INTRODUCTION
Infectious diseases have a leading role in morbidity ranking of people all over the world, due to its widespread distribution, multiorganic injuries, adverse effects. According to WHO [1], respiratory infections are one of the most widespread causes of child morbidity and mortality. Around 11-13 million people suffer from influenza and Upper respiratory tract infections (URTIs) each year in Ukraine, that is 95% of all registered cases of infectious diseases [2, 3] and in the structure of child infections URTI occupies the first rank position [4]. In this regard, respiratory viral infections became one of the leading medical and social problems in world countries and have national importance in Ukraine [5, 6].

Whereas the leading role in pathogenesis of URTI has a general toxic, epileptotropic and vasopathic action of respiratory viruses, the rash on mucous membranes reflects the patterns of the infectious process in general [7, 8]. In patients with URTI, non-specific lesions of the oral mucous membrane are often developed in the form of catarrhal inflammation – an influenza stomatitis, which reflects local factors. Undoubtedly, increased susceptibility to respiratory viral infections has a close relationship with various functional mechanisms [9].

THE AIM
The aim: to characterize the state of oxidative-prooxidant system as one of the factors of non-specific resistance of children’s organism with influenza stomatitis.

MATERIALS AND METHODS
We conducted a survey of 384 children with acute respiratory viral infections from 6 months to 12 years in order to study the clinical course of URTI, the identification of risk factors, and the severity of the course. From the total number of examined patients, 318 children had lesions of oral cavity, that is 82% of all examined cases. The control group consisted of children without lesions of oral cavity (66 people).

Formation of clinical groups of children with URTI was based on the severity of the disease.

THE STATE OF OXIDATIVE HOMEOSTASIS IN CHILDREN WITH INFLUENZA STOMATITIS

STAN HEMOSTAZY OKSYDACYJNEJ U DZIECI Z ZAPALENIEM JAMY USTNEJ W PRZEBIEGU GRYPY

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ABSTRACT
Introduction: The clinical course of acute respiratory viral infections was not sufficiently studied, especially the state of oxidative homeostasis in children with influenza stomatitis. This fact became the base for our study.

The aim: to characterize the state of oxidative-prooxidant system as one of the factors of non-specific resistance of children’s organism with influenza stomatitis.

Materials and methods: A survey was conducted on 384 children with acute respiratory viral infections aged from 6 months to 12 years, among them 318 had lesions of oral cavity. The mild form was diagnosed in 52 children, moderately severe - in 185, severe - in 81 children. The control group consisted of children without lesions of oral cavity (66 people). To analyze lipid peroxidation we used a spectrophotometric determination of diene conjugates. The ceruloplasmin activity and the transferrin saturation in blood plasma by iron were determined by G. Babenko’s method.

Results: We found the intensification of lipid peroxidation: a significant increase of diene conjugates in serum up to 13.78 %, the level of which depended on the severity of disease. We also found the activity increase of ceruloplasmin in 1.8 times in patients with severe course of disease. The saturation of blood plasma transferrin by iron was significantly reduced – for 15.27 % in patients with severe course of influenza stomatitis.

Conclusions: Changes in antioxidant system happen due to the activation of lipid peroxidation, and because of the inability to neutralize toxic metabolites in the children’s body the intoxication syndrome developed.

KEY WORDS: influenza stomatitis, antioxidant-prooxidant balance, oxidation homeostasis
Conducted after a parents’ sign of Informed Agreement for patient and research conduction.

Taking into account the literature data [10, 11, 12, 13, 14] about the role of free radical oxidation in the process of infectious inflammation, we studied the state of the prooxidant and antioxidant systems as one of the factors of nonspecific resistance in children with URTI. We used spectrophotometric determination of diene conjugates (DC) - intermediate products of free radical oxidation of erythrocyte phospholipids in blood serum using method of A. Riaze in the modification of V. B. Gavrilova and M. N. Myshrokudna [15].

