharmacologic stimulation at baseline and 24 to 36 hours after smoking cessation. At baseline, 50% of subjects had abnormal peak systolic velocity and 75% had abnormal end-diastolic velocity values. After withdrawing from smoking, 0% of subjects had abnormal peak systolic velocity and only 15% had abnormal end-diastolic velocity values. This study implies that long-term smoking causes ED by predominately altering the veno-occlusive function of the penis. Also, it shows that even short-term smoking cessation can improve erectile function.

The conclusion from some studies that smoking cessation leads to a recovery of erectile function is challenged by the prospective analysis of men who stopped smoking during the 9-year Massachusetts Male Aging Study follow-up. The study showed that the covariate-adjusted incidence of ED was not statistically decreased after smoking cessation ($P = .28$). Of note, the men in this study started smoking at a young age (mean = 16.6 years) and had relatively long smoking exposure (mean = 39.4 pack-years).[34]

Derby et al[80] found that cessation during middle age, after a significant smoking exposure, can fail to improve ED because of the long-term vascular effects.

Travison et al[81] also analyzed the data from the Massachusetts Male Aging Study and found that smoking was associated with progression of ED only. The odds of a progression of ED doubled with smoking status. There was no notable corresponding decrease in ED by stopping smoking. They concluded that smoking cessation could halt the progression of ED but might have minimal effect on ED remission.

Harte and Meston[82] studied 20 subjects who successfully quit smoking using an 8-week program that involved nicotine patches and counseling. Self-report surveys and penile plethysmography were performed throughout the 8 weeks. Four-week follow-up after successful quitting showed increased penile tumescence and a fivefold improvement in time to maximum erection. At the program midpoint, there was no improvement in erectile function, suggesting that nicotine patches also contribute to ED.

Passive Smoking and Erectile Dysfunction

The effect of passive smoking, or second-hand smoking, on erectile function has not been studied extensively. However, passive smoking is common and studying its relation to ED is important.

Celermajer et al[83] studied 78 subjects 15 to 30 years old who were previously healthy. Twenty-six subjects were self-reported active smokers, 26 were self-reported passive smokers (exposed to tobacco smoke at home and/or work for ≥1 hour daily), and the control group of 26 who were not exposed to any smoke. Using an ultrasound-based technique to observe the brachial artery, flow-mediated vasodilation was measured. In the control group, flow-mediated dilation was found to be 8.2 ± 3.1%. However, in the passive and active smoking groups, flow-mediated dilation was found to be significantly decreased at 3.1 ± 2.7% and 4.4 ± 3.1%, respectively. Kupelian et al[14] used the Boston Area Community Health Survey to observe

the effects of passive smoking. They found a moderate, but statistically insignificant, increase in the risk of ED for passive smokers. The increased risk for passive smokers (OR = 1.33, 95% CI = 0.69−2.55) was similar to the increased risk in people smoking 10 to 19 pack-years (OR = 1.28, 95% CI = 0.71−2.32). Many of the animal studies throughout this review that analyzed the mechanism by which smoking affects rat, mouse, and dog erectile function were performed using passive smoke exposure. Because animals cannot be made to smoke actively, the animals were passively exposed to smoke in a cage.[9,17,42,44,51,65]

CONCLUSIONS

There is substantial evidence showing that cigarette smoking contributes to ED. This association is supported by case series, cross-sectional, and prospective population-based studies. The population-based studies provide a more accurate observational assessment, but the number of these studies is limited. The prospective studies confirm the temporal relation that smoking appropriately precedes ED. Several studies have reported an increased risk of ED with greater smoking exposure. Other studies have found that smoking cessation can lead to a recovery of erectile function, but only if the lifetime smoking exposure is limited.

The relation between smoking and ED also is supported by studies that indicate a plausible mechanism of disease. The nicotine in cigarettes is at least a partial contributor, because studies have shown an acute vasospasm of the penile arteries after nicotine exposure, which alters erectile blood flow, and an increase in sympathetic nervous system tone. The long-term effects of smoking result from impaired vascular physiology of the erectile tissue as seen by morphologic changes in the tissue of smokers. Other studies have shown that smoking adversely affects tissue-dependent erection regulatory factors, such as NOS, and can increase corpora collagen fibers.

Overall, the clinical and basic scientific studies support a causal relation between cigarette smoking and ED. Short- and long-term smoking have been shown to decrease erectile function by multiple mechanisms. Passive, second-hand smoking also leads to ED by the same mechanisms, although the adverse effect might be slightly less. Clinically, promoting smoking abstinence can help to prevent ED, and encouraging current smokers to quit could limit the risk of ED.

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