MICROINFLAMMATION AND CARDIORENAL SYNDROME

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OBJECTIVES

Nowadays, microinflammation is thought to play a significant role in cardiovascular diseases and their complications.

The reactants of the acute and chronic phase of the inflammation process are especially significant microinflammation markers. The reactants of the acute phase have the role of inhibiting of the inflammation process and are significant in the reestablishment of the homeostasis of the organism . The most significant one in this group is C reactive protein (CRP), which could indicate direct and indirect tissue damage and the activation of endothelial cells. The total cholesterol level is also one of the reactants in the acute inflammation phase. Cytokines are especially important in the estimation of the microinflammation process, and the most significant ones are interleukins . Interelukin-8 (IL-8) is a proinflammatory cytokine described as an early marker of acute renal damage.

The aim of the paper is to examine the representation of certain parameters of microinflammation in sufferers with cardiorenal syndrome and compare the obtained values.

METHODS

Eighty-eight examinees above the age of 18 were involved (36 women and 52 men, divided into four clinical subgroups and the fifth control group, comprising n-11 healthy volunteers. There were n-20 examinees in the first subgroup of the clinical group, with cardiorenal syndrome type 1 (CRS-1), The second study subgroup, or cardiorenal syndrome type 2 (CRS-2) was made up of n-22 examinees. The third study subgroup involved cardiorenal syndrome type 4 (CRS-4) with n-22 examinees, and the fourth study subgroup included patients with cardiorenal syndrome type five (CRS-5), with n-13 examinees. Cardiorenal syndrome type 3 (KRS-3) was represented by n-2 examinees. Therefore, owing to the low number, this group was excluded from the statistics. The full blood samples were centrifuged for 15 minutes to 1000 revolutions, after which 5ml of the serum was frozen to -20 0C. Immunoassays of Serpin E1/PAI-1 and interelukin-8 (IL-8) were performed with commercially procured tests i.e. quantitative sandwich enzyme immunoassay technique, and were expressed in ng/mL. The serum concentrations of C reactive protein (CRP) were determined quantitatively, with a nephelometric test «Orion Diagnostica»-Turbox®. The results were expressed as concentration units (mg/L). The fundamental laboratory analyses were determined with standard biochemical parameters on the automatic analyzer with a photometric test of the ERBA Mannheim XL 600® brand, manufactured in Germany, through routine biochemical methods, and a commercially procured brand, ERBA Diagnostics Mannheim GMBH, Baden-Wurttemberg Germany). The statistical analysis was performed with a standard data processing programs SPSS 12.0 and Sigma Stat 3.5. The values of the tested characteristics were presented as an arithmetic average value ± standard deviation (SD) and median. The differences in the average parameters between the groups were determined with the use of the Student T test and χ^2 test. The rank analysis of variance was performed with the Kruskal Wallis test, owing to inconsistent frequency distribution. The univariate linear regression analysis was performed on all the subgroups, formed according to the CRS, for the purpose of testing the impact of predictor variables IL-8, CRP, triglycerides concentrations (Tg), total cholesterol (HOL), low-density lipoproteins (LDL) and high-density lipoproteins (HDL) on the value of the dependent variable of serpin E1/PAI-1. The values of $p<0.05$ were taken as statistically relevant values.

Table 1. Analysis of Serpin E1/PAI-1, IL-8 and the C reactive protein among the examinees in subgroups

Groups	Serpin E1/PAI-1 (ng/ml)		IL-8 (pg/ml)		CRP (mg/L)	
Control	7.78 ±3.66[a**]	(9.45)	35.46 ± 26.05	(26.71)	1.27 ± 0.73	(1.10)
Study	6.76 ±7.37	(4.88)	162.19 ±467.13	(39.70)	55.28 ±75.48	c***
					(9.20)	
Type 1	8.82 ±8.11	(7.29)	110.31 ±188.38	(38.81)	82.29 ±87.23	c**
					(42.80)	
Type 2	7.72 ±7.52	(6.60)	78.58 ±102.14	(53.28)	49.01 ±76.94	
					c** (6.10)	
Type 4	3.43 ±3.62	(2.14)	151.12 ±401.41	(36.16)	38.83 ±52.95	
					c** (17.70)	
Type 5	7.02 ±9.33	(4.88)	405.67 ±971.56	(61.54)	72.03 ±96.94	
					c** (10.70)	

Table 2. The correlation of serpin E1/PAI-1 with CRP, Tg, HOL, LDL and HDL

Data are given as mean value±SD (median)

a – vs Type 4, c – vs control; * – p<0,05, ** – p<0,01, *** – p<0,001 (Kruskal-Wallis Test)

	IL-8 (pg/ml)	CRP (mg/L)	Tg (mmol/L)	HOL (mmol/L)	LDL (mmol/L)	HDL (mmol/L)
Type 1	0.33	0.16	-0.17	0.01	0.52	0.32
Type 2	0.52	0.18	-0.25	0.24	0.17	0.01
Type 4	0.56	-0.27	0.01	-0.01	-0.24	0.79
Type 5	0.64	0.22	0.55	0.57	0.14	0.22

Table 3. The estimation of the impact of the factors relevant to the value of serpin E1/PAI-1 for CRS-1; the results of univariate linear regression analysis

