

**FEATURES OF VEGETATIVE HOMEOSTASIS IN CHILDREN WITH  
JUVENILE RHEUMATOID ARTHRITIS**

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**ANNOTATION:** Rheumatic diseases occupy one of the highest places in terms of frequency and prevalence among children and adolescents. The socio-economic significance of this problem is enormous, since rheumatic diseases lead to significant loss of working capacity and early disability. According to WHO data, rheumatic diseases account for 1/10 of disability and 1/3 of disability. In recent years, significant progress has been made in the diagnosis and treatment of rheumatoid arthritis in adults. Nevertheless, many aspects of the problem of rheumatoid arthritis have not yet been studied. In particular, significant work should be carried out to identify the main risk factors, pathogenesis, features of the clinical course of chronic juvenile arthritis in children, to study the causes of the transition of the inflammatory process to a chronic form, to improve diagnostic criteria and treatment methods. This plays an important role in preventing early disability.

**Keywords:** Juvenile rheumatoid arthritis, children, autonomic tone, heart rhythm, orthostasis.

### **INTRODUCTION**

Rheumatic diseases represent a significant and prevalent health burden among children and adolescents, contributing substantially to long-term morbidity and early disability. Among these conditions, Juvenile Rheumatoid Arthritis (JRA) stands out for its complex pathogenesis and severe socio-economic impact. While significant progress has been made in the diagnosis and treatment of rheumatoid arthritis in adults, many facets of JRA remain inadequately understood. Critical gaps persist in identifying its primary risk factors, the mechanisms driving the inflammatory process to a chronic state, and the full spectrum of its systemic effects.

One of the crucial, yet often under-examined, aspects of JRA is its impact on the autonomic nervous system (ANS), which governs the body's vegetative homeostasis. The chronic inflammatory state of JRA may induce significant imbalances in autonomic regulation, affecting cardiovascular function, metabolic processes, and the neuro-immune axis. Understanding the nature of this autonomic dysfunction is vital for developing more comprehensive diagnostic criteria and effective, holistic treatment strategies. Therefore, this study aims to investigate and characterize the specific features of vegetative homeostasis, including autonomic tone and reactivity, in children diagnosed with Juvenile Rheumatoid Arthritis.

### **MATERIALS AND METHODS**

The study involved 102 children diagnosed with Juvenile Rheumatoid Arthritis (JRA). The state of their vegetative homeostasis was assessed and compared against data from a control group of healthy children from the same region.

A preliminary assessment of vegetative tone was conducted using a unified and standardized research method, specifically cardiointervalography (CIG), performed in a state of relative rest. Based on the calculated stress index (SI), patients were categorized into three groups: eutonia (SI 30.0-90.0 conventional units), vagotonia (SI <30.0 conventional units), and sympathicotonia (SI >90.0 conventional units). The internal structure of the heart rhythm (including parameters such as Mo, AMo, and ΔX) was analyzed in relation to the initial vegetative tone.

Vegetative reactivity was evaluated using a clinooortostatic test (COT). Changes in autonomic tone in response to the orthostatic load were analyzed to determine the reactivity state. Responses were classified as normal, hypersympathicotonic, or asympathicotonic based on the ratio of the stress index post-test (SI2) to the initial stress index (SI1).

The impact of complex treatment on vegetative homeostasis was also assessed by comparing initial autonomic tone and reactivity data before and after the therapeutic intervention. Statistical significance of the differences between groups was evaluated, with results presented as  $M \pm m$ .

### RESEARCH AND RESULTS

Preliminary assessment of vegetative tone was carried out according to a unified and standardized research method (cardiointervalography (CIG), clinooortostatic test (COT)). The results of the study of initial vegetative tone in a state of relative rest (eutonia - 30.0-90.0 conv. units, vagotonia - <30.0 conv. units, sympathicotonia - >90.0 conv. units) showed a significant predominance of cases of initial sympathicotonia - 57 children (55.9%;  $P < 0.001$ ), a decrease in the proportion of eutonia - in 27 children (26.5%;  $P < 0.01$ ) and vagotonia - in 18 patients (17.6%;  $P < 0.05$ ) in relation to the healthy population of this region. The results of the study of the internal structure of the heart rhythm in the patients with JRA observed by us depending on the initial vegetative tone (Table 1) showed that the structure of the heart rhythm in patients differs from that of healthy children. Thus, in patients with initial eutonia, a decrease in the Mo value ( $P < 0.01$ ), an increase in ΔX ( $P < 0.01$ ), VPR, and SI ( $P < 0.05$ ) were observed.

