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CHANGES OF THE BLOOD PLASMA CONTENT OF SOME FACTORS OF APOPTOSIS AND A SOLUBLE FORM OF THE FACTOR OF THE RECEPTOR OF THE STEM CELLS IN PATIENTS WITH DIFFERENT TYPES OF VEGETOVASCULAR DYSTONIA

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Abstract. It has been established that the blood content of protein P53 diminishes by 27 %, the blood level of sTRAIL increases by 22 %, sCD 117 by 44% in patients with vegeto-vascular dystonia of the hypertonic type that is accompanied with an increase of the activity of caspase-1, however, the activity of caspases-3 and – 8, as well as the blood content of TNF-α do not change. With vegeto-vascular dystonia of the hypotonic type the concentration of blood plasma protein P53, TNF-α and sTRAIL and the activity of caspases-1,-3,-8 correspond to the control values against a background of an almost twofold increase of the plasma sCD 117 level. A considerable elevation of the blood content of type II apoptotic factors is characteristic of the mixed type of vegeto-vascular dystonia: the level of protein p53 increases 2,4 times, TNF-α – 1,9 times, sTRAIL – 2,3 times that is accompanied with an increased activity of caspase-1 – 4,1 times, caspase-3 – 3,3 times, caspase-8 – 3,8 times and an increase of the plasma concentration of sCD 117 – 3,5 times.

Key words: vegeto-vascular dystonia, protein P53, TNF-a, sTRAIL caspases-1,-3,-8, sCD 117.

Introduction. According to modern concepts apoptosis is not only a physiological process which regulates the volume of the cell mass and its form in an organism that develops, but under certain conditions is engaged in the mechanisms of the pathogenesis of many diseases associated with a disturbance of cell division [1, 2, 3]. The highest apoptotic intensity in an adult organism is observed in cell populations that are constantly formed and renewed where this process plays an important role of a factor which balances the processes of proliferation and corrects the processes of differentiation [5]. Endotheliocytes, among others, belong to such cells as well.

Therefore, it is not excluded, that a certain role is played by apoptotic disturbances in the pathogenesis of vegetovascular dystonia in the pathogenesis at the level of endothelial cells that in consequence of a hyper-and hypofunction of endotheliocytes may lead to the development of a hypo- and hypertensive type of vegetovascular dystonia respectively. However, this particular aspect of possible mechanisms of the development of vegetovascular dystonia remains obscure.

The object of the research. To investigate the blood plasma level of some markers of the apoptotic intensity of the endothelial cells (P 53, TNF-α, sTRIAL, caspases-1,-3,-8) and a soluble form of the receptor of the factor of the stem cells CD117 in patients with different types of VVD with a view of specifying the role of apoptosis in the development of various variants of the VVD course.

Material and methods. Forty eight patients with constitutionally stipulated VVD (17 men, 31 women aged from 14 to 30 years (22,8±2,1 on the average) were examined. The hypertensive type was diagnosed in 18 patients among them, the hypotonic type in 12 persons and a mixed type of the disease – in 18 persons.

The control group was made up of 15 apparently healthy persons of the corresponding age. The blood was drawn from the ulnar artery on an empty stomach in the morning. During the research the following assay kits were made use of for an immune-enzyme analysis – P53, TNF-α, sTRIAL and sCD117 (Diaclone Res., France) and for a biochemical study of the activity of caspases-1,-3,-8 (Bio Vision, USA) with a registration on the reader "Uniplan-M" (Russia).

A statistical analysis of the obtained findings was carried out on the basis of the "Biostat" program with an evaluation of Student´s t-test.

Results and their discussion. The indices of the content of protein P53, TNF-α, sTRAIL, sCD117 and the activity of caspases-1,-3,-8 in different groups of the examined patients are presented in a table. The blood content of protein P53 in the patients with VVD after the hypertensive type is statistically reliably lower than the control indices and does not differ from the control in the patients with hypotonic type of the disease, as it is evidenced by the results of the research presented in the table. In case of a mixed VVD type the blood plasma protein P53 concentration exceeds considerably that of both the apparently healthy persons and other groups of patients.

The blood TNF-α level in patients with VVD of the hyper-and hypotonic types did not differ from the control values, whereas in the patients with the mixed type of the disease, the plasma concentration of TNF-α exceeded statistically reliably the control values.

The blood plasma sTRAIL concentration in VVD after the hypertensive and mixed type was statistically considerably higher than the similar indices in the apparently healthy persons and corresponded to the control indices in the patients with the hypotonic type of the disease.

