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## Immune Changes at Patients with Primary Arterial Hypertension.

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**ABSTRACT**

Lack of apparent inflammatory processes at arterial hypertension does the problem of immune violations in many respects new and interesting. In research, changes of indexes of the immune status at patients with primary arterial hypertension depending on the disease stage are defined. Immunologic efficiency of reference treatment at patients with primary arterial hypertension of various stage is analyzed. To an assessment of efficiency of treatment and outcome prediction at patients with primary arterial hypertension concentration of IL-1, IL-8, neopterine, $C_{3a}$, $C_4$ are the most valuable in blood. Need of inclusion in reference treatment of patients with primary arterial hypertension of II and the III stages of immunologic preparations are proved.

**Keywords:** primary arterial hypertension, immunity, cytokines, complement system.

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# INTRODUCTION

Primary arterial hypertension falls into number of the most widespread diseases of cardiovascular system. In spite of the fact that the fissile studying by primary arterial hypertension is around the world conducted, the reasons still are not established. Now it is considered that primary arterial hypertension is a disease multifactorial [1, 2]. The problem of treatment and prevention of the complicated arterial hypertension today is one of the leaders in the modern medicine because of premature mortality [3].

Lack of apparent inflammatory processes at an arterial hypertension does a problem of immunologic violations in many respects disputable [4, 5]. However the increase in concentration of IgG, IgA was shown at arterial hypertension, especially with a heavy current. The increase in concentration of IgG is bound to development of cardiovascular complications [6]. In studying of question of value of immunologic violations at arterial hypertension the increase in level of autoantibodies to antigens from tissue of aorta and heart is shown. The revealed strengthening of autoantibodies to the endothelium of vessels points to development of remodeling of vessels at arterial hypertension [7, 8, 9]. Fully the question of the condition of immune system at primary arterial hypertension remains almost not studied [8, 10, 11].

Research objective was establishment of changes of level of cytokines and components of complement system at primary arterial hypertension of various stage.

## Technique

In work these inspections and treatments of 52 patients with the diagnosis primary arterial hypertension of I, II, III stages are presented. The blood plasma was exposed to research. The group of monitoring consisted of 12 healthy volunteers of the same age. All patients were divided into 3 groups. To all patients reference therapy was carried out: patients with primary arterial hypertension of the I stage received enalaprilum, patients with primary arterial hypertension of the II stage – enalaprilum and a hydrochlorothiazide, and patients with the III stage – enalaprilum and hydrochlorothiazide and bisoprololum. All preparations entered according to the recommendations explained in instructions on application of medicinal preparations.

The quantitative assessment levels of the TNF, IL-1, IL-6, IL-2, IL-8, IL-10, the receptor antagonist of IL-1, neopterine, $C_3$, $C_4$, $C_{3a}$, $C_5$, $C_{5a}$-components of complement systems, factor H and $C_1$-inhibitor was carried out by means of test-systems ("Cytokine", St. Petersburg) by the method of solid-phase enzyme immunoassay in the first day and for the 30th days.

## Main part

At the request for the medical care at patients primary arterial hypertension of the I stage in blood plasma revealed increase of level of pro-inflammatory cytokines (IL-1, TNF, IL-6, IL-8), anti-inflammatory cytokines (the IL-10, IL-Ra), IL-2 and neopterine, decrease level of in the $C_3$ and C5a-components of complement system (tab. 1).

At patients with primary arterial hypertension of the II stage in the blood plasma still more raised levels of the IL-1, IL-10, IL-1Ra, neopterine, $C_{5a}$, $C_4$ components of complement system and the factor H (tab. 1). The maximum level of cytokines was revealed at patients with primary arterial hypertension of the III stage whom the levels of IL-10, IL-1Ra, neopterine, factor H was much higher, than at patients of the previous groups is (tab. 1).

**Table 1: Level of cytokines and components of complement system at patients with primary arterial hypertension of various stages (M±m)**