**Table 1.**

**Structure of the heart rhythm in patients with juvenile rheumatoid arthritis depending on the initial vegetative tone ( $M \pm m$ )**

Юрак ритми курсаткичларин	Эйтония n = 27	Ваготония n = 18	Симпатикотония n = 57	P1	P2	P3
1. Mo, сек.,	0,627± 0,008	0,655 ± 0,012	0,546± 0,005	<0,001	<0,001	<0,001
2. AMo,%	14,80± 0,22	11,49± 0,11	32,16± 0,64	<0,01	<0,05	>0,05
3. ΔX, сек.,	0,215± 0,001	0,378± 0,002	0,093± 0,004	<0,01	>0,05	<0,01
4. ВПР., усл.ед.	8,39 ± 0,22	4,15± 0,05	22,91± 0,76	<0,05	>0,05	<0,01
5. ТИ., усл.ед.	60,42± 1,72	21,41± 0,78	374,8± 14,90	<0,05	>0,05	<0,01
6. AMo/ ΔX	75,09± 2,02	31,10± 0,74	388,7± 14,19	<0,05	<0,05	<0,01
7. AMo/ Mo	24,10± 0,66	17,88± 0,52	60,30± 1,18	<0,05	>0,05	<0,05

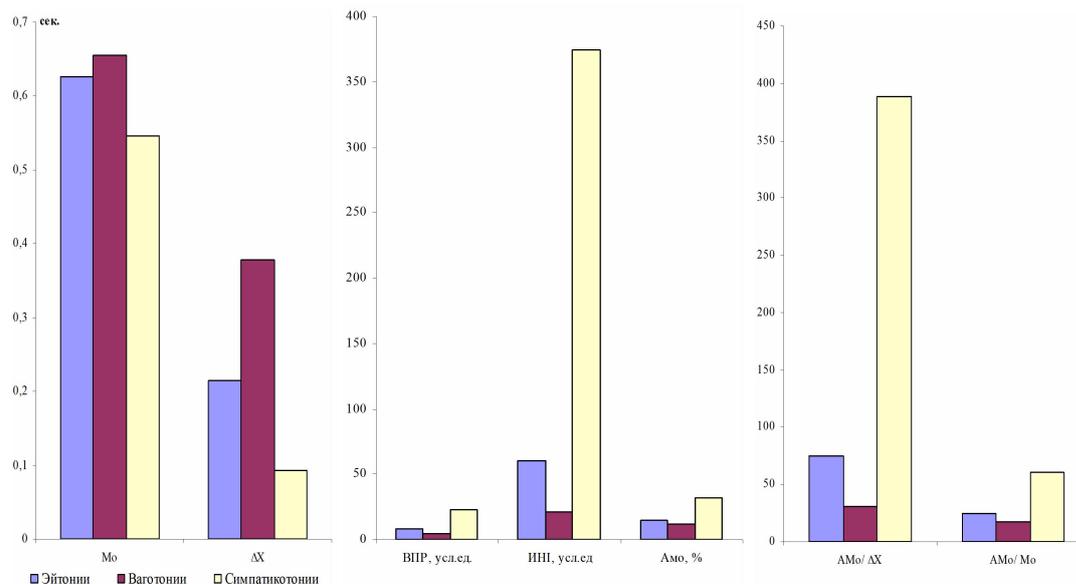
**Note:** P1, P2, P3 - significance of differences between healthy children and eu-, vago- and sympathicotonia, respectively

In initial eutonia, a certain balance is observed between adrenergic (AMo) and cholinergic (ΔX) effects on heart rhythm. However, in patients with initial eutonia, this balance was disrupted towards an increase in the humoral control contour (increase in Mo), a decrease in the activity of neural control (decrease in AMo), resulting in decreased AMo/ΔX and AMo/Mo ratios ( $P < 0.05$ ).

