ORIGINAL ARTICLE

CONTENTS

Dynamic indicators of the antioxidant system in children with acute respiratory pathology depending on the therapy scheme

Olesya M. Horlenko, Iryna Yu. Pikina, Lyubomyra B. Prylypko, Gabriella B. Kossey, Olga A. Pushkarenko, Iryna M. Boisak, Ivan I. Pushkash
UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

ABSTRACT

Aim: To improve the early diagnosis, course, prediction of the development of Acute Respiratory pathology in children, taking into account the state of antioxidant system (AOS).

Materials and Methods: The research group included school-age children (10-14 years old) with Acute Respiratory pathologe (n=111) and a control group (n=25).diseases in comparation.

Results: The highest positive correlation between ferritin and TNF- α (r=0,41, p=0,001); Cortisol with Glutathione peroxidase (r=0,35, p=0,006) were observed. Ascorbic acid presented positive interactions on the values of Il-6 and Il-2 (r=0,27, 0,26, respectively). The value of vitamin D is represented in positive interactions with γ-IFN (r=0,30), leptin (r=0,38) and Cu (r=0,32). The negative relationship of Zn with Il-6 was transformed for supporting immune barriers and protein metabolism.

Conclusions: The level of Glutathione peroxidase increased in 1,6 times, on the other hand, when the basic therapy was prescribed - in 1,1 times (p_3<0,01; p_4<0,01; p_5<0,01), cortisol level had a reliable tendency to decrease in 1,6. The values of Ascorbic acid increased by almost in 2 times in first group andin 1,4 times in the second group (p_3<0,01; p_4<0,01; p_5<0,01). After the treatment, the level of vitamin D was identified within the physiological range in the first group. There are also positive effects of optimized therapy on the state of Copper (p_3<0,01), Zinc (p_3<0,01), Iron (p_3=0,04) trace elements in comparison with the data of the second group.

KEY WORDS: acute respiratory disease (acute pharyngitis, acute bronchitis, acute tonsillitis), antioxidant system, reactive changes of the hepatobiliary system, treatment, children

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INTRODUCTION

Oxidative stress (OS) is widely studied in the pathology of various diseases and their effects on the development of an imbalance in the links of homeostasis. The mechanisms of formation of free radicals and regulation of their levels with the participation of oxidant and antioxidant systems have been studied, but there is a need for scientific research on the identification of early and highly sensitive biomarkers of OS in patients and their role [1]. The main target of oxidative stress is phospholipid membranes. Violation of the integrity of the protective membrane leads to an increase in its permeability to viruses, changes in the receptor apparatus and, as a result, the penetration of free radicals into the cell with subsequent damage to DNA and mitochondria, which is accompanied by a decrease in the transmembrane potential and an acceleration of the release of apoptosis factors [2,3].

In the cells of a living organism, there is a balance between the synthesis of reactive molecules and their leveling by protective mechanisms. As a rule, this balance is aimed at maintaining pro-oxidant conditions, which ensures permanent moderate oxidative eustress [4].

Disturbance of the balance can cause development of oxidative stress, that is, a state of the body characterized by an increase in the oxidative potential, which can lead to damage to the structure of DNA, proteins, carbohydrates and lipids and, thus, physiological homeostasis is disturbed. As a result, there is a shift in cell functioning and redox signal transmission, accumulation of cytotoxic compounds. Stress is defined as an imbalance between the formation of oxidants and antioxidant protection in favor of oxidants, which leads to cellular dysfunction and tissue damage, apoptosis. An imbalance of pro-oxidants and antioxidant system components is at the root of many diseases, as well as in acute respiratory pathology [5].

Among all the systems of the body, the respiratory tract, especially the lungs, are the most sensitive to oxidative stress compared to other organs and systems, due to the effect on them of a higher concentration of oxygen, exogenous oxidants that increase the synthesis

of oxidants and activate the formation of free radicals as markers of inflammation. Thus, free radicals are constantly formed in the human body during normal metabolism. They have both positive and negative properties [6].

AIM

To improve the early diagnosis, course, prediction of the development of Acute Respiratory pathology in children, taking into account the state of Antioxidant system for the development of optimized therapy.

