

Role of dietary α -tocopherole in correction of oxidative stress resulted from chronic cadmium exposure in rabbits

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Abstract

The aim of this study was to determine the adverse effects of cadmium sulfate administration & role vit E in correction these adverse effect on urinary system parameters, 30 six month old ,clinically healthy new Zealand white rabbits were divided in to three group (ten in each group) T1 control group, T2 givin normal diet and tap water has 250mg/L for 60days, T3 givin also normal diet, tap water has 250mg/ml & 500mg/day dietary administration of Alpha-tocophenol there were a significant variation ($p \leq 0.01$) between T2&T3 groups in the levels of blood urea nitrogen, uric acid & plasma glutathione peroxidase, while there were some improvement in the levels of creatinin & kidney glutathione peroxidase for T3 group than T2 group, but this improvement don't reach the significant value. urine protein percentage for T3 group was less sever than T2 group. histopathological alteration in the kidney tissue for T3&T2 groups were confirm these results as general, Alpha-tocophenol play important role in diminishing oxidative stress of urinary system that resulted from chronic cadmium exposure.

Introduction

Among heavy metals, cadmium (Cd) poses a number of environmental problems in addition to being detrimental to human health ^[1] Cadmium has an extremely long half life (20–30 years) in the human body and is highly cumulative, especially in the liver and kidney ^[2]. Cadmium toxicity is responsible for alterations in various metabolic processes ^[3] and the inhibition of nucleic acid and proteinsynthesis^[4]. A syndrome called Itai-itai, first described in Japan, has been associated with chronic ingestion of cadmium. It is accompanied by the classical renal effects of industrial cadmium poisoning: proteinuria and often glucosuria and aminoaciduria ^[5] Daily cadmium intake by ingestion in the endemic area has been estimated to be 0.6 mg ^[6] but it would have been considerably greater before 1955, when pollution control measures were instituted in the nearby mine. Epidemiological studies carried out indicate that the incidence of proteinuria is significant in cadmium-polluted areas another study at autopsy has revealed that the principal renal effects of chronic cadmium poisoning are seen in the tubules but are pronounced only in the most severe cases ^[7] Cadmium toxicity also include renal disturbance that includes the excretion of low-molecular-weight proteins

in the urine and an increase in amino acids ^[15] It has been proposed that the minimum critical level of cadmium in the kidney required to produce renal tubular damage is approximately 0.2 mg/g ^[8] There is some evidence of an increase in the incidence of renal stones in those with prolonged exposure to cadmium ^[9] In chronic cadmium exposure, bones appear to be secondarily affected or may be directly impaired before renal tubular damage develops. Oxygen radical scavengers such as vitamin E, glutathione (GSH), glutathione peroxidase (GSH-Px), superoxide dismutase, and catalase are protective against chemical-induced oxidative damage in rats ^[10] Vitamin E is a family of lipid-soluble vitamins, of which α -tocopherol is the most potent. Vitamin E has been shown to act as an antioxidant in cells, interrupting the propagation of lipid peroxidation in the plasma membrane and thus preserving membrane integrity ^[11] Recently, ^[12] demonstrated that Cd-induced alterations in liver and kidney biochemistry could be reduced by simultaneous administration of α -tocopheryl acetate in rats. The relationship between vitamin E intake and endogenous cellular defense mechanisms is not yet fully understood. However, the activity of

some antioxidant enzymes and the levels of certain antioxidants appear to be controlled by regulatory mechanisms that respond to oxygen metabolite

concentration^[13].aim of this study was role assess of vit. E in modulation of antioxidant defense mechanism against cadmium exposure.

Materials and methods

Animals:

Six months old clinically healthy New Zealand white rabbits weighing 2500 ± 115 gm, randomly divided into three groups of 10 animals each. They were kept in warm place 28°C in individual cages, all animals were given basic diet, the second group T2 was giving tap water with 250mg/l cadmium sulphate for 60 days, the third group T3 was given tap water and cadmium sulphate 250mg/l plus α -tocopherole 500mg per day by oral administration

Sample collection:

At 10 weeks whole blood was collected via cardiac puncture from anesthetized (ketamine 50mg/kg-xylazine 10mg/kg), rabbits were then euthanized with a single cardiac injection fatal plus (concentrated pentobarbital, 360 mg/kg),

kidney tissues was collected in For histological studies, while some kidney tissue collected into 0.25 mol/l sucrose and stored immediately on ice. Subsequently homogenized on ice for 20 second then centrifuged at 30000 cc for 30 minutes at 4°C and the supernatant collected for laboratory studies.

Blood and urine chemistries

Blood urea nitrogen, creatinine, uric acid concentration in plasma, urine protein were determined using commercially available kit (sigma), glutathione peroxides determined as in^[14].

Statistical analysis

Mean $\pm$ SE was carried. All data are analyzed using Duncan's multiple range test^[15] to determine if the treatment were significantly ($P \leq 0.01$) different or not.