These changes in the humoral contour of heart rhythm occur against the background of decreased activity in the parasympathetic part of the ANS ( $\Delta X$ ;  $P < 0.01$ ) and a certain degree of strain on compensatory mechanisms in heart rhythm regulation (increase in VPR and SI;  $P < 0.05$ ). In patients with JRA exhibiting initial vagotonia, heart rhythm indicators ( $\Delta X$ , VPR, SI, AMo/Mo) showed no significant differences ( $P > 0.05$ ) compared to healthy children ( $\Delta X = 0.395 \pm 0.020$  sec; VPR =  $3.45 \pm 0.12$  conv. units; SI =  $24.8 \pm 1.49$  conv. units; AMo/Mo =  $18.8 \pm 2.48$ ). In patients of the same group, there was a decrease in cardiac cycle density (Mo,  $P < 0.001$ ), a decrease in AMo value ( $P < 0.05$ ) and a decrease in the AMo/ $\Delta X$  ratio ( $P < 0.05$ ) compared to healthy children (Mo =  $0.755 \pm 0.02$  sec; AMo =  $14.30 \pm 1.02\%$ ; AMo/ $\Delta X$  =  $39.8 \pm 4.38$ ). These data are similar to the case observed in initial eutonia - an increased influence of the humoral contour on heart rhythm against the background of decreased central regulation. In patients with initial sympathicotonia, there was a further increase in the humoral contour ( $P < 0.001$ ), a maximum decrease in the  $\Delta X$  index ( $P < 0.01$ ), and a significant increase in VPR and SI indicators ( $P < 0.01$ ) compared to healthy children (Mo =  $0.607 \pm 0.06$  sec;  $\Delta X = 0.16 \pm 0.05$  sec; VPR =  $11.3 \pm 0.43$  conv. units; SI =  $179.70 \pm 7.05$  conv. units). An increase in the AMo/Mo ( $P < 0.05$ ) and AMo/ $\Delta X$  ( $P < 0.01$ ) ratios relative to healthy children ( $50.3 \pm 2.14$  and  $28.2 \pm 3.1$  respectively) indicates weakened compensatory capabilities of the parasympathetic part of the ANS, significantly strengthened central (nervous) circuits, and an increased degree of centralization in heart rhythm regulation. The structure of heart rhythm in patients with juvenile rheumatoid arthritis depending on the initial vegetative tone is clearly shown in Figure 1.

Thus, the regulation of heart rhythm in patients with JRA depends on the initial autonomic tone. In initial eu- and vagotonia, negative changes in heart rhythm occur, which is expressed by an increased heart rate. An increase in the influence of the humoral contour against the background of decreased influence of neural mechanisms on heart rhythm organization indicates less adaptive control mechanisms. Unlike patients with eu- and vagotonia, in initial sympathicotonia, the parasympathetic division of the ANS is weakened, and the neural contour of heart rhythm control is significantly enhanced.

**Figure 1. Structure of heart rhythm depending on the initial vegetative tone in patients with juvenile rheumatoid arthritis**



This indicates the beginning of an "emergency" stage in the body's compensatory capabilities for maintaining and organizing heart rhythm. Since the assessment of initial autonomic tone by the stress index (SI) under conditions of relative rest does not always accurately reflect the actual

state of autonomic tone, we focused on changes in autonomic tone during orthostasis (ORT). This is shown in Table 2 and Figure 2.

