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Oxidative stress and damage induced by abnormal free radical reactions and IgA nephropathy

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Abstract: Objective: To estimate the oxidative stress and oxidative damage induced by abnormal free radical reactions in IgA nephropathy (IgAN) patients' bodies. Methods: Seventy-two IgA N patients (IgANP) and 72 healthy adult volunteers (HAV) were enrolled in a random control study design, in which the levels of nitric oxide (NO) in plasma, lipoperoxide (LPO) in plasma and in erythrocytes, and vitamin C (VC), vitamin E (VE) and β-carotene (β-CAR) in plasma as well as the activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) in erythrocytes were determined with spectrophotometric mothods. Results: Compared with the HAV group, the averages of NO in plasma, and LPO in plasma and in erythrocytes in the IgANP group were significantly increased (P<0.0001), while those of VC, VE and β-CAR in plasma as well as those of SOD, CAT and GPX in erythrocytes in the IgANP group were significantly decreased (P<0.0001). Linear correlation analysis showed that with the increase of the values of NO, and LPO in plasma and in erythrocytes, and with the decrease of those of VC, VE, β-CAR, SOD, CAT and GPX in the IgAN patients, the degree of histological damage of tubulointerstitial regions was increased gradually (P<0.0001); and that with the prolongation of the duration of disease the values of NO, and LPO in plasma and erythrocytes were increased gradually, while those of VC, VE, β-CAR, SOD, CAT and GPX were decreased gradually (P<0.005). The discriminatory correct rates of the above biochemical parameters reflecting oxidative damage of the IgAN patients were 73.8%–92.5%, and the correct rates for the HAV were 70.0%–91.3% when independent discriminant analysis was used; and the correct rate for the IgAN patients was increased to 98.8%, the correct rate for the HAV was increased to 100% when stepwise discriminant analysis was used. The above biochemical parameters' reliability coefficient (alpha) were used to estimate the oxidative damage of the IgAN patients as 0.8145, the standardized item alpha=0.9730, F=53273.5681, P<0.0001. Conclusions: A series of free radical chain reactions caused serious pathological aggravation in the IgANP' bodies, thus resulting in oxidative damage in their bodies. In treating IgANP, therefore, it is necessary that suitable dose antioxidants should be supplemented to them so as to alleviate the oxidative damage in their bodies.

Key words: Chronic glomerulonephritis, Free radicals, Oxidation, Lipoperoxidation, Nitric oxide, Lipoperoxide, Antioxidant, Antioxidase, Oxidative stress, Oxidative damage

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INTRODUCTION

IgA nephropathy (IgAN) is a set of renal diseases induced by pathologic change of glomerulus, and its inciting causes include a variety of infectious agents such as upper respiratory and dermal streptococcal infections and bacterial endocarditis as well as the deposition of immune complexes in autoimmune diseases such as SLE (Appel, 1996; Kasiske and Keane, 1999). Some authors reported that their study of pathophysiology of glomerulonephritis showed that the content of nitric oxide in the exhaled air of chronic glomerulonephritis patients markedly increased (Kakoki *et al*., 1999); and that in the bodies of chronic glomerulonephritis patients (or experimental animals with chronic glomerulonephritis) the serum level of lipoperoxide or malondialdehyde (MDA) significantly increased; but that the activities of superoxide dismutase, catalase and glutathione peroxidase significantly decreased (McCarthy *et al*., 1998;

Zima *et al*., 1996). However, up to now, we are not aware of reports on abnormal metabolism of nitric oxide and abnormal change of free radical chain reactions in IgAN patients' bodies, or about the relationship between IgAN and oxidative stress, and oxidative damage. To investigate the relationship between the oxidative damage induced by abnormal free radical reactions and the IgAN, 72 IgAN patients (IgAN P) and 72 healthy adult volunteers (HAV) were enrolled in a random control study design, in which the levels of nitric oxide (NO), and lipoperoxide (LPO) in plasma and erythrocytes, and vitamin C (VC), vitamin E (VE) and β-carotene (β-CAR) in plasma as well as the activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) in erythrocytes were determined by spectrophotometric methods. At the same time, the differences in the averages of the above biochemical parameters between the IgAN group and the HAV group were analyzed. The linear correlation between the biochemical parameters with the degree of histological damage of tubulointerstitial regions and that between the duration of disease with the biochemical parameters for 72 IgAN patients were analyzed. Discriminant analysis was carried out for 72 IgAN patients and 72 HAV, and the above biochemical parameters' reliability coefficient (alpha) was used to estimate the oxidative damage of the IgAN patients' bodies.

