

# CHARACTERIZATION OF VEGETATIVE CHANGES IN BRONCHIAL ASTHMA OF VARIOUS SEVERITIES IN CHILDREN



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## ABSTRACT

This article presents a study of the state of vegetative balance and prognostic possibilities of quantitative parameters of functional activity of VNS to estimate a state of bodily adaptive reserves in children with severe BA. Bronchial asthma, being one of the most common chronic diseases in childhood, requires further research into predisposing and causally-significant factors, mechanisms of pathogenesis and peculiarities of a clinical course, improvement of methods of diagnostics, treatment, and prevention. Great importance in the development of bronchial asthma in children is given to genetically-fixed functional insufficiency of barrier tissues of the respiratory system, increased ability to synthesize allergic antibodies and produce certain cytokines, high bronchopulmonary sensitivity to mediators of allergic inflammation, lowered sensitivity of 3g-adrenoreceptors to endogenous catecholamins, changes in immunologic responsiveness, and disorder of neuroendocrinal regulation of immune responses. Implementation of genetic predisposition to bronchial asthma development is promoted by influence of adverse environmental factors.

## UDC CODE & KEYWORDS

■ UDC: 618 ■ Bronchial asthma ■ Catecholamins ■ Neuroendocrinal regulation ■ Bronchopulmonary sensitivity

## INTRODUCTION

As Guryanova, Igisheva, & Galejev (2003) wrote considering a leading role of allergy and immune inflammation in the development of bronchial asthma, a team of authors of the Research and practical program proposed the following determination of the disease: bronchial asthma is an allergic disease characterized by repeated episodes of bronchial obstruction, the pathogenetic basis of which is laid by immune inflammation of respiratory airways and bronchial hyper-reactivity. A disorder of bronchial patency is manifested by dyspnea, sibilant rales in lungs, which are quite often heard in the distance, a cough, and a feeling of chest congestion. The bronchial obstruction occurred is reversible under the influence of a treatment undertaken or resolved spontaneously.

During the last years a certain progress has been achieved in studying of mechanisms of development of bronchial asthma in children, clinico-functional criteria of the disease are specified, new technologies of treatment of disease exacerbations and programme of preventive treatment are introduced that increased a life quality of sick children and their parents. Modern multimodality therapy of children with bronchial asthma is carried out with due consideration to severity of its course and a period of the disease and stipulates utilisation of bronchodilators and mucolytic agents, basic anti-inflammatory drugs, antileukotriene and antitransmitter agents, specific immunotherapy, physiotherapeutic procedures, reflex - and psychotherapies. As Guryanova et al. (2003), Klyucheva, Ryvkin, & Troitskaya (2005), and Mizernitski (2003) wrote, the urgency and social importance of the problem are determined by high prevalence of the disease (10-15%) in childhood, a tendency to "rejuvenation" and an annual increase in a number of patients with BA, adverse influence on growth and development of the child and early disability. Analysis of medical data suggests on a doubtless role of the central and peripheral parts of the vegetative nervous system (VNS) not only in development of bronchial obstruction pathogenesis, but also in provision of processes of adaptation of respiratory and cardiovascular systems in BA. Disorders of vegetative regulation in BA concern both adrenergic and cholinergic links. Maintenance of a vegetative balance in the course of development of a pathological process makes it possible to keep the level of compensation achieved, to ensure an adequate peripheral blood flow and a normal bronchial tonus. As Bolova, Uvarova, & Yakushenko (2008) wrote at the same time, the adolescent age being an especial period of ontogenetic development of the child is characterised by a pronounced reorganisation of all functional bodily systems, a rise in a number of transitional disorders of the cardiovascular system and various types of a vegetative imbalance. Taking into account such a background for studying of pathogenetic mechanisms of development and prognosis of the disease course, the importance of estimation of vegetative interactions in patient with BA is doubtless. To evaluate the state of regulatory bodily systems, analysis of variability of cardiac rhythm is optimal.

Medical sources point at an important role of VNS disorders in occurrence and development of bronchial asthma, and researches into studying a balance and responsiveness of VNS in BA are not numerous and controversial. Some authors state that parasympathetic influences prevail in vegetative provision in a majority of patients with BA, other researchers note a more frequent occurrence of BA attacks in patients with prevalence of a sympathetic tonus, while third ones find a reliable growth of prevalence of a tonus of parasympathetic nervous system with age and increase of the disease duration. There is also an opinion that BA develops on the background of a rise in activity of the central contour of regulation of a vegetative tonus and pronounced sympathicotonia. Analysis of medical data allows drawing a conclusion that estimation of a wave structure of a sinus rhythm in patients with BA reveals an imbalance of all links of VNS and a possible depletion of its adaptive reserves. However, a degree of these changes as well as their reversibility (a possibility of re-adaptation) remain to be studied insufficiently.

The goal of our work was to study the states of vegetative balance and prognostic possibilities of quantitative parameters of the VNS functional activity to evaluate a state of adaptive bodily reserves in children with severe BA.