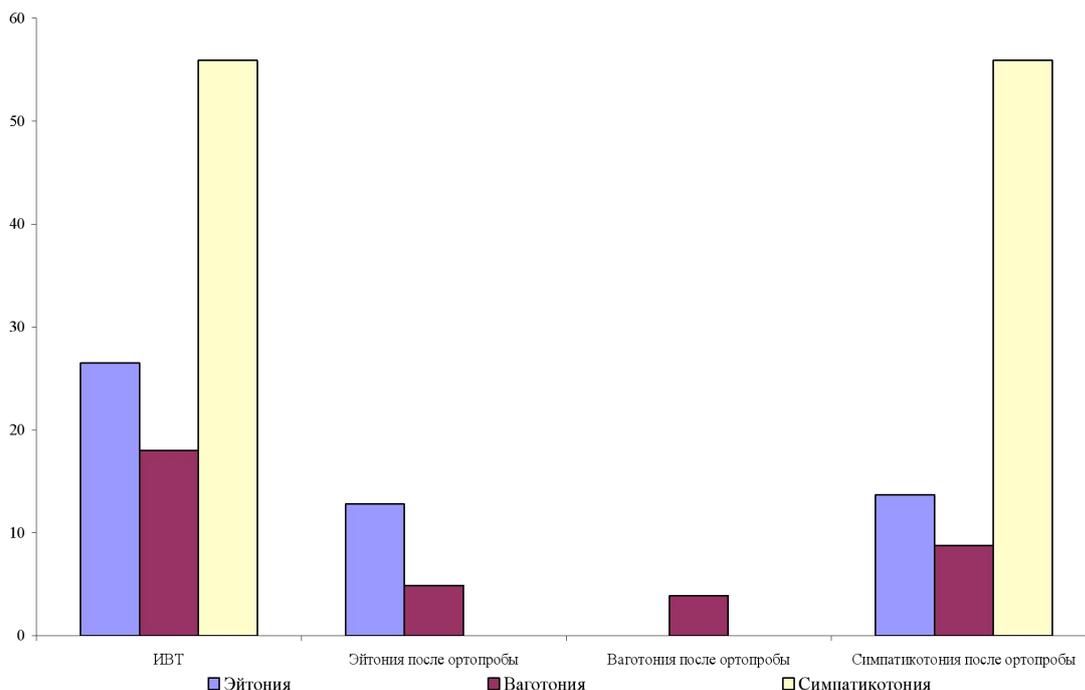
**Table 2.**

**Dynamics of initial vegetative tone (IVT) in the orthostatic state in patients with juvenile rheumatoid arthritis (%)**

Initial vegetative tone		Dynamics of IVT after orthotesting					
		Eitonia		Vagotonia		Sympathicotonia	
		п	%	П	%	п	%
1	<b>Eitonia</b> п=27 (26,5%)	13	12,8	-	-	14	13,7
2	<b>Vagotonia</b> п=18 (17,6%)	5	4,9	4	3,9	9	8,8
3	<b>Sympathicotonia</b> п=57(55,9%)	-	-	-	-	57	55,9
<b>Total п=102 (100%)</b>		<b>18</b>	<b>17,7</b>	<b>4</b>	<b>3,9</b>	<b>80</b>	<b>78,4</b>

As evident from the data in Table 2, patients with juvenile rheumatoid arthritis (JRA) maintained initial vegetative tone - either eutonia (SI1=30.0-90.0 conventional units) or vagotonia (SI1 <30.0 conventional units) - in a state of relative rest due to excessive tension in the parasympathetic part of the autonomic nervous system. This indicates that half of the children with JRA exhibited dystonic characteristics in their initial eu- and vagotonia from the outset. In JRA patients during orthostatic testing, the values of ΔX and Mo decreased (heart rate increased), while indicators of AMo, VPR, SI2, and derivatives of AMo, Mo, and ΔX increased (P<0.05-0.001). More pronounced changes were observed in patients with initial eutonia and vagotonia compared to those with sympathicotonia. This aligns with the law of initial value: the lower the initial level of activity, the greater the changes. This pattern was further confirmed by a significant increase in the SI2/SI1 ratio in eutonia (6.32±0.59; P<0.01) and vagotonia (7.42±0.57; P<0.001) compared to sympathicotonia (2.47±0.08). The dynamics of Initial vegetative tone (IVT) in orthostasis are clearly illustrated in Figure 2.

**Figure 2.** Dynamics of initial autonomic tone in orthostasis



The results of complex treatment in patients with JRA led to certain positive changes in the initial autonomic tone - a decrease in the number of sympathicotonic states from 55.9% to 43.1% ( $P < 0.01$ ) and an increase in the proportion of eutonia from 26.5% to 43.1% ( $P < 0.001$ ) were observed. However, the dynamics of the initial autonomic tone during orthostasis in patients with eu- (16.7%;  $P > 0.05$ ), vago- (8.8%;  $P > 0.05$ ), and sympathicotonic (74.5%;  $P > 0.05$ ) states compared to pre-treatment indicators (17.7%, 3.9%, and 78.4% respectively) did not confirm "the positivity of these two changes." Consequently, the specific therapeutic measures conducted have a temporary and unstable effect. The results of the study of autonomic reactivity in patients with JRA are presented in Table 3. The table data show that overall, only 34.3% of patients with JRA (compared to 77.7% in healthy individuals;  $P < 0.001$ ) responded to orthostatic load with normal values.

