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ASSOCIATION OF CIGARETTE SMOKING WITH 24 HOUR URINARY ALBUMIN EXCRETION AND CREATININE CLEARANCE IN NON-DIABETICS

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ABSTRACT

BACKGROUND: - *Many studies have shown adverse effects of smoking on urinary albumin excretion and creatinine clearance in diabetics, but little is known about effects of smoking on renal function in non-diabetics.*
Objective: - To observe renal functions alteration in healthy non-diabetic smokers.
SUBJECTS AND METHODS: *A total of 90 subjects, 30 non-smokers as control, 60 smokers apparently healthy subjects of either sex were randomly selected from different parts of Karachi.*
RESULTS: *24 hour urinary albumin excretion was significantly increased (P<0.001) in smokers (mean ± s.e.m 34.54 ± 0.51 mg/day) as compared to non-smokers (mean ± s.e.m 19.06+ 0.46 mg/day). Creatinine clearance was significantly increased (P<0.001) in smokers (mean ± s.e.m 120.16± 1.75 ml/min/1.73m^2) as compared to non-smokers (mean ± s.e.m 107.25± 1.93 ml/min/1.73m^2). More over significant positive correlation was found between number of cigarettes and 24 hour urinary albumin excretion showing r = 0.33; P<0.05. While no correlations were observed with anthropometric parameters.*
CONCLUSION: *Cigarette smoking is associated with mild microalbuminuria and mild hyperfiltration in smokers as compared to nonsmokers.*

KEY WORDS: Smoker, urinary albumin excretion, creatinine clearance.

INTRODUCTION

In recent past smoking has emerged as a major risk factor for the progress in renal disease; these adverse effects to impair renal function have gained more attention through investigation in diabetic patients[1]. Extensive investigations have not been taken for adverse effects of smoking on renal function in non-diabetic smokers[2]. A number of potentially harmful chemicals in tobacco smoke cause injury. This injury leads to a number of important diseases[3].

In healthy volunteers smoking causes an increases in renovascular resistance accompanied by a decrease in glomercular filtration rate (GFR) and filtration fraction in parallel with an increase in blood pressure and heart rate associated with sympathetic activation[4]. Some studies indicate that smoking increases the risk to develop microalbuminuria[5], shortens the interval from microalbuminuria to overt nephropathy[6]. Urinary albumin excretion and glomerular filtration rate in both diabetic and non-diabetic subjects may be affected by cigarette smoking[7].

Endothelial dysfunction may occur in the systemic arteries of even very light smokers from adolescence onward, although the likelihood of vascular physiological abnormalities increases with total amount smoked[8].

Smoking may also cause injury through nonhemodynamic pathways by causing damage to the renal and particularly microvasculature as a result of its effect on platelet function, thromboxane metabolism and endothelial cell function[9]. Atherogenic effects of smoking in the kidney are partially mediated by its unfavorable effects on lipoprotein and glycosaminoglycans metabolism[10]. Oxidative stress is probably another major player in genesis of smoking induced vascular renal injury[11,12]. In current smokers creatinine clearance is slightly higher in men. The effect on creatinine clearance is reversible in current smokers on discontinuation of smoking. This evidence is compatible with the notion of early hyperfiltration. A relative risk dependent on dose for end-stage renal failure (ESRF) is found in smokers as compared with nonsmokers[13]. Smoking is associated with risk of higher glomerular filtration rate and proteinuria[14].

Therefore this study was carried out in order to see above effects by using a series of healthy non diabetic smokers.

MATERIALS AND METHODS

This study was carried out in the Department of Physiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi.

A total of 90 subjects; 30 nonsmokers, 60 smokers apparently healthy subjects of either sex; age ranging between 25-40 years were randomly selected from different parts of the Karachi. On the basis of history and clinical examination, the subjects were evaluated for having cardiovascular, renal or liver disease. Subjects were further screened with the help of ultrasound and routine urine examination for having any problem in the urinary system. History of any kind of drugs was taken. A blood sample was drawn under aseptic conditions to measure plasma glucose level.

The subjects fulfilling inclusion/exclusion criteria were invited for second visit to bring 24 hour urinary collection in the container provided to them. Measurement of urinary volume, albumin concentration and creatinine concentration were performed. A blood sample was drawn for serum creatinine.

INCLUSION CRITERIA

For non-smokers apparently healthy subjects of either sex; age between 25-40 years, who never smoked and avoided passive smoking; for smokers apparently healthy subjects of either sex age between 25-40 years, who were smoking cigarettes regularly for the last five years or more.

EXCLUSION CRITERIA

Subjects were excluded from the study if they had a history of cardiovascular disease, renal disease or chronic liver disease. Diabetics and drug user were also excluded.

