THE CONNECTION OF ENDOTHELIAL FUNCTIONS INDEXES IN BLOOD SERUM WITH HEMOSTASIS OF PATIENTS WITH ALLERGIC VASCULITIS

Tashkenbayeva U.A.
Tashkent medical academy,
skin and venereal diseases department,
e-mail: umidatashkenbaeva@mail.ru

The combination of vascular and hemostasiological disturbances in skin can act as an important pathogenetic moment in the development of allergic vasculitises. It is known that NO affects the processes of blood coagulation [4]. The mechanism of its inti-trombous effect is conditioned by the decrease in platelet aggregation and the adhesion of shaped blood elements to the vascular endothelium. The disturbances in the NO-system can lead to the disbalance of these natural laws, the intensity degree of which is dependent on the degree of the pathological process intensity.

One of the most widespread mechanisms of allergic vasculitises is the endothelial dysfunction, which is usually an inadequate production of nitrogen oxide (NO) by the vascular endothelium in response for the adequate stimulus (geodynamical impact, cholinergic stimulation etc).

The NO level in endothelial cells is regulated by the activity if NO-synthase (NOS), from which important are the endothelial NOS (eNOS). In the conditions of the disturbances in NO synthesis an induced NO (iNOS) can be involved, which is 100-1000 times more active in the intensity of NO synthesis than eNOS [7, 8]. The iNOS marker – nitrate reductase (NP) which acts synchronously with iNOS is usually used to estimate its activity [65]. When the iNOS activity in tissues and cells is high the NO content is increased avalanche-like. NO forms a toxic and high-reactive compound – peroxinitrites ($ONOO^-$) [63] under conditions of hypoxia and the high concentration of superoxide anion O_2 caused by it. The alterations in NO, eNOS, iNOS, and $ONOO^-$ levels reflect the condition of endothelium NO-synthas mechanism of vascular tone regulation [4, 5, 6, 7, 8].

Materials and methods of the research

The research of endothelium function was based on the clinic-laboratory inspection of 226 patients with vasculitis and 20 almost healthy people of the same age.

The NO level was defined according to the sum of the major metabolites (NO_2^- and NO_3^-), endothelial NO-synthas (eNOS), nitrate reductase (NR), and peroxinirites ($ONOO^-$) [3]. The data obtained once from almost healthy volunteers served as a control for all groups. ADP-induced platelet aggregation (APA), fybrinolitic activity of euglobul clot (FAEC), Villebrand factor (Vf), and anti-aggregation activity of the vascular wall (AAVW) were also studied within the same patients.

The results and their analysis

The NO level in blood serum within the patients of the first group increased of 31,1 % and within the patients of the second group – of 36,9 % comparative to the data of the control group. The activity of endothelium eNOS within the first group decreased of 20,3 % and within the patients of the second group – of 27,5 %, and the nitrate reductase increased of 32,5 % within the patients of the first group and of 61,3 % comparative to the control group.

With the increase in NO concentration under the conditions of hypoxia and the high concentration of superoxide anion O_2 forms toxic and highly-toxic compound peroxinitrites ($ONOO^-$) with it, which increases up to 0,12 within the patients of the first group and up to 0,16 withi the patients of the second group.

The credibility of the alterations proves that the increase in NO level and free radicals level creates the conditions for the $ONOO^-$ synthesis and leads to a significant increase in its local concentration in the vascular wall. $ONOO^-$ is extremely toxic in high concentration, it induces apoptosis, breaks the prostacycline synthetase system function (by blocking the prostacycline synthesis and strengthening the tromboxane synthesis), causes the fragmentation of proteins by nitrating of amino acids and lipid proteins, induces the oxidation of low-dentisy lipid proteins (LDLP), in other words, leads to the irreversibility of the reversible tissue breath oppression under the influence of NO and $ONOO^-$.

The received results of the NO-system research reflect the presence and the degree of endothelium functions disturbance, and the endothelium dysfunction within the patients with allergic vasculitis is one of the early forerunners of tromboxic complications. The formation of free oxygen radicals suppresses the NO-synthas activity which is the catalyst of the NO synthesis and the platelet aggregation inhibitor that shows anti-trombous impact in the vascular endothelium [1, 2]. In turn, as a result of the endothelium damage the concentration of Villebrand factor is increased which leads to the strengthening of platelet aggregation and their adhesion to subendothelium, the formation of trombuses in micro-vessels, and the worsening in rheological blood characteristics disturbances.

This data testifies the disbalance between the oxygen radicals formation level and anti-oxidant organism system that affect the interaction of cellular factors and vessels endothelium thus creating the conditions for the development of hemocoagulation and immune regulation disturbances under the allergic vasculitis.

In the acute phase of allergic vasculitis a significant worsening of all hemostasis indexes and, first of all, those that are dependent on endothelium is revealed.

The ADP level of induced platelet aggregation within the second group was increased of 27,7% more than the indexes of the first group ($P < 0,001$), and of 54,2% more that the data of the control group($P < 0,001$). The maximum platelet aggregation activity was revealed within the group of patients with acute allergic vasculitis course.

The AAVW study within the patients with allergic vasculitis revealed its decrease. AAVW within the second group was lower than first group indexes by 26,0% ($P < 0,001$), and by 43,2% lower than those of the control group ($P < 0,001$).

The FAEC within the patients of the first group was in average oppressed down to 184,5 ± 1,2 min, and within the second group patients – down to 219,7 ± 1,6 min. Thus, within the patients of the second group the oppression of fibrinolytic activity of 19,1% lower than that within the patients of the first group($P < 0,001$), and of 51,5% lower than the control group level ($P < 0,001$) . The FAEC level of the control group was in average 145,0 ± 1,8 min.

A correlation average straight connection (correlation coefficient $r = 0,42$) was revealed between the NO level in blood serum and the ADP level of induced platelet aggregation. Along with the increase in NO synthesis the ADP content of induced platelet aggregation id also increased.

Also the relations between No level and highly-reactive compound peroxinirites ($ONOO^-$) was revealed (correlation coefficient $r = 0,70$). Correlation analysis showed that a strong straight connection exists between the increase in NO synthesis.

Resume

Under allergic vasculitis the disturbances of NO-synthas mechanism are observed. They are expressed by the decrease in the formation of NO that is produced by endothelium cells and its quick inactivation as a result of the formation of highly-toxic product $ONOO^-$ by the increase in HP ferment activity that leads to the suppression of NO-synthas activity that promotes for the creation of NO. This disbalance in NO-system under the allergic vasculitis leads to the progression of endotoxicosis and the disturbances in hemostasis systems and immunity.

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