

Formation of Mesenteric Lymph Nodes in the Dynamics of Early Postnatal Ontogenesis under Chronic Exposure to Pesticides Through the Mother's Body

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Abstract The purpose of this article is 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

1. Introduction

Despite the fact that the health of children and adolescents is a pressing problem and a matter of primary importance, throughout the world in recent decades there has been an increase in the incidence of allergic, autoimmune, infectious and oncological diseases in children, which is due to significant quantitative and qualitative deficiencies in various components of the immune system [1,10,11,12,14,15].

According to many experts, changes in the functioning of the immune system of children may be a consequence of disruption of its development in the prenatal period, caused by the action of various exogenous and endogenous factors on the mother's body during pregnancy. Of the exogenous factors, environmental factors have recently received special attention. The increasing introduction of the achievements of chemistry into our lives, the large-scale use of chemicals has led to progressive pollution of the environment. The predominant part of environmental pollutants are pesticides, without the use of which further development of the agricultural industry is impossible [8,9].

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 make it possible 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 prenatally to exogenous factors.

Purpose of the study: to study the morphological features of postnatal development and formation of mesenteric lymph nodes in the offspring of female rats exposed to chronic intoxication with pesticides.

2. Material and Methods

The experiments were carried out on white mature virgin female Wistar rats weighing 150-180 g. The females were divided into experimental (25) and control (25) groups. The experimental group of rats was administered fipronil diluted in physiological solution at a dose of 4 mg/kg, which was 1/100 of the LD50 of the drug, daily for 75 days until the end of the experiments. The control group received an equal volume of sterile saline solution. On the 31st day of the experiments, males were added to the females of both groups. Fertilization was recorded using vaginal smears. Mesenteric lymph nodes (MLN) of rat pups born from experimental and control animals were studied on days 3, 7, 14, 21 and 30 after birth using morphological, morphometric and electron microscopic research methods. All digital data were

statistically processed using a computer program package; differences satisfying $P > 0.05$ were considered significant.

3. Results and Its Discussion

Studies have shown that in control rat pups on the 3rd day after birth, the MDR parenchyma did not have morphologically distinguishable structural and functional zones and consisted of diffuse lymphoid tissue. Among the cells, lymphoblasts, medium and small lymphocytes were differentiated, and single macrophages were identified.

On the 7th day of postnatal life, significant quantitative and qualitative rearrangements of the parenchyma and stroma of the organ were noted. Along with an increase in the area and volume of the node, the cortex and medulla were distinguished for the first time. The cortex consisted of diffuse lymphoid tissue, where areas of dense and sparse arrangement of lymphocytes were noted. Dense accumulations of lymphoid cells were mainly located along the periphery of the cortex, and they represented zones of developing lymphoid follicles. Among the cellular elements there were a large number of lymphoblasts, prolymphocytes, single macrophages and plasma cells.

The 14th day after birth was characterized by significant rearrangements in the structure of the MDR: lymphoid follicles, the paracortical zone, brain cords and components of lymph circulation - the sinuses - were actually formed.

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

Analysis of the ratio of the T- and B-dependent zones of the organ responsible for the immune function in the dynamics of postnatal development in control rat pups showed that by the 14th day the T-dependent (cortical plateau, paracortical zone) zone occupied 42.3%, the B-zone (lymphoid follicle, brain cords) - 33.6%, and by the time of transition to definitive nutrition (21 days), a sharp increase in the volume of B-dependent zones was observed - they occupied 40% of the entire area of the node.

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

Maternal exposure to fipronil resulted in significant impairment of postnatal MDR development in their offspring. The formation of structural and functional T- and B-dependent MDR zones in experimental rat pups was significantly delayed, occurring 7-9 days later compared to

the control. Thus, if the complete formation of structural and functional zones of MDR in control rat pups occurred on the 21st day after birth, then by this time in experimental rat pups only the beginning of the formation of lymphoid follicles was observed and complete differentiation of the structural and functional compartments of MDR was completed by the 30th day of postnatal life.

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

Electron microscopy studies revealed high functional activity of macrophages and destructive changes in subcellular organelles of lymphoid cells, especially in T-dependent zones 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 the formation of MDR in their offspring. These disorders manifest themselves in the form of retarded 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 areas of MDR may be due to the direct toxic effect of fipronil and its metabolites on developing immune-competent cells, hormonal imbalance in the form of a decrease in the level of thyroid hormones and severe oxidative stress [2,3,4,5,6,7,13,16,17]. A decrease in the level of thyroid hormones and the accumulation of free radicals formed during oxidative stress suppress the proliferation of MDR T and B lymphocytes and simultaneously stimulate the process of their apoptosis.

4. Conclusions

1. Exposure to pesticides through the mother's body leads to a slowdown in the postnatal growth of lymphoid tissue of the mesenteric lymph nodes, as well as the formation of their structural and functional zones.
 2. Disturbances in postnatal immunogenesis due to the immunotoxic effects of pesticides through the mother's body can be the main cause of secondary immune deficiencies in newborns and infants, which necessitates targeted pharmacological correction.
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