

“EFFECT OF SHORT TERM CIGARETTE SMOKING ON INSULIN RESISTANCE AND LIPID PROFILE IN ASYMPTOMATIC ADULTS”

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Abstract : Present study examined the effect of short-term cigarette smoking on insulin resistance and lipid profile in asymptomatic healthy adults. This case control study comprised of 44 healthy male subjects in the age group of 18–40 yrs having BMI 25+3 and WHR < 1.0. Of these 22 smokers were included in the study group and 22 non-smokers in the control group. Subject selection was done such that one smoker and one non-smoker sibling or first degree male relative were selected from the same family. We compared fasting plasma glucose, insulin, lipid profile, and homeostatic model assessment index (HOMA Index) as a measure of insulin resistance between both the groups. Our observation showed that significantly higher values of serum glucose (133.36 ± 23.45 mg/dl; $P < 0.001$), serum insulin (32.04 ± 6.0 μ U/ml; $P < 0.001$) and HOMA index (3.62 ± 0.21 ; $P < 0.001$) were found in smokers as compared to non-smokers (serum glucose 86.95 ± 19.32 mg/dl, insulin 20.09 ± 4.8 μ U/ml, HOMA index 3.29 ± 0.30). No significant difference was observed for number of subjects having insulin resistance (HI > 3.8) and lipid profile in both the groups. Thus it appears that smokers are prone to develop hyperinsulinemia, hyperglycemia and the metabolic syndrome.

Key words : cigarette smokers insulin resistance fasting glucose
gasting insulin lipid profile HOMA index

INTRODUCTION

Smokers have been found to be at high risk compared to non-smokers for development of diabetes and a strong relationship between tobacco smoke and metabolic syndrome among adolescents has been observed (1). Various studies show that long term smoking decreases the insulin sensitivity (2–4), Adverse effects due to

short-term smoking have been also observed (5–8); however very few studies (1, 8, 9) are available regarding the effect of short-term cigarette smoking on insulin resistance in human. Previous studies have defined long-term smoking as smoking of > 1 pack/day for more than 15 years and short-term smoking as >1 pack/day for less than 10 years (7). In present study we have examined the effects of short-term (acute)

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smoking on serum lipid profile and insulin resistance in young apparently healthy male subjects, who were smoker for at least six months to maximum for two years and smoking more than five cigarette per day. We recruited non-smoking male subjects either siblings or first-degree male relatives from the same family as control. Thus objective of this study was to evaluate the acute effects of cigarette smoking on insulin resistance and serum lipid profile in apparently healthy subjects.

METHODS

This was a cross sectional case control study. Male smokers smoking at least five filter cigarettes per day for at least six months and maximum for two years, aged between 18–40 years (mean±SD 33.4±7.8 yrs) having BM 25±3 and waist to hip ratio <1.0 (mean±SD 0.9±0.22) were taken as study group. Subjects with IBM >27 and WHR >1.0 have high risk for development of metabolic syndrome (10, 11) so they were excluded from the study. BMI (mean±SD: 26.3±2.7), WHR (mean±SD: 0.86±0.25), physical activity and diet-matched non-smokers of similar age group (mean±SD: 32±6.9 yrs) from same families (non smoking male siblings or first degree male relatives) were taken as control group. This was done so the effect of other confounding factors including genetic factors on observations of the study could be minimized. All the subjects included in the study were normotensive, non-alcoholic, and non-diabetic and were from similar socioeconomic status having no other systemic and metabolic diseases. Family history of metabolic diseases including diabetes, IHD, and hypertension was obtained. Subjects

with any metabolic or systemic diseases, addicts of other form of tobacco intake (12) and alcohol were excluded from the study.

After taking clearance from the ethics committee of King George's Medical University and informed consent from the subjects for participation in the study; 60 subjects from 30 families of Lucknow city were enrolled in the study initially; out of which 16 subjects (8 families) did not turn up for the study. Hence finally 22 smokers and 22 non-smokers participated in the study.

Five ml of fasting blood was collected from each subject and serum was separated for glucose, insulin and lipid profile estimation. Estimation of serum glucose was done by GOD-POD method (Randox Laboratories Ltd., Antrim, U.K.). Serum insulin was estimated by immuno radiometric assay method using insulin IRMA kit (Immunotech Radiova Prague) and lipid profile by enzymatic method (Randox Laboratories Ltd., Antrim, U.K.) Insulin Resistance (IR) was calculated by Homeostatic model assessment index (HOMA Index) (13).

$$\text{HOMA Index} = \frac{\text{Fasting Glucose (mmole/l)} \times \text{Fasting Insulin (}\mu\text{U/ml)}}{22.5}$$

If subjects had no clinical and biological criteria of IR, a laboratory diagnosis of IR is made when the value of HOMA index is equalled or exceeded 3.8 (14). Subjects with HOMA index >3.8 are prone for development of metabolic syndrome. All data was statistically analyzed by using unpaired student t test and Fisher–Irwin test.

RESULTS

The observed values for fasting serum lipid profile, glucose, insulin and insulin resistance are given in Table-I. There were no statistically significant difference in the levels of TG, VLDL, and HDL between smokers and non-smokers. Serum cholesterol and LDL levels were slightly higher in smokers than nonsmokers but the difference was not statistically significant (Table-I).

Fasting serum insulin, plasma glucose and values for HOMA index (Table-I) were observed to be significantly higher in smokers ($P>0.001$) than non-smokers. However no significant numbers of subjects were observed having IR (HOMA index >3.8) in study as well as control groups. Only two smokers and one non-smoker from respective groups had HOMA index >3.8 .

