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The effect of vitamin E supplementation on antioxidant enzyme activities and lipid peroxidation levels in hemodialysis patients

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Abstract

Background: This study has been undertaken to investigate the possible alterations of oxidant/antioxidant status in uremic patients undergoing hemodialysis (HD) and the effects of vitamin E supplementation. *Methods*: Erythrocyte antioxidant enzyme activities [glutathione peroxidase (GSHPx), superoxide dismutase (SOD) and catalase (CAT)] and thiobarbituric acid reactive substance (TBARS) concentrations as a measure of lipid peroxidation in HD patients have been determined and compared with healthy controls. The patient group consisted of 36 uremic patients 21–75 years of age undergoing maintenance HD three times weekly for an average of 41 months. The efficiency of Vitamin E therapy in dialysis patients was also assessed by re-evaluating antioxidant status of the same patients after supplementation of the vitamin E in a dosage of 600 mg/daily for 14 weeks. *Results*: A significant decrease in the activities of erythrocyte SOD, CAT and GSHPx and a significant increase in TBARS concentrations were found in patient group compared to control group ($p < 0.001$). A significant correlation between GSHPx activities and duration of HD therapy was also observed ($r = -0.46$, $p < 0.01$). Vitamin E supplementation caused an increase in GSHPx and SOD activities and a decrease in TBARS concentrations. A slight but not significant increase in CAT activity was also observed by Vitamin E. *Conclusions*: The results suggest the presence of an oxidative activity and the possible preventive role of Vitamin E therapy in uremic patients undergoing HD.

Keywords: Hemodialysis; Oxidative stress; Antioxidant enzymes; Lipid peroxidation; Vitamin E

1. Introduction

In recent years, a growing interest has evolved in regard to the increased oxidative stress associated with uremia. In spite of controversial data, it is generally suggested that uremic patients undergoing hemodialysis (HD) are at a high risk of oxidative stress, which has been defined as an imbalance between formation of reactive oxygen species (ROS) and antioxidant defense mechanisms [1–4]. In HD patients, oxidative stress appears to exist from the consequences of (i) an abnormal production of ROS by activated leukocytes and possibly by other cells; (ii) the presence of uremic toxins with prooxidant properties; (iii) the decompartmentalisation of transition metals and enzymes from

Abbreviations: HD, Hemodialysis; TBARS, Thiobarbituric acid reactive substances; GSHPx, glutathione peroxidase; SOD, superoxide dismutase; CAT, catalase; ROS, reactive oxygen species; LDL, low density lipoprotein; RBC, red blood cell.

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the cells which catalyse the reaction of ROS; and (iv) defective antioxidant defenses. Although dialysis restores the quality of life in patients encountering end-stage renal failure, the long-term dialysis therapy causes the complications possibly due to the imbalance between the generation and the scavenging of oxygen radicals [5–9]. Despite the continuous improvement in techniques, biomaterials and the adequacy of HD therapy, frequent and severe complications have still remained. Cardiovascular disease is the major cause of morbidity and mortality in chronic renal failure patients on long-term HD and atherosclerotic complications are reported to account for more than 40% of the deaths [10–12]. It has been suggested that increased oxidant stress in these patients may trigger endothelial cell damage and oxidation of low-density lipoprotein (LDL), which leads to the accelerated development of atherosclerosis. On the other hand, impaired red blood cell (RBC) deformability, increased hemolysis, anemia, platelet dysfunction, accelerated aging, cataract can also be observed as HD-related complications in uremic patients [13–16]. Therefore, in order to protect the uremic patients against the complications of HD caused by oxidative stress, antioxidants and particularly vitamin E supplementation or use of HD filters with vitamin E-coated surface have been proposed. Vitamin E is an effective chain-breaking, lipid-soluble antioxidant in biological membranes that includes eight naturally occurring compounds in two classes designated as tocopherols and tocotrienols. It is abundant in vegetable oils and it has been widely used in the defense against oxidative stress [5,17]. It protects critical cellular structures against damage caused by oxygen free radicals and reactive products of lipid peroxidation. It is not only a powerful lipophilic antioxidant, but also contributes to the regulation of processes such as metabolic activity, proliferation and death, in different types of cells, including vascular smooth muscle cells, endothelial cells and leukocytes [18–22]. Since vitamin E deficiencies have also 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 [23–26].

