Level of uric acid and its' relationship with lipid peroxidation in sera of patients with acute coronary syndrome

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Abstract

Unstable angina pectoris often leads to acute myocardial infarction.
Since uric acid is thought to be risk factor for cardiovascular disease and considered a major antioxidant in human blood .The level of uric acid and lipid peroxidation in the sera of patients with unstable angina and myocardial infarction were measured and compared to the healthy individuals. Twenty-nine patients with unstable angina and twenty-nine patients with myocardial infarction were studied and compared to twenty-five healthy individuals. Uric acid was measured by using Human Kit. Malondialdelyde (MDA) a lipid peroxidation marker, was measured by thiobarbituric acid method .Significant elevation of uric acid and MDA were observed in the sera of patients with unstable angina and myocardial infarction compared to the control group , while a non significant correlation between uric acid and lipid peroxidation were found in the present study in the sera of patients with unstable angina and myocardial infarction.

Key words: uric acid, acute coronary disease, lipid peroxidation

Introduction

Acute coronary syndrome (ACS) encompass a continuum of ischemic heart disease from unstable angina (UA) with reversible myocardial cell injury through myocardial infarction (MI) with large areas of necrosis[1,2]. The definition of acute coronary syndrome depends on specific characteristics of each elements of triad of clinical presentation including a history of coronary artery disease electrocardiographic changes and biochemical cardiac markers [3]. Unstable angina and myocardial infarction have a common aetiology in the formation of thrombus on an inflamed and complicated atheromatous plaque[4]. Over the last 40 years, a number of clinical and laboratory variables have proven predictive of the incidence of cardiovascular disease and thus qualify as cardiovascular disease risk factores [5]. Recent studies have shown that in addition to the classic risk factores, such as age, male gender, hypertension , hyperlipidemia, diabetes mellitus , obsity , high serum uric acid concentration is a cardiovascular factor[6-9].

Uric acid generated from xanthine by xanthine oxidase is the final product of purine metabolism in human[10] .Sources of purine are either endogenous from de nova synthesis and nucleic acid breakdown, or exogenous from dietry purine intake[11] .The association between uric acid and coronary artery disease was not limited to the hyperuricemic range[12] . Jelic I. et. al. were demonstrated that uric acid determination ould be useful as one of the markers of clinically significant

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coronary artery disease[12]. Despite elevated of uric acid associated with increased risk for cardiovascular disease, its considered a major antioxidant in human blood that may protect against aging and oxidative stress[13,14] .Oxidative stress is defined as the tissue damage resulting from an imbalance between an excessive generation of oxidant compounds and insufficient antioxidant defence mechanisms [15,16].

It is thought to play an important role in the pathogensis of acute coronary disease[17,18].Given that free radicals have very short half-livers (seconds) the clinical assessment of oxidative stress is based on the measurement of different stable oxidized compounds such as lipid peroxidation[19].The process of lipid peroxidation is one of oxidative conversion of polyunsaturated fatty acid to products known as malondialdehyde or lipid peroxides which is the most studied , biologically relevant , free radical reaction[20] .

The persent study aims to evaluate levels of uric acid and it's relationship with lipid peroxidation in sera of patients with unstable angina and myocardial infarction diseases.

Subject and Methods

Subjects :- This study included 58 patients (29 with unstable angina and 29 with myocardial infarction) attending Albitar hospital in Baghdad city ,and diagnosed by Dr. Mahdi Al Zaydi .As a control ,25 healthy individuals were included in the present study .

Serum Sampling :- Venous blood (5ml) were taken from healthy donors and patients . Blood samples were centrifuged at (3000 rpm) for 10 min after blood coagulation , serum thus separated and stored at -20^{o}C until being used .

Methods :-

Determination of uric acid :- Serum levels of uric acid were determined by enzymatic colorimetric test [(21),(22)] using uric acid kit (Human Company) .

Determination of lipid peroxidation:- Malondialdehyde a lipid peroxidation marker was measured by the thiobarbituric acid method[(23)], according to the modified method of satoh[(24)].

Statistical Analysis: - The results are expressed as mean ± SD . Statistical and correlation analysis were undertaken using student t-test, and pearson's correlation coefficients . Values of $P<0.05$ were considered significant.

Results:-

Uric acid was measured in the sera of control and patients with UA and MI using Human Kit . The mean values presented in Table (1) reflect a highly significant increase in uric acid levels in sera of patients with UA ($P<0.001$) and patients with MI ($P<0.001$) in comparison with that of the control group . Since the serum levels of uric acid is higher in males than in females , gender specific serum uric acid levels was also investigated .