**Table 3.**

**State of vegetative reactivity based on initial vegetative tone in patients with JRA (according to CIG data)**

Initial vegetative tone		VR dynamics after orthoptest					
		Normal		Hypersympathicotonic		Asympathicotonic	
		π	%	π	%	π	%
1	Eitonia π=27(100%)	9	33,3	13	48,1	5	18,6
2	Vagotonia π=18 (100%)	9	50,0	9	50,0	-	-
3	Sympathicotonia π=57 (100%)	17	29,8	35	61,4	5	8,8
<b>Total n=102 (100%)</b>		<b>35</b>	<b>34,3</b>	<b>57</b>	<b>55,9</b>	<b>10</b>	<b>9,8</b>

(SI2/SI1) and in 65.7% of cases (in healthy children - 22.3%;  $P < 0.01$ ), the reactions were pathological (of which 55.9% of patients had hypersympathicotonic and 9.8% had asympathicotonic reactions), which significantly differed from the indicators of healthy children (12.1%;  $P < 0.001$  and 10.2%;  $P > 0.05$ , respectively). A comparative analysis of vegetative reactions in patients with JRA showed a decrease in normal eu- ( $P < 0.001$ ), vago- ( $P < 0.01$ ), and sympathicotonic ( $P < 0.001$ ) reactions compared to healthy children of this region (Yakhudayev E.M., 1992). In healthy children, normal vegetative reactions were observed in 81.7%, 71.9%, and 76.9% of cases, respectively. Among patients, the frequency of hypersympathicotonic reactions significantly increased: reaching 48.1% in eutonia, 50.0% in vagotonia, and 61.4% in sympathicotonia. These indicators are significantly higher than those of healthy children (10.4%, 22.8%, and 7.1%, respectively). In patients with eutonia, the frequency of asympathicotonic reactions increased (18.6% versus 7.8% in healthy individuals;  $P < 0.05$ ), while in initial sympathicotonia, it decreased (8.8% versus 16.7% in healthy children;  $P < 0.05$ ). Thus, patients with JRA exhibit peculiarities in vegetative homeostasis, manifested by high initial sympathicotonia, hypersympathicotonic vegetative reactivity, as well as insufficient and mixed forms of vegetative provision. The study of the internal structure of heart rhythm and COP results in patients with JRA indicates "exhaustion" and a decrease in the reserve capabilities of the sympathoadrenal and hypothalamic-pituitary-adrenal systems. Positive changes in vegetative homeostasis after specific treatment are observed only in male patients and in the articular form of the disease, while in girls and in the systemic form of the process, such improvements are not observed. Therefore, further refinement of JRA treatment methods is required in terms of correcting vegetative homeostasis and the use of vegetotropic drugs.

**CONCLUSION**

This study demonstrates the presence of significant disturbances in vegetative homeostasis among children with Juvenile Rheumatoid Arthritis. The findings reveal a marked predominance of initial sympathicotonia, indicating a state of heightened sympathetic nervous system activity at rest. The regulation of heart rhythm was found to be directly dependent on this initial autonomic tone, with evidence pointing to a decrease in adaptive control mechanisms. Specifically, patients with initial eu- and vagotonia exhibited an increased influence of the humoral contour and decreased neural control, while those with sympathicotonia showed weakened parasympathetic compensatory capabilities and a significantly enhanced neural contour, suggestive of an "emergency" stage of regulation.

Furthermore, orthostatic testing confirmed this autonomic instability, revealing that a majority of patients (65.7%) exhibited pathological vegetative reactivity, primarily hypersympathicotonic reactions. These results strongly suggest a state of "exhaustion" and a significant reduction in the reserve capabilities of the sympathoadrenal and hypothalamic-pituitary-adrenal systems.

Importantly, while complex treatment led to some positive changes in resting autonomic tone, these improvements were found to be unstable and did not normalize vegetative reactivity during orthostatic stress. This highlights the insufficiency of current therapeutic protocols in addressing the full scope of autonomic dysfunction in JRA. Consequently, further refinement of JRA treatment methods is imperative. Future strategies should aim to correct vegetative homeostasis, potentially through the targeted use of vegetotropic drugs, to improve systemic regulation and prevent the long-term disabilities associated with this chronic disease.

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