MATERIALS AND METHODS

The research group included school-age children (10-14 years old). The general group of inflammatory diseases of the respiratory tract (J06, 106.8, 106.9) with a diagnosis of Acute Respiratory infection (ARI) of bacterial origin was considered (n=111) and included local inflammatory lesions of the upper respiratory tract with presentation of acute Pharyngitis, J02 (68,0%), acute Bronchitis, J20, J20.9 (22,0%) acute Tonsillitis J03, J03.9 (10,0%) and a control group (n=25), identical in age and gender. Two research groups were created, depending on the method of treatment: 1st group - 60 patients (optimized therapy), 2nd group - 51 patients (basic therapy) and general clinical, biochemical, immunological studies were performed in the dynamics under the influence of the addition of mineral -vitamin complex and lysozyme.

RESULTS

In our research, we used the classification of natural antioxidants. The vast majority are exogenous components obtained from natural sources [7]. In the group of exogenous antioxidants, there are several subgroups that a person receives mainly with food, in particular, vitamins D3, C, minerals (Zinc, Iron and Copper).

The scientific study included determination of the levels of the following antioxidants (AO) in the blood of the examined patients:

a) representative of the enzyme link - glutathione-peroxidase (GPO);

b) non-enzymatic link:

1) low molecular weight AO – Bilirubin, Urea; Thyroxine (T4), steroid hormones (cortisol), vitamins D3, C);

2) macromolecular antioxidants of protein nature - total Protein, Ferritin;

3) trace elements: Zn, Fe, Cu.

Compounds that slightly inhibit or stimulate the action of antioxidants, but have no effect on the intensity of BRO processes, are also considered.

The obtained data on the studied indicators of AOS in children is presented in the following table (Table 1).

Based on the obtained date, the level of GPO increased by 1,6 times, when receiving basic therapy – by 1,1 times. Dynamic data varied within reference values, but with significant differences between groups and control group data ($p3<0,01$; $p4<0,01$; $p5<0,01$). It is known that the general cohort of biological antioxidants creates a buffer antioxidant system that has a certain capacity and spheres of influence, and the interrelationships of prooxidants/antioxidants determine the AO status of a child's organism. Antioxidant enzymes form a single metabolic chain, in which the product of the first reaction is the substrate of the next one, therefore, for the normal functioning of the entire system, it is important to maintain certain ratios in the activity of individual enzymes of the chain. The enzymatic link of the AOS of the body has significant associative links with the non-enzymatic link to protect cells from free radical oxidation products, taking into account their hydrophobic and hydrophilic characteristics and as a result, the formation of a complex antioxidant effect [4].

Dynamic changes in indicators under the influence of various treatment methods are observed. The predominance of positive probable differences in the group of children with an optimized therapy scheme in the levels of total bilirubin ($p5=0,002$), total protein ($p5<0,01$), and urea ($p5=0,03$) are especially worth noting.

The level of ferritin varied within the reference range, but with a tendency to increase ($p1=0,003$; $p2=0,46$; $p3=0,36$; $p4=0,2$; $p5=0,004$). The values of vitamin D3 at the initial stage were equal, below the reference range ($18,77 \pm 4,14$ and $18,41 \pm 3,26$ ng/ml, respectively, by group). After the treatment, the level of vitamin D3 was identified within the physiological range in the first group ($32,12 \pm 3,48$ ng/ml; $p1<0,01$, $p2<0,01$), while the upper limit was not reached in the second group ($28, 43 \pm 4,43$; $p3<0,01$, $p4<0,01$), but with a significant upward trend. The values of ascorbic acid increased almost 2 times in the first group and 1,4 times in the second group with reliable indicators ($p3<0,01$; $p4<0,01$; $p5<0,01$) and within the reference range. There are also positive effects of optimized therapy on the state of copper ($p5<0,01$), zinc ($p5<0,01$), iron ($p5=0,04$) trace elements. Increasing the level of zinc, which is part of approximately 300 different proteins and plays an enormous role in the functioning of the body, contributes to the reaction of antioxidant protection, stabilization of biological membranes and functioning of the endocrine glands. The trace element copper participates in the immune reactions of the child's organism, tissue respiration, mechanisms of enzymatic catalysis, contributes to the processes of cell proliferation, which