Results

From data of table1. was showed that the chronic cadmium administration on the rabbits lead to important change biological models of urinary activity, α -tocopherole in order correct really the oxidative stress for urinary system that resulted from cadmium exposure. Results revealed significant ($p \leq 0.01$) variation in blood urea nitrogen and uric acid in blood for T1 group than T2 and T3 groups, while T3 was significantly less than T2 group Creatinine level has significant increment in T2 group then T1 and T3 group while

there was no significant variation ($p > 0.01$) between T1 and T3 groups. Urine protein percent in T2 group was about 80% while urine protein in T3 group was less than T2 group, about 40%. Both glutathione peroxidase activity in blood and tissue had reduced significantly in T2 treatment group than normal group also there was significant difference between T1 and T3 groups in plasma GPX level while there was no difference in kidney tissue GPX between T1 and T3 groups.

Table 1 explain role of α -tocopherole in correction of oxidative stress resulted from cadmium exposure in different biochemical parameters.

Biochemical parameters	T1 control group	T2 cd. only	T3 cd+ α -tocopherole
Blood urea nitrogen	46.8 $\pm$ 1.489 a	67 $\pm$ 1.855 c**	54.2 $\pm$ 1.19 b**
Creatinine	0.4 $\pm$ 0.025 a	0.93 $\pm$ 0.047 b	0.46 $\pm$ 0.052 b
Uric acid	2.14 $\pm$ 0.056 a	4.39 $\pm$ 0.113 c**	3.12 $\pm$ 0.162 b**
Urine protien	0%	80%	50%
Plasma glutathione peroxidase	69.05 $\pm$ 0.427 a	54.04 $\pm$ 0.712 c**	64.8 $\pm$ 1.533 b*
Glutathione peroxidase in kidney tissue	37.99 $\pm$ 0.17 a	34.9 $\pm$ 0.173 b	37.93 $\pm$ 0.316 b

Results are expressed as mean $\pm$ standard error.

a: no significant variation

Different letters between groups refer to significant difference ($p < 0.01$).

** refer to significant variation under difference ($P < 0.01$)

* refer to significant variation under difference ($P < 0.05$)

Degree of freedom :2, 29.

These result were supported by histopathological examination of kidney tissue, Results revealed marked dilation and congestion of renal convoluted tubules and renal tissue with atrophy of glomeruli

for T2 animal group, histopathological examination of kidney tissue for T3 group revealed mild degenerative signs with normal glomeruli and renal convoluted tubules as explained in fig(1) and fig(2).

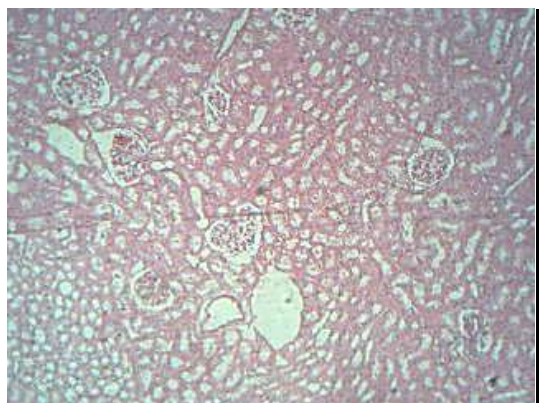
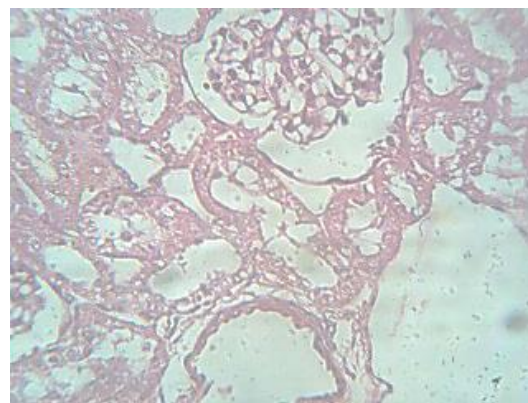
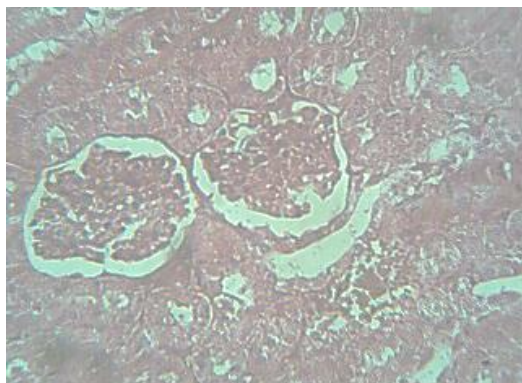


Fig (1)

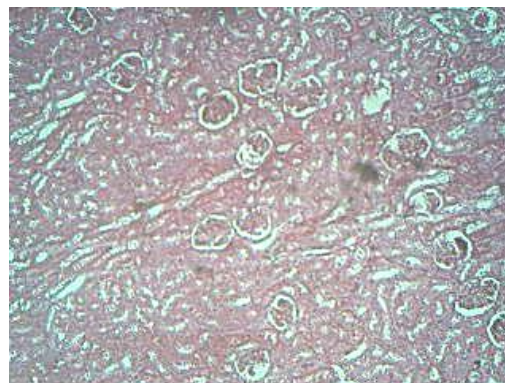


Fig(2)

Fig: Photomicrographs of haematoxylin and eosin stained sections of rabbit kidney fig.1 and fig 2(A)H&E, (10 $\times$), (1,2) Group II represented a severe congestion and dilatation of renal tissue and renal tubules with atrophy of glomeruli.



