Serum uric acid in smokers

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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 ٢٠٠٨ in Mosul city as a case control study.

Participants: Subjects enrolled in this study were divided into two groups; nonsmokers and smokers composed of ٤٧ and ٤٠ apparently healthy male volunteers respectively with the same dietary habit, no pastmedical 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 , urine 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

ألخلاصة

أهداف البحث: لعَرْض التأثير المحتمل للتدخين على مستوى الحامض البولي في مصل الدم.

الطرق:-أجريت الدراسة في الفترةِ مِنْ آذار ولغاية حزيران من عام ٢٠٠٨ في مدينه الموصل بطريقة مقارنة الحالات ألمرضيه مع ألمجموعة الضابطة.

المشاركون: قسم المشاركون في البحث إلى مجموعتين: غير مدخنين ومدخنين تتكون من ٤٧ و ٤٠ على التوالي من الذكور المتبرعين الأصحاء بنفس النمط الغذائي وبدون تاريخ مرضي سابق لداء السكري، ارتفاع مستوى الحامض البولي أو داء الملوك، أمراض الكلى، الرئة أو القلب أو تاريخ دوائي يوثر على مستوى الحامض البولي. مجموعة المدخنين قسمت بدورها إلى شديدي ، معتدلي و لطيفي التدخين .

من كلتا المجموعتين تم استحصال عينات دم في حالة الصوم وعينات عشوائية للإدرار لقياس تركيز الحامض البولي والكرياتنين . تم حساب نسبة الحامض البولي /الكرياتينين في الإدرار وطرح كسر الحامض البولي .

النَّتائِج: عدم وجود اختلافات معنوية في العُمر ، كرياتينين مصل الدم، نسبة الحامض البولي /الكرياتينين في الإدرار وطرح كسر الحامض البولي بين المجموعتين بينما هنالك انخفاضا معنويا في تركيز الحامض البولي في مصل الدم في المدخنين.

في المدخنين هنالك ارتباط سلبي معنوي بين العدد المتوسط للسجائر المدخنة / يوم ومدّة التدخين وبين تركيز الحامض البولي في مصل الدم.

أظهر شديدي ، معتدلي و لطيفي التدخين عدم وجود اختلافات معنوية في العُمر ، نسبه الحامض البولي /الكرياتينين في الإدرار، طرح كسر الحامض البولي ، كرياتينين مصل الدم و تركيز الحامض البولي في مصل الدم باستثناء وجود انخفاضا معنويا في تركيز الحامض البولي في مصل الدم لشديدي التدخين مقارنة بمعتدلي و لطيفي التدخين.

الاستنتاجات :- إن سبب المستوى المنخفض للحامض البولي في مصل الدم في المدخنين يعود لانخفاض الإنتاج الذاتي كنتيجة للتعرّض المُزمن إلى دخان السيجارةِ الذي هو مصدرُ هامٌ لإجهاد الاكسدة ولكون هذا الانخفاض متكافئٌ مع مدة وعدد السيكائر باليوم و يُهيّئُ للإصابة بأمراض الأوعية القلبيةِ كما أثبتته الدراسات الأخرى، لذا ما يوصّى به للمدخنين للتَوَقُف أو تَخفيض التدخين وإستعمال قياس الحامض البولي لمصل الدم كاختبار روتيني للمتابعة كونه بسيط و رخيص لعَكس مستوى مانع التأكسد.

Cigarette smoking is a well-known risk factor for the development of atherosclerosis and its complications including cerebral and cardiovascular diseases(CVD)[١,٢] through vascular endothelial damage.[٣] 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.[٤]

As cigarette smoke contains superoxide and reactive nitrogen species that readily react with various biomolecules,[١,٥,٦] 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[١,٧,٨] that regulate vascular tone and accelerate insufficiency of coronary artery and vasoconstriction in many different tissues.[٣,٩] Therefore imbalance between oxidants and antioxidants may play an important role in the susceptible smoker.[١٠,١١] In addition cigarette smokers also have increased inflammatory responses that further enhance their oxidative stress.[٥,٦]

Since in humans, uric acid(ur) is the most abundant aqueous antioxidant, accounting for up to ٦٠% of serum free radical scavenging capacity[١٢] and is an important intracellular free radical scavenger during metabolic stress including smoking,[١٣,١٤] therefore, measurement of serum ur reflect the antioxidant capacity.[١٢]

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 ٢٠٠٨ in Mosul city. Subjects enrolled in the study were divided into two groups (group١ and group ٢).

Group ١ considered as control composed of ٤٧ apparently healthy nonsmoker male volunteers, their ages ranged from (٢٠-٤٠) years.

