

PECULIARITIES OF PLATELET HEMOSTASIS CHANGES IN COPD - HYPERTENSIVE DISEASE MIXED PATIENTS

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Abstract

Disorders in the hemostasis system have a major impact on the disease course and complication in the hypertensive disease and chronic obstructive pulmonary disease patients. To assess the platelet hemostasis we examined 62 persons: 15 apparently healthy (Control Group), 15 HD patients without COPD, 17 HD patients with COPD associated, and 15 COPD patients of Degree II and III. We have found out that HD, COPD and the mix patients demonstrate an increased thrombocyte functional activity expressed in a higher degree of spontaneous aggregation, and significant activation of arachidonic acid induced thrombocyte aggregation. The HD patients feature a specific increase of adrenalin induced aggregation, contrary to other examined groups, that may be explained by a role of sympathetic nervous system in the HD pathogenesis. Chronic inflammation in the COPD patients is accompanied with a significant increase of arachidonic acid thrombocyte reaction (the highest among all examined groups) that should be taken into account when establishing a treatment policy with anti-inflammatory agents included.

Key words: hypertensive disease, chronic obstructive pulmonary diseases, hemostasis, thrombocytes, aggregation.

Introduction. Hypertensive disease (HD) is one of the most wide-spread diseases in the world as about 40% of adult population have an elevated blood pressure. Given the current level of social and economic conditions and an evolution stage of clinical medicine, a particular attention is paid to studies of peculiarities of comorbid state course and treatment, with several diseases mixed, particularly those of cardiovascular and respiratory systems. This mix is objectively preconditioned: integrity of some pathogenetic mechanisms, general risk factors (smoking being the first one), manifest attributes of diseases.

There are different views on pathogenetic relationship between arterial hypertension and chronic obstructive pulmonary disease (COPD): some scientists think that both diseases evolve independently under risk factor impact, others consider COPD to be HD evolution reason, while there are those declare such HD symptomatic. (2,6)

Diseases of cardiovascular and respiratory systems are known to be the most wide-spread in the world today. HD as well as COPD classified as non-communicable diseases are a cause of over 36mln death cases per year in the world.

As to Ukraine, respiratory diseases are ranked the first in the morbidity structure, with COPD that 8 to 22% of adults over 40 suffer from, being the most wide-spread. Chronic obstructive pulmonary disease is a key reason for life quality deterioration, disability, and mortality in the

whole world. The World Health Organization forecasts that COPD will have become the fifth disease in the world by prevalence rate and the third common reason for death by 2020.

HD prevalence rate is 4 to 27% in bronchopulmonary pathology patients, reaching 62% in the older age group. The growing number of COPD – HD mixed patients results from increased case rate for these diseases as well as gain of patient geriatric population where these diseases are frequent. Case rate of arterial hypertension mixed with bronchial obstruction increases with age. Arterial hypertension in most patients develops associated with pulmonary diseases, with only 12.5% cases when arterial hypertension precedes pulmonary pathology. (4,5,7,8,10)

Risk factors associated with blood pressure and metabolism potentiate each other and result into increased cardiovascular risk. Therefore management of such patient groups provides for accounting all risk factors affecting the disease prognosis. Assessment of plasma, vasculo-platelet and lipid homeostasis indicators are of value. Indicator rate depends on activity degree of inflammation and respiratory disturbance. With inflammation reduced and airway conductance improved, the hemostasis indicators stabilize. (1,3,9,11,12)

Taking into account an essential role of thrombocytes in thrombus development, platelet hemostasis study is a key to identify patients with thrombosis high risk in order to resolve an issue of Atherothrombosis prevention. Given that thrombocytes may have a direct impact on the chronic inflammation, a pathogenetic concept of contribution of platelet hemostasis and its regulation mechanisms to the development and progression of arterial hypertension as well as COPD is of interest.

Purpose. To assess a thrombocyte functional activity state in chronic obstructive pulmonary and hypertensive disease mixed patients.

Materials and methods. In the course of study 62 persons were examined: 15 apparently healthy (Control Group), 15 HD patients without COPD (Group I), 17 HD patients with COPD associated (Group II), and 15 COPD patients of Degree II and III (Group III). There were 36 men and 26 women among the patients examined. Average age of patients was 51.7 ± 1.2 . Most patients were in age groups of 40-49, 50-59 and 60-69 (22.5%, 50% and 20%, correspondingly).

Platelet hemostasis was studied with special laboratory methods (to resolve tasks set): spontaneous and induced thrombocyte aggregation, with ADP, arachidonic acid, collagen, and adrenalin used as aggregation inductors.

Findings and discussion.