Table (1) Mean values of uric acid levels in the sera of control and patients with UA and MI

Group		Sample Number(n)	Range mg\dL	Mean mg\dl	±Standard deviation
Control (Age:- 21-69 years)	All subjects	25	(1.6-7.8)	4.10	1.38
	Male	17	(2.2-7.8)	4.38	1.43
	Female	8	(1.6-4.6)	3.43	1.06
Patients with UA (Age:46-78 years)	All subjects	29	(3.3-12.8)	6.92	3.00
	Male	21	(3.3-12.8)	6.77	2.76
	Female	8	(3.5-11.2)	6.16	2.38
Patients with MI (age:48-75 years)	All subjects	29	(3.4-9.8)	6.37	1.6
	Male	22	(3.4-9.8)	6.60	1.67
	Female	7	(4.5-7.6)	5.91	1.10

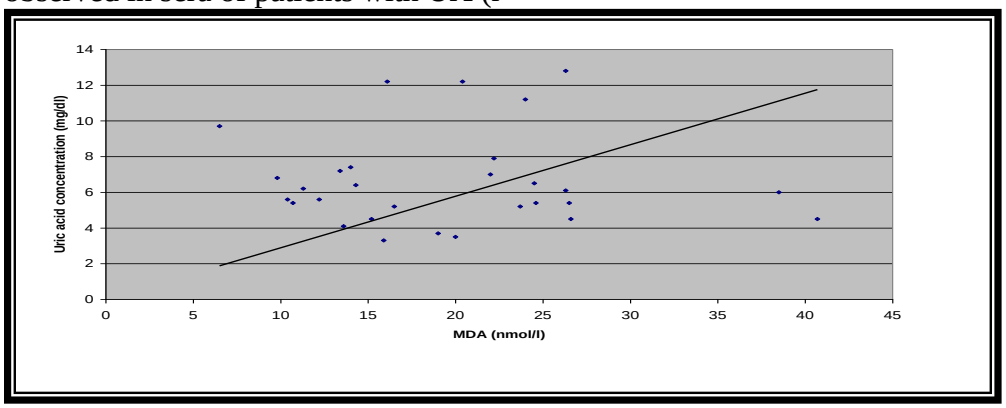
A highly significant increase in uric acid levels were observed in the sera of male patients with UA ($P<0.001$) and male patients with MI ($P<0.001$) in comparison with that of the control group . Meanwhile in female serum uric acid levels were significantly higher in patients with UA ($P<0.001$) and patients with MI ($P<0.005$) in comparison with that of the control group.

Malondiadehde was measured as a marker of lipid peroxidation in the sera of control and patients with UA and MI . The mean values presented in Table (2) show a presence of highly significant increase ($P<0.001$) in lipid peroxidation level in both sera of patients with UA and patients with MI in comparison with that of the control group.

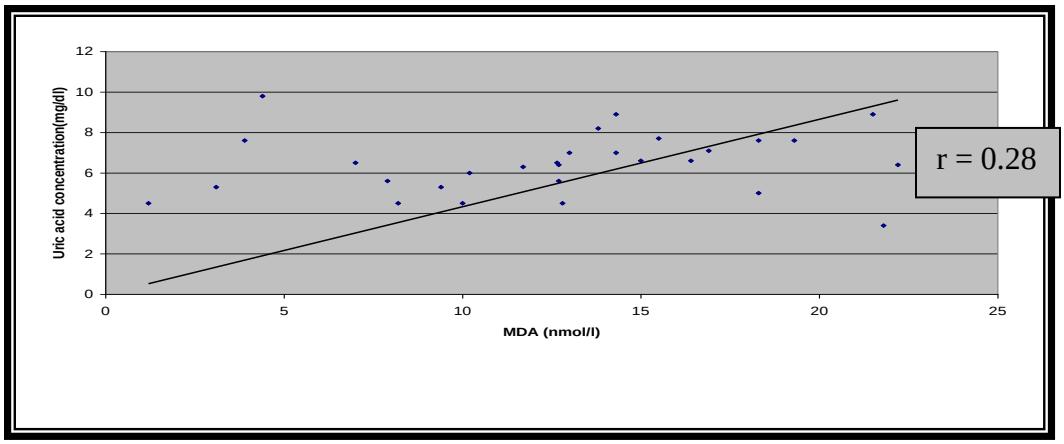
Table (2) Mean values of MDA in sera of control and patients with UA and MI

Group	Sample number(n)	Range (nmol/L)	Mean (nmol/L)	± Standard deviation
Control	25	(3.0-13.8)	7.03	2.65
Patients with UA	29	(6.5-40.7)	19.49	8.08
Patients with MI	29	(1.15-22.2)	12.68	5.60

A non significant correlation between uric acid and lipid peroxidation were observed in sera of patients with UA ($r = -0.243$, $P>0.05$) and patients with MI ($r = 0.28$, $P>0.05$) as in figures (1&2).