Group ٢ is the smoker group composed of ٤٠ cigarette smoker male volunteers, their ages ranged from ٢٠ to ٤٠ years . According to the number of cigarette smoked/day, this group is subdivided into heavy (≥٤٠ cigarettes smoked/day, n=٩), moderate (٢٠-٣٩ cigarette smoked/day, n=١٤) and mild (١-١٩ cigarette smoked/day, n=١٧) smokers.[١٥]

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

Neither group ١ nor group ٢ members had pastmedical 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[١٦] using a kit supplied by biomeriux company

(France) respectively and are performed using Cecil spectrophotometer-CE ١٠١١ 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[١٧] and fraction excretion of ur (FEur) by the formula [FEur = (Uur*Scr/Sur*Ucr)*١٠٠][١٧] 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[١٨,١٩] with computer software programs including Microsoft excel ٢٠٠٣ and SPSS ١١.٥ to evaluate the relation between different parameters. Differences between observations were considered not significant at P>٠.٠٥.

Results

Table ١ 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>٠.٠٥). Serum ur was significantly lower in group ٢ compared with group ١ (P<٠.٠١).

Table ٢ demonstrates the mean ± SD and the range of the average number of cigarette smoked/day and the duration of smoking in group ٢.

Table ٣ demonstrates the subclassification of smoker group according to the number of cigarette smoked/day into heavy (≥ ٤٠ cigarettes smoked/day) , moderate (٢٠-٣٩ cigarette smoked/day) and mild (١-١٩ 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>٠.٠٥) except a significant lower serum ur value in the heavy compared with moderate (P<٠.٠١) and mild (P<٠.٠٠١) smokers .

Figure ١ and ٢; demonstrate a significant negative correlations (P<٠.٠٠٥) between serum ur and both the number of cigarette smoked/day and the duration of smoking respectively in group ٢.

Table ١: Comparison between parameters of group١ and ٢

Parameter	Group I (Control) n = ٤٧ mean ± SD	Group II (Smokers) n = ٤٠ mean ± SD	P-Value
Age (years)	٢٨.٤ ± ٦.٠	٣٠.٥ ± ٦.١	NS
Serum cr (μmol/L)	٩٤.٥٥ ± ١٧.٥٩	٨٦.٤٠ ± ٢٧.٢٨	NS
Serum ur (mmol/L)	٠.٢٧± ٠.٠٥	٠.٢٤ ± ٠.٠٧	P < ٠.٠١
Uur/Ucr	٠.٤٣ ± ٠.١١	٠.٤٦ ± ٠.١٨	NS
FEur (%)	١٠.٠١ ± ٢.٦١	١١.٨٦ ± ٦.٨٣	NS

NS : Not Significant

Table ٢: Number of cigarette/day and duration of smoking in group ٢

Parameter	Mean ± SD	Range
Number of cigarette/day	٢٢.٢٥ ± ١٣.٦٣	٥ - ٦٠
Duration of smoking (Years)	٩.٣٤ ± ٥.٧٣	١.٥ -٢٢

Table ٣: Comparison between parameters (between each subgroup with the other two subgroups) of heavy, moderate and mild smokers

Parameter	Heavy Smokers n = ٩ mean ± SD	Moderate Smokers n = ١٤ mean ± SD	Mild Smokers n = ١٧ mean ± SD
Age (years)	٣٣.٧ ± ٦.٠ NS	٢٩.٣ ± ٥.٦ NS	٢٩.٩ ± ٦.٥ NS
Serum cr (µmol/L)	٨٩.٩٨ ± ٢٠.٨١ NS	٩٤.٥٦ ± ٣٥.٠٢ NS	٧٧.٧٧ ± ٢١.٣٦ NS
Serum ur (mmol/L)	٠.١٨ ± ٠.٠٥ ↓	٠.٢٤ ± ٠.٠٥ NS	٠.٢٧ ± ٠.٠٧ NS
Uur/Ucr	٠.٣٩ ± ٠.١١ NS	٠.٤٣ ± ٠.٢٠ NS	٠.٥٢ ± ٠.١٨ NS
FEur (%)	١٣.٥٣ ± ٣.٠ NS	١٢.٥٠ ± ١٠.٦١ NS	١٠.٥٢ ± ٣.٧٩ NS

↓ Significant lower in heavy compared with moderate (P<٠.٠١) and mild (P<٠.٠٠١) smokers