Table 1. Indicators of AOS links in children with Acute Respiratory diseases

Indicator	Group 1 (n=60)		Group 2 (n=51)		Control Group (n=25)
	Before treatment	After treatment	Before treatment	After treatment	
1	2	3	4	5	6
GTP (4171-10881, U/1)	3774,08±124,85	5974,29±344,22 (p1<0,01; p2=0,13)	3807,88±111,89	4192,81±219,25 (p3 <0,01; p4 <0,01; p5 <0,01)	6108,72±425,93
Ascorbic acid (5,0 – 15,0 mg/l)	4,30±0,25	8,09±0,57 (p1<0,01; p2=0,66)	4,34±0,21	6,25±0,45 (p3 <0,01; p4 <0,01; p5 <0,01)	8,21±1,96
Vitamin D3 (30-70 ng/ml)	18,77±4,14	32,12±3,48 (p1<0,01; p2 < 0,01)	18,41±3,26	28,43±4,43 (p3 <0,01; p4 <0,01; p5 <0,01)	39,57±5,86
Total protein g/l	66,49±7,04	74,42±3,98 (p1<0,01; p2= 0,20)	67,72±7,30	71,09±3,18 (p3 =0,003; p4=0,06; p5 <0,01)	73,03±5,68
Total bilirubin, µmol/l	15,72±9,3	12,68±2,91 (p1=0,02; p2= 0,19)	15,98±9,01	14,75±3,95 (p3 =0,37; p4=0,31; p5=0,002)	13,74±4,26
Ureal, µmol/l	4,72±1,26	3,87±0,82 (p1 < 0,01; p2= 0,77)	4,92±1,37	4,27±1,05 (p3 =0,008; p4=0,07)	3,81±0,99

Table 2. Correlation relationships of AOS indicators in children at the initial stage

Laboratory parameters		Correlation coefficient (r)	Statistical significance (p)
Free thyroxine	Total protein	-0,29	0,002
GPO	Thyroid hormone	-0,43	<0,01
Ascorbic acid	Vitamin B_{12}	0,25	0,007
Vitamin D3	CRP	-0,21	0,03
	ATPO	0,21	0,03
	IL-1	0,22	0,02
	TNF-α	0,26	0,005
Ferritin	Urea	-0,27	0,004
	Na	0,19	0,04
	TNF-α	0,23	0.01
Total protein	IL-4	0,19	0,05
Urea	CRP	-0,26	0,005
Cu	Bilirubin	0,20	0,03
	Creatinine	0,30	0,001
Zn	IL-6	-0,19	0,04
Fe	Urea	0,19	0,05
	Na	0,22	0,02
	Neoptein	-0,26	0,005
Cortisol	Creatinine	0,22	0,02
	Adiponectin	0,27	0,005
	IL-1	-0,26	0,005

determines its importance in the regeneration of the mucous membrane. Its biological significance is due to the fact that Cu+ and Cu2+ ions are components of numerous enzymes and proteins. Currently, about 20 are known, in particular, cytochrome C oxidase is a terminal protein complex that plays a decisive role in the regulation of the entire respiratory chain [8]. Also, Cu/Zn-dependent Superoxide dismutase is the starting chain of the antioxidant defense system of the child's body. Interdependence with iron exchange is demonstrated by presence of copper in Ceruloplasmin. Scientists have proven the existence of physiological

Table 3. Correlation relationships of AOS components under the optimized therapy influence

Laboratory parameters		Correlation coefficient (r)	Statistical significance (p)
Glutathione peroxidase	Cortisol	0,35	0,006
Ascorbic acid	IL-6	0,27	0,04
	IL-2	0,26	0,05
Vitamin D3	Y-IFN	0,30	0,02
	Leptin	0,28	0,003
	Cu	0,32	0,01
ferritin	Total protein	0,26	0,04
	TNF-α	0,41	0,001
	Antibodies to thyroperoxidase	0,39	0,02
Urea	IL-2	0,30	0,02
	IL-4	0,26	0,005
	IgG	0,29	0,02
Cortisol	IgE	-0,28	0,03
Bilirubin	Vitamin B_{12}	-0,28	0,03
Cu	Glucose	-0,34	0,007
	Alkaline phosphatase	0,28	0,03
	Vitamin D3	0,32	0,01
Zn	Creatinin	0,27	0,04
Fe	-	-	-

antagonism between copper, on the one hand, and zinc, molybdenum, and magnesium, on the other. Iron participates in the synthesis of hemoglobin and myoglobin, catalase and peroxidase; in direct and indirect oxidative processes (includes 72 enzymes), ensuring normal functioning of the Immune system [9].

The level of thyroid hormones also varied within the reference range with unreliable differences between groups (free Triiodothyronine, p5=0,37; free Thyroxine, (p5=0,16) in contrast to the level of Antibodies to Thyroperoxidase (p5=0,009), with a predominance of decrease of the level in the first group, but also within the reference values.