This study has been undertaken to investigate the possible alterations of antioxidant status and lipid peroxidation levels in uremic patients undergoing HD and to assess the efficiency of antioxidant protection of Vitamin E supplementation for 14 weeks.

2. Materials and methods

2.1. Chemicals

Cacodylic acid, pyrogallol, diethylentriaminpentaacetic acid, superoxide dismutase, 1,1,3,3,tetraethoxypropane, thiobarbituric acid, were obtained from Sigma (St. Louis, USA). Hydroxymethyl aminomethane, hydrochloric acid, sodium hydrogen phosphate, sodium dihydrogen phosphate, sodium hydroxide, perchloric acid, *n*-butanol were purchased from Merck (Darmstadt, Germany). Hydrogen peroxide was from Aldrich (Dorset, UK). RANSEL glutathione peroxidase kit was from RANDOX (Crumlin, UK).

2.2. Subjects

The study group was composed of 36 uremic patients (12 woman and 24 men), 21–75 years of age (mean 49 ± 14 years) undergoing maintenance HD three times weekly for an average of 41 months (range 5–108 months) at Gazi University Hospital in Ankara city. HD was performed for 4 h using cuprophan hollow-fiber dialyser (Hairdylena Medical, Germany) with blood flow rates of 200–300 ml/min. The adequacy of dialysis was monitored by measuring serum urea nitrogen and creatinine levels of patients, monthly. Patients with diabetes, chronic respiratory insufficiency, intercurrent infection and malignant tumors were excluded from the study. None of the patients had received any drug that could interfere with the measured parameters considered in our evaluation.

Table 1
Demographic and clinical details of study groups

	Hemodialysis group ($n=36$)	Control group ($n=36$)
Age, years (range)	49 ± 14 (21–75)	49 ± 14 (20–75)
Sex, M/F	24:12	24:12
Duration of dialysis therapy, months	41.4 ± 29.6	–

All dialysis patients (except two) underwent therapy with oral α-tocopherol (Ephynal-Roche) in a dosage of 600 mg/day (2 × 300 mg) for 14 weeks. Thirty-six healthy subjects of comparable age, sex, socioeconomic life style and smoking habits and with no history of renal disease chosen from university