| Indexes | Units of measure | Healthy donors | Primary arterial hypertension | | |
|---|---|---|---|---|---|
| | | | I stage | II stage | III stage |
| | | 1 | 2 | 3 | 4 |
| TNF | pg/ml | 3,2±0,2 | 5,4±0,1[*1] | 5,6±0,3[*1] | 10,1±0,2[*1-3] |
| IL-1 | pg/ml | 4,7±0,3 | 8,2±0,2[*1] | 9,4±0,2[*1,2] | 14,2±0,4[*1-3] |
| IL-6 | pg/ml | 5,8±0,08 | 7,3±0,1[*1] | 8,0±0,6[*1] | 13,7±0,2[*1-3] |
| IL-8 | pg/ml | 4,7±0,3 | 8,2±0,2[*1] | 8,5±0,2[*1] | 11,6±0,3[*1-3] |
| IL-10 | pg/ml | 0,8±0,1 | 2,6±0,3[*1] | 10,1±0,5[*1,2] | 15,0±0,3[*1-3] |
| IL-1Ra | pg/ml | 519,7±49,9 | 616,0±37,4[*1] | 871,4±62,3[*1,2] | 1047,5±49,9[*1-3] |
| Neopterine | pg/ml | 1,4±0,3 | 2,5±0,2[*1] | 3,8±0,2[*1,2] | 5,4±0,3[*1-3] |
| IL-2 | pg/ml | 0,8±0,1 | 2,6±0,3[*1] | 2,7±0,2[*1] | 3,9±0,3[*1-3] |
| $C_3$ | mg/dl | 114,4±4,5 | 97,2±2,8[*1] | 98,4±2,6[*1] | 100,8±2,4[*1] |
| $C_3$ | ng/ml | 66,0±7,9 | 71,3±5,4 | 74,2±6,1 | 80,3±4,7[*1] |
| $C_4$ | mg/dl | 39,3±3,5 | 44,7±1,6 | 49,7±2,8[*1] | 50,8±1,1[*1,2] |
| $C_5$ | ng/ml | 39,6±3,1 | 41,4±2,8 | 43,5±3,3 | 52,7±4,8[*1-3] |
| $C_5$ | ng/ml | 71,2±6,1 | 47,8±2,4[*1] | 94,1±2,0[*1,2] | 95,8±8,4[*1,2] |
| Factor H | ng/ml | 223,8±16,9 | 248,9±10,3 | 267,9±9,3[*1] | 308,5±14,8[*1-3] |
| $C_1$-inhibitor | ng/ml | 29,9±2,7 | 31,7±1,7 | 27,4±2,8 | 37,6±2,1[*1-3] |

Note. [*] – reliable differences of arithmetic averages ($p<0,05$); figures – in relation to what indexes of group these distinctions are reliable.

At patients with primary arterial hypertension I stage against reference therapy in the blood plasma concentration of IL-6, component $C_3$ of complement system were normalized, concentration the IL-1Ra and IL-10 were increased.

Application of reference pharmacological therapy for patients with primary arterial hypertension of the II stage allowed normalized in blood concentration of IL-6, $C_3$- and $C_5$ components of complement system. At patients with primary arterial hypertension of the II stage reference treatment partially normalized concentration in blood plasma the TNF, neopterine, IL-2 and raised level of IL-10.

At patients with primary arterial hypertension of the III stage carried-out reference treatment allowed to normalize completely in the blood plasma concentration of components of complement system ($C_3$, $C_{3a}$, $C_4$), $C_1$-inhibitor and to raise level of anti-inflammatory cytokines (IL-1Ra, IL-10).

At an assessment of couplings between changes of concentration of cytokines and components of complement system at patients with primary arterial hypertension the large number of communications was revealed. The greatest number of positive and negative communications are characteristic for IL-1, IL-8, neopterine, $C_{3a}$ and $C_4$.

## CONCLUSION

The received results testify to the expressed changes of the immune status at patients with primary arterial hypertension proportional to weight of a disease. The established changes of the immune status are eliminated with reference treatment especially at patients with II and the III stages of a disease insufficiently.

- At patients with primary arterial hypertension of the I stage in the blood plasma concentration of pro-inflammatory and anti-inflammatory cytokines, a neopterine, the IL-2 is increased, level of components of complement system ($C_3$ and $C_{5a}$) is lowered.
- At patients with primary arterial hypertension of the II stage level in the blood plasma of anti-inflammatory cytokines (IL-1Ra, IL-10) is follow-up raised.
- At patients with the III stage of primary arterial hypertension concentration of pro-inflammatory and anti-inflammatory cytokines, components of complement system is follow-up increased.
- Reference pharmacological therapy at patients with the I stage of primary arterial hypertension reduces quantity of the changed indexes of the immune status by 26,5%, at patients the II stage – for 20,3%, and patients with the III stage have 16,3% of the studied indexes. All this testifies to poor correction of immune violations.
- The most significant for an assessment of effectiveness of treatment and prediction of an outcome of a disease at patients primary arterial hypertension are in blood of concentration of IL-1, IL-8, neopterine, C3a, $C_4$.

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