Cortisol values during our study varied within the physiological range, but with a reliable tendency to decrease by 1,6 times in the group of children with an optimized treatment regimen (p4<0,01; p5<0,01).

An important stage of scientific research is the analysis of correlation relationships of the obtained values at the initial stage and at the end of the treatment.

The components of the antioxidant protection of the child's organism at the initial stage are presented in Table 2.

The most numerous (n=5) correlations of vitamin D3 were with CRP (r =-0,21, p=0,03) with a positive direction from antibodies to thyroperoxidase, Il-1, and TNF-a (r=0,21-0,26 with p=0,02-0,005). The correlations of ferritin with the levels of urea (r=-0,27, p=0,004), the positive direction - with the levels of Na (r=0,19, p=0.04), TNF-α (r=0,03, p=0,01) and the indicator of Fe with urea (r=0,19, p=0,05), Na (r=0,22, p=0,02, neopterin (r =-0,26 , p=0,005) should be noted. The cortisol level was positively correlated with the values of creatinine (r=0,22, p=0,02) and adiponectin (r=0,27, p=0,005) and negative interactions were found with IL-1 (r=-0,26, p=0,005).

According to our data, AOS indicators have a suppressive effect on the inflammatory process in the organism, in particular, Fe on the level of neopterin (r=-0,26), Zn on the level of IL-6 (r=-0,19), cortisol on IL-10 (r=-0,26), vitamin D3 on CRP (r=-0,21), free thyroxine on the level of total protein (r=-0,29).

Glutathione peroxidase correlates with the level of Creatinine (r=-0,27), which is involved in the energy exchange of tissues. Ascorbic acid has a positive interaction with the level of vitamin B12 (r=0,25), which regulates carbohydrate and fat metabolism. This way, the results of these indicators testify the positive effects on the main metabolic processes in order to preserve energy exchange. The level of copper correlates with the levels of bilirubin and creatinine, as the final product of the exchange of protein compounds, which indicates the positive effects of this trace element on the biliary function of the hepatobiliary system and energy metabolism [10, 11]. In clinical pediatric Gastroenterology, the vast majority of diseases of the hepatobiliary system are of a functional nature, accompanying and aggravating the course of the underlying disease. An

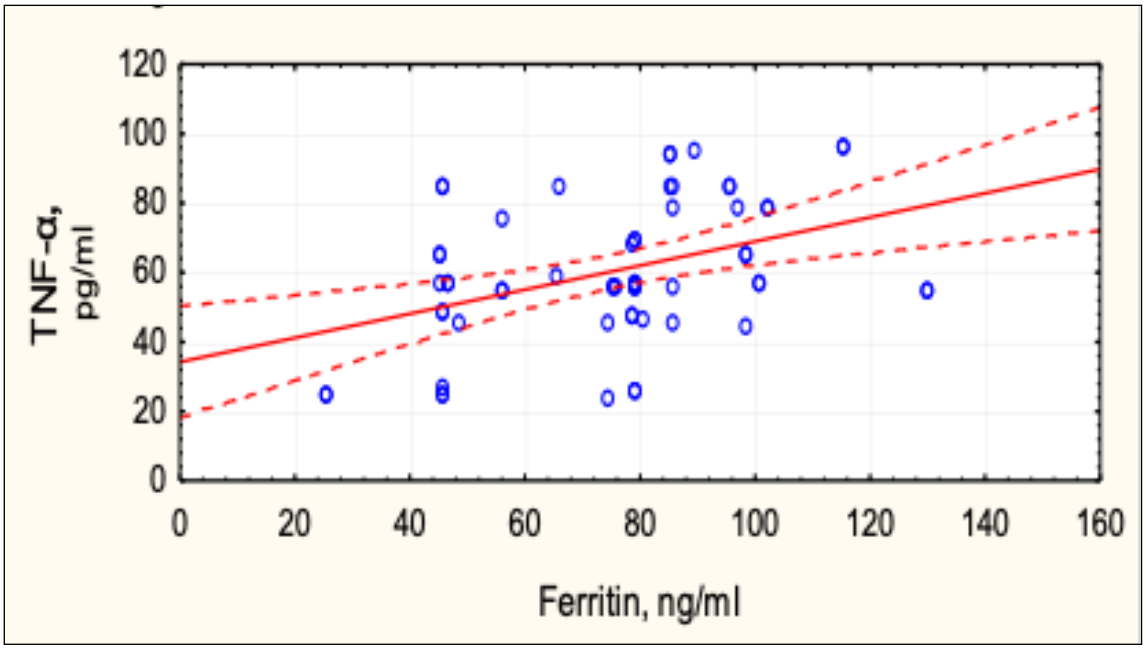

Fig.1. Correlation between the levels of TNF-a and ferritin levels (r= 0,41; p=0,001).

