P194

THE ACTIVITY OF INFLAMMATION AND THE BLOOD REDOX STATUS IN PATIENTS WITH CORONARY HEART DISEASE AND TYPE 2 DIABETES MELLITUS

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Abstract

The systemic inflammation process and pathogenic role of its mediators hold a firm position in the study of coronary heart disease (CHD) occurrence mechanisms and development and associated cardiovascular diseases. The importance of the whole inflammatory reactions cascade in the vascular wall, a pro-inflammatory and pro-oxidant potential in a dramatic cardiovascular risk increase, encumbrances and fatal outcomes in patients with impaired glucose metabolism were established [1, 2].

Objectives

To determine the relationship between indicators of inflammation and the blood redox status of type 2 diabetic (T2DM) patients with and without coronary heart disease.

Materials and methods

44 patients with T2DM and CHD (group 1), 67 patients with T2DM without cardiovascular complications (group 2), 89 healthy subjects (group 3) were included in this study. Serum concentrations of IL-6 and IL-8 were determined by ELISA using commercial kits. Concentrations of thiobarbituric acid reactive substances (TBARS) both in plasma and in atherogenic lipoprotein, total glutathione (GSHt) and oxidized glutathione (GSSG), as well as the activity of glutathione peroxidase (GP) and glutathione reductase (GR) in erythrocytes, and that of catalase (CAT) in plasma and blood superoxide dismutase (SOD) activity were determined by spectrophotometric methods. The concentration of erythrocytes glutathione in reduced (GSH) forms calculated using the formula: GSH = [GSHt] – 2 × [GSSG].
The red blood cells redox potential (E_h) is calculated with the Nernst equation $E_h = (– E^0 + 59,1 / 2 \times \log [GSSG] / [GSH]^2$, where E^0 – standard reduction potential, mV (E^0 = –252 mV at pH 7.2) [3].

Results

The fall the SOD and CAT activities were detected in groups 1 and 2, whereas decreased antioxidant capacity of the erythrocytes glutathione system and increased E_h values were most expressed in patients with T2DM and CHD.

Table 1. The indicators of the erythrocytes glutathione system in analyzed groups.

Characteristic	T2DM and CHD	T2DM	Healthy Subjects	*p*
	1	3	4	
GSHt, mmol/l	1,37 [1,09; 2,37]	2,93 [1,60; 5,66]	3,23 [2,17; 4,54]	p_{1-2}=0,007 p_{1-3}=0,000 p_{2-3}=0,760
GSSG, mmol/l	0,36 [0,32; 0,40]	0,36 [0,31; 0,38]	0,31 [0,27; 0,36]	p_{1-2}=0,463 p_{1-3}=0,004 p_{2-3}=0,289
GSH, mmol/l	0,76 [0,35; 1,84]	2,86 [0,86; 5,14]	2,64 [1,53; 4,06]	p_{1-2}=0,020 p_{1-3}=0,000 p_{2-3}=0,850
2GSH/GSSG, relat.units	2,10 [0,93; 4,74]	5,95 [2,18; 15,40]	9,82 [5,07; 14,91]	p_{1-2}=0,024 p_{1-3}=0,000 p_{2-3}=0,402
E_h, mV	–169,02 [–191,70; –151,99]	–192,48 [–220,49;–173,27]	–207,39 [–216,91; –195,84]	p_{1-2}=0,023 p_{1-3}=0,000 p_{2-3}=0,432
GP, mmol/l	56,65 [37,57; 67,63]	50,61 [34,46; 81,56]	80,28 [59,26; 100,35]	p_{1-2}=0,974 p_{1-3}=0,000 p_{2-3}=0,007
GR, mmol/l	1,13 [0,81; 1,33]	0,81 [0,78; 1,25]	0,97 [0,74; 1,11]	p_{1-2}=0,281 p_{1-3}=0,046 p_{2-3}=0,689

Table 2. Correlations between the erythrocytes GR activity and glutathione system parameters, oxidative stress in analyzed groups.

Characteristic	T2DM and CHD	T2DM	Healthy Subjects
TBARS	R = –0,4770**	R = –0,2895	R = –0,1154
GSHt	R = –0,6841***	R = –0,5117	R = 0,1052
GSSG	R = –0,1855	R = 0,7510**	R = 0,1476
GSH	R = –0,6957***	R = –0,5117	R = 0,0786
2GSH/GSSG	R = –0,5882**	R = –0,6270*	R = 0,0628
E_h	R = 0,7305***	R = 0,5968*	R = –0,0058
GP	R = 0,1829	R = –0,4021	R = 0,4391**

Significance levels of: * – $p < 0,05$; ** – $p < 0,01$; *** – $p < 0,001$.

Table 3. Correlations between the interleukin and glutathione system parameters and glucose concentrations in analyzed groups.

a) the IL-6 concentration

Characteristic	T2DM and CHD	T2DM	Healthy Subjects
GSHt	R= 0,0180	R= –0,5272	R= 0,0017
GSSG	R= –0,5508	R= 0,6695*	R= 0,1620
GSH	R= –0,5798	R= –0,6109	R= –0,0130
2GSH/GSSG	R= –0,5798	R= –0,5030	R= –0,0814
E_h	R= 0,5798	R= 0,5030	R= –0,0319
GP	R= –0,3784	R= –0,0418	R=0,3892
GR	R= 0,7928*	R= 0,2008	R= –0,0376
Glucose	R= 0,9487*	R= –0,1071	R=0,0843

b) the IL-8 concentrations

Characteristic	T2DM and CHD	T2DM	Healthy Subjects
GSHt	R= –0,3571	R= 0,0167	R= –0,4876**
GSSG	R= 0,0857	R= 0,3000	R= 0,2073
GSH	R= –0,826*	R= –0,1000	R= –0,4367*
2GSH/GSSG	R= –0,8286*	R= 0,2857	R= –0,4633*
E_h	R= 0,8286*	R= –0,2857	R= 0,4418*
GP	R= 0,0357	R= –0,1833	R= –0,0465
GR	R= 0,8571**	R= 0,2833	R= –0,2985
Glucose	R= 0,7379	R= –0,1071	R= –0,0602

Significance levels of: * – $p < 0,05$; ** – $p < 0,02$; *** – $p < 0,01$; **** – $p < 0,001$.

Conclusion

Consequently, patients with T2DM and CHD are different from diabetic patients without cardiovascular complications to have increased pro-inflammatory cytokine IL-6. The increased in IL-6 concentration was found in group 1 (87%, p=0,000) and group 2 (20%, p=0,007) compared to group 3, the IL-8 concentration was increased only in group 1 (56%, p=0,041).
Correlation between E_h, GSH, GSSG and GR activity in patients groups 1 and 2 indicates a impairment the erythrocytes reduction potential due to the activation process of glycosylation and chronic oxidative stress.
High cytokine concentrations and changes in glutathione level as well as E_h can be considered as prognostic markers for assessing the risk of CHD progression in diabetic patients.
The necessity of control and correction of the cellular redox potential in patients with CHD and T2DM.

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For further information

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