In the VVD patients after the hypertensive type the activity of the blood plasma caspase-1 statistically reliably exceeded the control values. At the same time, the indices of the activity of caspase-3 and caspase-8 didn't differ essentially from the control values.

Table

The blood plasma content of P53, TNF-a, sTRAIL, sCD117 and the activity of caspases-1,-3,-8 in patients with different types of VVD (x±Sx)

Groups of patients	P53 u/ml	TNF-a p/ml	sTRAIL p/ml	caspase-1 u/ml	caspase-3 u/ml	caspase-8 u/ml	sCD117 ng/100 mkl
Control (apparently healthy volunteers), n=15	26,64±2,64	35,97±3,68	390,80±16,39	0,049±0,004	0,080±0,007	0,102±0,008	2,35±0,32
Patients with VVD after the hypertensive type, n=18 Group 1	19,36±1,70 p<0,05	44,07±3,47 p>0,1	476,90±30,56 p<0,05	0,077±0,007 p<0,01	0,098±0,009 p>0,1	0,139±0,016 p>0,06	3,38±0,33 p<0,05
Patients with VVD after the hypotonic type, n=12 Group 2	31,75±4,47 p>0,3 p1-2<0,01	41,23±4,84 p>0,3 p1-2>0,6	382,80±37,28 p>0,8 p1-2>0,06	0,041±0,003 p>0,1 p1-2<0,001	0,063±0,005 p>0,07 p1-2<0,01	0,087±0,005 p>0,1 p1-2<0,02	4,48±0,36 p<0,001 p1-2<0,05
Patients with VVD after the mixed type, n=18 Group 3	63,39±4,60 p<0,001 p1-3< 0,001 p2-3< 0,001	68,41±4,32 p<0,001 p1-3<0,001 p2-3<0,001	916,70±61,41 p<0,001 p1-3<0,001 p2-3<0,001	0,199±0,023 p<0,001 p1-3<0,001 p2-3<0,001	0,265±0,031 p<0,001 p1-3<0,001 p2-3<0,001	0,390±0,046 p<0,001 p1-3<0,001 p2-3<0,001	8,28±0,71 p<0,001 p1-3< 0,001 p2-3< 0,001

Footnotes. p – a degree of the authenticity of differences in relation to the control; p_{1-2}, p_{1-3}, p_{2-3}, – a degree of the authenticity of differences of the indices in the respective groups of patients; n – a number of observations

Reliable changes of the activity of caspases-1,-3 and -8 were not observed in relation to the control ones in the patients with the hypotonic type of the disease.

The indices under study underwent the greatest changes in case of the mixed VVD type when the activity of all the investigated caspases turned out to be reliably higher compared to the control one and in comparison with other groups of patients under study.

The results, dealing with an evaluation of the blood content of molecules sCD117 – a soluble form of the receptor of the factor of the stem cells (SCF), deserve special attention. The level of sCD117 statistically reliably exceeded the control indices and reached the maximal values in the patients with VVD after the mixed type in all the groups of examined patients.

Thus, no essential changes of the initial and effector mechanisms of type II apoptosis was observed according to the results of our study in case of the hyper –and hypotonic types of VVD. At the same time, there is every reason to assert about a certain pathogenetic role of apoptotic disorders in case of the mixed type of VVD, so far as a sharp growth of the blood content of proapoptotic factors – p53, TNF-α and sTRAIL is not only accompanied with a considerable elevation of the activity of caspases 1,-3 and -8, but takes place against a background of an essential rise of the sCD117 plasma concentration – a factor which protects the stem cells from death due to apoptosis [2].

Conclusions

In accordance with the results of the research carried out by the author it may be assumed that in case of the mixed type of vegetovascular dystonia there occurs a sharp increase at the endothelial level of the intensity of both the division of cells and their apoptosis, a process capable of bringing on an uncontrolled and unbalanced release of biologically active substances of the endothelium which possess a powerful and functionally antagonistic effect (for example, endothelins – the endothelial factor of relaxation) on the tonus of the vessels of the resistive type.

Outlooks of further investigations. Further investigations of the apoptotic processes of the endothelial cells in vegetovascular dystonia are promising for the purpose of elaborating methods of preventing cardiovascular and cerebrovascular diseases in this particular category of patients.