Table 4. Correlation relationships of data in children with Acute Respiratory diseases when using basic therapy

Laboratory parameters		Correlation coefficient (r)	Statistical significance (p)
Ascorbic acid	Urea	0,31	0,03
	K	0,27	0,04
Cu	Adiponectin	-0,31	0,03
	C-peptid	0,32	0,02
Zn	Glucose	0,37	0,008
	Ferritin	0,28	0,04
	TNF-α	0,35	0,01
Fe	CRP	-0,30	0,03
	Alkaline phosphatase	0,36	0,01
Free Thyroxine	Leucocyres	0,35	0,01
	Ca	-0,33	0,02
	Adiponectin	-0,33	0,02
	Leptin	-0,31	0,03
Vitamin D3	CRP	-0,39	0,004
	IgM	-0,30	0,03
	Vitamin B12	-0,39	0,005
	GPO	-0,36	0,009
Total Protein	Vitamin B12	-0,28	0,04
	IL-1	-0,36	0,009

interesting fact is that the development of hepatopathies with acute respiratory pathology, which have a short-term course and clinical presentation, are often undiagnosed and ignored. However, there are cases of functional disorders that dynamically transform into organic pathology. In particular, metabolic disorders and violations of components of AOS in acute Respiratory pathology can lead to the development of nonalcoholic fatty liver disease [12].

To optimize the treatment of ARD, we have developed a complex of vitamin-mineral composition and Lysozyme. The main regularities and relationships of the investigated components of AOS are considered in the following table (Table 3).

It should be noted that the number of relationships decreased from 22 to 18, of which 15 were positive (r=0,26-0,41, p=0,05-0,006). The highest positive correlation was observed in ferritin from TNF-α (r=0,41, p=0,001). The correlogram is presented on the following figure (Fig. 1).

The relationships between the levels of Fe, free Thyroxine, and Adiponectin were reduced, which indicates the positive effects of therapy in this study group. Negative relationships were observed between the levels of Cortisol and IgE (r=-0,28, p=0,03), which is evidence of suppression of allergic complications in respiratory pathology. Bilirubin values have a negative correlation with vitamin B12 (r=0,28, p=0,03), proving the effect on the biliary system and the decrease of Bilirubin depending on the increase of vitamin B12. Correlations of the level of Cu with glucose values (r=- 0,34, p=0,007) characterize the influence on the regulation of carbohydrate metabolism.

As for positive correlations, there is a synergism of the action of GPO with cortisol (r=0,35, p=0,006), which means the balancing of the antioxidant action in the organism, when negative relationships with Creatinine were observed at the beginning of the research. Cortisol at the initial stage was also positively correlated with Creatinine and Adiponectin with negative influence with pro-inflammatory IL-1. The final studies presented the synergism of the relationship between cortisol and GPO and the suppressive effects on the level of IgE.

Ascorbic acid presented positive interactions on the values of pro-inflammatory IL-6 and IL-2 (r=0,27 and 0,26, respectively at p=0,04, 0,05) in contrast to the initial interactions on vitamin B12 (r=0,25), which regulates carbohydrate and fat metabolism. It indicates there is still a need for the child's organism to regulate pro-inflammatory cytokines (IL-2,6) as means of preventing the development of the inflammatory process and promoting the secretion of immunoglobulins.

The value of vitamin D is represented by positive interactions with γ-IFN (r=0,30), Leptin (r=0,38) and Cu (r=0,32). The data can be interpreted as suppression of the activity of affected cells, stimulation of immunogenesis and its maintenance due to γ-IFN and the irreplaceable trace element Cu, taking into account the metabolic component represented by the leptin indicator. Correlations of the ferritin level have interactions with the values of total Protein (r=0,26), TNF-**α** (g=0,41) and Antibodies to Thyroperoxidase (r=0,39).

The level of Urea is positively correlated with Il-2 (r=0,30), Il-4 (r=0,26) and IgG (r=0,29), which indicates stabilization of the cytokine profile and prevention of chronic respiratory pathology.