DETERMINATION OF PARAMETERS;

Urinary albumin concentration was estimated by colorimetric test, serum creatinine by method of Brod and Sirota, urinary creatinine was determined by Jaffe's reaction by Alkaline Picrate and creatinine clearance by the formula uv/p and was corrected for surface area. Students 't' test was performed in order to see any significance among various parameters.

CORRELATION COEFFICIENT

The computer package Microsoft Excel was used for data entry. Correlation between different variables was detected by using Pearson Coefficient of Correlation on SPSS-10. Only P values (<0.05) are considered significant.

TABLE 1

AGE, BODY MASS INDEX, BODY SURFACE AREA, PULSE RATE, SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE IN NON-SMOKERS (CONTROL) AND SMOKERS

(All The values are expressed in mean±s.e.m)

Variables	Non-smokers (Control) (n=30)	Smokers (n=60)
Age (Years)	29.83 ±0.71	30.53 ±0.38
Body Mass Index (Kg/m^2)	24.30 ±0.11	24.10 ±0.07
Body Surface Area (m^2)	1.74 ±0.01	1.74 ±0.008
Pulse Rate (beat/min)	71.50 ±0.22	71.93 ±0.22
Systolic Blood Pressure (mmHg)	119.00 ±0.90	118.16 ±0.66
Diastolic Blood Pressure (mmHg)	78.33 ±0.73	78.25 ±0.60

n = Number of subjects.
All the values are non significant as compared to control.

TABLE 2

24 HOUR URINARY ALBUMIN EXCRETION, SERUM CREATININE, URINARY CREATININE, 24 HOUR URINARY VOLUME AND CREATININE CLEARANCE IN NON-SMOKERS (CONTROL) AND SMOKERS

(All The values are expressed in mean±s.e.m)

Variables	Non-smokers (Control) (n=30)	Smokers (n=60)
24 Hour Urinary Albumin Excretion (mg/day)	19.06±0.46	*** 34.54±0.51
Serum Creatinine (mg/dl)	0.92±0.02	** 0.85±0.01
Urinary Creatinine (mg/dl)	122.93±2.37	NS 123.85±1.15
24 Hour Urinary Volume (ml)	1157.66±28.14	NS 1193.00±15.07
Creatinine Clearance (ml/min/1.73m^2)	107.25±1.93	*** 120.16±1.75

NS = Non-significant.
** P <0.01 when compared to control.
*** P <0.001 when compared to control.

RESULTS

Table 1 shows comparison of Mean (±s.e.m) of age, body mass index (BMI), body surface area (BSA), pulse rate, systolic blood pressure and diastolic blood pressure in non-smokers (control) and smokers. Non-significant differences were found in these variables.

Mean values of serum creatinine, urinary creatinine, 24 hour urinary volume, creatinine clearance, and 24 hour urinary albumin excretion are depicted in table 2. It shows comparison between non-smokers (control) and smokers. Urinary creatinine and 24 hour urinary volume were statistically

insignificant when smokers were compared with non-smokers. Serum creatinine was significantly low (P<0.01) in smokers when compared with control. The mean (± s.e.m) of values of creatinine clearance, and 24 hour urinary albumin excretion were significantly high (P<0.001) in smokers as compared to non-smokers.

Table 3. Shows correlation of number of cigarettes per day and duration of smoking in years with creatinine clearance, and 24 hour urinary albumin excretion. Significant positive correlation r =0.33, P<0.05 was found between number of cigarettes and 24 hour urinary albumin excretion.

TABLE 3

CORRELATION COEFFICIENT

	Creatinine clearance (ml/min/1.73m^2)	**24 Hour Urine Albumin (mg/day)**
No. of Cigarettes (per day)	r = -0.03	* r = 0.33
Duration of Smoking (year)	r = 0.01	r = 0.01

r Coefficient of correlation.
* P<0.05

DISCUSSION

The diabetics are usually followed for their diabetic complications and their renal function usually becomes well known. The alteration in renal function is less likely known in non-diabetics until they develop some renal damage; this explains why little is known about abnormalities in these subjects[15]. An increased risk for end stage renal failure (ESRF) was found for smokers as compared to non-smokers. Such increased relative risk of ESRF in smokers up to 1.69 for heavy smokers was independent of age, ethnicity, income, blood pressure, diabetes mellitus and prior history of myocardial infarction or serum cholesterol[16]. Our study is in agreement with this trial because in our study the subjects were healthy, non-diabetic, normotensive and non-obese having body mass index (BMI) within normal limits. In our study serum creatinine was significantly low in smokers as compared to non-smoker creatinine clearance was significantly high in smokers as compared to non-smokers. This is in agreement with study conducted by Halimi et al[17] who have shown significantly higher creatinine clearance in current smokers as compared to non-smokers and serum creatinine significantly low in smokers as compared to non- smoker. Our study is in agreement with study conducted by Pinto-Sietsma et al[2] who have shown increased creatinine clearance ml/min/1.73m^2 and 24 hour urinary albumin excretion in smokers.