METHODS

Study design

A random control design was used in this research. To obtain an objective conclusion, the principles of random sampling, control, replication and equilibrium, and the management factor, experimental effect and subjects, and the inclusion criteria and exclusion criteria of subjects, were taken into full consideration, and were strictly followed in the study (Lang and Secic, 1997; Zhou *et al*., 2000). The pathologist reading the biopsies did not know the laboratory data, the laboratory assistant doing each of the above experiments did not know the results of the biopsies.

Subjects

1. IgA nephropathy patients (IgANP)

Following "Select Cases–Random Sample" of "SPSS 11.0 for Windows", 72 IgAN patients were randomly sampled from 95 IgAN patients whose diagnoses were confirmed by renal biopsy, and accorded with the diagnostic criteria and the inclusion criteria and exclusion criteria (Appel, 1996; Kasiske and Keane, 1999), in the Second Affiliated Hospital of College of Medicine, Zhejiang University. Pathology included mesangial proliferative glomerulonephritis, mesangiocapillary glomerulonephritis, focal glomerulonephritis and sclerosing glomerulonephritis. The clinical situation involved hypertension (9.7%), nephrotic range proteinuria (38.9%) and hematuria (100%). Their ages, gender, blood pressures, serum creatinines, 24-hour urinary protein excretion, duration of disease since renal biopsy-proven, smoking history and alcohol abuse history are presented in Table 1. The patients' extent of histological damage of tubulointerstitial regions was divided into four gradings by Masson Coloration and randomly sampled 50 sights, I: the interstitial regions were basically normal, mild tubule degeneration and dilataltion; II: fibrosis of the interstitial regions, tubule atrophy <20%, inflammatory cells infiltration scattered; III: fibrosis of the interstitial regions and tubule atrophy was 30%–50%, inflammatory cells infiltration scattered and/or widespread; IV: fibrosis of the interstitial regions and tubule atrophy >50%, inflammatory cells infiltration scattered and/or widespread (Liu and Li, 1992). Routine feces examination, radiographs and electrocardiograms of these IgAN patients were all within normal ranges. Their medical history associated with brain, heart, lung, liver, hypertension, hyperlipidemia, chronic bronchitis, diabetes, atherosclerosis and tumors were all excluded, and patients with chronic systemic inflammation, such as patients with systemic vasculitis, patients with elevated C-reactive protein, etc., were all excluded. They were all volunteers in this study.

2. Healthy adult volunteers (HAV)

Following "Select Cases–Random Sample" of "SPSS 11.0 for Windows", 72 HAV were randomly sampled from 200 HAV whose diagnoses were confirmed by comprehensive physical examinations at the Second Affiliated Hospital of the School of Medicine, Zhejiang University. Their ages, gender, blood pressures, smoking history and alcohol abuse

history are presented in Table 1. They were within normal ranges in their routine blood, urine and feces examinations, radiographs and electrocardiograms. Those with medical history associated with brain, heart, lung, liver, kidney and other organs as well as hypertension, hyperlipoidemia, chronic bronchitis, autoimmune disease, diabetes, atherosclerosis and tumors were all excluded. They were all volunteers in this study.

There was no significant difference between the averages for age, gender, blood pressure in the IgANP group and in the HAV group. All the above subjects did not have history of smoking and alcohol abuse (Table 1).

The demographic data and some other data of the 72 IgANP and 72 HAV are presented in Table 1.

The above subjects were never exposed to radiation, or engaged in work exposing them to intoxicating materials or pesticides. Within the prior month, all the subjects had not taken any antioxidant supplements such as vitamin C, vitamin E, β-carotene, ginkgo biloba, tea polyphenols or other similar substances before they enrolled as volunteers in this study. And the IgAN patients, in general, had not taken fruits and green foodstuff containing rich antioxidative vitamins because their diets were restricted strictly.

3. Collection and pretreatment of blood samples

Fasting venous blood samples of all the subjects were collected in the morning and heparin sodium was added as anticoagulant. The separated plasma and erythrocytes were stored at −50 °C immediately (Zhou *et al*., 2000).