Correlation between Zinc and Creatinine levels were also considered (r=0,7, p=0,04). Zinc is an important trace element, a representative of AOS, which modulates the functions of approximately 2,000 enzymes and 750 transcription factors to participate in various biological and physiological processes. There are scientific studies on its maintenance of the integrity of immune barriers as a Cofactor in Metalloenzymes, enhancement of cytotoxic activity of natural killers, proliferation and differentiation of innate immune cells, production of interferon. It has anti-inflammatory properties due to the modulation of the release of cytokines and the production of antibodies, mainly IgG [13]. According to our data, negative connections of Zn with IL-6 as a pro-inflammatory marker were transformed at the final stage into modulating characteristics of the trace element. both in terms of supporting immune barriers and protein metabolism. Although at the initial stage, there was a negative correlation with CRP and a positive correlation with the levels of pro-inflammatory Cytokines - IL-1, TNF-a. We will analyze the state of the links of AOS homeostasis in the treatment of children with basic therapy for Acute Respiratory diseases (Table 4).

Positive correlations are presented in the values of Ascorbic acid with the levels of Urea (r=0,31) and Potassium (r=0,27). Ascorbic acid is a non-enzymatic component of AOS. Ascorbic acid is an unusual antioxidant, because it reacts mainly with radicals, and not with non-radical compounds. The protective function of this vitamin includes the prevention of damage to protein, lipid and carbohydrate compounds and the acceptance of active forms of oxygen, nitrogen, and carbon. Vitamin C can also act as a pro-oxidant, especially in the presence of transition metals such as iron and copper, triggering various dangerous radical reactions and behaving as a radical promoter [14].

The formation of urea is a necessary link in protein synthesis and amino acid metabolism, it also participates in osmoregulation, affects the distribution of fluid between body cells and the extracellular space. The urea level indicator also correlates in a positive range with IgG values (r=0,29, p=0,02), as components of the body's protein metabolism.

The next element of the studied triad is the value of potassium. Which, as the main intracellular cation, regulates intracellular osmotic pressure and participates in protein metabolism.

The next investigated component is vitamin D level. The value of the indicator is presented by negative correlations with CRP (r=-0,39, p=0,004), IgM (r=-0,30, p=0,03), vitamin B12 (r=-0,39, p=0,005), GPO (r=-0.36, p=0.009). According to our data, the value of vitamin D3 has a suppressive effect on the synthesis of inflammatory markers IgM, CRP. The negative interactions on GPO level, on the background of

the metabolic factor vitamin B12, suggest a suppressive direction, which can be explained by vitamin D3 levels below reference, even after treatment. However, at the initial stage, there was a negative correlation with CRP and a positive correlation with the levels of pro-inflammatory cytokines - IL-1, TNF-a.

Thyroxine correlations are also informative. Thyroxine is one of the hormones that is synthesized by the thyroid gland and regulates energy metabolism in the human body. The study of the features of the antioxidant reaction shows that thyroxine stops oxidation by reacting with common types of chain oxidation. Studies confirms the hypothesis that thyroxine participates in the system of free radical reactions and as a result of these reactions it decomposes [15].

According to our data, there is a predominance of negative correlations of Thyroxine with Ca levels (r=-0,33, p=0,02), Adiponectin (r=- 0,33, P=0,02), Leptin (r=-0,31, p=0,03), except for the level of the Leukocyte pool (r=0,35, p=0,01), which is presented by positive relationships. Regarding the initial correlations, negative correlations with the levels of Total Protein (r=-0,29) and TSH (r=-0,43) were observed. Thyroxine functions as a highly specific antioxidant. According to the final results, it can be suggested that the level of thyroxine stabilizes the metabolic component and mineral exchange in the organism after treatment [16].

As for the correlation relationships of the total protein indicator, negative effects on the level of vitamin B12 (r=-0,28, p=0,04), IL-1 (r=-0,36, p=0,009) and positive correlations with the level of Neopterin (r=0,31, p=0,03) were observed. The anti-inflammatory effects of the Total Protein level with IL-1 are particularly pronounced, with a high degree of reliability, along with positive effects on the Neopterin level , which characterizes the state of the Immune system.

Correlative interrelationships of microelements are indicative as well. In particular, Cu presents multidirectional effects on adipose tissue hormones - with Adiponectin (r=-0,31, p=0,03), C-peptide (r=0.32, p=0.02), which indicates a metabolic component in copper exchange.