### Material and method

As Baevski, Ivanov, & Chireikin (2001) wrote, estimation of initial vegetative tonus was carried out according to unified and standardised technique of study; cardiointervalography (CIG), clino-orthostatic test (COT). The results of study of initial vegetative tonus in conditions of a relative rest showed an appreciable prevalence of cases of initial sympathicotonia in 72 children (64.7%,  $P < 0.001$ ), a decrease in the share of eutony in 22 children (20.8%;  $P < 0.01$ ) and vagotonia in 17 patients (15.2%,  $P < 0.05$ ).

The data obtained during the study were processed statistically on personal computer Pentium-IV using Microsoft Office Excel-2003 software including utilisation of built-in functions of statistical management.

### Results and discussion

Results of studying the internal structure of a cardiac rhythm in patients with BA followed-up by us depending on initial vegetative tonus show (Table 1) that the structure of a cardiac rhythm in patients differs from that of healthy children.

Table 1: Structure of heart rhythm in children with bronchial asthma depending on initial vegetative tonus

Heart rhythm indicators	Eutony n = 22	Vagotonia n = 17	Sympathicotonia n = 72
1. Mo, sec.	0.612±0.009	0.659±0.010	0.541±0.004
2. MoA,%	14.60±0.20	11.51±0.10	32.85±0.26
3. ΔX, sec.	0.211±0.001	0.357±0.002	0.097±0.003
4. VIR, c.u.	8.36±0.16	4.14±0.09	23.12±0.32
5. IS1, c.u.	60.13±1.56	21.87±0.54	345.82±7.65
6. MoA/ΔX	74.89±2.76	31.67±0.98	376.91±18.23
7. MoA/Mo	25.43±0.88	16.97±0.76	62.32±1.66

Source: Authors

In initial eutony in patients with a decrease in Mo ( $P < 0.01$ ), ΔX ( $P < 0.01$ ) values, an increase in indicators of VNR and IS1 ( $P < 0.05$ ) is observed. It is known that in initial eutony, a certain balance between adrenergic (MoA) and cholinergic influence (AX) on heart rhythm is observed. However, in patients in initial eutony, this balance is impaired toward an increase of a humoral contour of regulation (a rise in Mo), a decrease in activity of the nervous control (reduction of MoA) due to which MoA/ΔX and MoA/Mo ratios ( $P < 0.05$ ) are lowered. These shifts in a humoral contour of cardiac rhythm occur on the background of a fall in activity of a parasympathetic part of VNS (ΔX,  $P < 0.01$ ) and some tension of compensatory mechanisms in regulation of cardiac rhythm (a rise in VIR and IS1,  $P < 0.05$ ).

In BA patients in initial vagotonia, no reliable differences in cardiac rhythm indicators (ΔX, VIR, IS1, MoA/Mo) were observed in comparison with healthy children (ΔX = 0.395±0.020 sec; VIR = 3.45±0.12 c.u.; IS1 = 24.8±1.49 c.u.; MoA/Mo = 18.8±2.48) ( $P > 0.05$ ). In the same group of patients, inspissation of a cardiac cycle (Mo,  $P < 0.001$ ), a decrease of MoA value ( $P < 0.05$ ) and MoA/ΔH ratio ( $P < 0.05$ ) in comparison with healthy children (Mo = 0.755±0.02 sec.; MoA = 14.30±1.02%; MoA/ΔH = 39.8±4.38) is noted. These data are similar to what happened in initial eutony, viz. intensification of influence of a humoral contour on the background of reduction of the central influence on heart rhythm.

Patients with initial sympathicotonia show further enhancement of a humoral contour ( $P < 0.001$ ), a maximum fall of a ΔX indicator ( $P < 0.01$ ), a substantial rise in VIR and IS1 rates ( $P < 0.01$ ) in comparison with healthy children (Mo = 0.607±0.06 sec.; X = 0.16±0.05 sec.; VIR = 11.3±0.43 c.u.; IS1 = 179.70±7.05 c.u.). It should be noted that a decrease of ΔX rate to low values (0.093±0.004 sec.) on the background of high VIR, IS1 rates suggests to a state of limited strain and deterioration in a quality of circulation regulation, i.e. the onset of an "emergency" phase in regulation of a cardiac rhythm. An increase in ratios of MoA/Mo ( $P < 0.05$ ) and MoA/ΔX ( $P < 0.01$ ) in comparison with healthy children (50.3±2.14 and 28.2±3.1 respectively) suggests on depletion of compensatory possibilities of the parasympathetic part of VNS and appreciable enhancement of central (nervous) contours and a rise of a degree of centralisation of cardiac rhythm management.

