

# EFFECT OF VITAMIN E IN CHRONIC RENAL FAILURE AND RENAL ANAEMIA <sup>+</sup>

تأثير فيتامين E لمرضى الفشل الكلوي المزمن والانييميا الكلوية

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## Abstract:

In this study we aimed to evaluate the role of oxidative stress as a contributing factor on the extent of free radical damage on lipid (measured as malondialdehyde, MDA) and their effect on antioxidant defense mechanism (measured as vitamin E in the serum of chronic renal failure patients, CRF prediallytically and renal anaemia) through studying the effect of vitamin E supplementation as an antioxidant on the markers of oxidative stress as well as on hemoglobin in haemodialysis (HD) patients.

**Methods:** Plasma malondialdehyde(MDA), plasma creatinine, urea and haemoglobin (Hb) concentration were measured in 40 HD patients(both sex) and compared with 20 healthy(both sex), matched controls. After 3 months of vitamin E supplementation in a dosage of 600mg/day (not to accede the safety daily dose) [1], the baseline parameters were reassessed in the same patients group

## المستخلص :

تهدف هذه الدراسة معرفة تأثير فيتامين E كعامل مضاد للاكسدة وبجرعة ٦٠٠ ملغم/يوم للمرضى الذين يستعملون الكلية الصناعية. (دفاع وقياس معدلات تركيز اليوريا والكرياتينين وخضاب الدم)، كعامل مساعد تعتمد عليه الجذور الحرة في اكسدة الدهون وذلك بقياس المالوندايديه، تركيز الهيموغلوبين، قياس كفاءة الكلى plasma creatinin و blood urea لـ ٤٠ مريض (لكلا الجنسين) بمرض الفشل الكلوي المزمن ومقارنة النتائج مع ٢٠ اصحاء (من كلا الجنسين) بعد ٣ اشهر من التزود بأخذ فيتامين E بجرعة ٦٠٠ ملغم/يوم لـ ٢٠ مريض (من كلا الجنسين) و ٢٠ مريض (من كلا الجنسين) بدون فيتامين E حيث يستعمل نفس التقييم للنتائج لكلتي المجموعتين. اظهرت النتائج التي تم الحصول عليها كون مستوى MDA قبل التزود بفيتامين E خطر حيث معدلاته الاحصائية اقل من  $p < 0.0001$  اما بعد التزود بفيتامين E فقد ارتفعت معدلات مستوى MDA اما تركيز الهيموغلوبين فلم يتأثر تقريبا. كما تبين ان عدم اتوازن لمرضى الفشل الكلوي ممكن ان يساهم في زيادة فقر الدم الكلوي. العلاج بالتزود بفيتامين E ممكن ان يقلل تكوين الجذور الحرة بشكل فعال لمرضى الفشل الكلوي ولكنه لم يؤثر على معدلات فقر الدم لهم.

## Introduction:

Reactive oxygen species (ROS) play a significant role in pathogenesis of chronic renal failure (CRF) [2], leading damage protein, lipid and DNA. Oxidative stress, increased lipid peroxidation, and decreased activity of antioxidant systems may contribute to the accelerated development of atherosclerosis in patients receiving hemodialysis therapy for chronic renal

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failure. Renal anaemia is one of the main complications seen in HD patients and resulting from many pathogenic factors. Oxidative stress defines an imbalance between generation of reactive oxygen species (ROS) and antioxidative defense mechanisms protection from oxidant injury involves complex pathways of antioxidant defence mechanisms at both the blood and intracellular levels. In view of the profound biological effects of ROS, in recent years numerous clinical and experimental studies focused on detection of signs of oxidative stress in renal patients [3].

Vitamin E has been used extensively in clinical medicine but careful examination of the evidence available reveals that in the majority of instances there is inadequate evidence to prove its value. There is, however, well founded evidence for the value of large doses of tocopherol (400-600 mg per day over a prolonged period) in intermittent claudication. In addition there is a reasonable evidence [4] for the administration of tocopherol (up to 400 mg per day) to patients with stasis ulcers and in certain fibrous tissue degenerations.

Vitamin E, particularly in the form of  $\alpha$ -tocopherol has been proposed for the prevention or treatment of many health conditions, often based on its antioxidant and anti-inflammatory properties. There is a growing interest in the possible benefits of Vitamin E in kidney diseases with high oxidative stress [5].

Hemodialysis is known to be one major cause of oxidative stress due to the activation of polymorphonuclear neutrophil leukocytes through contact of the blood with the dialysis membranes. Activated polymorphonuclear neutrophil leukocytes are able to mediate lipid peroxidation (LPO) in red blood cells (RBC), which results anaemia in uremic patients [6]. The latter may result from haemodialysis membrane-induced activation of macrophages on the surface of dialysis membranes during the dialysis session. Loss or deficiency of antioxidant activity (e.g. vitamin E deficiency) could also contribute to enhanced oxidative stress in uraemia.

## **Methods:**

Forty patients (23 males and 17 females), range (18-47) years with CRF on maintenance HD referred from the Dialysis Department, Hawari Hospital, Banghazi, were enrolled in the study.