As an indicator of antioxidant activity in blood serum, we determined the activity of the copper-containing protein - ceruloplasmin (CP), which was determined with transferrin (TF) in blood plasma, taking into account its importance for normal processes of hemotopoesis, iron transport and antioxidant defense, using the method of G. A. Babenko [16].

All the research methods which were used meet the requirements for examination of patients and conducting scientific researches meet the requirements of norms and principles of bioethics. In carrying out the work, the rules of patient safety, the rights and canons of human dignity, as well as the moral and ethical norms in accordance to the main conditions of the GSP (1996); European Convention on Human Rights and Biomedicine (dated 04.04.1997); a set of ethical principles regarding human experimenta
tion developed for the medical community by the World Medical Association (WMA) – The Declaration of Helsinki (1964-2000); the Order of the Ministry of Health of Ukraine №281 dated November 1, 2000; a code of ethics for scientists of Ukraine (2009) are followed and which is confirmed by the protocol of the Bioethics Commission of the I.Horbachewsky Ternopil State Medical University (protocol №21 dated January 8, 2014).

RESULTS

It is known that inflammation caused by respiratory viruses and microorganisms is an inducer of oxidative stress, which results in appearance of free radicals, whose excessive amount is limited by the antioxidant system [8,18]. Accumulation of lipid peroxidation toxic products causes a change in phospholipid structure of membranes, which can be analized as one of the possible adaptive mechanisms of the body in response to infectious and inflammatory process in patients with URTI.

According to our data all forms of URTI lead to the intensification of lipid peroxidation: the amount of DC in blood serum of children with URTI correlated with the increase of disease severity. In mild form of the disease the amount of DC was 1.51±0.02 cond.units/ml (in group of healthy children - 1.44±0.08 cond. units/ml). There was an accumulation of DC in the blood serum in patients with URTI of moderate intensity, which was 1.580±0.002 cond. units/ml. Significant intensification of lipid peroxidation activity occurred in patients with severe URTI, when the amount of DC significantly increased and was 1.670 ± 0.001 cond.units/ml. Therefore we established reliable (P <0.001) increase in amount of DC in serum of all patients with acute respiratory infections, the severity of which depended on the severity of disease, which reflected the activity of inflammatory process.

Activation of lipid peroxidation process in children with acute influenza stomatitis leads to significant changes in antioxidant system (AS), activating the production of its components even in the mild form of the disease. Clinically, in patients with mild form of URTI, signs of general intoxication (headache, loss of appetite, sleep disturbance) and weakly expressed cattarrhal phenomena in the form of rancid and coughing were weakly expressed. An increase in body temperature to 37.2° - 37.8 °C was observed for not more than 2-3 days. The overall condition of patients was evaluated as satisfactory. While studying the antioxidant activity in serum, we found that activity of ceruloplasmin in patients with URTI of mild form is significantly higher (P <0.01) than in the control group and raises up to 48.19±0.81 cond.units (in group of healthy children - 37.16±0.52 cond.units). Further activation of AS occurs in patients with severe URTI, when the activity of the CP is 59.85±0.55 cond.units.

At the same time, all the signs of influenza intoxication were expressed in the examined children: body temperature increased to 39 °C and was accompanied by dizziness, general weakness, chills, noise in the ears, pain in the eyeballs, myalgia and arthralgia, sweating, sleep disturbances; tracheitis was accompanied by an overhead dry cough. The effects of local factors reflect non-specific changes in oral cavity: cattarrhal stomatitis, serous inflammation, manifested by hyperemia, swelling of the mucous membrane of gums, lips, cheeks, the appearance of impressions on the cheek’s mucous membrane along the line of teeth contact, increase and bleeding of gums papillae. Nonspecific changes were due to the effect of taking medications, which led to a violation of the acid-base balance of the oral fluid, dysbiosis, local immunity, hypovitaminosis, which we confirmed in laboratory [19].