4. Measurement of biomedical substances

The spectrophotometry of coloration of α-naphthylamine and nitrite was used to determine plasma NO level expressed as nmol/L; the spectrophotometry of thiobarbituric acid reactive substances (TBARS) was used to determine plasma LPO level expressed as μmol/L; the spectrophotometry of TBARS was used to determine erythrocytic LPO level expressed as nmol/(g·Hb); the spectrophotometry of ferrozine coloration was used to determine plasma VC and VE levels expressed as μmol/L; β-CAR was extracted from plasma with a mixture of ethanol and petroleum ether, and plasma β-CAR level was assayed with spectrophotometry and expressed as μmol/L; the spectrophotometry of inhibiting pyrogallol auto-oxidation was used to determine erythrocytic SOD activity expressed as U/(g·Hb); the spectrophotometry of coloration of hydrogen peroxide and acetic acid-potassium dichromate was used to determine erythrocytic CAT activity expressed as K/(g·Hb); improved Hafeman's spectrophotometry was used to determine the erythrocytic GPX activity expressed as U/(mg·Hb) (Zhou *et al*., 2000).

In the determination of the above biochemical substances and enzymes, the main analytical reagents, such as vitamin C, vitamin E, β-carotene, disodium 5,6-diphenyl-3-(2-pyridyl)-1,2,4-triazinedisulfonate (ferrozine), Cu/Zn-superoxide dismutase, catalase, α-naphthylamine, 1,2,3-trihydroxybenzene (pyrogallol), 1,1,3,3-tetraethoxypropane, 2-thiobarbituric acid, were all purchased from SIGMA® Chemical Company, USA; and the other analytical reagents were all produced in China. The fresh quadruply distilled

Table 1 The demographic data and some other data on the IgANP group and the HAV group

Item	CGNP (n=72)	HAV (n=72)	
Age (year)	21–30 (25.0±2.4)	21–30 (25.3±2.4)	t=0.2267*, P=0.7191
Gender	M=52, F=20	M=50, F=22	χ^2=1.0123**, P=0.3858
Systolic pressure (mmHg)	122–138 (132.12±3.42)	117–135 (131.05±3.60)	t=1.9862*, P=0.0545
Diastolic pressure (mmHg)	76–84 (80.08±3.32)	70–85 (81.14±4.11)	t=1.7400*, P=0.0838
Serum creatinine (μmol/L)	155.32–370.45 (251.68±37.04)	–	–
Urinary protein excretion (g/24 h)	0.89–6.75 (3.41±1.71)	–	–
Duration of disease since renal biopsy-proven (year)	1–5 (2.9±0.9)	–	–
Smoking history	NO	NO	–
History of alcohol abuse	NO	NO	–

* Independent samples t test, ** Pearson chi-square test

water was prepared with a quartz glass distilling apparatus. In the determination of the above biochemical substances and enzymes, the main analytical instruments included Hewlett Packard 8453-Spectrophotometer, USA, etc.

In the determination of the above biochemical substances, the standardization of experiment, e.g. the same batch number of each reagent, the same quality control, the same lab assistant, and identical analytical apparatus were strictly used for every experiment in order to control and decrease the error and bias produced during the determining process of the above experiment, and to ensure the analytical quality of determinations (Lang and Secic, 1997; Zhou *et al*., 2000).

5. Medical statistical analysis

All data were statistically analyzed with SPSS 11.0 for Windows statistic software using a Compad Pentium IV/2.4 MHz computer. All the parameters in this study followed normal distributions (as shown by Kolmogorov-Smirnov Z test), and are expressed as mean plus or minus standard deviation ($\bar{\chi} \pm s$) at 95% confidence interval (95% CI). Hypothesis testing methods included independent-samples t test, chi-square test (χ^2 test), Pearson product-moment correlation analysis, Spearman correlation analysis, discriminant analysis, and reliability analysis. In the statistical analysis, the level of hypothesis testing (α) was set at ≤0.05 in order to avoid false positives (α-error), and the hypothesis testing power was set at ≥0.80 to avoid false negatives (β-error) (Lang and Secic, 1997; Zhou *et al*., 2000).

RESULTS

Comparison between the averages ($\bar{\chi} \pm s$) of the biochemical parameters in the IgANP group and the HAV group

Compared with the HAV group, the averages of NO in plasma, and LPO in plasma and erythrocytes in the IgANP group were significantly increased (P<0.0001), and those of VC, VE and β-CAR in plasma as well as those of activities of SOD, CAT and GPX in erythrocytes in the IgANP group were significantly decreased (P<0.0001) (Table 2).

