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Relationship of Blood Oxyproline Level with the Severity of Obstructive Bronchitis in Children

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Abstract: The article presents data on the state of collagen metabolism in terms of oxyproline in the blood, its clinical significance for assessing the severity and outcome of the disease, the criterion for the effectiveness of therapy in children of early age with acute obstructive bronchitis and bronchiolitis. The author recommends to determine the level of free and protein-bound oxyproline in blood plasma, an increase in which reflects the degree of destruction in the bronchopulmonary apparatus. The inclusion of immunomodulin into the basic treatment contributes to an increase in the effectiveness of therapy, a reduction of treatment duration.

Keywords: children, oxyproline, bronchitis and bronchiolitis, treatment.

One of the most important components of lung collagen is hydroxyproline. Compared to other parenchymal organs, the collagen content in the lung is the highest [4, 7, 20, 21,]. When oxyproline metabolism is impaired, unfavorable conditions are created for the stability of the pulmonary framework of the surfactant system of the alveoli and for the lungs to perform their main gas exchange function [1, 3,].

In recent years, in the violation of the regulation of collagen synthesis during inflammatory processes in the lungs, a certain place is given to shifts in immune reactivity. In this case, excessive collagen formation is associated with the manifestation of autotoxicity of lymphocytes. The dependence of the activation of collagen production on the damaging effect of T-lymphocytes has been revealed [5,6, 7, 16,]. A number of researchers associate the intensity of collagen formation in acute inflammatory diseases in the lungs with metabolic disorders associated with proteins, in particular, hydroxyproline [2, 14, 15]. With a prolonged course of the disease, a high level of hydroxyproline in the blood plasma against the background of a fairly good clinical condition of patients may indicate an unfavorable prognosis [3, 12, 13].

In recent years, there has been a certain trend towards an increase in the incidence of bronchial obstruction syndrome in young children [2, 10, 11].

The pathogenesis of bronchial obstruction is rather complicated and not fully understood [4, 8, 9]. Until now, metabolic disorders of the connective tissue structures of the lungs, collagen degradation in obstructive bronchitis have been insufficiently studied. In the literature, there are practically no data on the state of metabolism of oxyproline and its relationship with the course of acute obstructive bronchitis and bronchiolitis in young children.

The purpose of our work is to study the clinical significance of oxyproline shifts for assessing the severity and outcome of the disease, and to develop adequate methods for correcting oxyproline metabolism in the treatment of young children with acute obstructive bronchitis and bronchiolitis.

We examined 95 children aged from 1 month to 3 years (average age 1.5 ± 0.63 years), who were treated in the somatic department of the Tashkent City Children's Clinical Hospital. The observation was carried out by the method of random sampling. The diagnosis of acute obstructive bronchitis and bronchiolitis was based on the data of the clinical picture of the disease, the results of general clinical studies in accordance with the proposed classification of clinical forms of bronchopulmonary diseases in children, adopted in Moscow at the symposium "Nonspecific lung diseases in children".

According to the modern classification, the diagnosis of acute obstructive bronchitis and bronchiolitis was made in children who fell ill for the first time, whose lung radiographs showed no focal and infiltrative shadows in the lungs in dynamics, there was a pronounced cough, dry and moist rales, prolonged and difficult exhalation. Acute obstructive bronchitis was diagnosed in 63 (66.3%) children, and acute obstructive bronchiolitis in 32 (33.7%) children.

All examined children were divided into 2 groups. The first group included patients with acute obstructive bronchitis, in whom the level of oxyproline was studied before and after treatment, of whom 38 received traditional treatment and 25 - along with traditional Immunomodulin. The 2nd group consisted of children with acute obstructive bronchiolitis, of which 15 patients were treated with the traditional method, 17 were additionally injected with Immunomodulin.

The drug Immunomodulin was developed by Uzbek scientists and approved by the Main Directorate for Quality Control of Medicines and Medical Equipment of the Ministry of Health of the Republic of Uzbekistan for use in medical practice as a biostimulating and immunocorrecting agent (registration certificate No. 96 671 22 dated 06.21.1996).

Immunomodulin was administered intramuscularly at a 0.1–0.014% solution per 10 kg of body weight once a day for 5-7 days.

The control group consisted of 20 apparently healthy children of the same age.

The material for the study was blood plasma with a volume of 0.5 ml. Blood sampling was performed in the morning on an empty stomach. The study was carried out before and after the corresponding course of therapy. Oxyproline in blood plasma was investigated by the method of M.A. Osadchuk and V.M. Kapustin [5]. Analysis of our research results showed that before the treatment, the level of free and protein-bound oxyproline in the blood plasma of young children with acute obstructive bronchitis and bronchiolitis was significantly higher than in the control group.

It should be noted that in the blood plasma before treatment in children with acute obstructive bronchiolitis, the concentration of free and protein-bound oxyproline was higher, respectively, by 13.8% ($p < 0.05$) and 14.6% ($p < 0.01$) than in children with acute obstructive bronchitis.

Consequently, the increase in the level of oxyproline in the blood plasma is associated with the severity of the pathological process and the form of the disease.

The difference in the change in the level of free and bound oxyproline, their high content in the blood in children with acute obstructive bronchitis and bronchiolitis, may be determined by the peculiarity of the pathogenesis of the disease.

