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.

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/1.73m²) as compared to non-smokers (mean ± s.e.m 107.25± 1.93 ml/min/1.73m²). 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. Extensive investigations have not been taken for adverse effects of smoking on renal function in non-diabetic smokers. A number of potentially harmful chemicals in tobacco smoke cause injury. This injury leads to a number of important diseases.

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

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. 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. Atherogenic effects of smoking in the kidney are partially mediated by its unfavorable effects on lipoprotein and glycosaminoglycans metabolism. Oxidative stress is probably another major player in genesis of smoking induced vascular renal injury. 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. Smoking is associated with risk of higher glomerular filtration rate and proteinuria.
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.

TABLE 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-smokers (Control) (n=30)</th>
<th>Smokers (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>29.83 ±0.71</td>
<td>30.53 ±0.38</td>
</tr>
<tr>
<td>Body Mass Index (Kg/m²)</td>
<td>24.30 ±0.11</td>
<td>24.10 ±0.07</td>
</tr>
<tr>
<td>Body Surface Area (m²)</td>
<td>1.74 ±0.01</td>
<td>1.74 ±0.008</td>
</tr>
<tr>
<td>Pulse Rate (beat/min)</td>
<td>71.50 ±0.22</td>
<td>71.93 ±0.22</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>119.00 ±0.90</td>
<td>118.16 ±0.66</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78.33 ±0.73</td>
<td>78.25 ±0.60</td>
</tr>
</tbody>
</table>

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

TABLE 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-smokers (Control) (n=30)</th>
<th>Smokers (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 Hour Urinary Albumin Excretion (mg/day)</td>
<td>19.06±0.46</td>
<td>34.54±0.51</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dl)</td>
<td>0.92±0.02</td>
<td>** 0.85±0.01</td>
</tr>
<tr>
<td>Urinary Creatinine (mg/dl)</td>
<td>122.93±2.37</td>
<td>NS 123.85±1.15</td>
</tr>
<tr>
<td>24 Hour Urinary Volume (ml)</td>
<td>1157.66±28.14</td>
<td>NS 1193.00±15.07</td>
</tr>
<tr>
<td>Creatinine Clearance (ml/min/1.73m²)</td>
<td>107.25±1.93</td>
<td>*** 120.16±1.75</td>
</tr>
</tbody>
</table>

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

10. Only P values (<0.05) are considered significant.

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
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.

**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 subjects15. 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 cholesterol16. Our study is in agreement with this trial because in our study the subjects were healthy, non-diabetic, normotensive and nonsmokers of 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 al17 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 al18, who have shown increased creatinine clearance ml/min/1.73m2 and 24 hour urinary albumin excretion in smokers.

Our results do not agree the study of Ritz et al19, who observed decreased glomerular filtration rate and Gambaro et al19, 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 flow20,21 and glomerular filtration rate22. 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 glomeruli19.

**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 cessation may help prevent alteration in renal function.

**REFERENCE**