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PECULIARITIES OF UNSPECIFIC IMMUNOLOGIC REACTIVITY IN PATIENTS WITH ISCHEMIC HEART DISEASE AFTER STENTING

Особенности неспецифической иммунологической реактивности у больных ишемической болезнью сердца после проведенного стентирования

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Abstract

Nowadays more and more attention is paid to the status of unspecific immunologic reactivity in patients suffering from ischemic heart disease. This is due to the fact that immunologic reactivity serves for the background of progressing pathologic process. The aim of our research is in the following: to

determine the features of unspecific immunologic reactivity in patients with ischemic heart disease before and after stenting coronary arteries. In the issue of our research it has been assessed incomplete phagocytosis in neutrocytes and monocytic links secondary to the intact functional and metabolic neutrocytes' reserve in patients with angina of effort on the II – III f. cl. after stenting at any time of our research.

Резюме

На сегодняшний день все большее внимание уделяется значению состояния неспецифической иммунологической реактивности организма у больных ИБС. Это обусловлено тем, что иммунологическая реактивность является фоном, на котором развивается патологический процесс. Все это и определило цель нашего исследования: установить особенности неспецифической иммунологической реактивности у больных ИБС перед и после проведения стентирования коронарных артерий. В результате исследования было установлено, что у больных стенокардией напряжения II-III ф. кл. после проведенного стентирования во все сроки исследования наблюдается незавершенность фагоцитоза нейтрофильного и моноцитарного звеньев, на фоне сохраненного функционально-метаболического резерва нейтрофилов.

Atherosclerosis and ischemic heart disease as one of its complications are the most frequent and severe cardiovascular diseases of social significance. They take one of the leading positions among the causes of morbidity, mortality, temporary and persistent invalidity. According to the statistic data within some recent years these values in Ukraine tend to the growth. Besides, the mortality caused by ischemic heart disease in Ukraine considerably exceeds the average values in Europe [1].

During the recent years the particular interest is paid to the status of immunologic reactivity in patients with ischemic heart disease at early post-operative period in surgical and interventional techniques of treatment. On one

side, the initial alteration of immunologic reactivity determines the origin and the course of disease and on the other side – the disease exerts the influence on the status of immunologic reactivity [2-4].

Last years a considerable progress has been achieved in endovascular treatment of coronary arteries (CA) with using balloon angioplasty and stenting [5]. In stenting atherosclerotic plaque, which closes the lumen in the vessel or sharply narrows it, is affected and changes its shape [6]. A different traumatism rate of the plaque and its adjacent endothelium is observed and results in activation of inflammatory cells in the plaque such as: monocytes, macrophages, as well as, cells arriving from the blood circulation to the point damaged.

Implantation of stents covered with rapamycin into coronary arteries results in changing the values of unspecific link in immunologic system which may reflect the features of local and systemic responses to the implantation of the stent covered with drugs and can be significant for the forecast of disease [7, 8].

All mentioned above defined the *aim* of our research: to reveal the features of unspecific immunologic reactivity in patients suffering from ischemic heart disease before and after stenting coronary arteries.

Materials and methods

45 patients have been examined: 15 donors (1 group); 15 patients with ischemic heart disease and angina of effort of III- IV f. cl., submitted to the coronarography for confirming the requirement of stenting (2 group); 15 patients with ischemic heart disease and angina of effort III-IV f. cl. submitted to coronary arteries stenting according to the indications (3 group). The indication for stenting was a such stenosis localization, when balloon angioplasty gives unsatisfactory results (anastomoses' stenoses, bifurcation stenoses, stenoses in proximal segment of anterior interventricular branch of the left coronary artery).

The assessment of phagocytes activity of neutrophiles and monocytes in the blood, based on the method of assessment of absorptive and digestive capacities relatively to microbe test-culture after their joint preincubation (by H. Frimel) has been performed for studying unspecific immunologic reactivity [9].

The assessment of oxygen depended metabolism of neutrophiles (NBT- test) and functional cells reserve (stimulated NBT-test) by M. E. Viksman, A. N. Mayansky has been carried out [10]. This method is based on the capacity of neutrophiles to absorb nitroblue tetrazolium which is reduced to insoluble deep blue formazan in phagosomes of the cell.