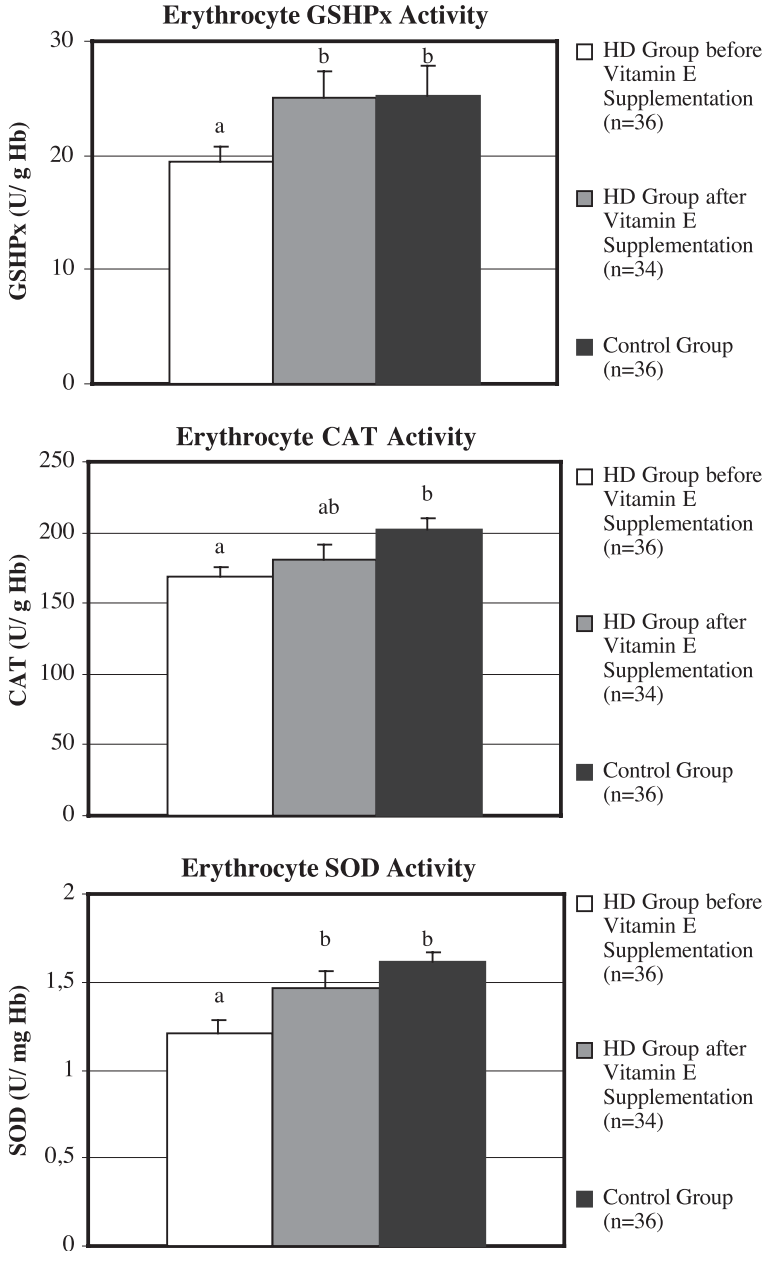

Fig. 1. Erythrocyte antioxidant enzyme activities (GSHPx, SOD and CAT) in the study groups. Superscripts of different letters (a, b) differ significantly ($p < 0.001$) from each other. Values are given as mean ± S.E.M.

staff were used as the control group (12 woman and 24 men). The age range of the controls was 20–75 years with a mean age of 49 ± 14 years.

The study was approved by an Ethical Committee according to the "Declaration of Helsinki". All subjects participated in the study voluntarily and all of them provided oral consent (in Turkish) before blood samples were drawn.

2.3. Sampling

Venous blood samples were collected in heparinized tubes in the morning after breakfast for the determination of lipid peroxidation levels and antioxidant enzyme activities [Glutathione peroxidase (GSHPx), superoxide dismutase (SOD), catalase (CAT)]. Centrifugation was performed at 800 × *g*, plasma was separated, and erythrocyte packages were prepared as recommended. All samples were immediately aliquoted and stored in a freezer at −80 °C until analysis.

2.4. Analytical measurements

2.4.1. Antioxidant enzyme activities

The activity of GSHPx was determined by using the RANSEL glutathione peroxidase kit, which is based on an enzymatic cycling assay as described by Paglia and Valentine [27]. The decrease in NADPH concentration, which is proportional to the enzyme, was measured spectrophotometrically by using cumen hydroperoxide as the substrate. One enzyme unit was defined as the amount of enzyme that transforms 1 μmol of NADPH to NADP per minute at 37 °C.

The activity of CAT was measured spectrophotometrically at 240 nm as the decomposition of H_2O_2 [28]. One unit of CAT activity was defined as the amount of enzyme required to decompose 1 μmol of H_2O_2 in 1 min. The specific activities for GSHPx and CAT were expressed in units per gram of hemoglobin. The SOD activity was determined by monitoring the auto-oxidation of pyrogallol at 420 nm [29]. One enzyme unit was defined as the amount of enzyme required to inhibit the rate of pyrogallol auto-oxidation by 50%. The specific activity for SOD was expressed in units per milligram of hemoglobin.

2.5. Lipid peroxidation levels

Lipid peroxidation levels were quantified by measuring thiobarbituric acid reactive substances (TBARS) by spectrofluorometric assay described by Richard et al. [30]. TBARS is expressed as nanomoles of malondialdehyde per litre of plasma.

2.6. Statistical analysis

Experimental data were analysed with ANOVA followed by LSD test using SPSS Software version 10.0 (SPSS, Chicago, IL, U.S.A.). Correlations be-

