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TO CONSIDER THE PARAMETERS OF IMMUNOLOGICAL MARKERS IN THE DYNAMICS OF THE DEVELOPMENT OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN PATIENTS WITH ACUTE POISONING BY DRUGS AFFECTING THE CENTRAL NERVOUS SYSTEM

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Relevance. The severity of the condition of patients with acute severe poisoning by drugs affecting the central nervous system is due to pronounced dysfunctions of various organs and body systems due to the specific action of xenobiotics (Luzhnikov E.A. et al., 2016), as well as developing hypoxia (Livanov G.A. et al., 2014; Hashemian M. et al., 2016) which leads to the development of life-threatening complications, which often determines the outcome of a chemical injury. A number of authors note that hypoxia in critical conditions causes the formation of a systemic inflammatory response consisting of increased production of pro-inflammatory mediators, activation of cytokines and kinins, increased vascular permeability, increased blood viscosity and microthrombosis (Chereshnev V.A. et al., 2019; Cavaillon J.M. et al., 2016; Ramakrishnan S. et al., 2019). Systemic inflammatory reaction and hypoxia are always associated with activation of proteolytic processes, coagulation and fibrinolytic systems (Sanotsky V.I., 2013; Alekhnovich A.V., 2020). Numerous authors have shown in their works that with the intensive and prolonged action of inflammatory factors, numerous disorders develop both at the cellular and organ levels (Gusev E.Yu. et al., 2018; Savelyev V.S. et al., 2017; Alberti C. et al., 2015). There are reports in the literature about widely used diagnostic algorithms for systemic inflammatory response syndrome in patients with intensive care, therapeutic, and surgical profiles, which allows early diagnosis of infectious complications and timely initiation of therapy (Zhevlakova Yu.A., 2017; Akimova V.N. et al., 2016; Ratzinger F. et al., 2015; Boehme A. K. et al., 2014).

However, the possibility of their use in clinical toxicology has not been considered or investigated to date. There are no comprehensive studies on the problem of systemic inflammation in acute poisoning with drugs affecting the central nervous system, and methods for correcting this component of the pathogenesis of acute exotoxicosis have not been sufficiently defined.

The mechanisms of pharmacological action on pathological reactions that are components of the systemic inflammatory reaction syndrome, in particular, such as proteolysis and the blood coagulation system, have not been determined, which seems relevant. There is no information about the role of systemic inflammatory reaction syndrome in the development of infectious complications in patients with acute poisoning by drugs affecting the central nervous system, which are one of the reasons for the increased duration of treatment of patients and the possible risks of death in the somatogenic phase of acute poisoning. Of no small importance are the long periods and difficulties in treating the developed inflammatory complications.

Thus, these issues require detailed study, since their solution involves the possibility of improving the effectiveness of treatment of this patient population. In connection with these arguments, the solution of the above problems through the implementation of the planned research work is timely and relevant. In the presence of certain clinical diagnostic criteria (according to Bone R.C., 1996), CB acquires a purely clinical concept - systemic inflammatory response syndrome (SIRS), which is considered as an important pathogenetic link in critical conditions of various etiologies of a non-infectious and

infectious nature with a risk of developing multiple organ failure syndrome (Gusev E.Yu. et al., 2017; Levit D.A. et al., 2017; Savelyev V.S. et al., 2016; Bone R.C. et al., 1992). Cytokines, products of hemostasis activation, free radicals, biogenic amines, nitric oxide, platelet aggregation factor, neuroendocrine humoral factors and other mediators play an important role in the development of the body's CVD to damaging factors of various nature (Chereshnev V.A. et al., 2012; Gusev E.Yu. et al., 2014; Olson N. et al., 2011; Neri M. et al., 2013; Bernstein H.G. et al., 2014; Boehme A. K. et al., 2014).

There is practically no complete information in the literature on the comprehensive assessment and diagnostic capabilities of CVD in patients with acute poisoning by neurotropic agents. The possible connection between acute poisoning, purulent infection and the outcomes of acute poisoning with substances of neurotropic action is not considered. In this regard, the subject of this study will be the diagnosis of CVD and the assessment of its role in the pathogenesis of acute poisoning with substances of neurotropic action, as well as the development of a pathogenetically sound method of its treatment.