When indicators of thrombocyte functional activity in the patients (HD, COPD and mix) are assessed, a significant increase of spontaneous aggregation compared to Control Group is observed, including all three examined groups of patients (Table 1). The spontaneous aggregation degree change is the least expressed in HD patients, however it exceeds the Control Group in 2.77 times

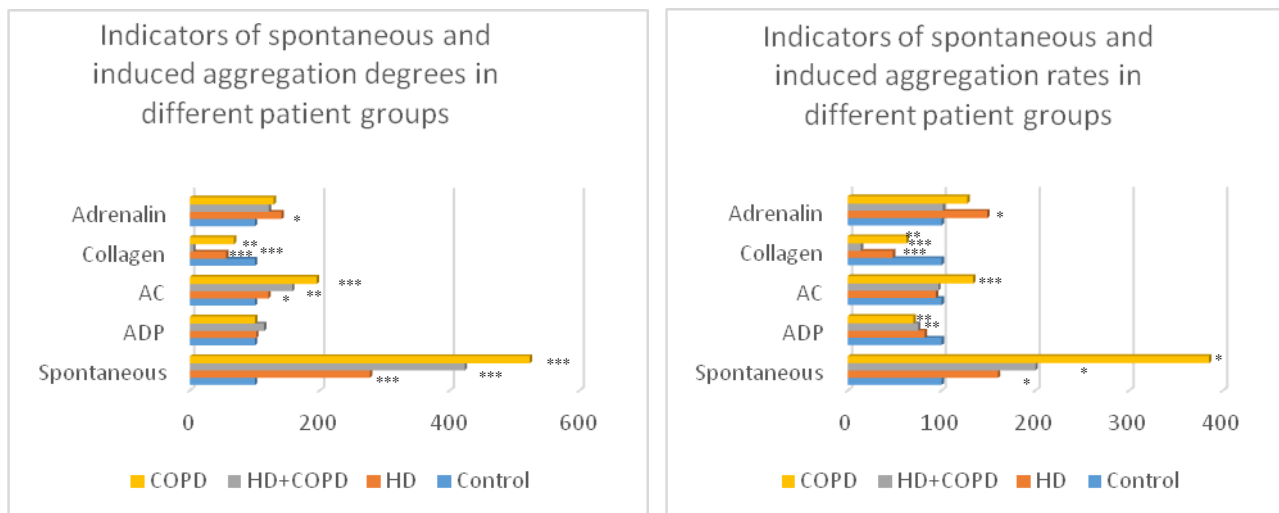
($p < 0.001$). The highest expressed spontaneous aggregation is in the COPD patients. It differs from the Control Group in 5.24 times ($p < 0.001$), the HD patients by 52.8% ($p < 0.05$) and the mixed pathology patients by 23.5% ($p > 0.05$).

When assessing the induced aggregation, we observed that ADP thrombocyte reaction of examined patient groups was practically the same as in the Control Group. Furthermore, no statistically significant differences of these indicators were noted either with the Control Group or among the patient groups. However, we found out that all patient groups demonstrated a slowdown of aggregation process as response to ADP that differed significantly from the Control Group by 18% ($p < 0.05$) in the HD patients, by 25% ($p < 0.05$) in the mixed pathology patients, and by 30% ($p < 0.05$) in the COPD patients.

We revealed expressed aggregation changes when the thrombocytes were stimulated with arachidonic acid. The thrombocytes in the HD patients were seen to be 20.8% more sensitive to AC than the thrombocytes in the Control Group persons, though in the COPD patient group this indicator turned out to exceed not only the value of Control Group – in 1.95 times ($p < 0.001$), but also that of HD patient group – by 30.2% ($p < 0.05$). It is interesting that HD – COPD mix caused less expressed indicators of AC induced aggregation degree than in the COPD patients, i.e. by 23.8% ($p < 0.05$), while assessment of aggregation process rate in response to AC demonstrated a statistically significant acceleration only in the COPD patient group – by 33.6% ($p < 0.001$).

Rather unexpected results were received when we studied the collagen induced thrombocyte aggregation. It is of interest that aggregation degree indicators in response to collagen were well below in all three patient groups than in the Control Group. Furthermore, if the aggregation degree was 1.78 times ($p < 0.001$) and 1.48 times ($p < 0.01$) lower in the HD group and the COPD group, correspondingly, than in the Control Group, in the mixed pathology group this indicator was 1.06% comparing to 20.9% in the Control Group ($p < 0.001$), i.e. was 19.7 times decreased as well as differed significantly from the HD group and COPD group – 11 times ($p < 0.001$) and 13.3 times ($p < 0.001$), correspondingly. The rate of collagen induced thrombocyte aggregation turned out to be also well slowed down in all three examined groups.