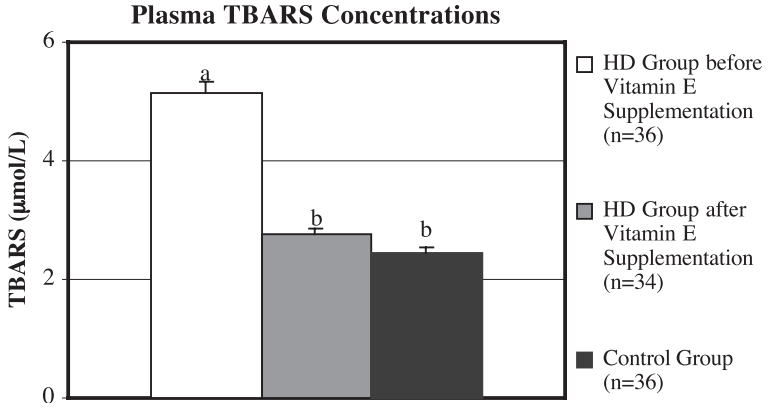

Fig. 2. Plasma TBARS concentrations in the study groups. Superscripts of different letters (a, b) differ significantly ($p < 0.001$) from each other. Values are given as mean ± S.E.M.

tween variables were evaluated by using Pearson's correlation coefficients. Values are given as mean ± S.E.M.

3. Results

Information relating to each patient including sex, age and duration of HD therapy is shown in Table 1. There was no significant difference among the groups studied with respect to demographic and clinical data.

HD therapy caused significant decreases in the activities of antioxidant enzymes compared to the control values ($p < 0.001$ by LSD test) (Fig. 1). It was also observed that lipid peroxidation levels in HD patients measured as TBARS levels were increased significantly ($p < 0.001$ by LSD test). A significant correlation was only found between GSHPx activity and duration of dialysis in HD patients ($r = -0.46$; $p < 0.01$).

Vitamin E supplementation (600 mg/day) for 14 weeks caused a significant decrease in the elevated TBARS levels by HD ($p < 0.001$) (Fig. 2). It was also observed a significant increase in GSHPx and SOD activities by Vitamin E supplementation ($p < 0.001$). The observed enhancement in the CAT activity in HD group after vitamin E supplementation was found not to be statistically significant compared to the values before supplementation (Fig. 1). There was no sex difference for any parameter within the groups.

4. Discussion

Although a direct cause–effect relationship between HD and oxidative stress-related diseases has not been definitively demonstrated, it has been suggested that oxidative damage can play a role in many conditions associated with end-stage renal complications such as cardiovascular and infectious diseases, cancer, diabetes, disorders of peripheral and central nervous system, anemia and accelerated aging [1,4,31–33]. There may be several potential sources of increased free radical production in chronic renal failure and the presence of oxidative stress appears to be a multifactorial phenomenon. An increased production of prooxidants, including ROS generated by activated leukocytes, auto-oxidizing carbonyl, transition metals and probably other toxins with different molecular weight, defective antioxidant protection and increased susceptibility to plasma lipid oxidation can cause the production of oxidative damage during HD. It is also reported that HD membrane materials have been described to play a central role in ROS production interfering with the activation of polymorphonuclear cell and monocyte oxygen metabolism [34,35]. A weakening of antioxidant defenses caused by HD may be characterized by leakage and consumption of hydrophilic antioxidants during dialysis; consumption of liposoluble/lipoprotein-associated antioxidants; changes in the lipid composition of biological fluids and cell membranes and/or a deficit in cofactors and damage to antioxidant enzymes. Altered antioxidant defense mechanisms seem to be one of the important factors leading to peroxidation. However, the data of HD patients about antioxidant enzyme activities (GSHPx, SOD and CAT) are controversial. The activities of these enzymes were variably reported to be decreased, increased or unchanged in erythrocytes of HD patients [36–40]. In the present study, erythrocyte GSHPx, SOD and CAT activities in HD group before supplementation were found to be lower compared to the control group ($p < 0.001$) in agreement with some of these reports. On the other hand, there are several reports showing the increase in the lipid peroxidation levels in patients with chronic renal failure, particularly undergoing HD [36,38,41–43]. However, some studies indicated that an individual dialysis session lowered plasma MDA [44] or that MDA levels were not enhanced in HD patients [45]. The findings of the present study demonstrated a weakening of antioxidant defense system and the increased levels of lipid peroxidation in HD patients. Moreover, the significant correlation between duration of HD therapy and GSHPx activity in our study suggested the importance of therapy period in the complications of HD related to defective antioxidant system.