Fig(1)The correlation between uric acid concentration and MDA n sera of patients with unstable angina



Fig(2)The correlation between uric acid concentration and MDA in sera of patients myocardial infarctio

Discussion

Unstable angina pectoris and acute myocardial infarction are halmarke of acute coronary syndromes[25]. The association between elevated serum uric acid and coronary artery disease has been observed in numerous studies[12]. Despite this , there is still no agreement on whether uric acid is a cause, a consequence or just a marker of cardiovascular disease[8],[12],[26].

In the present study increased level of uric acid was observed in sera of patients with UA and patients with MI in comparison with that of the control group . This results were in agreement with the results obtained by Gur M. et. al. who found that serum uric acid levels in patients with coronary artery disease were significantly higher than those of the control group[27] .

Also Tatt E. et. al. have showed that high serum uric acid levels were associated with critical coronary artery disease in young patients < 35 years with acute myocardial infarction[28]. Kojima S. et. al. have suggested that serum uric acid level is suitable marker for predicting acute myocardial infarction[29].

Although the mechanisms by which uric acid may play a pathogenetic role in cardiovascular disease is unclear , hyperuricemia is associated with deleterious effect on endothelial dysfunction , oxidative metabolism, platelet adhesivenes hemrheology , and aggregation[9].

Serum uric acid levels reflect circulating xanthine oxidase activity and oxidative stress production[29]. Ames et. al. have proposed that uric acid may act as an important physiological antioxidant defence against such oxidative injuries[30]. The basis for this hypothesis was the observation that uric acid is oxidized to allantoin (and other product) in a process that scavengers singlet molecular oxygen , hydroxyl radicals , lipid hydroperoxide , and oxohaem oxidant , while inhibiting lipid peroxidation[31]. Another important antioxidant property of uric acid is the ability to form stable co-ordination complexes with iron ions[29],[31]. Increasing appreciation of the causative role of oxidative injury in many disease states great importance on the reliable assessment of lipid peroxidation . Malondialdehyd is one of several low molecular weight end product formed via the decomposition of certain primary

and seconedary lipid peroxidation products[32]. Most often , malondialdehyde assay used its reactivity at high temperature and low pH , towards thiobarbituric acid[33]. In the present study lipid peroxidation was observed to be significantly higher ($P<0.001$) in sera of patients with UA and patients with MI in comparison to the healthy controls .These results were in agreement with the results obtained previously which indicated that plasma MDA levels were highly significant in patients with acute coronary syndrome compared to the control[34],[35]. Dubois – Ramde JI. et. al. have reported that plasma MDA levels of patients presenting with unstable angina and acute myocardial infarction were higher than those of patients with stable angina and of normal angina and non - Q wave myocardial infarction groups[36].

A non significant correlation ($P>0.05$) between uric acid and MDA in sera of patients with UA and MI were found in the present study . This finding can be supported by the results obtained from previous stadies which suggested that uric acid has a variable behavior where is not necessary an antioxidant and , depending on the chemical milieu , may become a prooxidant[13],[30],[37] . In the presence of lipid peroxides uric acid even becomes a strong prooxidant[38]. Muraoka S. and Miura T. reported that uric acid loses its antioxidant ability in the hydrophobic environment . Morover it can form free radicals either alone or in combination with peroxynitrite[39].

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مستوى حامض اليوريك وعلاقته بتفاعل الدهون مع البيروكسيد في امصال مرض القلب المزمن

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الخلاصة

تؤدي الذبحة الصدرية غير المستقرة في اغلب الأحوال إلى الإصابة بالاحتشاء العضلي القلبي الحاد ، ونظرا لإمكانية اعتبار حامض اليوريك عامل مسبب لمرض القلب الوعائي ولكونه عامل اساسي مضاد للاكسدة تم قياس مستوى حامض اليوريك ومالون داي الديهايد في مصول دم المرضى المصابين بالذبحة غير المستقرة والاحتشاء العضلي القلبي حيث تضمنت الدراسة الحالية جمع 29 عينة من مرضى المصابين بالذبحة غير المستقرة و29 عينة من مرضى المصابين بالاحتشاء العضلي القلبي وتمت مقارنتها ب 25 عينة من الاشخاص الاصحاء .

تم قياس حامض اليوريك باستخدام عدة Human وقياس مالون داي الديهايد كدالة الأكسدة الفوقية للدهون باستخدام حامض ثايو باربتريك . حيث لوحظ وجود زيادة معنوية في مستوى كلا من حامض اليوريك ومالون داي الديهايد في مصول دم كلا المرضى المصابين بالذبحة غير المستقرة والمصابين بالاحتشاء العضلي القلبي مقارنة مع مستوياتها في مصول دم الاصحاء في حين تبين عدم وجود علاقة معنوية بين حامض اليوريك ومالون داي الديهايد في مصول دم كلا المرضى المصابين بالذبحة غير المستقرة ومرضى الاحتشاء العضلي القلبي .