ISSN NO: 2770-2936
Date of Publication:03-11-2022

Pathological changes in blood cells in herbicide poisoning

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Abstract: The aim of this work was to elucidate the structural bases of the reaction of blood system cells in acute and chronic herbicide poisoning and to find spores for their correction with metal-containing biocomplexes. Based on the goal, the following tasks were set:
- to study the morphofunctional state of various (copper-containing cobalt) biocomplexes on the morphofunctional state of the cells of the blood system in acute and chronic herbicide poisoning.

Keywords: Herbicide Poisoning, Blood System

Relevance. The development of industrial and household chemicals, the intensive use of various chemicals in agriculture has created a new problem for physicians and environmentalists. The expansion of the use of pesticides has led to environmental pollution and an increase in the number of people in contact with these drugs. This contributed to the development of various acute and chronic lesions, the manifestation of mutagenic, allergenic and other undesirable pathological effects. One of the most sensitive tissues to toxic effects is hematopoietic tissue, which contains a pool of rapidly proliferating cells. It clearly manifests the negative effects of pesticides, which determine the value of its study in elucidating the mechanisms of action of one or another pesticide. The works devoted to the study of the pathomorphological state of the cells of the blood system in case of pesticide poisoning do not allow revealing the patterns of changes in the blood system.

The development of rational methods of prevention and pathogenetic methods for correcting the toxic effects of pesticides is one of the urgent tasks of modern medicine. Unfortunately, so far there are only a few reports on the use of drugs that have an antidote and therapeutic effect in case of poisoning with certain pesticides.

In this regard, the most promising are biocomplexes of various microelements with organic compounds, which have a high protective therapeutic effect in case of poisoning with pesticides and ionizing radiation.

However, the effect of these biocomplexes on the body, in particular, on the blood system during acute and chronic administration of organophosphorus pesticides, remains not fully understood.

The foregoing indicates the relevance and timeliness of the study of the morphological and functional characteristics of the response of cells in acute and chronic herbicide poisoning and its correction with biocomplexes.

Purpose and objectives of the study:

The aim of this work was to elucidate the structural bases of the reaction of blood system cells in acute and chronic herbicide poisoning and to find spores for their correction with metal-containing biocomplexes. Based on the goal, the following tasks were set:
- to study the morphofunctional state of various (copper-containing cobalt) biocomplexes on the morphofunctional state of the cells of the blood system in acute and chronic herbicide poisoning.

Scientific novelty of the work:

In the work, for the first time, using complex general morphological, hematological, cytochemical, radioautographic, and electron microscopic methods, the pathomorphological bases of the reaction of blood cells and hematopoiesis to acute and chronic herbicide poisoning were studied. General and specific patterns of pathomorphological changes in the blood system in the dynamics of acute and chronic intoxication with herbicides have been established. It was found that the most characteristic changes in the system blood in case of herbicide poisoning are anemia, leukocytosis with a shift to the left and thrombocytopenia of cellular and subcellular mechanisms, which constitute inhibition of proliferation and differentiation of hematopoietic

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cells in the bone marrow, increased destructive changes in their subcellular organelles, and as a result, disorganization of metabolic processes in circulating blood cells. For the first time, metal-containing biocomplexes were tested, which have a pronounced protective and therapeutic effect in acute and chronic herbicide poisoning, an appropriate biocomplex was established and recommended for use in practice.

Scientific and practical value of the study:

The obtained data on shifts in blood parameters and cytochemical changes in neutrophilic leukocytes are additional differential diagnostic tests in the examination of persons working with the herbicide. Data on the cellular and sub-cellular bases of the reaction of blood cells in case of herbicide poisoning can be used in the educational process at medical institutes for a more in-depth explanation of the body's reactions to various toxic effects. The facts established in the work on the pronounced antidote and therapeutic effect of biocomplexes make it possible to recommend these preparations for wide use in conditions of work with herbicides.

The main scientific provisions made:

I. Structural and functional basic reactions of blood system cells in acute and chronic herbicide poisoning have common patterns and are characterized by suppression of the processes of proliferation and differentiation of hematopoietic cells.

II. Biocomplexes have a pronounced protective and therapeutic effect in both acute and chronic herbicide poisoning.

Our work is experimental and performed on laboratory rats. However, there are relatively few data on the cells of the blood system of laboratory rats in the literature, and in the vast majority of studies, only the quantitative content of certain cellular forms of hematopoiesis is considered.