DISCUSSION

In our study, the two groups of subjects (smokers and non-smokers) were of comparable sex, age, BMI, WHR, physical activity level and diet, even genetic composition to some extent (as we have taken control and study groups from the same family). They were non-diabetic, non-alcoholic, normotensive subjects belonging to same socioeconomic status.

Our study examined the effect of smoking for less than two years on insulin resistance and lipid profile. In contrast, earlier studies have shown that long-term nicotine consumption or chronic cigarette smoking increases insulin resistance (15-19). We observed significantly higher fasting serum insulin, glucose and values of HOMA index in smokers (Table-I) as compared to nonsmokers. However only two smokers and

TABLE I: Showing fasting serum lipid profile, insulin, glucose and HOMA index in 22 smokers and 22 non-smokers.

	Smokers (n=22)	Non smokers (n=22)	P
Age (yrs)	33.4±7.8	32±6.9	
BMI	25±3.0	26.3±2.7	
WHR	0.9±0.22	0.86±0.25	
No. of cigarettes/day	12.4±6.3	Nil	
Smoking duration (months)	21.4±5.4	Nil	
TG (mg/dl)	105.45±32.64	103.64±47.62	0.91
VLDL (mg/dl)	23.07±06.51	21.25±11.24	0.95
Cholesterol (mg/dl)	150.84±26.51	138.05±22.56	0.12
HDL (mg/dl)	45.49±12.51	48.27±9.67	0.13
LDL (mg/dl)	72.94±18.29	63.40±23.28	0.33
Cho/HDL ratio	2.71±0.67	2.86±1.12	0.58
LDL/HDL ratio	1.28±0.55	1.37±0.85	0.69
Insulin (μ U/l)	32.04±6.02	20.09±4.80	0.00092
Glucose (mg/dl)	133.36±23.45	86.95±19.32	0.00089
HOMA index	3.62±0.21	3.29±0.30	0.00068

(All values are mean±sd)

Abbreviations : Cho = Cholesterol, TG = Triglyceride, VLDL = Very Low Density Lipoprotein, HDL = High Density Lipoprotein, LDL = Low Density Lipoprotein, HOMA = Homeostatic Model Assessment.

one non-smoker had IR. We have observed only the short-term effect of cigarette smoking on insulin resistance. On the contrary earlier studies have shown the effect of long-term smoking on IR. The degree of IR and the extent of the related metabolic abnormalities are strongly associated with smoking habits (15). However significantly high value of HOMA index in smokers as compared to non-smokers shows that even short-term cigarette smoking decreases insulin sensitivity.

The increase in fasting glucose level in smokers could be due to decrease in cellular glucose uptake and utilization, thereby suggesting that smoking affects a mechanism involving early steps in insulin action (e.g. signal transduction, glucose transport, and/or glucose phosphorylation) or by mechanisms operating simultaneously on different biochemical pathways. Nicotine may have direct or indirect effect via interaction with insulin receptors and for post receptive events. Smoking causes increased release of catecholamines (20), which might reduce the number of insulin binding sites as well as decreasing the synthesis of glucose transporters. There may also be other indirect effect of smoking on insulin action; for instance, elevated levels of FFA, which impair insulin mediated glucose uptake (21).

In our study smokers had significantly high fasting insulin levels as compared to non-smokers. Other cross sectional studies have also demonstrated that chronic smokers were hyperinsulinemic during an OGTT (15, 22, 23). The two groups of subjects were comparable regarding the variables known

to affect insulin action and glucose tolerance. Thus, it seems reasonable to speculate that the difference in fasting insulin and glucose levels we observed between the two groups were secondary to cigarette smoking and, theoretically, could be caused by the direct effects of nicotine, carbon monoxide, or other agents in cigarette smoke.

The observations of the present study are consistent with experimental studies demonstrating that cigarette smoking can acutely impair insulin action (8, 24, 25) and with previous cross-sectional findings of the presence of hyperglycemia and 27 hyperinsulinemic in nondiabetic smokers (22, 26, 27). These observations show that even short-term smokers are prone for development of diabetes because of hyperinsulinemia, hyperglycemia and decrease insulin sensitivity.

In our study the values of fasting serum cholesterol and LDL in smokers were not significantly different from levels in non-smokers (Table-I). However others have shown raised post absorptive levels of TG, low HDL, and increased total cholesterol and increased LDL in smokers than non-smokers (26, 27, 29, 30), which were compatible with IR (29). In our study we have not found any significant statistical difference between smokers and non-smokers in terms of fasting lipid profile probably because we have included only non-diabetic, non-hypertensive healthy, college going students and young male subjects. Smokers registered for our study did not have a long smoking record. Very few subjects had demonstrable IR (HOMA index ≥ 3.8) and an increase in TG, LDL and total cholesterol are hallmarks of IR.

In the present study no significant harmful effects of passive smoking regarding lipid profile, fasting glucose, insulin and on insulin sensitivity have been observed in non-smokers compare to smokers; as we have recruited non- smokers from the same family. However some experimental observations have shown that acute exposure to cigarette smoking in both smokers and non-smokers have been seen to significantly impair glucose tolerance; higher insulin levels in smokers (8) also accompanied this. In our study probably the passive exposure to smoking was not enough to show the harmful effect in non-smokers. However passive smokers are undeniably at risk from exposure to cigarette smoke, the extent of the risk and the passive nature of their exposure to this risk requires to be examined separately.

Thus we conclude that although hyperglycemia, hyperinsulinemia, and high HOMA index was seen in smokers but their lipid profile was unaffected. So, smokers can be counselled that discontinuation of smoking especially in early stages could bring substantial reversal of the damage caused, if any, and hence this is a strong motivating factor for smokers to discontinue early.

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