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DYNAMICS OF IMMUNE STATUS INDICATORS IN PATIENTS WITH NON-SPECIFIC AORTO-ARTERITIS ON THE BACKGROUND OF COMBINED THERAPY

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SUMMARY

The article considers the results of the study of the immune status in patients with non-specific aortoarteritis in the dynamics of combined therapy.Calcium antagonists, ACE inhibitors, and antiplatelet agents. Data were obtained on the undeniable advantages of combined antihypertensive therapy with equator and plavix, which affect a large number of different parts of the pathogenesis of NAA - the activity of immune inflammation, endothelial dysfunction, myocardial hypertrophy and vascular wall.

KEYWORDS: *Nonspecific aortoarteritis, immune status.*

INTRODUCTION

Nonspecific aortoarteritis (NAA) is one of the rare vascular diseases characterized by circulatory disorders in various arterial basins, which causes a variety of clinical manifestations of this pathology.[6,8] The leading clinical syndrome of this disease is arterial hypertension (AH), which is observed in about 70% of patients. Hypertension in patients with non-specific aortoarteritis, is a consequence of immune inflammation of large and medium-sized arteries, promotes remodeling of the heart and blood vessels. Recent studies have shown that the defeat of the endothelial layer of the vascular wall in the formation of cardiovascular diseases occurs at the earliest stages of the pathogenesis of NAA.[7,9,12] It is known that calcium antagonists and ACE inhibitors have a vasoprotective effect, cause regression of vascular remodeling[2,3,5], contribute to the correction of endothelial dysfunction by reducing the formation of angiotensin II, reduce the activity of monocytes-macrophages, inhibit the activation of adhesion molecules and inflammatory mediators, migration of smooth muscle cells to the inflammatory lesion, and growth of smooth muscle cells of the vascular wall.[10,11,13] These processes underlie the anti-inflammatory and angioprotective effects of equator, which is a fixed combination of the angiotensin-converting enzyme inhibitor lisinopril, with the calcium antagonist amlodipine. The presence of a sulfhydryl group in the structure of the equator molecule determines the ability of the product to counteract oxidative stress, elimination of reactive oxygen species and other free radicals that initiate the development of immuno-inflammatory processes in the vascular wall, and the formation of endothelial dysfunction. This combination is pathophysiologically and clinically justified, highly effective, and has independent evidence of a beneficial effect on the cardiovascular prognosis. The fixed combination of lisinopril with amlodipine appeared in the clinical practice of Uzbekistan as the first of this combination and in just a few years has taken a fairly strong place among modern therapeutic approaches for hypertension. Both components belong to the first-line treatment of hypertension with a good level of evidence for positive effects on cardiovascular prognosis.[1,4] Plavix (clopidogrel) is an antiplatelet drug, a representative of the thienopyridine class. By blocking platelet receptors for adenosine diphosphate, it reduces their activity and ability to aggregate, and ultimately reduces the risk of serious thrombotic complications in various manifestations of stenotic diseases of the aorta and arteries.

The aim - is to study the dynamics of immune status indicators in patients with NAA on the background of combined therapy with equator and plavix.

MATERIALS AND METHODS

Taking into account the role of immune disorders in the progression of endothelial dysfunction in patients with NAA, a control study of immune status indicators was conducted after equator monotherapy and when equator is combined with plavix. 37 patients with NAA were examined. The control group included 30 healthy donors: 12 men and 18 women aged 22 to 38 years, with an average age of 24.2±6.3 years. All patients were randomly selected into two groups: the first group consisted of 19 NAA patients who took equator at a dose of lisinopril 10 mg / day + amlodipine 5 mg / day and

plavix (clopidogrel) 75 mg/day; the second group included patients (18 people) whose therapy included taking equator at a dose of lisinopril 10 mg/day + amlodipine 5 mg / day. The duration of therapy was 6 months. All examined patients with NAA received pathogenetic therapy with prednisone at a dose of 40 mg/day, respectively, with the degree of activity of the disease.

RESULTS

Evaluation of the effectiveness of the influence of the equator and antiagregantaplavix on the immune status, endothelial function(ED), thrombosis resistance of the vascular wall and Central hemodynamics of patients with NAA co IIED showed the following results.

