THE PHARMACOLOGIC EFFECT OF ORAL α-TOCOPHEROL SUPPLEMENTATION ON OXIDATIVE STRESS IN CHRONIC RENAL FAILURE

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The pharmacological effect of α-tocopherol on plasma and erythrocyte lipid peroxidation were investigated in chronic renal failure (CRF) patients. The indices of oxidative stress were measured in 4 CRF patients of before and after oral supplementation of α-tocopherol 100 mg daily for 30 days and in 7 unsupplemented CRF patients using as control. In supplemented group, the results showed a significant increases in plasma and erythrocyte vitamin E levels, while the levels were unchanged in unsupplemented patients. In patients receiving α-tocopherol, both plasma and RBC lipid peroxidation values were significantly decreased. In addition, the osmotic fragility of red blood cells represented by median glycerol lysis time was significantly increased ($p<0.01$). In conclusion, oral supplementation of α-tocopherol may be of protective value on oxidative stress in chronic renal failure patients and may have clinical benefit in alleviating the associated by reducing the fragility of red blood cells.

KEY WORDS : α-Tocopherol, oxidative stress, chronic renal failure

INTRODUCTION

Chronic renal failure remains a major medical problem in Thailand. The progression of chronic renal disease occurs with the ongoing process of the loss of a critical number of nephron population.[1] Evidences showed that oxidative stress played an important role in pathogenesis of renal disease and the progress of the disease to end stage.[2]

The chronic effects of reactive oxygen species (ROS) on kidney have been demonstrated by animal models. An experimental model of chronic deficiency of selenium and vitamin E has also been well documented. The chronic deficiency of these two antioxidants are associated with structural and functional injuries in intact rat's kidney.[3] Another well known medel is the chronic puromycin amino-nucleoside nephropathy (PAN).[4] Progressive renal damage in these two models is partly mediated by excessive production of reactive oxygen species. Dietary supplementation with vitamin E, an endogenous lipophilic antioxidant, ameliorates the severity of the progressive renal damage.[3,4]

It is obvious that development of progressive renal damage in animal model should be reduced by the beneficial effects of supplementation of vitamin E.[3,4] Prior study showed that Thai chronic renal failure patients suffered serious decrease in vitamin E level in the erythrocyte.[5] Increased levels of plasma thiobarbituric acid reactive substances, a marker of lipid peroxidation, have also been reported in patients with chronic renal failure[5,6,7] and the beneficial effect of vitamin E should also be essential for chronic renal failure patients.[8,9]

In the present work, we have investigated the pharmacologic effect of vitamin E supplementation against plasma and erythrocyte lipid peroxidation in Thai chronic renal failure patients.

MATERIALS AND METHODS

Fresh and heparinized blood samples were obtained before and after vitamin E treatment. The erythrocyte,

plasma lipid peroxide were determined by malondialdehyde (MDA) formation[10,11] The erythrocyte and plasma antioxidant vitamins were performed by high-performace liquid chromatography.[12,13] The osmotic fragility test of red blood cell was carried out with a slight modification by the method of Eugene *et al.*[14] and Zanella *et al.*[15] All results are expressed as the mean ± SD. Statistical analysis were analyzed using paired two-tailed student's t-test. Statistical significance level was defined as $p<0.05$.

RESULTS

The experiment was performed in 11 patients with mild degree renal failure (6 males and 5 females), aged from 27.0 to 69.0 years (average 48.91 ± 14.87) with informed consents. All patients were of chronic glomerulonephritis and were free from diabetes mellitus, chronic respiratory insufficiency, intercurrent infection, hepatic disorder, alcoholic ingestion and cigarette smoking. None had received either blood or plasma during the last 4 months preceding the study. Iron, vitamins or aluminium hydroxide were stopped for one month before blood and urine determinations. The patients were divided into two groups. Four patients, group I, 2 males and 2 females, aged from 42.0 to 62.0 years (average 52.0 ± 10.46) received oral supplementation of 100 mg vitamin E daily with routine medication for 30 days. Seven patients, group II, 4 males and 3 females received only routine medication but not vitamin E, aged from 27.0 to 69.0 years (average 47.14 ± 17.43), were served as controls.

