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The Evaluation of Thiol/Disulfide Homeostasis in Diabetic Nephropathy

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Abstract

Thiol/disulfide homeostasis plays a critical role in antioxidant defense, detoxification, apoptosis, enzyme activities, transcription and cellular signal transduction. It is known that thiol levels decrease due to thiol oxidation, disulfide levels increase and thiol/disulfide ratio increase in diabetics. However, it is not known that how diabetic thiol/disulfide balance changes in diabetic nephropathy. Therefore, we aimed to investigate thiol/disulfide balance in diabetic patients with nephropathy.

61 patients with type 2 diabetes and 26 healthy volunteers were included. Proteinuria was tested by measuring microalbumin/creatinine ratio in spot urine. The groups named as follows: healthy volunteer group 1, normal albuminuric group 2 (n=17), middle albuminuric group 3 (n=24) and severe proteinuric group 4 (n=20). Thiol/disulphide homeostasis concentrations were measured using method developed by Erel et al.

Mean blood urea and creatinine levels were found to be significantly higher and GFR level was found to be significantly lower in group 4 than in the other 3 groups. Native thiol levels are significantly lower in diabetic groups than in healthy controls and in diabetic subjects with moderate and severe proteinuria, compared to healthy and diabetics with normal proteinuria. Total thiol level was significantly lower in groups 2 and 3 than group 1 and 2. Disulfide/native thiol and disulfide/total thiol ratios were significantly higher in the diabetic groups than in the healthy control group and in the group 4 than in the group 2.

In our study, it was determined that the level of native and total thiols decreased significantly in diabetic patients with nephropathy and the balance was disrupted in favor of disulfide. We conclude that the reduction in thiol levels associated with increased oxidative stress may be one of the important factors in the development and progression of diabetic nephropathy.

Table 1. Clinical and laboratory parameters between groups.

Parameters	Group 1 (n=26)	Group 2 (n=17)	Group 3 (n=24)	Group 4 (n=20)	p
Gender (female/male)	13/13	7/10	15/9	9/11	NS
Age (year)	48.7±10.4	50.7±10.1	54.6±9.0	53.4±9.1	NS
Glucose (mg/dL)	90.4±8.8[a,b,c]	155.9±37.0[d]	216.0±98.4	198.0±89.0	<0.001
A1c (%)	-	7.9±2.1[e]	8.7±1.6	9.5±2.3	0.046
Urea (mg/dL)	31.1±9.9[c]	30.0±5.5[f]	33.3±15.3[g]	50.6±30.0	0.001
Creatinine (mg/dL)	0.8±0.1[c]	0.8±0.1[h]	0.9±0.2[i]	1.1±0.5	<0.001
GFR (mL/dk)	87.2±6.8[j]	98.1±14.6[h]	90.5±16.3[i]	72.5±27.8	<0.001
Total cholesterol (mg/dL)	169.9±37.4	176.1±43.8	189.0±49.3	189.3±40.9	NS
Triglyceride (mg/dL)	138.9±55.4[k]	189.4±88.9	237.7±176.0	189.3±77.7	0.025
HDLC (mg/dL)	46.2±9.5[l]	40.9±9.7	37.2±10.5	41.5±8.5	0.015
LDLC (mg/dL)	97.8±33.3	97.4±39.1	109.7±28.7	109.9±32.5	NS

[a]: p=0.003 between Group 1 and Group 2; [b]: p<0.001 between Group 1 and Group 3; [c]: p<0.001 between Group 1 and Group 4; [d]: p=0.007 between Group 2 and Group 3 a; [e]: p=0.014 between Group 2 and Group 4; [f]: p=0.001between Group 2 and Group 4; [g]: p=0.002between Grup 3 and Grup 4; [h]: p<0.001between Grup 2 and Grup 4; [i]: p=0.001 between Grup 3 and Grup 4; [j]: p=0.006 between Grup 1 and Grup 4; [k]: p=0.002between Grup 1 and Grup 3; [l]: p=0.001between Grup 1 and Grup 3.

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Table 2. Comparison of thiol and disulfide parameters between groups.

Parameters	Group 1 (n=26)	Group 2 (n=17)	Group 3 (n=24)	Group 4 (n=20)	p
Native thiol (µmol/L)	426.4±44.3[a.b.c]	386.2±35.3[d.e]	329.1±63.3	318.2±53.3	<0.001
Total thiol (µmol/L)	468.4±52.4[b.c]	448.7±51.6[f.g]	388.9±62.6	390.3±71.8	<0.001
Disülfide (µmol/L)	20.5±7.9[a.b.c]	31.2±11.8	29.9±12.0	36.1±18.9	0.002
Disülfide/ native thiol (%)	4.9±1.8[h.b.c]	8.0±2.7[i]	9.6±4.8	11.4±6.2	<0.001
Disülfide/ Total thiol (%)	4.4±1.5[j.b.c]	6.8±2.0[k]	7.8±3.3	8.9±7.8	<0.001

[a]: p=0.013 between Group 1 and Group 2; [b]: p<0.001 between Group 1 and Group 3; [c]: p<0.001 between Group 1 and Group 4; [d]: p=0.001 between Group 2 and Group 3; [e]: p=0.001 between Group 2 and Group 4; [f]: p=0.002 between Group 2 and Group 3; [g]: p=0.004 between Group 2 and Group 4; [h]: p=0.019 between Group 1 ile Group 2; [i]: p=0.018 between Group 2 ile Group 4; [j]: p=0.007 between Group 1 ile Group 2; [k]: p=0.028 between Group 2 ile Group 4.