Serum uric acid in smokers

Bassam E Hanna, Luma M Tohala, Jamal M Hamed

Department of Biochemistry, Nineveh College of Medicine, University of Mosul, Iraq

ABSTRACT

Objectives: To demonstrate the possible effect of smoking on serum uric acid level.

Methods: The study was conducted during the period from March to June 2008 in Mosul city as a case control study.

Participants: Subjects enrolled in this study were divided into two groups; nonsmokers and smokers composed of 47 and 40 apparently healthy male volunteers respectively with the same dietary habit, no past medical history of diabetes mellitus, hyperuricemia and gout, renal, lung or heart diseases or drug history affecting uric acid level. Smoker group is subdivided into heavy, moderate and mild smokers.

Fasting blood and random urine samples were obtained from both groups for measurement of uric acid and creatinine. Calculation of both urine uric acid/urine creatinine ratio and fraction excretion of uric acid were done.

Results: No significant differences in the age, serum creatinine, spot urine uric acid/urine creatinine ratio and fraction excretion of uric acid between two groups where as serum uric acid was significantly lower in smokers.

In smokers there are significant negative correlations of the average number of cigarette smoked/day and the duration of smoking with serum uric acid level.

Heavy, moderate and mild smokers showed no significant differences in the age, serum uric acid/urine creatinine ratio, fraction excretion of uric acid, serum creatinine and serum uric acid except a significant lower serum uric acid value in the heavy smoker compared with moderate and mild smokers.

Conclusion: The significant low serum uric acid level in smokers is due to the reduction of endogenous production as a result of chronic exposure to cigarette smoke that is a significant source of oxidative stress and as this reduction is proportionate with the duration and number of cigarette smoked/day and as low uric acid predispose to cardiovascular diseases as proved by other studies, therefore, its recommended for smokers to stop or reduce smoking with the use of serum uric acid as a routine test for follow-up as it is inexpensive, simple to reflect antioxidant level.

Keywords: Smokers, uric acid, cardiovascular disease

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Cigarette smoking is a well-known risk factor for the development of atherosclerosis and its complications including cerebral and cardiovascular diseases (CVD), through vascular endothelial damage. This damage occurs possibly through the production of oxygen free radicals as superoxide radicals, hydrogen peroxide and hydroxyl radicals. Several enzymes can produce oxygen free radicals including xanthine oxidase, NADPH oxidase, myeloperoxidase, and endotoxin.

As cigarette smoke contains superoxide and reactive nitrogen species that readily react with various biomolecules, it has been hypothesized that some of the adverse effects of smoking may result from oxidative damage to endothelial cells, which results in nitric oxide shortage that regulate vascular tone and accelerate insufficiency of coronary artery and vasconstriction in many different tissues. Therefore imbalance between oxidants and antioxidants may play an important role in the susceptible smoker.

In addition cigarette smokers also have increased inflammatory responses that further enhance their oxidative stress.

Since in humans, uric acid (ur) is the most abundant aqueous antioxidant, accounting for up to 10% of serum free radical scavenging capacity and is an important intracellular free radical scavenger during metabolic stress including smoking. Therefore, measurement of serum ur reflect the antioxidant capacity.

The aim of this study is to demonstrate the possible effect of smoking on serum ur level.

**Patients and Methods**

The study was conducted during the period from March to June 2008 in Mosul city. Subjects enrolled in the study were divided into two groups (group 1 and group 2).

- Group 1 considered as control composed of 34 apparently healthy nonsmoker male volunteers, their ages ranged from (20-40) years.
- Group 2 is the smoker group composed of 40 cigarette smoker male volunteers, their ages ranged from 20 to 40 years. According to the number of cigarette smoked/day, this group is subdivided into heavy (≥40 cigarettes smoked/day, n=14), moderate (10-39 cigarette smoked/day, n=14) and mild (1-9 cigarette smoked/day, n=16) smokers.

A complete record of history was obtained, including name, age, average number of daily cigarette smoking, duration of smoking, dietary habit, past medical and drug history.

Neither group nor group members had past medical history of diabetes mellitus, hyperuricemia and gout, renal, lung or heart diseases or drug history affecting ur and creatinine (cr) level or interfere with its measurement. Members of both groups had the same dietary habit.