In children with severe course of pathological process, the activity of CP increased in 1.8 times compared to control and raised up to 67.23±1.50 cond.units. In the clinical picture, this form of pathology dominated by symptoms of central nervous system intoxication, which was manifested by nausea, vomiting, nasal haemorrhage, seizures, delusions, short-term loss of consciousness, meningeal symptoms. The febrile reaction, which lasted 3-7 days, corresponded to the severe course of the disease. Sharp impairment of the general condition in which hyperthermic, neurotoxic syndromes occurred, was studied as severe course of disease. Cattarrhal phenomena as coughing, congestion and mucous secretion from the nose, pain and sore throat, dry cough were present. Attention was drawn to hyperemia of the face, conjunctivitis, lacrimation, eye shine, moderate cianosis of the lips. The red lobe of the lips is covered with blisters and serous exudate or suffocated bloody crust. On the lips and nostrils often appeared...
herpes rashes. Local manifestations in the oral cavity were manifested by catarrhal stomatitis, dryness, multiple rashes on the mucous membrane of the mouth with a tendency to merge and the formation of extensive erosive surfaces.

It is known that important role in children susceptibility to infection, especially in early childhood when other mechanisms of protection are not yet completely formed [8, 9], plays a bacteriostatic effect of the transferrin (TF) [10, 12]. The study of TF saturation by iron, which is provided by the ferroxidase activity of the CP, showed the following results. In the mild form of acute respiratory infections in children, the saturation of plasma TF was significantly lower in comparison with healthy children - 0.178±0.002 cond. units. (0.190±0.002 cond.units in the control group). In acute respiratory infections in the form of moderate-intensity saturation of blood TF was 0.165±0.003 cond.units. The most significant decrease in saturation of blood TF (P<0.001) was in patients with severe URTI - 0.161±0.001 cond.units.

DISCUSSION

It is known that in human body, the regulator of copper balance is ceruloplasmin - a protein with properties of enzymes specific to serum, which has protective, anti-infectious function in the form of antibodies and in the composition of the properdine-complementary system. Transferin, being a metalloprotein of blood, refers to factors that block free radical oxidation and, together with ceruloplasmin, forms a prooxidation-antioxidant buffer system of blood involved in the maintenance of oxidative homeostasis. Insufficiency of iron and iron-binding proteins has a secondary effect on the immune system and the function of leukocytes, which affects the mechanism of protection of the host from the invasion of microorganisms and viruses. As a result of infectious agent action, the child’s body undergoes changes that lead to a violation of metabolic processes, including the metabolism of trace elements, which result in the distortion of the stability and strength of organometallic compounds in biological fluids. The dynamics of ceruloplasmin activity, the saturation of blood serum transferrin and the content of protein fractions are sensitive tests, which may indicate the morphological changes in mucous membrane of child oral cavity. This fact is partially confirmed by information from a number of authors [10, 20, 21], which indicate that the complete elimination of morphological changes is accompanied by the normalization of protein metabolism.

CONCLUSIONS

Respiratory infections lead to increase of activity in one of the most powerful antioxidant enzymes – ceruloplasmin in blood serum, which stimulates the process of hematopoesis and regulates the blood function with the transferrin, on the background of significant decrease in the saturation of its iron. As a result of our clinical and laboratory studies, there was a disturbance in transportation of transferrin and ceruloplasmin in the body of children with viral influenza stomatitis, the depth of which depends on the severity and duration of the disease. As the severity of acute viral stomatitis increases, the lipid peroxidation activity increases, what is confirmed by the indexes of diene conjugates. Due to the lipid peroxidation activation, changes occur in the antioxidant system - the development of components of antioxidant protection of transferrin and ceruloplasmin. Because of the inability of detoxification systems to neutralize toxic metabolites in the body - an intoxication syndrome develops. Such changes in the functioning of the antioxidant defense system, in our opinion, are the manifestation of compensatory reactions and indicate a gradual increase in the level of catabolic processes with increasing severity of the disease, which must be taken into account when choosing the optimal method of treatment.

REFERENCES


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