The activity of myeloperoxydase (MP) has been assessed by modified cytochemical method of R. P. Nartsissov [11]. This method consists in the fact that benzidine is oxidized by hydrogen peroxide to the brown oxybenzidine in the presence of peroxidase.

The assessment of the content of cations proteins (CP) in neutrophiles has been carried out by the method with bromphenol blue (M.G. Shubich [12]). This method consists in elective staining of cation protein with bromphenol blue.

Statistic analysis of the data has been performed according to the routine technique by the method of variation statistic with a set of applied programs "Excel". Arithmetical mean (M), error of mean (m) have been calculated. The authenticity of results has been assessed by 1-criterion of Student. Comparative result was considered reliable at $P< 0,05$.

Results of research

While studying the values of functional and metabolic status of neutrophiles and monocytes in patients of the second group in comparison with control data it has been revealed decreasing neutrophiles' functional activity (NPI – neutrophiles phagocytic index) both at the 30-th and at the 120-th minutes by 13 % and 7 % respectively, that in the last case is statistically unauthentic, but clinically significant. But the absorptive capacity of neutrophiles (NPN – neutrophiles' phagocytic number) at the 30-th minute and digestive capacity at the 120-th minute have been increased by 300 % and by 33 % respectively (table 1.)

On the contrary, the functional activity of monocytes (MPI – monocytes' phagocytic index) has been increased both at the 30-th and at the 120-th minutes by 20 % and 130 % respectively. Their absorptive capacity was increased by 50 %,

at the 30-th minute, but digestive capacity at the 120-th minute didn't exceed control data.

The values of the spontaneous NBT-test were higher than control values by 8 % that is statistically unauthentic, but clinically significant, whereas the values of the stimulated NBT-test were decreased by 16 %.

Table 1. Dynamics of the values of functional and metabolic status of neutrophiles and monocytes in patients with ischemic heart disease after stenting coronary arteries (M + m)

Index, Unities of measure	Donors (n= 15)	Patients before operation (n= 15)	Terms after stenting		
			1day (n= 15)	3 day (n= 15)	5 day (n= 15)
1	2	3	4	5	6
NPI at 30 min, %	67,5±4,1	59,3±4,4*	57,2±1,1*	62,7±1,7	62,0±1,3
NPN at 30 min, c. u.	1,10±0,04	3,9±0,8*	2,5±0,5*·**	2,9±0,5*·**	1,7±0,4**
NPI at 120 min, %	57,4±1,3	53,4±2,2	52,7±0,4*	55,3±0,2	56,7±0,1
NPN at 120 min, c. u.	2,8±0,3	4,2±0,7*	3,8±0,5*	3,2±0,4*	2,9±0,3**
MPI at 30 min, %	34,5±1,3	42,1±5,6*	44,2±2,7*	42,1±5,05	35,3±1,2**
MPN at 30 min, c. u.	1,2±0,2	2,1±0,7*	1,8±0,5*	1,7±0,4*·**	1,4±0,7**
MPI at 120 min, %	19,5±0,1	45,7±2,7*	37,4±2,1*	30,0±1,3*	25,3±2,0*·**
MPN at 120 min, c. u.	2,50±0,05	2,7±0,8	2,2±0,1*·**	2,4±0,8	2,4±0,7
NBTsp, c. u.	1,20±0,01	1,30±0,09	1,10±0,03	1,20±0,04	1,10±0,02
NBTst, c. u.	1,30±0,08	1,1±0,1	1,10±0,01	1,30±0,02	1,30±0,01
CP, c. u.	2,2±0,2	1,10±0,04*	1,40±0,02*	1,70±0,01**	2,00±0,03**
MP, c. u.	2,3±0,2	1,60±0,06*	1,70±0,07*	2,00±0,04**	2,00±0,03**

Notes: * - authentic difference (P <0,05) relative to the donors' group;
** - authentic difference (P <0,05) relative to the preoperative patients' group.

The values studied of bactericidal system were decreased: content of cation proteins (CP) – by 30 %, myeloperoxidase activity (MP) – by 50 % relatively to the donors' group.