Fasting blood samples for the measurement of serum ur and cr and random urine samples for the measurement of spot urine cr and ur were obtained from all subjects. The measurement of both serum and urine cr and ur were done by Jaffe's kinetic method using a kit supplied by biolabo company (France) and by uricase method using a kit supplied by biomeriux company.
(France) respectively and are performed using Cecil spectrophotometer-CE in the biochemistry laboratory at Nineveh College of Medicine in Mosul.

From the data of serum and urine ur and cr, the calculation of both urine ur/urine cr (Uur/Ucr) ratio by dividing urine ur with urine cr and fraction excretion of ur (FEur) by the formula $[FEur = (Uur*Scr/Ur*Ucr)^{\cdot\cdot\cdot}]$ were done in both groups.

The results were statistically evaluated by standard statistical methods including mean, standard deviation (SD), range (minimum-maximum), Linear regression analysis (Pearson correlation coefficient r), student’s t-test, with computer software programs including Microsoft excel and SPSS to evaluate the relation between different parameters. Differences between observations were considered not significant at $P>0.50$.

**Results**

Table 1 demonstrates the mean ± SD of the age, serum cr, serum ur, spot Uur/Ucr ratio and FEur in both groups. No significant differences in the age, serum cr, spot Uur/Ucr ratio and FEur between two groups ($P>0.05$). Serum ur was significantly lower in group 2 compared with group 1 ($P<0.01$).

Table 2 demonstrates the mean ± SD and the range of the average number of cigarette smoked/day and the duration of smoking in group 2.

Table 3 demonstrates the subclassification of smoker group according to the number of cigarette smoked/day into heavy ($\geq 40$ cigarettes smoked/day), moderate ($11-39$ cigarette smoked/day) and mild ($1-10$ cigarette smoked/day) smokers with the mean ± SD of their corresponding parameters including the age, serum cr, serum ur, spot Uur/Ucr ratio and FEur. No significant differences in the age, Uur/Ucr ratio, FEur, serum cr and serum ur ($P>0.05$) except a significant lower serum ur value in the heavy compared with moderate ($P<0.01$) and mild ($P<0.001$) smokers.

Figure 1 and 2; demonstrate a significant negative correlations ($P<0.001$) between serum ur and both the number of cigarette smoked/day and the duration of smoking respectively in group 2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (Control) n = 14 mean ± SD</th>
<th>Group II (Smokers) n = 40 mean ± SD</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.1 ± 7.3</td>
<td>30.0 ± 6.1</td>
<td>NS</td>
</tr>
<tr>
<td>Serum cr (µmol/L)</td>
<td>94.3 ± 17.0</td>
<td>86.4 ± 19.2</td>
<td>NS</td>
</tr>
<tr>
<td>Serum ur (mmol/L)</td>
<td>0.73 ± 0.5</td>
<td>0.76 ± 0.7</td>
<td>$P &lt; 0.01$</td>
</tr>
<tr>
<td>Uur/Ucr</td>
<td>0.43 ± 0.11</td>
<td>0.41 ± 0.18</td>
<td>NS</td>
</tr>
<tr>
<td>FEur (%)</td>
<td>11.0 ± 2.71</td>
<td>11.8 ± 2.83</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS : Not Significant

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Table 2: Number of cigarette/day and duration of smoking in group γ

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cigarette/day</td>
<td>22.0 ± 13.22</td>
<td>5-60</td>
</tr>
<tr>
<td>Duration of smoking (Years)</td>
<td>9.34 ± 0.73</td>
<td>1.5-22</td>
</tr>
</tbody>
</table>

Table 3: Comparison between parameters (between each subgroup with the other two subgroups) of heavy, moderate and mild smokers

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Heavy Smokers n = 9 mean ± SD</th>
<th>Moderate Smokers n = 14 mean ± SD</th>
<th>Mild Smokers n = 17 mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.7 ± 7.4 NS</td>
<td>29.3 ± 6.7 NS</td>
<td>29.9 ± 6.0 NS</td>
</tr>
<tr>
<td>Serum cr (µmol/L)</td>
<td>89.9 ± 20.81 NS</td>
<td>94.0 ± 30.2 NS</td>
<td>77.77 ± 21.36 NS</td>
</tr>
<tr>
<td>Serum ur (mmol/L)</td>
<td>0.78 ± 0.06 NS</td>
<td>0.84 ± 0.06 NS</td>
<td>0.77 ± 0.07 NS</td>
</tr>
<tr>
<td>Uur/Ucr</td>
<td>0.39 ± 0.11 NS</td>
<td>0.43 ± 0.09 NS</td>
<td>0.32 ± 0.18 NS</td>
</tr>
<tr>
<td>FEur (%)</td>
<td>13.5 ± 7.0 NS</td>
<td>12.0 ± 10.71 NS</td>
<td>10.0 ± 3.79 NS</td>
</tr>
</tbody>
</table>

