

Smoking and Type 2 Diabetes Mellitus

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Cigarette smoking is a well-known risk factor in many diseases, including various kinds of cancer and cardiovascular disease. Many studies have also reported the unfavorable effects of smoking for diabetes mellitus. Smoking increases the risk of developing diabetes, and aggravates the micro- and macro-vascular complications of diabetes mellitus. Smoking is associated with insulin resistance, inflammation and dyslipidemia, but the exact mechanisms through which smoking influences diabetes mellitus are not clear. However, smoking cessation is one of the important targets for diabetes control and the prevention diabetic complications.

Keywords: Diabetes complications; Diabetes mellitus; Smoking

INTRODUCTION

Smoking is one of the modifiable risk factors for many chronic diseases, such as cardiovascular disease (CVD), cancer, chronic obstructive lung disease, asthma, and diabetes. However, the adverse effects of smoking on diabetes have been generally under recognized. In the guidelines from the Korean Diabetes Association, smoking cessation is recommended as one of the most important steps in preventing the cardiovascular complications of diabetes [1]. Many studies have shown that the adverse effects of smoking on diabetes mellitus are not only diabetic macrovascular complications but the causal nature of its association with diabetes and the progression of diabetic microvascular complications has yet to be explored.

Although smoking is known to decrease body weight, it is associated with central obesity [2]. Smoking also increases inflammation and oxidative stress [3], to directly damage β -cell function [4] and to impair endothelial function [5].

The prevalence of smoking in Korean men is near 50%, which is the highest smoking rate in the Western Pacific region. In addition to obesity, the high prevalence of smoking is one of the major health problems for Korea's public health.

This review is about the various smoking effects on diabetes mellitus, diabetic complications, and diabetic incidence. Understanding the hazardous effects of smoking on diabetes mellitus may lead to more emphasis on smoking prevention and smoking cessation as important strategies in the management of diabetes mellitus.

SMOKING AND DIABETES INCIDENCE

There is much evidence that smoking increases the risk of diabetes. Several cohort studies in Korea have reported that smoking was associated with an increased risk for the development of diabetes. Cho et al. [6] followed 4,041 men for 4 years in rural and urban settings in Korea, and found that past and current smokers had a significantly increased risk for type 2 diabetes, and the risk increased with the number of cigarettes smoked. Another study reported a 14-year-long prospective cohort study, in which the risk of diabetes among men and women who smoked 20 cigarettes or more per day was 1.55 (95% confidence interval [CI], 1.51 to 1.60) compared to those who never smoked [7].

A Japanese study reported similar results of a positive cor-

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relation between cigarette consumption and risk for diabetes [8]. The health professionals' follow-up study demonstrated that the risk for diabetes among men who smoked ≥ 25 cigarettes per day was 1.94 (95% CI, 1.25 to 3.03) [9]. Another British study showed the risk for diabetes in smoking men was around 1.7, after adjusting for confounding factors, such as age, body mass index, physical activity, alcohol intake, social class, and antihypertensive treatment [10].

There have been few studies on the effect of smoking on the risk of diabetes in women as generally the prevalence of smoking is lower in women than men. However, the results from the Nurses' Health Study in the United States (114,247 women, 1,227,589 person-years follow-up) showed that the risk for diabetes in smokers was 1.42 after adjustment for other risk factors [11].

The same cohort was followed for 16 years, and a new analysis was performed. The predictable risk factors for diabetes were overweight and obesity, as in men, low physical activity, a poor diet, current smoking, and abstinence from alcohol were all independently associated with the risk for diabetes. The adjusted risk for diabetes in smokers was 1.4 compared with non-smokers [12].

THE EFFECT OF SMOKING ON INSULIN ACTION

The exact mechanism for why smoking increases the risk of diabetes and deteriorates glucose homeostasis has not been fully elucidated, but the available evidence shows that smoking increases insulin resistance.

In healthy young men, acute smoking showed an increased insulin resistance [13]. Smokers had a significantly increased homeostatic model assessment insulin resistance index an hour after smoking [14]. The smoking reduced insulin mediated glucose uptake by 10% to 40% in men who smoked compared with non-smoking men [15,16]. In type 2 diabetic subjects, insulin and C-peptide responses to oral glucose load were significantly higher in smokers than non-smokers and the insulin resistance, as determined by the euglycemic clamp technique, was positively correlated in a dose dependent manner [17]. Thus smoking induced insulin resistance in patients with type 2 diabetes, as well as healthy subjects.

In addition to increased insulin resistance, smoking also showed dyslipidemia prone to atherosclerosis. Smokers had higher fasting triglycerides and lower high density lipoprotein

cholesterol levels, and an increased proportion of small dense low density lipoprotein particles. Fibrinogen levels and plasminogen activator inhibitor 1 activity were also elevated in smokers [18].

In terms of glucose homeostasis, smoking has a negative effect on glucose control. In a population-based prospective study, cigarette smoking was positively associated in a dose dependent manner with elevated HbA1c after adjustment for possible confounding by dietary variables [19]. This finding was also reported in patients with diabetes in Sweden; smoking type 1 and type 2 patients had a higher mean HbA1c but a lower mean body mass index than non-smokers [20].