The purpose of the work. To identify the importance of immune system dysfunction in the pathogenesis of inflammatory complications in acute poisoning by drugs affecting the central nervous system and to identify ways of correction in order to improve the effectiveness of basic detoxification therapy. Research objectives. 1. To determine the clinical symptoms of the systemic inflammatory response in acute severe poisoning by agents affecting the central nervous system. 2. To consider the parameters of immunological markers in the dynamics of the development of systemic inflammatory response syndrome in patients with acute poisoning by drugs affecting the central nervous system. 3. To identify a possible relationship between laboratory markers of systemic inflammatory response syndrome and the severity of hypoxia, hemostatic disorders and endotoxemia in patients with acute severe poisoning by drugs affecting the central nervous system. 4. To investigate the importance of immunological markers of systemic inflammatory response syndrome for predicting inflammatory complications and adverse outcome in patients with acute poisoning by drugs affecting the central nervous system of severe degree. 5. To develop an algorithm for the early detection of inflammatory complications in patients with acute poisoning by drugs affecting the central nervous system of severe severity using the parameters of the systemic inflammatory response syndrome. 6. To study the effectiveness of the immunomodulatory agent “Immunofan” and the proteolytic enzyme inhibitor “Aprotinin” as part of complex detoxification and anti-inflammatory therapy in patients with acute poisoning with drugs affecting the central nervous system of severe degree. The object and subject of the study. To achieve this goal and solve the problems, a scientific methodology was used, including standardization, analysis, comparison and generalization of the research results. The scientific work will analyze the data on the diagnosis and treatment of 260 patients with acute poisoning. neuroleptics and substances of severe narcotic effect. The patients will be examined at the base of the toxicology department of the Bukhara branch of the RNCEMP. The patients will be divided into 2 groups: Group I of patients with basic treatment (120 patients) and group II of patients (140 patients) who will use the immunomodulatory agent Immunofan and the proteolytic enzyme inhibitor Aprotinin as part of a complex basic detoxification and anti-inflammatory therapy in patients with acute poisoning with drugs affecting the central nervous system. a severe degree system. Research methods. Patients with severe acute poisoning, with a level of depression of consciousness on the Glasgow coma scale of 7 points or lower, which corresponds to superficial and deep comas complicated by disorders of external respiration and central hemodynamics, will be selected for the study. General clinical laboratory tests will include a general blood test with a detailed leukocyte formula and a biochemical analysis with the determination of glucose, lactate, total protein, electrolytes (K, Na, Cl), bilirubin with fractions, urea, creatinine, amylase, AlT, AsT, LDH, coagulograms. All patients will undergo a comprehensive examination, including X-ray examination of the chest organs, ultrasound examination of the abdominal organs, electrocoagulography, electrocardiography, chemical and toxicological examination of urine, biochemical, hematological, immunological laboratory tests.

Immunological studies will include determination of the concentration of cytokines TNFa, IL-1b, IFN-γ IL-10 with a set of reagents (Vector-Best, Russia) by solid-phase enzyme immunoassay (ELISA). To

determine the indicators taken as the physiological norm, 20 healthy donors will be examined. As a result of the conducted research, the fact of the development of CVD will be established and the patterns of its formation in response to the ingestion of a toxic dose of drugs affecting the central nervous system will be determined. New data will be obtained that expand the understanding of the pathogenesis of inflammatory complications, including hospital-acquired pneumonia, in acute poisoning with drugs affecting the central nervous system associated with the development of CVD, and allow us to identify new ways to prevent these complications. For practical application, an algorithm for the diagnosis of CVD will be proposed, which includes an assessment of the level of consciousness, respiratory rate, heart rate, body temperature, clinical and biochemical blood tests, chest X-ray examination, dynamic determination of blood markers of inflammation and hemostasis activation. The use of this algorithm will allow timely prevention of the development of inflammatory processes and complications and will make it possible to optimize the complex of therapeutic measures in a timely manner. An algorithm for the use of pathogenetic treatment using the immunomodulatory agent Immunofan and the proteolytic enzyme inhibitor Aprotinin will be developed and proposed as part of a comprehensive basic detoxification and anti-inflammatory therapy in patients with acute poisoning with drugs affecting the severe central nervous system, which will reduce the incidence of inflammatory complications. Upon completion of the work, it is planned to develop and put into practice methodological recommendations, scientific articles will be published in scientific journals of the republic and abroad. It is planned to participate in congresses, conferences, seminars and other scientific forums.

Conclusion. A patent application will be filed for the effectiveness of the developed complex immunocorrective, anti-inflammatory therapy as part of a complex basic detoxification and anti-inflammatory therapy in patients with acute poisoning with drugs affecting the severe central nervous system, based on clinical and immunological shifts, the deposit of scientific development, and certificates for a computer program for the created scientific and innovative development. The research results will be introduced into the educational process of medical universities on the subject of immunology and skin and venereal diseases.

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