The level of Zn is characterized by positive correlation effects with the values of Glucose (r=0,37, p=0,008), Ferritin (r=0,28, p=0,04) and TNF- α (r=0,35, p=0,01). The level of Fe correlates in a negative range with suppression of the synthesis of the inflammatory marker CRP (r=-0,30, p=0,03) and with a positive vector with the value of Alkaline Phosphatase (r=0,36, p=0,01). Oxidative stress is a common denominator in the pathogenesis of various chronic diseases. Therefore, Antioxidants are often used to protect cells and tissues and eliminate oxidative damage. It is well known that iron metabolism is the basis of the dynamic interaction between Oxidative stress and antioxidants in many pathophysiological processes. Both Iron deficiency and Iron overload can affect the redox state.

DISCUSSION

Oxidative processes and the formation of free radicals are an integral part of human metabolism. Redox biology encompasses events involving a shift in the balance between reactive oxygen species (ROS) and their removal [17]. Infection with respiratory viruses is generally associated with cytokine production, inflammation, cell death, and other pathological processes that can be triggered by increased ROS production. [18].

The Respiratory tract occupies the second place after the Gastrointestinal tract in terms of the area of the mucous membranes. Therefore, understanding the unique nature of the Immune system of the respiratory mucosa is extremely important [19]. The consequence of vitamin A hypovitaminosis is, in particular, poses damage to the mucous membranes of the Respiratory tract: the glandular epithelium is replaced by a keratinized one due to keratinization. The loss of the mucociliary epithelium of the Respiratory tract reduces the barrier role of the mucous membranes. Also, vitamin A deficiency reduces the production of Lysozyme and Interferons, further weakening the body's non-specific resistance. One of the consequences of vitamin A deficiency is also the weakening of specific resistance during reproduction, growth and differentiation of Immunocompetent cells [20]. Therefore, Hypovitaminosis A results in increased susceptibility to the causative agents of Acute Respiratory nfections and their more severe course [21]. At the same time, the presence of Hypovitaminosis A, taking into account the involvement of vitamin A in the synthesis of Iron (insufficiency of which leads to a decrease in the Oxygen capacity of the blood) and the synergistic effect of vitamins A and D3 (activation of receptors for Calcitriol), is being actively investigated [22].

Nowadays, scientific literature contains more and more data on the role of vitamin D3 and its metabolites in the regulation of body homeostasis, the effect on cell differentiation and proliferation, the expression of antimicrobial peptides, as well as its involvement in the formation of innate and adaptive immunity. It is recommended to prevent vitamin D3 deficiency and maintain a serum 25(OH)D level >75 nmol/L. [23, 24]. It is vitamin D3 that is receiving special attention regarding the risk of acute respiratory tract infections in the pediatric

population. Children with respiratory tract infections were found to have significantly lower mean vitamin D3 levels compared to control groups. A relationship between the level of vitamin D3 and the frequency and severity of infections was also observed [23].

A disease caused by vitamin C deficiency can affect susceptibility to respiratory infections [24]. The level of vitamin C in human blood plasma rapidly decreases under conditions of physiological stress, including infection. The antioxidant, anti-inflammatory and immunomodulatory effect of vitamin C makes it a potential therapeutic agent both for the prevention and relief of the course of respiratory infections, and as an adjunctive therapy as well [25].

Therefore, oxidative processes, including a shift in the balance between active forms of oxygen and their removal, are an integral part of human metabolism. Infection with respiratory viruses, which is associated with the production of cytokines, inflammation, cell death and other pathological processes, can be provoked by oxidative stress, changes in the content of certain vitamins and trace elements, which creates conditions for the development of a number of pathological processes, including acute and recurrent respiratory diseases.