95% CI of the averages of the biochemical parameters in the IgANP group and the HAV group

The lower limits of the 95% CI of the averages of NO in plasma, and LPO in plasma and erythrocytes in the IgANP group were greater than the upper limits

Table 2 Comparison between the averages ($\bar{\chi} \pm s$) of the biochemical parameters in the IgANP group and in the HAV group

Group			IgANP	HAV	t^*	P
	n		72	72		
Oxidative substances	Plasma	NO (nmol/L)	560.7±117.2 (534.5–586.9)	360.2±83.4 (343.1–381.5)	12.3675	0.0001
		LPO (μmol/L)	14.15±2.07 (13.61–14.71)	11.32±1.63 (10.83–11.61)	10.1568	0.0001
	Erythrocyte	LPO [nmol/(g·Hb)]	43.60±5.32 (42.54–45.00)	29.05±4.32 (28.31–30.10)	17.0128	0.0001
Antioxidative substances	Plasma	VC (μmol/L)	35.85±9.17 (34.21–38.39)	55.12±13.76 (52.71–58.03)	10.3165	0.0001
		VE (μmol/L)	16.62±4.53 (15.64–18.41)	25.88±4.57 (24.97–26.87)	13.5538	0.0001
		β-CAR (μmol/L)	1.23±0.34 (1.21–1.36)	1.73±0.45 (1.64–1.82)	7.4942	0.0001
	Erythrocyte	SOD [U/(g·Hb)]	1734.7±131.4 (1685.1–1754.2)	2111.5±150.6 (2069.4–2143.8)	16.9981	0.0001
		CAT [K/(g·Hb)]	226.8±56.1 (213.8–238.9)	306.4±75.1 (289.3–323.5)	7.3936	0.0001
		GPX [U/(mg·Hb)]	20.25±5.33 (18.79–21.22)	29.12±7.03 (27.65–30.77)	8.8657	0.0001

*Independent-samples t test. The figures in parentheses are 95% confidence interval (95% CI)

of 95% CI of the same biochemical parameters in the HAV group. The upper limits of the 95% CI of the averages of VC, VE and β-CAR in plasma as well as SOD, CAT and GPX in erythrocytes in the IgANP group were less than the lower limits of 95% CI of the same biochemical parameters as those in the HAV group (Table 2).

Linear correlation between the IgAN patients' every biochemical parameter with the degree of histological damage of tubulointerstitial regions

The results showed that with the increase of the values of NO in plasma, and LPO in plasma and erythrocytes, and with the decrease of those of VC, VE and β-CAR in plasma as well as those of SOD, CAT and GPX in erythrocytes in the IgAN patients, the degree of histological damage of tubulointerstitial regions (DHDTR) was increased gradually (Table 3).

Linear correlation between the IgAN patients' duration of disease with every biochemical parameter

The results showed that with prolonged duration of disease, the values of NO in plasma, and LPO in plasma and erythrocytes were increased gradually, while those of VC, VE and β-CAR in plasma as well as those of SOD, CAT and GPX in erythrocytes were decreased gradually (Table 4).

Discriminant analysis for 72 IgAN patients and 72 HAV

In the present study, the discriminatory correct rates for the IgAN patients were 73.8%–92.5%, and those for the HAV were 70.0%–91.3% when single biochemical parameter of the IgAN patients and the HAV was used for independent discriminant analysis (Table 5).

The discriminatory correct rate for the IgAN patients was increased to 98.8%, and that for the HAV was increased to 100%, and 99.4% of original cases correctly classified when the all the above biochemical parameters of the IgAN patients and the HAV were used to conduct stepwise discriminant analysis. The main details were as follows: Canonical discriminant function coefficients: D=19.018+0.075 VE–0.022 SOD+0.727 plasma LPO+0.290 erythrocytic LPO+0.002 NO; functions at group centroids (unstandardized canonical discriminant functions evaluated at group means): IgANP group=7.197, and HAV group=–7.197.

Reliability analysis for the above biochemical parameters used to estimate the oxidative damage of the IgAN patients

The results of reliability analysis for the values of NO in plasma, LPO in plasma and erythrocytes, those of VC, VE and β-CAR in plasma as well as those of SOD, CAT and GPX in erythrocytes reflecting the oxidative damage of the IgAN patients were as follows: the reliability coefficient (alpha)=0.8145, the standardized item alpha=0.9730. Single measure intraclass correlation=0.1962, its 95% CI was from 0.1418 to 0.2689, and average measure intraclass correlation=0.8145, its 95% CI ranged from 0.7494 to 0.8688, F=5.3678, P<0.0001.