Table 1 shows the effect of vitamin E therapy on vitamin E and MDA level in supplemented and non-supplemented groups of chronic renal failure patients. Vitamin E therapy resulted in a significant increase in plasma and erythrocyte vitamin E levels in treated group compared with untreated group. Levels of vitamin E in plasma and red blood cell in non-supplemented patients remained low. After vitamin E therapy, both plasma and RBC lipid peroxidation levels in vitamin E treated group was significantly decrease.

Table 1 The effect of vitamin E therapy on vitamin E and MDA levels in control and vitamin E treated group of chronic renal failure patients. Values represent mean ± SD.

	Control group		Vitamin E treated group	
Data	**Before therapy**	**After therapy**	**Before therapy**	**After therapy**
Plasma vitamin E (mg/dl)	1.422 ± 0.8	1.498 ± 0.15	1.547 ± 0.44	4.351 ± 2.14 *
RBC vitamin E (mg/ml prc.)	2.587 ± 0.42	2.483 ± 0.39	2.668 ± 0.34	4.909 ± 2.09 *
Plasma MDA (μmol/l)	129.37 ± 16.95	135.00 ± 23.92	142.50 ± 29.01	94.50 ± 10.54 *,*
RBC MDA (nmol/Cer)	298.80 ± 32.99	314.81 ± 32.81	318.038 ± 106.32	158.965 ± 23.72 *,**

Comparison based on values at one month after therapy versus before therapy :

* $p<0.05$ versus before therapy; * $p\leq0.01$ versus control; ** $p<0.0001$ versus control.

CONCLUSION AND DISCUSSION

Free radical-mediated oxidative damage has been implicated in pathogenesis and progression of chronic renal failure.[2] Since the observation by several reports both in vitro and in vivo studies[16,17] revealed that there was increased oxygen consumption per nephron as a consistent tubule adaptation which occurs with nephron loss. Increased oxygen utilization induced high level of generation of reactive oxygen species.[17] Superoxide anion radical and other reactive oxygen species (ROS) production is a direct consequence of increased oxygen consumption. The hyperactivity of these oxygen radicals is directed against lipids and proteins as well as nucleic acid. There are resulting in structural modification and fragmentation cause renal cell damage.[2] The degree of lipid peroxidation caused by these ROS depends largely on the activity of endogenous oxygen radical scavengers.[17]

α-Tocopherol is an effective antioxidant preventing peroxidation of lipid membranes and has a similar protecting action in the biological tissues. The previous study[5] indicated that Thai chronic renal failure patients were subjected to oxidative stress as indicated by deficiency in α-tocopherol in red blood cell and increasing of lipid peroxidation. Suffering from α-tocopherol deficiency or under peroxidant stress has been claimed to biochemical and sub-cellular damage by lipid peroxidation.[18] Oxidative damage to polyunsaturated lipids in tissue membranes (lipid peroxidation) a free radical process, is a widely accepted mechanism for cellular injury. Malondi-aldehyde is one of the products of lipid peroxidation which appears to be produced in relatively constant proportion to lipid peroxidation. It is therefore a good indicator of the rate of lipid peroxidation.

In conclusion, the results obtained in this study have clearly demonstrated that MDA levels in both plasma and red blood cell with susceptibility to lipid peroxidation were significantly decreased in chronic renal failure patients after α-tocopherol therapy. These beneficial effects on chronic renal failure and related signs are associated with significant reduction of oxidative stress, represented by decrease in malondialdehyde content and increase in antioxidative capacity. Therefore, α-tocopherol therapy may be a promising approach to prevent peroxidation of membrane lipids in chronic renal failure. Our study may also suggested that oral supplementation of α-tocopherol in chronic renal failure could be importance by slow down the progression of renal disease and the efficacy of long-term α-tocopherol administration in such patients should be further studies.

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