Thus, at preoperative stage the activation of monocytic system has been observed, whereas the adaptive capacities of neutrophiles system have been restricted. Evidently, the agents forming them had no reserves necessary for systemic adaptation. Decreasing values of bactericidal system has been revealed.

While studying the values of functional and metabolic status of neutrophiles and monocytes in patients of the 3-rd group on the first day after stenting performed it has been revealed decreasing functional activity of neutrophiles relatively to the donors' group by 16 % and slightly by 7 % at the 120-th minute (it is statistically unauthentic, but clinically significant).

As to the initial values statistically significant differences in functional activity of neutrophiles at the 30-th and 120-th minutes were not revealed.

Statistically important differences in the functional activity of neutrophiles both at 30-th and 120-th minutes on the third ant the fifth days were not revealed concerning the initial values and donors' ones.

On the first day the functional activity of monocytes at the 30-th and 120-th minutes has been increased by 20 % and 85 % relatively to the values in donors' group. As to the initial values at 30-th minute considerable statistic differences were not observed. At the 120-th minute the decrease of the values studied was 33%.

On the third day at the 30-th minute increasing functional activity of monocytes by 20 % was observed, whereas on the fifth day the values corresponded to donors' ones. Increasing by 50 % and 25 % respectively was observed at the 120-th minute. At the 30-th minute on the third day an absolute conformity to the initial values was observed and on the fifth day decreasing by 17% was registered. Decreasing functional activity of monocytes at the 120-th minute on the third and the fifth days was 35 % and 46 % respectively.

The absorptive capacity of neutrophiles on the first and on the third days exceeded the control values by 200 % and on the fifth day - by 50%. The absorptive capacity of monocytes within this period of research statistically considerably exceeded control values.

The digestive capacity of neutrophiles and monocytes gradually became normal: exceeding neutrophiles on the first and third days was 35 % and 14 % and monocytes' excess was by 12 % for the first day. In all other periods of research the digestive capacity of both neutrophiles and monocytes corresponded to donors' values.

With respect to preoperative values within the whole period of research (1, 3, 5 days) the absorptive capacity of neutrophiles was decreased by 25 %, 25 %, 50% respectively. The absorptive capacity of monocytes was decreased relatively to the initial means on the third and the fifth days. Decreasing digestive capacity of neutrophiles in average by 25 % was observed on the third and the fifth days. The same changes of monocytes' digestive capacity were observed on the first and the fifth days.

The tendency to decreasing the values of NBTsp relatively to the donors' values in average by 8 % on the first and fifth days, but on the third day these values corresponded to the donors values. As to the initial values the decrease was observed during the whole period of the study by 16 %, 8 % and 16 % respectively. NBTst values were decreased by 15 % relatively to the donors' values only on the first day and absolutely corresponded to them on the third and the fifth days. On the first day NBTsp value was the same as before the operation. An increase in average by 18 % was registered on the third and fifth days.

MP values relatively to the donors' ones within the whole period of study were decreased by 36 %, 23 % and 10 % respectively, but exceeded preoperative values by 27 %, 54 % and 81 % respectively.

Practically CP values corresponded to the donors' ones, whereas the initial values were slightly increased in average by 25 % on the first, third and fifth days.

Thus, in patients of the third group the functional activity of neutrophiles after stenting was decreased on the first day at 30-th and 120-th minutes, but at the same time the functional activity of monocytes was increased. On the third and the fifth days the functional activity both of neutrophiles and monocytes corresponded to the control values.

Phagocytic number (PN) dynamics of neutrophiles and monocytes both at the stage of absorption and at the stage of digestion displays incomplete phagocytosis secondary to the intact functional and metabolic reserves. The values of bactericidal system were decreased within the whole period of study.

Conclusions

1. As a result of the study performed the changes in the values of unspecific immunologic link have been revealed in patients suffering from ischemic heart disease.

2. When carrying out coronarography an activation of monocytic link in phagocytic system has been observed whereas the adaptive capacities of neutrophiles' link were restricted secondary to the deficiency of the functional and metabolic reserve.

3. Alterations of unspecific resistance in patients after stenting coronary arteries are characterized by incomplete phagocytosis in all periods of the study and by deficiency of functional and metabolic reserve, which was reduced on the fifth day.

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