DISCUSSION

NO plays an important role in renal hemodynamics and renal function, and if the dynamic balance of NO metabolism is destroyed the kidney and/or other organs will produce pathological changes (Kakoki *et al*., 1999). LPO and its metabolic products, such as MDA, conjugated diene (CD), etc., can strongly attack DNA, proteins, enzymes, biological membranes, polyunsaturated fatty acids (PUFAs) and others in the human body, leading to generation of a large number of free radicals (FRs), and to lipoperoxidative damage of mesangial cells and renal tubular epithelial cell (Templar *et al*., 1999; Zima *et al*., 1996; Girotti, 1998; Mayes, 2000; McKee and McKee, 2000; Shah, 1991). VC, VE, β-CAR, SOD, CAT and GPX are the most important antioxidants and antioxidases in the human body, and they play important roles in scavenging oxygen free radicals (OFRs), such as superoxide anion radical ($O_2^-\cdot$), hydroxyl radical ($\cdot OH$) and other free radicals (FRs) as well as singlet oxygen ($^1O_2$), hydrogen peroxide (H_2O_2) and other reactive oxygen species (ROS) that are excessive in the human body, and in preventing physiological and pathological aggravation of a series of FRs chain reactions induced by $O_2^-\cdot$, thereby protecting biological membranes of cells against oxidative and lipoperoxidative damages. Marked decrease of the

Table 3 Linear correlation between the IgAN patients' every biochemical parameter with the degree of histological damage of tubulointerstitial regions (DHDTR)

Correlative item	*n*	Correlative coefficient (*r*)	*t*	P^*
Plasma NO with DHDTR	72	0.6651	7.8658	<0.0001
Plasma LPO with DHDTR	72	0.6052	6.7143	<0.0001
Erythrocytic LPO with DHDTR	72	0.5149	5.3051	<0.0001
Plasma VC with DHDTR	72	– 0.5862	6.3911	<0.0001
Plasma VE with DHDTR	72	– 0.5716	6.1527	<0.0001
Plasma β-CAR with DHDTR	72	– 0.5569	5.9224	<0.0001
Erythrocytic SOD with DHDTR	72	– 0.5292	5.5083	<0.0001
Erythrocytic CAT with DHDTR	72	– 0.6005	6.6330	<0.0001
Erythrocytic GPX with DHDTR	72	– 0.6150	6.8886	<0.0001

*Spearman correlation analysis

Table 4 Linear correlation between the IgAN patients' duration of disease with every biochemical parameter

Correlative item	*n*	Correlative coefficient (*r*)	*t*	P^*
Duration of disease with plasma NO	72	0.3246	3.0305	0.0033
Duration of disease with plasma LPO	72	0.3477	3.2747	0.0016
Duration of disease with erythrocytic LPO	72	0.5878	6.4176	<0.0001
Duration of disease with plasma VC	72	– 0.3557	3.3609	0.0012
Duration of disease with plasma VE	72	– 0.5142	5.2943	<0.0001
Duration of disease with plasma β-CAR	72	– 0.3711	3.5295	0.0007
Duration of disease with erythrocytic SOD	72	– 0.3650	3.4630	0.0009
Duration of disease with erythrocytic CAT	72	– 0.3687	3.5026	0.0009
Duration of disease with erythrocytic GPX	72	– 0.3950	3.7978	0.0003

* Pearson product-moment correlation analysis

Table 5 Discriminant analysis for every biochemical parameter of the IgAN patients and the HAV

Item		Constant	χ	Correct rate of discrimination to the IgAN patients (%)	Correct rate of discrimination to the HAV (%)
Plasma	NO	–4.528	0.010	85.0	83.8
	LPO	–6.862	0.537	73.8	82.5
Erythrocyt	LPO	–6.771	0.186	87.5	91.3
Plasma	VC	–3.935	0.085	81.3	72.5
	VE	–4.935	0.232	77.5	90.0
	β-CAR	–3.935	2.632	76.3	70.0
Erythrocyte	SOD	–13.526	0.007	92.5	90.0
	CAT	–3.963	0.015	75.0	70.0
	GPX	–3.861	0.157	76.3	71.3

levels of the above antioxidants and antioxidases in the human body can cause metabolic disorders and pathological aggravation of a series of FRs chain reactions, thus inducing a variety of diseases related to the abnormal reactions of FRs (Templar *et al*., 1999; Mayes, 2000; McKee and McKee, 2000; Kasiske and Keane, 1999; Sharma *et al*., 2000; Goldstein and Schnellmann, 1998).