Plasma levels of free and protein-bound oxyproline in sick children early age with acute obstructive bronchitis and bronchiolitis before and after treatment

Indicators of oxyproline	Control group (n-20)	**Acute obstructive bronchitis**		
		before treatment (n=63)	traditional treatment (n=38)	traditional treatment + Immunomodulin (n=25)
Free	5,06±0,29	6,96±40,27[1]	5,88±0,23[1)2)]	5,30±0,49[2)]
Protein bound	13,81 ±0,45	18,67±0,43[1)]	15,30±0,39[1)]	13,72±0,27[2)3)]

Indicators of oxyproline	Control group (n-20)	Acute obstructive bronchiolitis		
		before treatment (n=32)	traditional treatment (n=15)	traditional treatment + Immunomodulin (n= 17)
Free	5,06±0,29	7,92±0,38[1)4)]	6,03±0,32[1)2)]	5,48±0,31[2)]
Protein bound	13,81 ±0,45	21,39±0,94[1)4)]	16,52±0,48[1)2)|]	13,90±0,24[2)3)]

There is no doubt that a more pronounced increase in the level of free and protein-bound oxyproline in the blood plasma in children with acute obstructive bronchiolitis compared with those in children with acute obstructive bronchitis is associated with significant disorders in the collagen metabolism of the bronchopulmonary system. On the other hand, changes in oxyproline metabolism indicate the heterogeneity of pathomorphological disorders in the bronchopulmonary system, which is accompanied by a different course and severity of the clinical picture of the disease. At the same time, the significant shifts in collagen metabolism found in our studies in the body of young children with acute obstructive bronchitis and bronchiolitis indicate the need to correct the revealed disorders.

As the results of our studies have shown, traditional therapy does not lead to a complete recovery to control values of the content of oxyproline in both free and protein-bound blood fractions in children with acute obstructive bronchitis and bronchiolitis. However, the level of free and protein-bound 011 is restored to the control level in children with acute obstructive bronchitis and bronchiolitis when immunomodulin is included in the traditional treatment regimen. As you know, Immunomodulin in patients with inflammatory lung diseases contributes to the restoration of impaired links of immunity - the activity of T-lymphocytes, immunoregulatory T-helpers and T-suppressors, B-lymphocytes, phagocytes, stimulates the production of interferon, antitelogenesis, enhances hematopoiesis, has vaso- and bronchodilating properties [1, 20, 21].

There are separate reports that Immunomodulin in acute inflammatory lung diseases increases the reduced cytochemical activity of mononuclear cells, stimulates immunogenesis in immunodeficiency, improves functional interactions between neutrophils, macrophages, lymphocytes and fibroblasts, i.e. those factors of pathogenesis that are involved in the regulation of collagen metabolism, in particular, oxyproline in the focus of inflammation [7, 18]. Perhaps, due to these mechanisms, we have established a high therapeutic effect and normalization of parameters of hydroxyproline (free and bound) in blood plasma when Immunomodulin is included in the complex treatment of children with acute obstructive bronchitis and bronchiolitis.

Along with the improvement of the indicators of oxyproline metabolism, we noted that the introduction of Immunomodulin promotes an earlier improvement in the clinical manifestations of the disease and a reduction in the recovery period. So, after 1-2 injections of the drug in children, the body temperature dropped to normal, the average duration of the febrile period remained 1.8 = ± 0.1 days, while in children with traditional treatment, the duration of body temperature was over 37.5 ° C (38— 39 'C) persisted for 2-3 days and averaged 2.5 ± 0.2 days ($p < 0.001$).

In children treated with the traditional method, symptoms such as cough, shortness of breath, dry wheezing, buzzing, as well as moist medium and fine bubbling rales, shortness of breath with a prolonged output with the participation of auxiliary muscles, disappeared on the 3rd-5th day, their average duration was 4.3 - ± 0.8 days, whereas when Immunomodulin was included in the complex therapy - on days 2-3 and the average duration was 2.2 ± 0.4 days ($p < 0.002$). In 4 (4.2) children undergoing traditional treatment, there was a protracted course of the disease (more than 10 days), while no such cases were observed with the introduction of Immunomodulin. It should be noted that children receiving Immunomodulin tolerated the drug well, no side effects were noted.

In addition, the analysis of the obtained research results showed that the duration of inpatient treatment of patients with acute obstructive bronchitis and bronchiolitis with the traditional

method averaged 11.8 ± 0.3 days, while with the additional conclusion of Immunomodulin - 7.5 ± 0.2 days ($p < 0.001$).

Thus, impaired metabolism of hydroxyproline is one of the important factors in the pathogenesis of acute bronchial obstruction and allows, in combination with the clinical picture, to judge the metabolic reactivity of the morphostructures of lung tissue in young children with acute obstructive bronchitis and bronchiolitis. At the same time, the revealed difference in the content of hydroxyproline in the blood plasma in patients with acute obstructive bronchitis and bronchiolitis indicates its diagnostic and prognostic significance for assessing the severity, nature of the course and outcome of the disease, as well as for analyzing the effectiveness of therapy.

The higher therapeutic effect of Immunomodulin revealed in our studies in comparison with the traditional treatment method allows us to recommend it for the treatment of young children with acute obstructive bronchitis and bronchiolitis, which will contribute to the optimization of therapy.

Thus, in acute obstructive bronchitis, an increase in the level of free and protein-bound hydroxyproline in the blood plasma indicates a severe course of acute broncho-obstructive disease in young children. The revealed relationship between the high concentration of oxyproline and the severity of the disease indicates that impaired collagen metabolism in the lungs is of no small importance in the datogenesis of acute broncho-obstructive syndrome in young children. When sick children with acute obstructive bronchitis and bronchiolitis are included in the complex treatment of Immunomodulin, a high therapeutic effect and normalization of oxyproline parameters are observed.

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