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FORMATION OF MESENTERIC LYMPH NODES IN THE DYNAMICS OF EARLY POSTNATAL ONTOGENESIS WITH CHRONIC EXPOSURE TO PESTICIDES THROUGH THE MOTHER'S BODY

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Abstract: Purpose: to study the features of the postnatal development of the lymph nodes of the offspring of females exposed to chronic intoxication with fipronil.

Materials and methods: mesenteric lymph nodes 3, 7, 14, 21 and 30-day old rats born from females with chronic intoxication with fipronil and from control rats that were subjected to morphological, morphometric and electron microscopic methods of research served as the material for the study.

Results: In experimental rat pups obtained from females under conditions of chronic intoxication with fipronil, there was a significant lag in the formation of structural-functional T- and B-dependent zones of mesenteric lymph nodes, which was carried out 7-9 days later than rat pups with the natural course of postnatal ontogenesis.

Conclusions: Chronic exposure to fipronil through the mother's body contributes to a significant disruption of the processes of postnatal growth and the formation of mesenteric lymph nodes in their offspring, which manifest themselves as a slowdown in the growth and formation of the lymphoid tissue of the organ and its structural and functional zones.

Keywords: fipronil, offspring, postnatal ontogenesis, mesenteric lymph nodes.

Despite the fact that the health of children and adolescents is an urgent problem and a matter of priority importance, in recent decades there has been an increase in the incidence of allergic, autoimmune, infectious and oncological diseases in children all over the world, due to significant quantitative and qualitative deficiencies in various components of the immune system. According to many experts, changes in the functioning of the immune system of children may be the result of a violation of its development in the prenatal period, due to the effect of various exogenous and endogenous factors on the mother's body during pregnancy. Of the exogenous factors in recent years, special attention is paid to environmental factors. In this regard, the greatest interest and scientific and practical significance is the study of the features of the postnatal development of the organs of immunogenesis of the offspring of females exposed to chronic intoxication with pesticides, which would allow to identify the mechanisms of development of certain disorders of the immune system, to create a scientifically based strategy for the prevention and treatment of diseases in children exposed to prenatal exposure to exogenous factors.

The purpose of the study: study of morphological features of postnatal development and formation of mesenteric lymph nodes of offspring of females exposed to chronic intoxication with pesticides.

Materials and methods of research. The experiments were carried out on white sexually mature virgin Wistar female rats weighing 150-180 g. The females were divided into experimental (25) and control (25) groups. The experimental group of rats was injected with fipronil diluted in saline solution at a dose of 4 mg/kg daily for 75 days until the end of the experiments using a probe through the mouth at a dose of 4 mg/ kg, which was 1/100 of the LD50 of the drug. The control group received an equal volume of sterile saline solution. On the 31st day of the experiments, males were hooked up to the females of both groups. Fertilization was recorded using vaginal smears. Mesenteric lymph nodes (MLU) of baby rats born from experimental and control animals were studied on the 3rd, 7th, 14th, 21st and 30th days after birth using morphological, morphometric and electron microscopic examination methods. All digital data were statistically processed using a computer software package, differences satisfying $P>0.05$ were considered reliable.

Results and their discussion. Studies have shown that in control rats on the 3rd day after birth, the MLU parenchyma had no morphologically distinguishable structural and functional zones and consisted of diffuse lymphoid tissue. Lymphoblasts, medium and small lymphocytes were differentiated among the cells, single macrophages were determined.

On the 7th day of postnatal life, significant quantitative and qualitative rearrangements of the parenchyma and stroma of the organ were noted. Along with the increase in the area and volume of the node, the cortical and cerebral substances were distinguished for the first time. The cortical substance consisted of diffuse lymphoid tissue, where areas of dense and sparse arrangement of lymphocytes were noted. Dense clusters of lymphoid cells were mainly located on the periphery of the cortical substance and they represented zones of forming lymphoid follicles. A large number of lymphoblasts, prolymphocytes, single macrophages and plasma cells were distinguished among the cellular elements.

The 14th day after birth was characterized by significant changes in the structure of MLU: lymphoid follicles, paracaortical zone, cerebral cords and components of lymph circulation - sinuses were actually formed.

On the 21st-30th day, almost complete completion of the formation of the structural and functional zones of the organ was noted. Among the lymphoid follicles, both follicles without germinative centers and with germinative centers were distinguished. Morphometrically, during this period, the areas of lymphoid follicles, cerebral cords, parafollicular zone and cortical plateau reached the level of adult animals.

Analysis of the ratio of the T- and B-dependent zones responsible for the immune function of the organ in the dynamics of postnatal development in control rats showed that by day 14, the T-dependent (cortical plateau, paracortical zone) zone

occupied 42.3%, the V-zone (lymphoid follicle, brain cords) - 33.6%, and by the time of transition for definitive nutrition (21 days), there was a sharp increase in the volume of V-dependent zones - they occupied 40% of the total area of the node.

Thus, the development and formation of mesenteric lymph nodes of offspring obtained from control animals in the dynamics of postnatal ontogenesis was accompanied by a regular restructuring of its structural and functional zones and cellular composition. These rearrangements mostly stabilized by the 3rd week of the animals' life, when they switched to definitive nutrition.

Exposure to fipronil through the mother's body led to a significant disruption of the postnatal development of MLU in their offspring. The formation of structural and functional T- and B-dependent zones of MLU in experimental rats lagged significantly, being carried out 7-9 days later compared to the control. So, if the complete formation of structural and functional zones of MLU in control rats occurred on the 21st day after birth, then by this time only the beginning of the formation of lymphoid follicles was observed in experimental rats and the complete differentiation of structural and functional compartments of MLU was completed by the 30th day of postnatal life.

Morphometrically, a significant decrease in the growth rate and formation of MLU in offspring obtained by exposure to fipronil on the mother's body was revealed. During all the study periods, the absolute area of lymphatic follicles in MLU remained 17-28% significantly smaller compared to the control ($P<0.05$). Analysis of the ratios of T- and B-dependent MLU zones showed that under the conditions of exposure to fipronil on the mother's body, the formation of T-dependent MLU zones of offspring suffered the most. The growth rates of the area of T-dependent zones of the organ in experimental rats were 25-35% behind the control indicators ($P<0.05$).

Electron microscopic studies revealed high functional activity of macrophages and destructive changes in subcellular organelles of lymphoid cells, especially in T-dependent areas of the organ.

Thus, the data obtained indicate that chronic exposure to fipronil through the mother's body contributes to a significant disruption of the processes of postnatal growth and formation of MLU in their offspring. These disorders manifest themselves in the form of a lag in the growth and formation of the lymphoid tissue of the organ and its structural and functional zones. The slowdown in the growth and formation of structural and functional zones of MLU may be due to the direct toxic effect of fipronil and its metabolites on developing immune cells, hormonal imbalance in the form of a decrease in thyroid hormone levels and pronounced oxidative stress [3,4,5]. A decrease in the level of thyroid hormones and the accumulation of free radicals formed during oxidative stress inhibit the proliferation of MLU T and B lymphocytes and simultaneously stimulate the process of their apoptosis.

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