Our results do not agree the study of Ritz et al[4], who observed decreased glomerular filtration rate and Gambaro et al[18], who showed normal glomerular filtration rate.

How can a smoking induced increase in glomerular filtration rate be explained in non-diabetic persons? In its acute phase smoking induces a transient decrease in renal plasma flow [4,18] and glomerular filtration rate[4]. These small repeated episodes of transient renal hypoperfusion may damage some glomeruli and finally result in alterations in the structure of preglomerular vessels and cession of function which may induce hypertrophy and hyperfiltration in the remnant glomeruli[19]

CONCLUSION

In conclusion chronic cigarette smoking is associated with mild microalbuminuria and mild hyperfiltration in smokers as compared to non-smokers. At this stage we recommend that non-diabetic chronic smokers be examined and investigated for renal function. Smoking has negative effect on renal function in subjects without renal disease. Smoking is preventable risk factor; so cession may help prevent alteration in renal function.

REFERENCE

1. Orth SR, Ritz E, Schrier RW. The renal risks of smoking. Kidney Int 1997; 51:1669-77.
2. Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE. Smoking is related to albuminuria and abnormal renal function in non-diabetic persons. Ann Intern Med 2000; 133:585-91.
3. Cotran RS. Environmental Diseases In: Robbins Basic Pathology. 7th ed. Kumar V, Cotran RS, Robbins SL eds. WB Saunders Company, Philadelphia, USA 2003; pp 274-275.
4. Ritz E, Benck U, Franek E, Keller C, Seyfarth M, Clorius J. Effects of smoking on renal hemodynamics in healthy volunteers and in patients with glomerular diseases. J Am Soc Nephrol 1998; 9:1798-1804.
5. Chase HP, Garg SK, Marshal G, Berg CL, Harris S, Jackson WE, Hamman RE. Cigarette smoking increases the risk of albuminuria among subjects with type I diabetes. JAMA 1991; 265:614-17.
6. Stegmayr B, Lithner F. Tobacco and end stage diabetic nephropathy. BMJ 1987; 295:581-82.
7. Nobukazu Ishizaka, Yuko Ishizaka, Ei-ichi Toda. Association between cigarette smoking and chronic kidney disease in Japanease men. Hypertension Research 2008; 31:485-95.
8. Celemajer DS, Sorensen KE, Georgakopoulos D, Bull C, Thomas O, Robinson J, Deanfield JE. Cigarette smoking is associated with dose related and potentially reversible impairment of endothelium dependent dilation in healthy young adults. Circulation 1993; 88:2149-55.
9. Nitenberg A, Antony I. Coronary vascular endothelium, a common target in patient with diabetes mellitus, cigarette smoking, hypercholesterolemia, hypertension and menopausal status. Nephrol Dial Transplant 1998; 13(Suppl 4):16-19.
10. Baggio A, Budakovic A, Gambaro G. Cardiovascular risk factors, smoking and kidney function. Nephrol Dial Transplant 1998; 13(Suppl 7): 2-5.
11. Oberai B, Adams CWM, High OB. Myocardial and renal arteriolar thickening in cigarette smoking. Atherosclerosis 1984; 52:185-90.
12. Black HR, Zeevi GR, Silten RM, Smith GJW. Effect of heavy cigarette smoking on renal and myocardial arterioles. Nephron 1983; 34:173-79.
13. Stephan R. Orth. Smoking and the Kidney. J Am Soc Nephrol 2002;13: 1663-72.
14. Hyung-Jin Yoon, Minseon Park, Hyeongseok. The differential effect of cigarette smoking on glomerular filtration rate and proteinuria in an apparently healthy population. Hypertension Research 2009; 32:214-19.
15. Pinto-Sietsma SJ, Janssen WM, Hillege HL, Navis G, de Zeeuw D, de Jong PE. Urinary albumin excretion is associated with renal functional abnormalities in a nondiabetic population J Am Soc Nephrol 2000; 11:1882-88.
16. Whelton PK, Randall B, Neaton J, Stamler J, Brancati FL, Klag MJ. Cigarette smoking and ESRD incidence in men screened for the MRFTT. J Am Soc Nephrol 1995; 6:408a.
17. Halimi JM, Giraudeau B, Vol S, Caces E, Nivet H, Lebranchu Y, Tichet J. Effects of current smoking and smoking discontinuation on renal function and proteinuria in the general population. Kidney Int 2000; 58:1285-92.
18. Gambaro G, Verlato F, Budakovic A, Casara D, Saladini G, Del Prete D, Bertaglia G, Masiero M, Checchetto S, Baggio B. Renal impairment in chronic cigarette smokers. J Am Soc Nephrol 1998; 9:562-7.
19. Remuzzi G. Cigarette smoking and renal function impairment. Am J Kidney Dis 1999; 33:807-13.