The hypothesis that increased oxidative stress is a factor in dialysis pathology has led to use antioxidant supplements or more compatible dialysis filter containing vitamin E coating on the blood-exposed surface. The utilization of vitamin E-enriched liposomes is proposed to be the most recent approach [46]. However, results from these investigations are not yet conclusive. Galli et al. [24] showed that oral

supplementation of vitamin E (800 mg/day for a period of 3 weeks) slightly but not significantly decreased TBARS levels, but a significant effect on the plasma fatty acid (PUFA) profile of HD patients was observed. However, a significant decrease in TBARS concentrations and an increase Vitamin E/triglyceride ratio were observed after 1 month of treatment with vitamin E-coated membrane dialyzer [24]. Mydlik et al. [47] found that HD with conventional HD membrane led to an increase of MDA levels. The activity of SOD was low and GSHPx activity was observed to be higher than normal range. No influence of oral supplementation with vitamin E (400 mg after each HD session) for 3 weeks on plasma MDA and RBC GSHPx was found. There was a tendency toward the normalization of the activity of SOD after the treatment with vitamin E-coated membrane and oral vitamin E supplementation. On the other hand, in agreement with our results, there are also some studies that indicated the protective effects of vitamin E on the increased lipid peroxidation in HD patients [25,26,41,42]. Bayes et al. [48] showed that oral administration of vitamin E (400 mg at the end of each HD session for 3 months) caused a significant decrease in MDA concentrations and oxidized anti-LDL antibodies, two lipid peroxidation markers, in HD patients. Cristol et al. [25] also demonstrated that oral vitamin E supplementation (500 mg daily) for 6 months progressively restored the abnormally low RBC vitamin E concentrations towards the normal levels in dialysis patients. It was also observed a concomitant progressive decrease in MDA concentrations, suggesting an associated diminution in oxidative stress [25]. Inal et al. [26] reported a significant enhancement in SOD and CAT activities along with a significant decrease in MDA levels by oral vitamin E therapy (200 mg/day) during 10 months. These results suggest that the efficiency of vitamin E has been dependent on the duration of therapy as well as its dose. Our findings also showed that a 14-week oral supplementation of vitamin E in a dosage of 600 mg/day caused a significant protective effect against oxidative damage in HD patients evidenced by decreased TBARS concentrations and increased antioxidant enzyme activities. Vitamin E is recognized as a powerful lipophilic chain-breaking antioxidant that delays lipid peroxidation. Apart from antioxidant properties, new functions of this antioxidant have been shown in polymorphonuclear leukocytes, especially a decrease of superoxide production by activated phagocytes [49]. It is also demonstrated that it contributes to the regulation of processes such as metabolic activity, proliferation and death in different types of cells [18–22]. Supplementation of HD patients with vitamin E has been found to reduce composite cardiovascular disease endpoints and myocardial infarction [50]. Present findings provided further evidence on beneficial effect of vitamin E in the patients undergoing maintenance HD due to antioxidant-dependent or independent properties of vitamin E.

In conclusion, a significant increase in TBARS concentrations as a marker of lipid peroxidation and significant decreases in the activities of antioxidant enzymes (GSHPx, SOD and CAT) were observed in the uremic patients undergoing maintenance HD. Oral vitamin E supplementation for 14 weeks caused an enhancement in the activities of GSHPx and SOD and a decrease in lipid peroxidation levels significantly. It was also observed a slight but not significant increase in the activity of CAT by vitamin E. These findings suggest the probability of an antioxidant defence damage and the possible preventive role of Vitamin E supplementation against this damage in HD patients.

References

[1] Galli F, Canestrari F, Bellomo G. Pathophysiology of the oxidative stress and its implication in uremia and dialysis. Contrib Nephrol 1999;127:1–31.
[2] Miyata T, Fu TX, Kurokawa K, Thorpe SR, Baynes JW. Autooxidation products of both carbohydrates and lipids are increased in uremic plasma: is there oxidative stress in uremia? Kidney Int 1998;54:1290–5.
[3] Giorillo C, Oliviero C, Rizzuti G, Nediani C, Pacini A, Nassi P. Oxidative stress and antioxidant defences in renal patients receiving regular hemodialysis. Clin Chem Lab Med 1998; 36:149–53.
[4] Hasselwander O, Young IS. Oxidative stress in chronic renal failure. Free Radic Res 1998;29:1–11.
[5] Galli F, Canestrari F, Buoncritiani U. Biological effects of oxidant stress in haemodialysis: the possible roles of vitamin E. Blood Purif 1999;17:79–94.
[6] Canaud B, Cristol J, Moreno M, leray-Moregues H, Bosc J, vaussenat F. Imbalance of oxidants and antioxidants in hemodialysis patients. Blood Purif 1999;17:99–106.
[7] Combe C, Pourtein M, Precigout V, et al. Granulocyte activa-