SMOKING AND DIABETIC MICROVASCULAR COMPLICATIONS

The smoking effects on microvascular diabetes complications vary across reports. Generally, several studies have shown that smoking has an adverse effect on diabetic nephropathy, but the influence of smoking independently with glucose control, on retinopathy and neuropathy are unclear.

SMOKING AND NEPHROPATHY

Several studies have demonstrated that smoking promotes diabetic microalbuminuria and exacerbates diabetic nephropathy. In the study by Biesenbach et al. [21], a 13-year follow-up study, the progression of nephropathy was clearly increased in smokers. The authors showed that smoking was a risk factor for diabetic kidney disease, independent of age, sex, and duration of diabetes and HbA1c levels.

In prospective studies by Chuahirun and Wesson [22] and Chuahirun et al. [23], the adverse effects on diabetic nephropathy in type 2 patients were confirmed, even in optimal hypertensive patients.

SMOKING AND RETINOPATHY

The association of smoking and diabetic retinopathy has not been clear. It was reported that retinopathy has been associated with glycemic control and not smoking state [24]. Some studies have reported no association with smoking and retinopathy in type 2 diabetes [24,25]. The United Kingdom Prospective Diabetic (UKPD) study to determine risk factors related to the incidence and progression of diabetic retinopathy

followed patients over 6 years from diagnosis. The development of retinopathy was associated with glycemia and higher blood pressure, but not smoking [26]. Thus in type 2 patients, the effects of smoking on diabetic retinopathy has not been as clear as with nephropathy.

SMOKING AND NEUROPATHY

There are few studies about smoking and diabetic neuropathy. Smoking may affect diabetic neuropathy differently according to the type of diabetes [27]. In type 2 diabetic patients, smoking was not a risk factor in the presence of polyneuropathy or sensory neuropathy as diagnosed by symptom and sign [27,28]. It was reported that there was no relationship between current or previous levels of smoking and the severity and duration of chronic painful neuropathy [29]. But in the study by Tamer et al. [30], while smoking was not associated with neuropathic complaints, using electromyography-supported neuropathy examination there were significant relationships with smoking, as well as HbA1c. Therefore, more studies are needed to evaluate the association between smoking and neuropathy.

SMOKING AND MACROVASCULAR COMPLICATIONS

Smoking has been shown to be a significant risk factor for all-cause mortality, and for mortality due to CVD and coronary heart disease (CHD) in diabetics. Smokers die on average 8 to 10 years younger than non-smokers, as age is entered into most multi-regression analysis.

SMOKING AND CHD

Smoking is a major risk factor for CVD in non-diabetic subjects, as well as diabetic subjects. In an 8-year prospective study, smoking was significantly associated with an increased risk for CHD in diabetic patients [31]. The UKPD study clearly showed that smoking was a significant and independent risk factor for CHD in type 2 diabetic patients [32]. In the Nurses' Health Study, in women with type 2 diabetes, it was demonstrated that cigarette smoking was associated in a dose-dependent manner with an increased mortality and CHD. Compared with never-smokers, the relative risks for CHD were 1.66 for current smokers of 1 to 14 cigarette per day, and 2.68 for current smokers of 15 or more cigarettes per day [33,34].

Recently, a meta-analysis in the Asia-Pacific region, in men with diabetes, the hazard ratio comparing current smokers with non-smokers was 1.42 for CHD. In Asia, where there are high rates of smoking, and a rapidly increasing prevalence of diabetes, the author concluded that cigarette cessation strategies there were huge benefits in terms of reducing the burden of CVD in men with diabetes [35].

SMOKING AND STROKE

Smoking also increases the risk of stroke in patients with diabetes, but may not be as strong as CHD. In the UKPD study, mathematical models were developed to estimate the risk of stroke, and the variables were smoking, duration of diabetes, age, sex, systolic blood pressure, total cholesterol to high density lipoprotein cholesterol ratio, and presence of arterial fibrillation [36]. In a study using the general practice research database in the United Kingdom, smoking was an additional risk factor for stroke in type 2 diabetic patients [37]. Another 4-year prospective study, also showed that smoking and HbA1c were predictors of stroke among the type 2 diabetic patients without a history of a previous stroke [38].

The relative risk of smoking for stroke has not been as high as that for CHD. In the Nurses' Health Study, in smokers who smoked 1 to 14 cigarette per day, the risk was significant for CHD but not for stroke. In those who smoked 15 cigarettes or more per day, the relative risk for CHD and stroke were 2.68 and 1.84, respectively [33]. Similar trends were shown in a Swedish study, in which the relative risk of smoking was higher in myocardial infarction (2.33) than for stroke (1.12) in 30 to 59 year-old patients [39].

CONCLUSIONS

There have been many studies showing that smoking has harmful effects on patients with diabetes. Smoking increases diabetic incidence and aggravates glucose homeostasis and chronic diabetic complications. In microvascular complications, the onset and progression of diabetic nephropathy is highly associated with smoking. In macrovascular complications, smoking is associated with a 2 to 3 times higher incidence of CHD and mortality. However, smoking prevention and smoking cessation may not be emphasized enough in diabetic clinics. Thus, educating patients on the importance of not smoking and engaging in smoking cessation programs are im-

portant strategies for the management of diabetes.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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