The main indicators of peripheral blood and bone marrow of rats are given in the works. They are mostly close to each other. Thus, the total content of erythroblast cells in the bone marrow is in the range of 17.65% - 23.6%, mitosis of erythroid cells - 0.29 - 0.75. The percentage of stab neutrophilosis in the bone marrow is relatively high. In the leukocyte formula of the peripheral blood of rats, lymphocytes predominate, sometimes reaching more than 70% of all leukocytes. Among granulocytes, mainly segmented neutrophils are found.

Thus, rats are characterized by a higher content of stab neutrophils in the bone marrow and the predominance of lymphocytes in the leukocyte formula.

Currently, a unitary scheme of hematopoiesis is generally accepted, reflecting the successive stages of histogenesis of blood cells. It has been established that all blood cells originate from a single ancestral hematopoietic stem cell, which a well-known histologist once wrote about.

But, going into the details of the discussion about the morphology of hematopoietic stem cells, we considered it appropriate to present the basic data on the morphology of the identifiable cells of the blood system.

The ultrastructure of morphologically identifiable cells of the human blood system and small-nourishing cells has been studied in some detail by now. However, these studies have been performed primarily in humans, mice, and rabbits, while studies Only a small number of works have been devoted to the ultrastructural features of rat hematopoietic cells.

The process of maturation of the cells of the erythroid germ is characterized by certain ultrastructural changes both in the nucleus and in the cytoplasm of the cells. The nucleus decreases in size, taking on a more rounded shape, while chromatin compaction occurs and the nucleolus disappears. The size and number of mitochondria decreases and the electron density of the mitochondrial matrix increases due to the accumulation of granular content. The content of free ribosomes and polysomes gradually decreases, while the amount of amphora material increases. The electron density of the cytoplasm increases due to the accumulation of hemoglobin. It has been established that the disappearance of the nucleus from normoblasts occurs by its expulsion. Mature erythrocytes have a high electron density and are surrounded by a membrane about 20 nm thick; cell organelles are absent.

In the process of maturation of neutrophils, two stages are morphologically distinguished, characterized by the formation of two structurally and chemically different populations of granules. The first stage of granulogenesis occurs at the pro-myelocyte stage, when primary or azurophilic granules are formed,

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Numerous electron microscopic studies have shown that the changes that occur in the process of differentiation of human eosinophilic leukocytes and other small-nourishing leukocytes are in many respects similar to those of neutrophilic leukocytes. The formation of specific eosinophilic granules is carried out in the components of the Golgi complex. A characteristic feature of small-feeding eosinophilic granules is the presence of an electron-dense crystalloid in their mainland.

Electron-cytochemically and biochemically, acid phosphatase, arylsulfatase, poxidase, esterase, basic proteins and phospholipids were detected in eosinophilic granules.

The ultrastructure of basophic leukocytes has been studied in less detail. According to the characteristics of the nucleus and cytoplasm, with the exception of granules, basophilic leukocytes practically do not differ from neutrophilic and eosinophilic ones. Specific basophilic granules vary in size and structure. They are predominantly round or oval in shape, 0.2 - 162 microns in size, surrounded by a membrane. The functional role of basophilic granulocytes has not yet been fully elucidated. It is assumed that they are involved in allergic reactions of the body and in the metabolism of histamine. A number of works have been devoted to the study of the ultrastructure of monocytopoietic cells. Currently, these cells are considered as precursors of tissue macrophages and are united in the system of iononuclear phagocytes. They are characterized by the presence of granules with the activity of myeloperoxidase and lysosomal enzymes.

In connection with the achievement of immunology, there is now a need for research that would simultaneously make it possible to judge whether lymphocytes belong to 1- or 2-immunity systems and evaluate their structural features. A broad perspective for solving this problem is opening up in connection with the introduction of methods of immune electron microscopy, which combines the achievements of morphology and immunochemistry. Studies of functionally heterogeneous rat lymphocytes using immune electron microscopy are still rare and insufficient for the development of morphological criteria for various cell populations.