CONCLUSIONS

1. Based on the analysis of dynamic indicators under the influence of optimized treatment, the level of GPO increased in 1,6 times, on the other hand, when the basic therapy was prescribed - in 1,1 times (p3<0,01; p4<0,01; p5<0,01), the level of Cortisol had a reliable tendency to decrease by 1,6 but within the physiological range (p4<0,01; p5<0,01), the level of Ascorbic acid increased in almost 2 times in the first group and in 1,4 times in the second group (p3<0,01; p4<0,01; p5<0,01). Vitamin D3 levels at the initial stage were equal, below the reference range (18,77 ± 4,14 and 18,41 ± 3,26 ng/ml, respectively, by group). After the treatment, the level of vitamin D3 was identified within the physiological range in the first group (32,12 ± 3,48 ng/ml; p1<0,01, p2<0,01), in contrast, the upper limit was not reached in the second group (28,43 ± 4,43; p3<0,01, p4<0,01, p5<0,01), but with a significant upward trend. There are also positive effects of optimized therapy on the state of Copper (p3<0,01), Zinc (p3<0,01), Iron (p3=0,04) trace elements in comparison with the data of the second group.
2. At the initial stage, the most numerous (n=5) negative correlations of vitamin D3 with CRP (r=-0,21, p=0,03) and a positive correlation with antibodies to TPO, IL-1, and TNF-α were found (r=0,21-0,26, p=0,02-0,005). AOS indicators had a suppressive effect on the inflammatory process in the body, in particular, Fe on the level of Neopterin (r=-0,26), Zn on the level of IL-6 (r=-0,19), Cortisol on IL-10 (r=- 0,26), vitamin D3 on CRP (r=-0,21), free Thyroxine on the level of Total Protein (r=-0,29). GPO was correlated with the level of Creatinine (r=-0,27), which is involved in the energy exchange of tissues. Ascorbic acid had a positive interaction with the level of vitamin B12 (r=0,25), the level of copper was correlated with the levels of Bilirubin and Creatinine, as the end product of the exchange of Protein compounds. In other words, the results of these indicators prove the positive effects on the main metabolic processes in order to preserve energy exchange.
3. The relationships between the levels of Fe, free Thyroxine and Adiponectin were reduced, which indicates the positive effects of therapy in this study group. The highest positive correlation was found between Ferritin and TNF-α (r=0,41, p=0,001); along with the the synergism of the action of cortisol with GPO (r=0,35, p=0,006) and the suppressive effect on IgE (r=-0,28, p=0,03), which indicates the balancing of the antioxidant action in the organism, ascorbic acid presented positive interactions on the level of pro-inflammatory IL-6 and IL-2 (r=0,27, 0,26, respectively at p=0,04, 0,05), which is considered as prevention of the development of the inflammatory process. Vitamin D3 is represented by positive interactions with γ-IFN (r=0,30), Leptin (r=0,38) and Cu (r=0,32), which can be interpreted as inhibition of the activity of affected cells, stimulation of immunogenesis and its maintenance due to γ-IFN and Cu taking into account the metabolic component - Leptin. The level of Urea was positively correlated with IL-2 (r=0,30), IL-4 (r=0,26) and IgG (r=0,29), which indicates stabilization of the Cytokine profile and prevention of Chronic Respiratory pathology.
4. Positive correlations are presented in the values of Ascorbic acid with the levels of Urea (r=0,31) and Potassium (r=0,27). The indicator of vitamin D3 presented negative correlations with CRP (r=-0,39, p=0,00 IgM (r=-0,30, p=0,03), vitamin B12 (r=-0,39, p=0,005), GPO (r=-0,36 and p=0,009), which can be regarded as a suppressive effect on the synthesis of inflammatory markers IgM, CRP. Negative interactions on the level of GPO against the background of the metabolic factor of vitamin B12 indicate a suppressive direction, which can be explained by the levels of vitamin D3 being below the reference range even after treatment. The level

of Zn is characterized by positive correlations with the levels of Glucose (r=0,37, p=0,008), Ferritin (r=0,28, p=0,04) and TNF-α (r=0,35, p=0,01). The level of Fe correlates in a negative way with the suppression of the synthesis of the inflammatory marker CRP (r=-0,30, p=0,03) and with a positive vector with the value of Alkaline Phosphatase (r=0.36, p=0.01).

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Olesya M. Horlenko
Uzhhorod National University
14 University St, 88000 Uzhhorod, Ukraine
e-mail:ohorlenko@gmail.com

ORCID AND CONTRIBUTIONSHIP

Olesya M. Horlenko:0000-0002-2210-5503 A B D F
Iryna Yu. Pikina: 0000-0003-1565-8174 B D F
Lyubomyra B. Prylypko:0000-0002-4131-5450 B C
Gabriella B. Kossey: 0000-0003-0811-4929 D E
Olga A. Pushkarenko:0000-0002-7143-029X D E
Iryna M. Boisak: 0009-0002-5279-3412 B F
Ivan I. Pushkash: 0000-0002-57282980 E F

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