NS : Not Significant

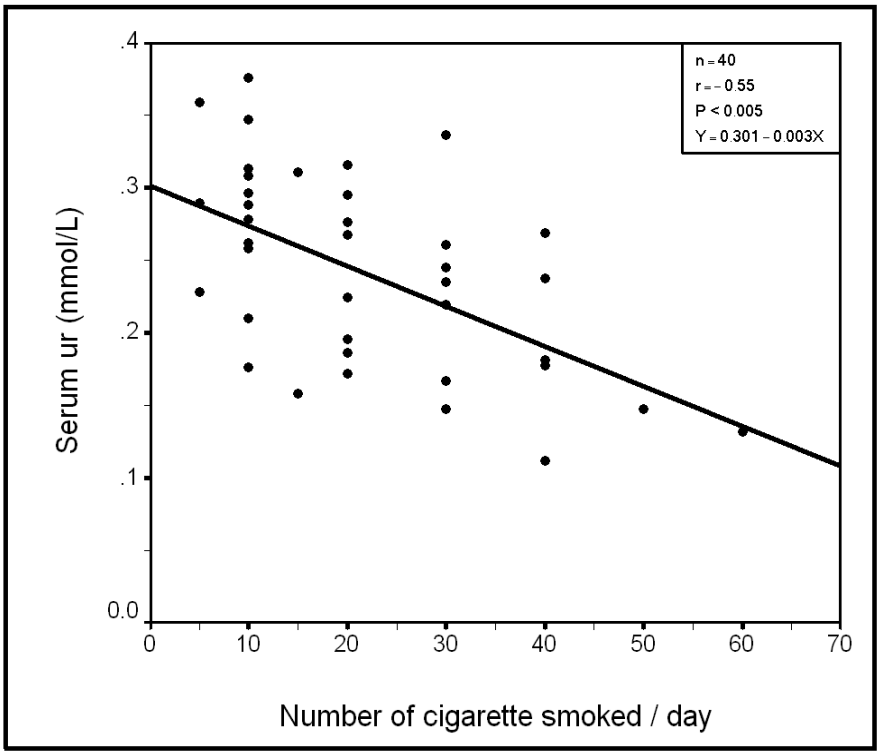

Figure ١: Correlation between serum ur and number of cigarette smoked/day in group II

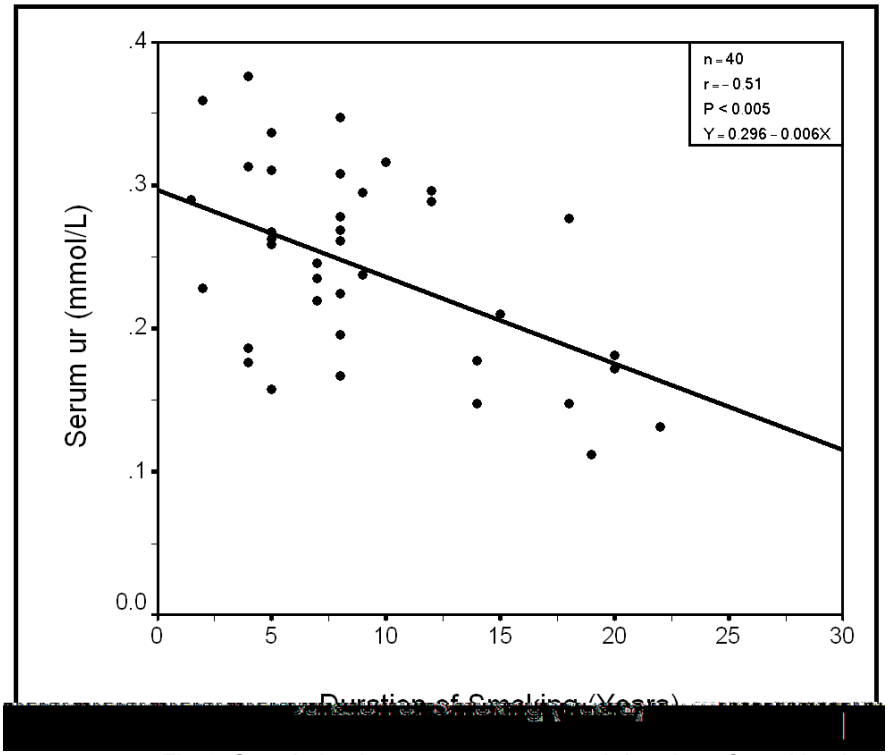

Fig ٢: Correlation between serum ur and duration of smoking in group II

Discussion

Although many, but not all epidemiological studies have suggested that high serum ur is a risk factor for CVD [٢٠,٢١] 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.[٢٢] The raised level of serum ur parallel to an increased risk of CVD could be either primary or secondary to underling causes of CVD.[٢٣-٢٥] However, the specific role of serum ur in this constellation remains uncertain[٢٦] 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.[٢٧,٢٨] 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.[٢٩]

The viability of administering ur in solution has been suggested[٢٧] 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.[٣٠]

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[١,٣١] and reduction of antioxidants including ur in smokers.[٣٢,٣٣] 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.[١] 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.[٣٢] 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.[١٢,٣٣] Therefore, high serum ur concentrations might be protective in situations characterized by increased cardiovascular risk and oxidative stress as in smoking[٨] and by reduction of serum ur level in smokers it increase the susceptibility to oxidative damage and account for the excessive free radical production,[٣٤] therefore, the possibility that ur confers protection against the development of atherosclerosis, in view of its antioxidant properties, has been recognized.[٣٥]

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 $\overline{X} \pm$ SD observed in the control group by other studies.[١٧,٣٦] Since these tests have been reported to be useful to evaluate renal handling of ur[٣٧]and as serum ur concentrations are highly dependent on endogenous production[٣٨] as well as renal excretion.[٣٩] Therefore , in this study it is concluded that the reduction of seum 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[٥,٣٤] which represent about ٦٠% of serum free radical scavenging capacity[١٢] and to the low intake of dietary antioxidants in smokers.[٤٠]

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.

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