Thus, regulation of cardiac rhythm in patients with severe BA depends on initial vegetative tonus. In initial eutony and vagotonia adverse changes in cardiac rhythm occur expressed by higher cardiac rhythm, less adaptive regulatory mechanisms, i.e. enhancement in the influence of a humoral contour on the background of a decrease of the influence of nervous mechanisms in the organisation of a cardiac rhythm. Unlike patients with vagotonia, in initial sympathicotonia exhaustion of the parasympathetic VNS occurs, and that means that enhancement of a nervous contour of cardiac rhythm regulation suggests on the onset of an "emergency" phase in compensatory possibilities of the body on provision and organisation of a cardiac rhythm. We consider a change in a vegetative tonus (Table 2) in orthostasis (CIG) to be important.

Table 2: Dynamics of initial vegetative tonus in children with severe bronchial asthma in orthostasis

Initial vegetative tonus	Dynamics of IVT after an orthostatic test			
	Eutony	Vagotonia	Sympathicotonia	Total
Eutony	11 (10.8)	0	11 (9.8)	22 (19.8)
Vagotonia	3 (2.9)	5 (4.9)	9 (6.9)	17 (15.3)
Sympathicotonia	0		72 (64.7)	72 (69.9)
Total	14 (13.7)	5 (4.9)	92 (81.4)	111 (100)

Source: Authors

As the data of Table 2 show, in BA patients an initial vegetative tonus - eutony and vagotonia of a relative rest were maintained due to excessive strains in the parasympathetic VNS. It suggests that in 1/2 of children with JRA, initial eutonies and vagotonias initially had a dystonic character. Results of a multimodality therapy of patient with BA resulted in certain favourable shifts in initial vegetative tonus, viz. a fall in a number of cases of sympathicotonia ( $P < 0.01$ ) and a rise in specific gravity of eutony ( $P < 0.001$ ). However, dynamics of initial vegetative tonus during orthostasis in patients with eutony, vagotonia and sympathicotonia did not confirm a "usefulness of these two shifts" in comparison with specific gravity of initial vegetative tonus in orthostasis prior to treatment. Hence, the measures undertaken, aimed at carrying out of specific therapy, produce a temporary and unstable effect. Results of studying vegetative responsiveness (VR) in patients with BA are presented in Table 3.

Table 3: The state of vegetative responsiveness in patients of bronchial asthma depending on the initial vegetative status

Initial vegetative tonus	Dynamics of VR after orthostatic test			
	Normal	Hypersympatricotonic	Symptom-free	Total
Eutony	7 (33.3)	12 (52.4)	3 (14.3)	22 (19.8)
Vagotonia	7 (46.7)	10 (53.3)	0	17 (15.3)
Sympatricotonia	15 (21.1)	52 (72.3)	5 (6.1)	72 (69.9)
Total	29 (27.5)	74 (65.7)	8 (6.8)	111 (100)

Source: Authors

The data of Table 3 suggest that, in general, patients with severe BA responded with normal values (IS2/IS1) only in 27.53% of cases (77.7%,  $P < 0.001$  in healthy subjects) to an orthostatic load and in 72.5% of cases (22.3%,  $P < 0.01$  in healthy subjects) responses were pathological (of them in 65.7% of patients had hypersympatricotonic and in 6.8% symptom-free responses), that differs considerably from the data obtained in healthy children (12.1%,  $P < 0.001$  and 10.2%,  $P > 0.05$ , respectively). A comparative analysis of vegetative responses in sick subjects showed a decrease in of normal responses in eutony ( $P < 0.001$ ), vagotonia ( $P < 0.01$ ) and sympathicotonia ( $P < 0.001$ ) in comparison with healthy children of this region (who had vegetative responses in 81.7%, 71.9%, and 76.9% respectively).

A vegetative status in the majority of adolescents with moderate BA in exacerbation is characterised by a background sympathicotonia, high vegetative responsiveness of a normal or hypersympatricotonic type in normal tonus of the parasympathetic part and a sufficient variant of vegetative provision of activity. Adolescents with severe BA have a pronounced imbalance of vegetative regulation characterised by a decreased tonus of a sympathetic part of the autonomic nervous system in rest, a symptom-free variant of reaction to an orthostatic load in insufficient vegetative provision of activity of organs and systems. During an exacerbation period of moderate BA in adolescents, electric instability of myocardium prevails on the background of sympathicotonia mainly in the form of disorders of a function of automatism. Patients with a severe course of the disease have various variants of a disorder of rhythm and conductivity in combination with a change in processes of repolarization of myocardium.

### Conclusion

Patients with severe BA have peculiarities in vegetative homeostasis expressed in high initial sympathicotonus, hypersympatricotonic vegetative responsiveness and insufficient and mixed types of vegetative provision.

Implementation of hyperactivity of a sympathetic link of the vegetative nervous system is carried out by means of influence on metabolism through prostaglandins and cyclic nucleotides with mobilisation of energy resources, activation and "exhaustion" of reserve possibilities of the hypothalamic-hypophyseal-adrenal system, a change in the level of released mediators of an allergic response.

The results obtained need further development of methods of treatment of BA in terms of correction of vegetative homeostasis and utilisation of vegetotropic drugs that can promote a more favourable course of the disease and improve a life quality of patients.

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