Bibliography

1. Кухарчук А.Л. Старение, стволовые пространства и иммунная система / А.Л.Кухарчук, В.В.Радченко, В.М.Сирман // International J. Immunorehabilitation. – 2003. – Т. 5, № 2. – С. 134.
2. Вплив алотрансплантації ембріональних плюрипотентних прогеніторних клітин на динаміку системного артеріального тиску в спонтанно гіпертензивних щурів / О.Л.Кухарчук, В.В.Радченко, В.М.Сірман [та ін.] // Фізіол. ж. – 2003. – Т. 49, № 4. – С. 68-71.

3. Лушников Е.Ф. Гибель клетки (апоптоз) / Е.Ф.Лушников, А.Ю.Абросимов. – М.: Медицина, 2001. – 192 с.
4. Apo2L/TRAIL-dependent recruitment of endogenous FADD and caspase-8 to death receptors 4 and 5 / F.C.Kischkel, D.A.Lawrence, A.Chuntharapai [et al.] // Immunity. – 2000. – Vol. 12. – P. 611-620.
5. Reed J.C. Mechanisms of Apoptosis / J.C.Reed // Am. J. Pathol. – 2000. – Vol. 157. – P. 1415-1430.

ИЗМЕНЕНИЕ СОДЕРЖАНИЯ В ПЛАЗМЕ КРОВИ НЕКОТОРЫХ ФАКТОРОВ АПОПТОЗА И РАСТВОРИМОЙ ФОРМЫ РЕЦЕПТОРА ФАКТОРА СТВОЛОВЫХ КЛЕТОК У БОЛЬНЫХ РАЗНЫМИ ТИПАМИ ВЕГЕТО-СОСУДИСТОЙ ДИСТОНИИ

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Резюме. Установлено, что у больных вегето-сосудистой дистонией по гипертоническому типу содержание в плазме крови белка p53 уменьшается на 27 %, уровень в крови sTRAIL возрастет на 22 %, sCD117 – на 44 %, что сопровождается повышением активности каспазы-1, однако активность каспаз-3 и -8, а также содержание в крови TNF-α не изменяется. При вегето-сосудистой дистонии по гипотоническому типу концентрации в плазме крови белка p53, TNF-α, sTRAIL и активность каспаз-1 -3, -8 отвечают контрольным величинам на фоне почти двукратного повышения плазменного уровня sCD117. Для смешанного типа вегето-сосудистой дистонии характерным является значительное повышение содержания в крови факторов апоптоза II типа: уровень белка p53 растет в 2,4 раза, TNF-α – в 1,9 раза, sTRAIL – в 2,3 раза, что сопровождается увеличением активности каспазы-1 в 4,1 раза, каспа зы-3 – в 3,3 раза, каспазы-8 – в 3,8 раза и повышением плазменной концентрации sCD117 – в 3,5 раза.

Ключевые слова: вегето-сосудистая дистония, белок P53, TNF-a, sTRAIL каспазы-1,-3,-8, sCD 117.

ЗМІНИ ВМІСТУ В ПЛАЗМІ КРОВІ ДЕЯКИХ ЧИННИКІВ АПОПТОЗУ ТА РОЗЧИННОЇ ФОРМИ РЕЦЕПТОРА ФАКТОРУ СТОВБУРОВИХ КЛІТИН У ХВОРИХ НА РІЗНІ ТИПИ ВЕГЕТО-СУДИННОЇ ДИСТОНІЇ

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Резюме. Встановлено, що у хворих на вегето-судинну дистонію за гіпертонічним типом вміст у плазмі крові білка p53 зменшується на 27 %, рівень у крові sTRAIL зростає на 22 %, sCD117 – на 44 %, що супроводжується підвищенням активності каспази-1, однак активність каспаз-3 та -8, а також вміст у крові TNF-α не змінюється. При вегето-судинній дистонії за гіпотонічним типом концентрації в плазмі крові білка p53, TNF-α, sTRAIL та активність каспаз-1 -3, -8 відповідають контрольним величинам на фоні майже дворазового підвищення плазмового рівня sCD117. Для змішаного типу вегето-судинної дистонії характерним є значне підвищення вмісту в крові факторів апоптозу II типу: рівень білка p53 зростає у 2,4 раза, TNF-α – в 1,9 раза, sTRAIL – у 2,3 раза, що супроводжується підвищенням активності каспази-1 у 4,1 раза, каспази-3 – у 3,3 раза, каспази-8 – у 3,8 раза та підвищенням плазмової концентрації sCD117 – у 3,5 раза.

Ключові слова: вегето-судинна дистонія, білок P53, TNF-a, sTRAIL каспази-1,-3,-8, sCD 117.

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