tion and adhesion molecules during hemodialysis with cuprophan and high flux biocompatible membrane. Am J Kidney Dis 1994;24:437–42.
[8] Kuwahara T, Market M, Wauters JP. Neutrophil oxygen radical production by dialysis membranes. Nephrol Dial Transplant 1988;3:661–5.
[9] Iuliano L, Colavita AR, Leo R, Pratico D, Violi F. Oxygen free radicals and platelet activation. Free Radic Biol Med 1997;22:999–1006.
[10] Foley RN, Parfrey PS, Sarnack MJ. Cardiovascular diseases in chronic renal failure. Am J Kidney Dis 1998;32:S112–9.
[11] Rigatto C, Singal PK. Oxidative stress in uremia: impact on cardiac disease in dialysis patients. Semin Dial 1999;12:91–6.
[12] Locatelli F, Del Vecchio L, Manzoni C. Morbidity and mortality on maintenance hemodialysis. Nephron 1998;80:380–400.
[13] Lindsay RM, Moorthy AV, Koens F, Linton AL. Platelet function in dialyzed patients with chronic renal failure. Clin Nephrol 1975;4:52–7.
[14] Kikuchi Y, Koyama T, Koyama Y, et al. Red blood cell deformability in renal failure. Nephron 1982;30:8–14.
[15] Ritz E, Deppisch R, Sitier E, Hansch G. Atherogenesis and cardiac death: Are they related to dialysis procedure and biocompatibility? Nephrol Dial Transplant 1994;9:165–72.
[16] Huysmans K, Lins RI, Daelemans R, Zachee P, DeBroe ME. Hypertension and accelerated atherosclerosis in endstage renal disease. J Nephrol 1998;11:185–95.
[17] Chow CK. Vitamin E and oxidative stress. Free Radic Biol Med 1991;11:215–32.
[18] Riccralelli R, Tasinato A, Clement S, Ozer NK, Boscoboinik A, Azzi A. Alpha tocopherol specially inactivates cellular protein kinase C alpha by changing its phosphorylation state. Biochem J 1998;15:243–9.
[19] Galli F, Rovidati S, Chiarantini L, Kulurianu H, Canestrari F, Buonaristani U. Bioreactivity and biocompatibility of a vitamin E-modified multi-layer hemodialysis filter. Kidney Int 1998;54:580–9.
[20] Devaraj S, Li D, Jialal E. The effect of alphatocopherol supplementation on monocyte function. J Clin Invest 1996;98: 756–63.
[21] Chan AC. Vitamin E and atherosclerosis. J Nutr 1998;128: 1593–6.
[22] Bendich A. Antioxidant vitamins and human immune response. In: Litwack G, editor. Vitamins and hormones. San Diego: Academic Press; 1996. p. 35–62.
[23] Satoh M, Yamasaki Y, Nagake Y, et al. Oxidative stress is reduced by the long-term use of vitamin E-coated dialysis filters. Kidney Int 2001;59:1943–50.
[24] Galli F, Varga Z, Balla J, et al. Vitamin E, lipid profile and lipid peroxidation in hemodialysis patients. Kidney Int 2001;59:S148–54.
[25] Cristol J.-P., Bosc J.-Y., Badiou S, et al. Erythropoetin and oxidative stress in hemodialysis: beneficial effects of vitamin E supplementation. Nephrol Dial Transplant 1997;12:2312–7.
[26] Inal M, Kanbak G, Sen S, Yetkin I, Akyuz F. The effect of long-term vitamin E therapy on the antioxidant enzymes and lipid peroxidation in hemodialysis patients. Ann Med Sci 1999;8:84–7.
[27] Paglia DE, Valentina WN. Studies on the quantitative and qualitative characterisation of erythrocyte glutathione peroxidase. J Lab Clin Med 1967;70:158–69.
[28] Aebi H. Catalase. In: Bergmeyer HU, editor. Methods of enzymatic analysis. New York: Academic Press; 1974. p. 673–7.
[29] Marklund S, Marklund G. Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. Eur J Biochem 1974; 47:469–74.
[30] Richard MJ, Portal B, Meo J, Coudray C, Hadjian A, Favier A. Malondialdehyde kit evaluated for determining plasma and lipoprotein fractions that react with thiobarbituric acid. Clin Chem 1992;38:704–9.
[31] Tetta C, Biasioli S, Schiavon R, et al. An overview of hemodialysis and oxidative stress. Blood Purif 1999;17:118–26.
[32] Halliwell B, Gutteridge JMC. Free radicals in biology and medicine. Oxford: Clarendon Press; 1989.
[33] Loughrey CM, Young IS, Lightbody JH, Mc Master D, Mc Namee PT, Trimble ER. Oxidative stress in hemodialysis. OJM 1994;87:679–83.
[34] Cristol JP, Canaud B, Rabesandratana H, Gailard I, Serre A, Mion C. Enhancement of reactive oxygen species production and cell surface markers expression due to hemodialysis. Nephrol Dial Transplant 1994;9:389–94.
[35] Naito H, Azuma M, Hashimoto Y. Clinical assessment of dialyzer using regenerated cellulose membrane with modified surface. Clin Rep 1994;28:589–95.
[36] Chen C, Liaw J, Juang J, Lin T. Antioxidant enzymes and trace elements in hemodialyzed patients. Biol Trace Elem Res 1997;58:149–57.
[37] Durak I, Akyol O, Basesme E, Canbolat O, Kavutcu M. Reduced erythrocyte defense mechanisms against free radical toxicity in patients with chronic renal failure. Nephron 1994;66:76–80.
[38] Turi S, Nemeth I, Vargha I, Matkovicks B, Dubos E. Erythrocyte defense mechanisms against free oxygen radicals in hemodialyzed uremic children. Pediatr Nephrol 1991;5: 179–83.
[39] Paul J-L, Sall N-D, Soni T, et al. Lipid peroxidation abnormalities in hemodialyzed patients. Nephron 1993;64:106–9.
[40] Asoyama K, Shiki Y, Ito H, et al. Antioxidant enzymes and lipoperoxide in blood in uremic children and adolescents. Free Radic Biol Med 1990;9:105–9.
[41] Taccone-Gallucci M, Giardini O, Ausiello C, et al. Vitamin E supplementation in hemodialysis patients: effect on peripheral blood mononuclear cells lipid peroxidation and immune response. Clin Nephrol 1986;25:81–6.
[42] Giardini O, Taccone-Gallucci M, Lubrano R, et al. Effects of alpha-tocopherol administration on red blood cell membrane lipid peroxidation in hemodialysis patients. Clin Nephrol 1984;21:174–7.
[43] Dasgupta A, Hussain S, Ahmad S. Increased lipid peroxidation in patients on maintenance hemodialysis. Nephron 1992;60:56–9.
[44] Daschner M, Lenhartz H, Botticher D, Schaefer F, Wollschlager M, Mehls O. Influence of dialysis on plasma lipid per-