On the contrary, the thrombocyte reaction to adrenalin differed statistically significant from the Control Group only in the HD patient group where the induced aggregation degree and its rate exceeded the Control Group by 41% ($p < 0.05$) and 48.7% ($p < 0.05$), correspondingly (Fig. 1).



Note: * – significance of changes against the Control Group.

* – $p < 0,05$; ** – $p < 0,01$; *** – $p < 0,001$

Fig. 1. Indicators of platelet hemostasis in different patient groups

Assessing the changes found out on studying the platelet hemostasis in the examined patient groups, one should make a conclusion that the platelet hemostasis changes are rather non-uniform in the HD, COPD and mixed patient groups. If all examined groups demonstrated activation of thrombocyte spontaneous aggregation, in terms of induced aggregation, the changes are rather heterogeneous. So, it should be noted the HD patients' thrombocytes react more on arachidonic acid and adrenalin, being also the only ones with a significant increase of adrenalin induced aggregation comparing to the Control group. The found changes allow for stating that the COPD patients, with a well increased degree of thrombocyte spontaneous aggregation exceeding the Control Group in 5.24 times, have the most expressed thrombocyte aggregation activity as this group demonstrated the most expressed thrombocyte reaction on the arachidonic acid stimulation. Given that the COPD patients suffer of chronic inflammation, and the arachidonic acid is a component of inflammation cascade metabolism, these findings should be considered expected. The most controversial changes were observed on stimulating the thrombocytes with collagen in all three examined groups. A significant decrease of collagen induced aggregation may be explained by exhaustion of thrombocyte granules involved into the inflammation response.

It should be noted that the thrombocyte activation in the HD patients has been presented earlier as well. Thus, it was demonstrated that the thrombocyte functional activity increased in response to ADP and adrenalin stimulation. However, in our study no significant changes with ADP stimulation were observed in any of examined groups that highlights once more a need of integrated approach to the thrombocyte functional activity studies, namely, use of several inductors to assess the platelet hemostasis status. In addition, inductors should be selected in the way to study impact on various receptors of platelet membrane.

Table 1

Indicators of thrombocyte functional activity in different patient groups

Indicator	Control	HD Patients (I)	COPD – HD Patients (II)	COPD Patients (III)	D 1-2	D 2-3
Spontaneous aggregation degree, %	0.84±0.3	2.33±0.37***	3.56±1.3***	4.4±0.8***	<0.05	>0.05
ADP induced aggregation degree, %	34.6±5.6	35.6±8.2	39.4±9.6	34.7±8.9	>0.05	>0.05
ADP induced aggregation rate, %/min	47.8±6.1	39.2±4.7**	35.9±10.23**	33.4±9.5**	>0.05	>0.05
AC induced aggregation degree, %	28.47±5.6	34.4±7.4*	44.8±10.14**	55.5±8.3***	<0.05	<0.05
AC induced aggregation rate, %/min	36.9±6.1	34.9±4.8	35.6±6.3	49.3±9.4***	>0.05	<0.001
Collagen induced aggregation degree, %	20.9±4.7	11.7±2.6***	1.06±0.47***	14.1±4.2**	<0.001	<0.001
Collagen induced aggregation rate, %/min	21.6±5.3	10.4±2.8***	3.0±0.8***	13.5±4.9**	<0.001	<0.001
Adrenalin induced aggregation degree %	18.7±9.9	26.4±6.5*	22.7±6.8	24.09±5.6	>0.05	>0.05
Adrenalin induced aggregation rate, %/min	14.05±6.5	20.9±4.4*	14.27±3.2	17.9±4.7	<0.01	>0.05

Notes:

* – significance of changes against the Control Group

* – p<0.05; ** – p<0.01; *** – p<0.001, p 1-2 – probability degree of indicator differences against those in HD and mixed pathology patients, p2-3 – probability degree of indicator differences against those in COPD and mixed pathology patients.

Conclusions

1. HD, COPD and the mix patients demonstrate an increased thrombocyte functional activity expressed in a higher degree of spontaneous aggregation, and significant activation of arachidonic acid induced thrombocyte aggregation.

2. The HD patients feature a specific increase of adrenalin induced aggregation, contrary to other examined groups, that may be explained by a role of sympathetic nervous system in the HD pathogenesis.

3. Chronic inflammation in the COPD patients is accompanied with a significant increase of arachidonic acid thrombocyte reaction (the highest among all examined groups) that should be taken into account when establishing a treatment policy with anti-inflammatory agents included.

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