Thus, the analysis of the literature data allows us to conclude that quite extensive information on the structural and functional features of the cells of the mammalian blood system has been accumulated to date. However, it reflects the state structures and functions of cells under physiological conditions and in various diseases of the blood system. The pathomorphological basis of adaptive rearrangements of blood cells and hematopoietic tissue in acute and chronic poisoning with pesticides, in particular, herbicides, remains practically unexplained. Meanwhile, the disclosure of the structural and functional regularities of the effect of herbicides on the cells of the blood system allows us to consider in depth the mechanism of changes observed in the body and contributes to the choice of the most optimal methods for their correction. In terms of pharmacological correction of the response of cells and tissues to the action of herbicides, preparations are the most promising.

The foregoing as a whole necessitates further research, which provides for the elucidation of the structural and functional features of the reactions of blood cells to the action of a widespread pesticide and the possibilities of pharmacological correction of these reactions using metal-containing biological complexes.

Materials and Research Methods

The experiments were carried out in 224 outbred male rats with a body weight of 140-150 g. The animals were kept under standard vivarium conditions. Before the experiments, the animals were quarantined for two weeks to exclude various diseases.

All animals were divided into two main groups.

The first group of animals (84 rats) was divided into 4 subgroups and was used to study the state of the reaction of the blood system during acute poisoning with herbicides and in the process of its correction with biocomplexes. Three subgroups of this group received a single dose of herbicide intragastrically at a dose of 150 mg/kg. The fourth subgroup, which received an equal volume of sterile saline, served as the control. Animals of subgroup I were slaughtered under ether anesthesia on days 1, 3 and 7 after herbicide poisoning. Animals of subgroup II, starting from the first day after poisoning, received biocomplex No. I once a day subcutaneously at a dose of 10 mg/kg for 7 days. Animals of the III subgroup similarly subcutaneously injected biocomplex No. 6 for 7 days at 10 mg/kg. Both (I and II) subgroups of animals were slaughtered on the 7th day of the experiments simultaneously with the control subgroups of rats in compliance with all conditions.

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The second main group of animals (120 rats) was also divided into 4 subgroups and used to study the reaction of blood system cells during herbicide poisoning with subsequent correction with biocomplexes. The first three subgroups of animals were daily intragastrically injected with herbicides at a dose of 2.8 mg/kg (1/100 LD50) and the fourth control subgroup received an equal volume of sterile saline. All slaughters were carried out in the morning, on an empty stomach, under ether anesthesia. In addition to these two groups, 20 intact rats of the same body weight were used in the work.

At the time of slaughter, blood was taken from all animals to determine the number of erythrocytes, leukocytes, hemoglobin content and serum cholinesterase activity according to the generally accepted method. Blood smears stained according to Romanovsky-Giemsa were used to calculate the leukocyte count and platelet count. Detection of acid and alkaline phosphatase activity, myeloperoxides and glycogen content was carried out according to the methods described in the manuals on blood cell cytochemistry. The results of the cytochemical reaction were evaluated by the five-point system.

The Result of Own Research

In our work, the main task was to identify the reaction of blood system cells to acute and storage exposure to herbicides. It is known that herbicides belong to the group of organophosphorus substances and, first of all, have an adverse effect on the nervous system. and the reproductive system. The results of our studies have shown that both acute and chronic herbicide poisoning is accompanied by pronounced structural and functional changes in the blood system, which are characterized by certain dynamics. In acute poisoning with herbicides, already starting from the 1st day of experiments, severe hypochromic anemia occurs in the peripheral blood, which is combined with absolute leukocytosis and thrombocytopenia.

Peripheral blood changes in acute herbicide poisoning are accompanied by pronounced shifts in myelograms. In the red bone marrow, there is a violation of the processes of proliferation and differentiation of cells of erythroid and myeloid germs.

Significantly increases the number of plasma cells and bone marrow macrophages. Quantitative changes in peripheral blood and bone marrow are combined with qualitative changes. They manifest themselves as inhibition of the activity of myeloperoxidase, alkaline phosphatase and a decrease in the glycogen content in neutrophilic leukocytes, while the activity of acid phosphatase increases. It has now been established that organophosphorus compounds, in particular herbicides, have the ability to inhibit redox enzymes. Fosalone is especially active in inhibiting the activity of cholinesterase in the blood and other tissues. Our data show that the inhibitory effect of fosalone is not limited to blocking cholinesterase, although on the 7th day the activity of this enzyme in the blood serum decreases by more than 2 times. In acute phosalone poisoning, the activity of intracellular leukocyte enzymes, in particular, myeloperoxidase and alkaline phosphatase, is significantly reduced.