The findings in the present study showed that in the IgAN patients' bodies the metabolism of NO presented serious disorders, that the dynamics between oxidation and antioxidation produced were gravely unbalanced, and that the oxidative stress led to bad pathological enhancement, thereby inducing severely oxidative damage and lipoperoxidative damage in their kidneys and bodies. There could be several interpretations. Evidence suggested that a variety of intraglomerular sources of NO (e.g., from

macrophages and endothelial cells), in response to inflammatory cytokines, mechanical stress, and other mediators (e.g., acetylcholine or bradykinin), affects the contractile state and therefore the physiological function of the mesangial cells (Kakoki *et al*., 1999). These inflammatory cytokines, especially interleukin-1 (IL-1), could activate immediately inducible nitric oxide synthase (iNOS), stimulate the synthesis and/or release of NO, thus producing a large amount of NO (Kakoki *et al*., 1999; Zhou *et al*., 2000). Excessive NO could inactivate antioxidants and antioxidases by reacting with some active groups in their molecular structures, could harm the function of mesangial cells (Goldstein and Schnellmann, 1998; Zhou *et al*., 2000). Meanwhile, the inflammatory cytokines and cells, phagocytes and other organic substances also released a large number of OFRs, ROS and other FRs, which provoked and accelerated the aggravation of the oxidative stress in the kidneys of the IgAN patients, resulting in large extent damage of kidneys and renal functions, such as the histological damage of glomeruli and tubulointerstitial regions, and so on (Mayes, 2000; McKee and McKee, 2000; Kasiske and Keane, 1999; Sharma *et al*., 2000; Goldstein and Schnellmann, 1998).

It has to be emphasized that most antioxidative vitamins, such as vitamin C and E, and β-carotene, have to be acquired from dietary sources because these vitamins cannot be synthesized in the human body. In general, everyday diets of IgAN patients were strictly restricted, their diets were very simple and lacked of nutrition, especially of VC, VE and β-CAR, due to the needs of dietotherapy. Nevertheless, the antioxidative-vitamins-poor diets cannot provide sufficient scavengers of OFRs, ROS and other FRs to keep the dynamic balance between oxidation and antioxidation (Zhou *et al*., 2000). In this condition, IgAN patients have to make use of a great quantity of antioxidants and antioxidases in their bodies in order to scavenge the excessive OFRs, ROS and other FRs, and to resume and keep dynamic balance between oxidation and antioxidation, and to decrease oxidative damage in their bodies, thereby further leading to the aggravation of the oxidative stress and the oxidative damage in the kidneys of the IgAN patients (Mayes, 2000; McKee and McKee, 2000; Kasiske and Keane, 1999; Sharma *et al*., 2000).

In this study, the findings of Spearman correlation analysis suggested that the biochemical parameters had close relation with the degree of histological damage of tubulointerstitial regions in the IgAN patients. And the findings of Pearson correlation analysis suggested that there were close relationship with the duration of disease in the IgAN patients. In addition, the findings of discriminant analysis for the IgAN patients and the HAV further proved this relationship.

The findings of reliability analysis all further showed that oxidation stress induced by excessive NO, OFRs, ROS and other FRs played very important roles in the oxidative damage and lipoperoxidative damage to the kidneys and renal function in the IgAN patients (Kasiske and Keane, 1999; Goldstein and Schnellmann, 1998).

In summary, the findings in the present study suggested that the dynamic balance between oxidation and antioxidation in the IgAN patients were in severe disorder, thereby leading to the oxidative damage and lipoperoxidative damage in their renal functions and bodies. We, therefore, recommend that antioxidant vitamins at suitable doses, such as vitamin C (300 mg, *tid*) and vitamin E (100 mg, *bid*), should be given to IgAN patients daily in order to alleviate oxidative damage and lipoperoxidative damage because these vitamins are free-radical scavengers and could have a protective effect against farther oxidative damage to IgA nephropathy patients (Templar *et al*., 1999; Zima *et al*., 1996; Shah, 1991; Sharma *et al*., 2000; Endreffy *et al*., 1991; Trachtman *et al*., 1996).

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