oxidation products and antioxidant levels. Kidney Int 1996; 50:1268–72.
[45] Erdogan C, Unlucerci Y, Turkmen A, Kuru A, Cetin O, Bekpınar S. The evaluation of oxidative stress in patients with chronic renal failure. Clin Chim Acta 2002;322:157–61.
[46] Wratten ML, Navino C, Tetta C, Verzetti G. Hemolipodialysis. Blood Purif 1999;17:127–33.
[47] Mydlik M, Derzsiova K, Racz O, Sipulova A, Lovasova E, Petrovicova J. A modified dialyzer with vitamin E and antioxidant defense parameters. Kidney Int 2001;59:S144–7.
[48] Bayes B, Pastor MC, Bonal J, Junca J, Romero R. Homocysteine and lipid peroxidation in hemodialysis: role of folinic acid and vitamin E. Nephrol Dial Transplant 2001;16:2172–5.
[49] Cachia O, Leger CL, Descomps B. Monocyte superoxide production is highly sensitive and inversely related to normal changes of low density lipoprotein in alpha tocopherol. Atherosclerosis 1998;138:263–9.
[50] Boaz M, Smetana S, Weinstein T, et al. Secondary prevention with antioxidants of cardiovascular disease in endstage renal disease (SPACE): randomized placebo-controlled trial. Lancet 2000;356:1213–8.