Our data showed that acute herbicide poisoning is accompanied by progressive leukocytosis with a shift of the leukocyte formula to the left, eosinophilia, lymphocytosis and monocytosis. Leukocytosis finds its explanation in the analysis of the myelogram of the bone marrow. It has been established that the number of young, stab and segmented neutrophils in the bone marrow significantly decreases, while the relative content of neutrophilic promyelocytes and myelocytes increases. This indicates that in the bone marrow, along with a violation of the processes of neutrophil differentiation, there is an intensive release of the bone marrow reserve of granulocytes in the peripheral blood. The increased release of young and mature neutrophils from the bone marrow into the blood causes leukocytosis in acute herbicide poisoning.

One of the most pronounced changes in peripheral blood in acute herbicide poisoning is severe anemia, which is hypochromic in nature. The mechanism for the development of anemia is complex and not fully understood. The cytochemical, radioautographic and electron microscopy studies carried out by us made it possible to elucidate the individual links in the pathogenesis of hypochromic anemia in acute phosalone poisoning. The study of the number of CHIC - positive erythroid cells reflects the degree of ineffective erythropoiesis and intramedullary destruction of erythroid cells. Consequently, acute exposure to herbicides is accompanied by an increase in the degree of ineffective erythropoiesis and increased intramedullary destruction of erythroid cells. Increased destruction of erythroid cells was also confirmed by our electron microscopy studies, which revealed many pronormocytes, normocytes with lysis of the nucleus and cytoplasm. At the same time, an increase in the number and functional activity of bone marrow

ISSN NO: 2770-2936
Date of Publication:03-11-2022

macrophages, which intensively phagocytize erythroid cells, was established. All this as a whole indicates that disturbances in the process of erythropoiesis and increased death of erythroid cells in the bone marrow itself are one of the causes. However, not only these mechanisms are involved in the development of anemia. Our radioautographic data showed that acute exposure to herbicides is accompanied by a pronounced decrease in the proliferative activity of erythroid germ cells and, above all, erythroblasts and pronormocytes.

Thus, hypochromic anemia that develops in acute herbicide poisoning is due to both an increase in the degree of destruction of erythroid cells and inhibition of the proliferative activity of the latter.

We found that acute poisoning with herbicides is accompanied by thrombocytopenia, which is most pronounced on the 1st-3rd day of the experiments. During this period, the number of bone marrow megakaryocytes decreased significantly. Electron microscopically in the cytoplasm of megakaryocytes revealed lysis of granules, the appearance of large vacuoles and reduction of demarcation membranes. This indicated a violation of the processes of platelet formation from megakaryocytes, and, apparently, is one of the causes of thrombocytopenia in the peripheral blood.

Thus, the studies carried out have established individual cellular and subcellular mechanisms of changes in the blood system during acute herbicide poisoning, which involve disruption of the processes of cell proliferation and differentiation, and increased destructive changes in their organelles.

Conclusions

With acute exposure to fosalone at a dose of 1/20 LD_50, against the background of signs of intoxication, severe hypochromic anemia develops leukocytosis with a shift to the left and thrombocytopenia. This is accompanied by inhibition of the activity of myeloperoxidase and alkaline phosphatase in neutrophilic leukocytes, destructive changes in subcellular organelles, and disruption of the process of granulogenesis in maturing granulocytes.

An increase in the degree of ineffective erythropoiesis and intramedullary destruction of erythroid cells, a decrease in their proliferative activity are separate links in the pathogenesis of anemia in acute and chronic intoxication with herbicides.

In the pathogenesis of thrombocytopenia in acute and chronic poisoning with phosalone, an important role belongs to the destructive changes in the organelles of megakaryocytes, the reduction of their demarcation membranes, and the slowing down of the processes of platelet lacing.

For the first time, a comparative study of the membrane-stabilizing and therapeutic properties of new microelement biocomplexes with vitamin U and amino acids was carried out. It has been established that biocomplexes of cobalt and copper have a rather high membrane-stabilizing and hemostimulating activity in both acute and chronic herbicide intoxication.

According to the results of cytochemical, radioautographic and electron microscopic studies, it was found that the biocomplex Co (II) is the most harmless and highly effective through the membrane stabilizing effect, helps to restore damaged subcellular organelles and has a stimulating effect on the proliferative activity of cells of the blood system.

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