↓ Significantly lower in heavy compared with moderate (P<0.01) and mild (P<0.001) smokers
NS: Not Significant

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Figure 1: Correlation between serum ur and number of cigarette smoked/day in group II

Figure 2: Correlation between serum ur and duration of smoking in group II

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Discussion

Although many, but not all epidemiological studies have suggested that high serum ur is a risk factor for CVD, and independent predictor of death in patients at high risk for CVD. Many studies are warranted to evaluate its prognostic implications and potential utility in the monitoring of therapy. The raised level of serum ur parallel to an increased risk of CVD could be either primary or secondary to underling causes of CVD. However, the specific role of serum ur in this constellation remains uncertain and the vital question is whether increased serum ur is a causal factor for CVD?. Observational data alone cannot answer that question.

In contrast, evidence suggesting that increase serum ur is protective against CVD since it acts as an endogenous antioxidant. The higher serum ur levels found in CVD patients suggests that any protective antioxidant effect which ur has is overwhelmed by other negative effects on pathogenesis.

The viability of administering ur in solution has been suggested and so the role of ur as an independent cardiovascular risk factor has not been proved and the raising serum ur concentrations protects against oxidative damage in the setting of acute oxidative stress as in smoking.

After exclusion of factors affecting serum ur level, the significant reduction of serum ur is attributed to smoking and is negatively correlated to the duration and the number of cigarette smoked daily in spite of no significant difference between mild and moderate smokers which probably due to the vague history given by smokers on the number of cigarettes smoked/day, this finding is in agreement with other studies that found low serum ur in regular smoker and reduction of antioxidants including ur in smokers. Other study proved that after smoking, a similar reduction in the concentration of plasma antioxidant compounds, such as cysteine, methionine and ur indicates that oxidative stress increases every time a cigarette is smoked. Others proved that cigarette smokers and nonsmokers exposed to cigarette smoke have a significantly lower plasma antioxidant status than do unexposed nonsmokers, independent of differences in dietary antioxidant intakes. Other studies proved that excess free radical activity and endothelial dysfunction in smokers cause low baseline serum ur concentrations and that administration of ur raises circulating antioxidant defenses and allows restoration of endothelium-dependent vasodilatation. Therefore, high serum ur concentrations might be protective in situations characterized by increased cardiovascular risk and oxidative stress as in smoking and by reduction of serum ur level in smokers it increase the susceptibility to oxidative damage and account for the excessive free radical production, therefore, the possibility that ur confers protection against the development of atherosclerosis, in view of its antioxidant properties, has been recognized.

In this study, serum cr, FEur and Uur/Ucr ratio are not significantly differ between two groups, in addition to that FEur and Uur/Ucr ratio values lie within the X ± SD observed in the control group by other studies. Since these tests have been reported to be useful to evaluate renal handling of ur and as serum ur concentrations are highly dependent on endogenous production as well as renal excretion. Therefore, in this study it is concluded that the reduction of serum ur level in smokers is due to reduction of endogenous production rather than increase renal excretion. This reduction of endogenous production is due to both chronic exposure to cigarette smoke that is a significant source of oxidative stress which led to consumption of antioxidants including ur which represent about 1-8% of serum free radical scavenging capacity and to the low intake of dietary antioxidants in smokers.

Conclusion

The significantly low serum ur level in smokers is due to the reduction of endogenous production as a result of chronic exposure to cigarette smoke that is a significant source of oxidative stress and as this reduction is proportionate with the duration and number of cigarette smoked/day, low ur is a predisposing factor to CVD as proved by other studies, therefore, it is recommended that for smokers to stop or reduce smoking with the use of serum ur as a routine test for follow-up as it is inexpensive and simple way to reflect antioxidant level.
References


Bloomer RJ. Decreased blood antioxidant capacity and increased lipid peroxidation in young cigarette smokers compared to nonsmokers: Impact of dietary intake. Nutr J. 2009;8:139.