All patients had been on regular haemodialysis for at least 5 months and dialysis sessions were performed three times a week and each session lasted 4 hours.

Twenty healthy subjects (12 males and 8 females), mean age ( $16 \pm 4$ ) were chosen as control. The blood samples were taken from the patients before the dialysis session and repeated at the end of three months of vitamin E supplementation.

**Assay;** 6 ml fasting blood samples were collected into polypropylene tubes containing EDTA (1.5 mg/ml), 1ml was used for measurement of hemoglobin (Hb) concentration, while the rest of the sample was separated into plasma and erythrocytes fraction by centrifugation at 3000g for 10 minutes. The separated plasma was used for assay of malondialdehyde (MDA), creatinine and urea levels.

**Haemoglobin concentration:** Hb was measured by (Quanti Chrom haemoglobin assay kit) according to [7] based on an improved cyanohaemoglobin method, in which the haemoglobin is converted into a uniform colored end product. The intensity of color was measured at 400nm.

**Determination** of plasma creatinine and urea: plasma creatinine levels were measured by spectrophotometric method according to [8] and Layne, (1957) respectively, while urea was

measured by an enzymatic method according to [9]. Plasma Malondialdehyed (MDA) level: plasma (MDA) level was measured spectrophotometrically at 532 nm using thiobarbituric acid reagents under acidic conditions to generate a pink colored product and recorded as nmol/L [10, 11].

In this study, the extent of free radical- mediated damage on lipids ( measured as MDA levels) and effect on antioxidant defense mechanism(measured as vitamin E) was studied in CRF patients before dialysis to show the role of antioxidant in preventing the progression of CRF and for monitoring and optimization of antioxidant therapy.

So, in this study we interested, if there is a possible role of redox imbalance in the development of renal anaemia, through studying the effect of vitamin E supplementation as an antioxidant on the haemoglobin levels, and studying the effect of vitamin E supplementation as an antioxidant on plasma creatinine, urea nitrogen in HD patients.

## **Results:**

Table (1) showed that, there was statistically significant increase in the MDA level in HD patients ( $p<0.0001$ ), also there was a significant decrease in Hb concentration in the patients when compared to control ( $p<0.0001$ ), table (1) also showed plasma creatinine and urea in HD patients before and after supplementation, there was significant decrease in plasma creatinine and urea levels after vitamin E supplementation ( $p<0.0001$ ). After vitamin E supplementation there was a insignificant decrease in MDA level ( $p<0.0001$ ) and there was insignificant increase in Hb concentration ( $p=0.082$ ).

Table 1: The studies parameters in HD patients before and after supplementation of vitamin E

Parameters	Control	HD patients		p-value
		Before vitE	After vitE	
MDA mmol/l	1.75±0.77	8.17±1.99	6.08±1.77	$p<0.0001$
Creatinine mg/dl	0.96±0.16	10.98±2.23	5.71±1.5	$P_1<0.0001$ $P_3<0.0001$
Urea mg/dl	27.7±6.56	210.32±26.12	84.40±15.9	$P_1<0.0001$ $P_3<0.0001$
Hb g/dl	11.30±8.77	7.14±0.98	7.98±1.34	$p<0.0001$ $p_4=0.082$

P: significance between HD before and after vitamin E supplementation

$P_1$ : significance between control and HD before vitamin E supplementation

$P_3$ : significance between control and HD after vitamin E supplementation

$P_4$ : significance between HD after vitamin E supplementation.

## **Discussion:**

Vitamin E deficiencies have been reported in uremic patients undergoing maintenance HD, beneficial effects of vitamin E, administered orally or bound to dialysis membranes have been suggested in these patients [12].

In this study re-evaluating indices of oxidative stress of the same patients after supplementation of the vitamin E in a dosage of 600 mg/daily for 14 weeks revealed a decrease in MDA concentration.

The oral vitamin E supplementation might be able to modify oxidative stress by an increase in total antioxidant capacity and decrease in lipid preoxidation: that could be considered as apreventive strategy in hemodialysis patients [13]. Vitamin E help to prevent cell membrane damage; still under [14].

In the current study there was decrease in Hb concentration in HD patients group before vitamin E supplementation which could be a consequence of oxidative stress in those patients

as reported by [14]. They stated that the vitamin E scavenger ROS generation with reactions in the body would contribute to the lipid peroxidation [15].

Although, haemoglobin levels did not increased significantly after the vitamin E supplementation, [16] have reported that vitamin E might improve the rheology of circulating red blood cells and reduce the requirement of erythropoietin doses in HD patients.

However, [17] have suggested that renal anaemia is caused probably by some high molecular weight or protein bound toxins that have a property to inactivate the antioxidant defense system.

The present findings allow us to conclude that: Redox imbalance in HD patients might be a contributing factor in renal anaemia. Treatment with vitamin E might decrease radical generation effectively in HD patients with insignificant effect on renal anaemia.

We suggest that the supplement of vitamin E is capable of regaining antioxidant defense in plasma and preventing oxidative damage induced by hemodialysis.

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