Factor	t	Sig	B	95% Confidence Interval for B	
				Lower Bound	Upper Bound
IL-8 (pg/ml)	2.11	0.0489	0.02	0.00	0.04
CRP (mg/L)	1.21	0.2558	0.03	-0.03	0.09
Tg (mmol/L)	-0.20	0.8443	-0.52	-6.05	5.02
HOL (mmol/L)	-1.18	0.2586	-1.52	-4.28	1.25
LDL (mmol/L)	0.85	0.4174	1.76	-2.98	6.50
HDL (mmol/L)	0.18	0.8579	1.71	-19.29	22.71

Table 4. The estimate of the impact of the factors relevant for the value of serpin E1/PAI-1 for CRS-2; the results of the univariate linear regression analysis

Factor	t	Sig	B	95% Confidence Interval for B	
				Lower Bound	Upper Bound
IL-8 (pg/ml)	2.13	0.0461	0.02	0.00	0.06
CRP (mg/L)	1.32	0.2081	0.02	-0.02	0.09
Tg (mmol/L)	-1.12	0.2788	1.81	-5.86	1.81
HOL (mmol/L)	1.31	0.2083	1.38	-1.12	4.74
LDL (mmol/L)	1.11	0.2838	1.47	-1.52	4.80
HDL (mmol/L)	-0.11	0.9158	6.40	-14.32	12.95

Table 5. The estimate of the factors relevant for the values of serpin for CRS-4; the results of the univariate regression analysis

Factor	t	Sig	B	95% Confidence Interval for B	
				Lower Bound	Upper Bound
IL-8 (pg/ml)	2.43	0.0247	0.004	0.00	0.01
CRP (mg/L)	-1.36	0.1925	-0.02	-0.06	0.01
Tg (mmol/L)	0.74	0.4683	0.72	-1.34	2.77
HOL (mmol/L)	-0.11	0.9139	-0.07	-1.41	1.27
LDL (mmol/L)	-0.96	0.3566	-0.82	-2.70	1.06
HDL (mmol/L)	3.36	0.0063	2.83	0.98	4.69

RESULTS

The correlation of parameter serpin E1/PAI-1 between the control group and the subgroups of the clinical group the parameter serpin E1/PAI-1 showed a statistical significance in cardiorenal syndrome type 4 (CRS-4) by a significance level of $p<0.01$, while the Kruskal Wallis test showed an impact of $p<0.05$ in all the subgroups. The correlation of interleukin 8 (IL-8) levels between the subgroups of the clinical group and the control group did not show any statistical significance. Correlation between the clinical subgroup and the control group for C reactive protein showed a statistical significance level of $p<0.01$ in cardiorenal syndrome type-1, while cardiorenal syndrome type 2 and 4 exhibited $p<0.001$ i.e. maximum statistical relevance, just like between the clinical group and the control group. In addition, the difference between the subgroups of the clinical group was $p<0.05$ and was considered less statistically relevant (Table 1).By testing the normality of the subgroups formed according to the CRS, the Shapiro-Wilk test established that the distribution of serpin E1/PAI-1 values deviated from the normal distribution in all the subgroups. Therefore, Spearman's correlation coefficient ρ was used for the purpose of determining the correlation between serpin E1/PAI-1 and biochemical parameters: CRP, Tg, HOL, LDL and HDL (Table 2) It was determined that serpin E1/PAI-1 positively and statistically significantly correlated with IL-8 in CRS-2 and CRS-4 with a statistically significant value of $p<0.05$, while the level was even more statistically relevant in CRS group 4 ($p<0.01$). A positive, but not statistically significant correlation was also present in CRS-1. There is no statistically significant differences between serpin E1/PAI-1 and the remaining parameters measured (CRP, Tg, HOL and LDL) in any of the subgroups, formed according to the CRS. Although it could be concluded that there is a positive and expressed correlation of serpin E1/PAI-1 in subgroup CRS-4 and Tg and HOL, and with LDL in subgroup CRS-1, based on the value of ρ, these correlations are not statistically significant, which is the consequence of the small sample size in the mentioned subgroups. A very strong positive and statistically significant ($p<0.01$) correlation between serpin E1/PAI-1 and HDL was recorded in CRS-4. In the CRS-1 group, the only statistically significant predictor variable was IL-8 ($p<0.05$). An increase in IL-8 by one led to an increase of the values of serpin E1/PAI-1 by 0.02 (Table 3).

In group CRS-2, IL-8 ($p<0.05$) also stood as the only statistically significant predictor variable. The increase of IL-8 by one led to the increase in the value of serpin E1/PAI-1 by 0.02 (Table 4). In the CRS-4 group, IL-8 ($p<0.05$) and HDL ($p<0.01$) proved to be statistically relevant predictor variables. An increase in IL-8 by one led to an increase in the value of serpin by 0.004, and by 2.83 in the case of HDL (Table 5).

CONCLUSIONS

The results of this research indicate that, among the markers of inflammation in the study group, the most prominent ones are interleukin 8 and serpin, while the process of microinflammation is the most expressed in the cardiorenal syndrome type-4. In addition, HDL cholesterol is present as a predictor variable for microinflammation in cardiorenal syndrome type-4, while triglycerides and total cholesterol are predictors in cardiorenal syndrome type-5.

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