Fig(3)



Fig(4)

(3,4) group III showed normal glomeruli and renal convoluted tubules. while fig 3 and 4 (B) H&E, (40×).

Discussion

In this work the effect of single doses of vitamin E on the basal serum and urine levels of some biochemical (blood urea nitrogen, uric acid, creatinine, urine protein, plasma glutathione peroxidase and kidney glutathione peroxidase) parameters in white newzeland rabbits exposed to chronic cadmium toxication were investigated. The results shows that vitamin E cause significant ($p \leq 0.01$) decrease in the basal level of blood urea nitrogen, uric acid and plasma glutathione peroxidase while creatinine and kidney glutathione peroxidase levels was improved by vitamin E administration but this improvement dose not reach to the significant level. Damage to certain tissues & organ results in the elevation of serum concentration of specific biochemical parameters of urinary system as presented by histopathological alteration of kidney tissue, this occur as a result of their release or secretion from the damaged tissue ^[16], The cadmium induced increases in serum level of urea nitrogen & creatinine suggest signs of renal toxicity ^[17] this may be due to the oxidative effect of cadmium which is a sulfhydryl-active & powerful oxidative metal ^[18], Treatment with Alpha-tocopherole reduced cadmium induced increment in serum level of urinary system parameters, which may be due to the

antioxidant effect of vitamin E is lipid soluble vitamin & has been established as very effective antioxidants ^[1] it scavenge free radicals by readily donating electrons to these unstable & highly reactive molecules (ROS) during biological reaction in the body & become oxidized themselves, as scavenges of free radicals, it therefore reduce the production of ROS & oxidative stress which be presented in significant increment of GPX levels in both plasma & kidney tissue of T3 group than T2 group. This will in turn prevent or reduced lipid peroxidation & tissue injury or damaged that may be induced by oxidative trauma/stress. the oxidative effects of cadmium are mediated through the activation of protein kinase C (pkc) during single transduction, PKC activity is interns dependent on cytosolic calcium ion concentration ^[7], vitamin E cause inhibition of PKC ^[21], in addition to action of vitamin E on protect against magnesium deficiency, which turn lead to reduction in intracellular calcium ^[16] this mechanism may explain the opposite (increasing & decreasing) effects of cadmium & the vitamin E on basal serum levels of the parameters & histological alteration that investigated in this study or their oxidative & antioxidative activates.

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دور ألفا-توكوفيرول الغذائي في تصحيح الإجهاد التأكسدي للجهاز البولي الناتج من التسمم المزمن بكبريتات الكادميوم في الأرانب

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الخلاصة

تهدف الدراسة الى تحديد مدى التأثير السلبي والتأكسدي لكبريتات الكادميوم على فعالية الجهاز البولي ودور ألفا-توكوفيرول في تقليل تلك التأثيرات. إذ تم قياس مستوى الكرياتينين، حامض اليوريك مع مستوى اليوريا (Blood urea nitrogen) في الدم إضافة إلى قياس مستوى البروتين في الإدرار كما تم قياس الأنزيمات المضادة للأكسدة glutathione peroxidase في الدم ونسيج الكلية في جسم الأرانب بعد شهرين من إجراء التجربة. قسمت الحيوانات إلى ثلاثة مجاميع تضم أعداد متساوية 10 حيوانات لكل منها مجموعة سيطرة ومجموعة معاملة ثانية أعطيت الماء والغذاء الاعتيادي وأضيف كبريتات الكادميوم بتركيز 250 ملغم/لتر ومجموعة معاملة ثالثة أعطيت الماء والغذاء الاعتيادي مع إضافة كبريتات الكادميوم 250 ملغم/لتر ثم تناولت 500 ملغم/لتر من الفا-توكوفيرول (BHD-England) ولمدة شهرين متتاليين. تبين النتائج وجود فروق معنوية ($P \leq 0.01$) في مستوى اليوريا وحامض اليوريك ومستوى الأنزيم المضاد للتأكسد glutathione peroxidase في البلازما بين مجموعتين المعاملة الثانية والثالثة، بينما انخفض مستوى الكرياتينين وارتفع مستوى الأنزيم المضاد للتأكسد في النسيج في مجموعة المعاملة الثالثة مقارنة بمجموعة المعاملة الثانية إلا أن هذا الانخفاض والارتفاع لم يصل إلى مستوى المعنوية ($P > 0.01$). كما تم دراسة الجانب النسيجي للكيتين في مجاميع المعاملة وجاءت نتائج النقطيع النسيجي موافقة للفحوصات السيولوجية. بصورة عامة أشارت الدراسة إلى وجود انخفاض نسبة الإجهاد التأكسدي لمعايير الجهاز البولي في الأرانب والناتج من قبل كبريتات الكادميوم نتيجة لاستخدام العامل المضاد للتأكسد α -tocopherole.