After 6 months of treatment with equator inclusion, patients with NAA co IIED showed a significant decrease in proinflammatory cytokinemia: (the level of TNF was 103.1±10.2 PG / ml; IL-1ß-111.4±12.2 PG / ml, IL-6-44.8±5.1 PG / ml). The use of the equator+plavix combination was accompanied by potentiation of anti-inflammatory activity, which was manifested by a decrease of approximately 2 times the serum concentration of the studied cytokines. (picture. 1)

Picture 1: Dynamics of the anti-inflammatory cytokine content in blood serum of patients with NAA co II ED on the background of therapy

Indicator	**Surveyed groups (n=37)**			
	Control (**n**=30)	Before treatment (**n**=37)	Therapy with the equator (**n**=18)	Therapy with the equator + plavix (**n**=19)
FNoaph/ml	39,4±3,6	170,4±9,2	103,1±10,2	66,3±5,8
IL-1ßpg / ml	36,4±4,1	175,9±12,3	111,4±12,2	56,3±4,1
IL-6pg / ml	17,8±3,9	80,1±6,2	44,8±5,1	23,1±3,8

In patients with NAA with grade III-IV ED, the use of equator alone against the background of basic prednisone therapy significantly reduced the hyperproduction of anti-inflammatory cytokines, the content of TNF decreased by 39.5%, IL-1β by 36.7%, and IL-6 by 44.1%. More significant changes in the level of anti-inflammatory cytokines were achieved in the group of patients receiving equator+plavix therapy, the content of TNF decreased by 61.1%, IL-1β - by 68%, and IL-6-by 71.2% in comparison with the indicators before treatment. When evaluating the effect of combined therapy with the inclusion of the equator and plavix on the cytokine concentration anti-inflammatory action in patients with various duration of the disease established that the equator compared to the combination of equator and plavix has less effect on the activity of the studied cytokines in patients with NAA with a history of illness less than 1 year. Equator+plavix therapy in patients of this group led to a decrease in anti-inflammatory cytokines to the level of control, the use of equator alone was accompanied by a significant decrease in the content of TNF, IL-1β, and IL-6. With a history of NAA from 1 to 3 years, only complex therapy (equator+plavix) had a significant corrective effect on anti-inflammatory cytokines, while it should be noted that the normalization of the level of anti-inflammatory cytokines in patients of this group was not achieved.

There was a significant corrective effect of the equator and basic therapy on the hyperproduction of anti-inflammatory cytokines in patients with NAA with II degree of ED, characterized by a significant decrease in the concentration of IL-4, IL-10 and Tfrß1 (up to 48.1±4.8 PG / ml; 26.5±1.8 PG / ml and 68.6±4.2 PG / ml, respectively). The use of equator + plavix was accompanied by a significant increase in therapeutic activity, achieving a lower concentration of anti-inflammatory cytokines (IL-4-37.2±3.9 PG / ml, IL-10-18.1±2.1 PG / ml, TFR-β1-60.8±4.1 PG / ml.).

In patients with grade III-IV ED, the appointment of both the equator and the equator+plavix combination was accompanied by less significant dynamics of these indicators. Thus, after 6 months of combined therapy (equator + plavix +prednisone), the content of IL-4, IL-10, and TFR-β1, respectively, was 62.1±3.8 PG/ml ($p<0.05$), 27.2±2.1 PG/ml ($p<0.05$), and 76.9±3.8 PG/ml ($p<0.05$) (Picture 2).

Picture 2: Dynamics of the anti-inflammatory cytokine content in serum of patients with NAA with III-IV degree of ED on the background of therapy.

Indicator	**Surveyed groups (n=37)**			
	Control (**n**=30)	Before treatment (**n**=37)	Therapy with the equator (**n**=18)	Therapy with the equator + plavix (**n**=19)
FNoaph/ml	23,2±4,5	88,8±4,2	75,9±3,6	62,1±3,8
IL-1ßpg / ml	13,4±3,6	47,2±2,3	38,2±2,9	27,2±2,1
IL-6pg / ml	40,9±6,9	99,8±3,2	89,2±2,8	76,9±3,8

At the same time, treatment only with the equator against the background of prednisone had a significantly lower corrective effect on the level of the studied cytokines. The effectiveness of the studied drugs on the level of IL-4, IL-10 and TFR-β1 also depends on the duration of the course of NAA. When the duration of NAA is less than 1

year, equator therapy caused a significant decrease in the level of these cytokines, complex therapy equator + plavix led to normalization of the serum spectrum of anti-inflammatory cytokines, with the duration of the disease from 1 to 3 years, only complex therapy (equator+plavix) significantly reduced the hyperproduction of IL-4, IL-10 and TFR-β1(by 34.2%, 18.3% and 44.6%, respectively).

CONCLUSION

The data was obtained by us to indicate the undeniable advantages of combined antihypertensive therapy equator + plavix, which is due to the potentiation of their action, this is due to the fact that different classes of drugs act on different parts of the pathogenesis of NAA, thereby complementing each other's action. Combined therapy with calcium antagonists, ACE inhibitors and antiplatelet agents allows you to immediately affect a large number of different parts of the pathogenesis of NAA - the activity of immune inflammation, endothelial dysfunction, myocardial hypertrophy and vascular wall, so it is the combined therapy that solves the problem of multifactorial NAA with hypertension syndrome.

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