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The effect of phosphorus organic mixtures on chromosome aberration and cells' mitotic activity of red bone marrow in the subacute experiment

Abstract: At 100 Wistar rats population in subacute experiment the effect of small sub-toxic doses of phosphorus detergents (Efasol, Polifos, Syntaf) on the level of chromosomal aberrations and cells' mitotic activity of red bone marrow was investigated. There were 9 research groups of animals and one control in certain clear relationship between dose intensity and toxic effects of restructuring chromosomal apparatus. The number of cells with chromosomal aberrations in a dose-dependent (1/10, 1/100 LD₅₀) increased from 5 to 10 times. The study of cells' mitotic activity of red bone marrow identified reducing mitotic index, which may indicate the cytostatic effect of phosphorus detergents in appropriate doses 1/10 and 1/100 LD₅₀. All xenobiotics in 1/1000 LD₅₀ dose did not affect the genetic apparatus of male rats.

Keywords: xenobiotics, phosphorus detergents, cells' mitotic activity, red bone marrow, rats.

Introduction

Investigation was performed at the Department of Clinical Pathophysiology, Topographic Anatomy and Operative Surgery at Kharkiv Medical Academy of Postgraduate Education according to the issue "Radiotoxins' pathophysiological mechanisms on the body and methods of early diagnostics and correction".

The result of mutagenic effects of chemical compounds in the germ cells is a genetically defective gametes formation, which can lead to death of zygotes, embryos, fetuses, offspring born with disabilities which are able to be transmitted from generation to generation and form the hereditary disease. In literature there is enough information on the impact of factors of production and the environment on

the development and formation of long-term effects, including the occurrence of chromosomal and gene mutations.

It is known that mutations in somatic cells lead to their death or their functional changes. The latter, in turn, can lead to compatible or incompatible with the life birth defects if mutations arose during embryogenesis, or diseases in an individual in somatic cells which emerged and consolidated unfavorable mutations.

Over recent years, strong evidence of the impact of environment factors on fetal development in women of childbearing age who contact with industrial chemicals is revealed. However, it is difficult to determine is this condition a result of complex chemical factors before pregnancy, or the result of embriotoxic action of xenobiotics. More reliable in this respect, contact with active chemicals.

So repeatedly had been shown the increase number of stillbirths and miscarriages in women, whose husbands contact with chemicals. Along with these, the analysis of questionnaires, describing the mental and physical development and overall health of future generations, attracted the attention of workers in often mourning on lag of their children in early development, poor performance in school, excitement, nervousness, increased disease and others [1-5].

Thus, the purpose of the study was the impact of new sub-toxic doses of phosphorus-containing organic compounds on the genetic apparatus of warm-blooded animals in subacute experiment on white rats.

Materials and methods

The choosing of organic phosphorus compound mixtures was justified by the necessity of exploring the pathophysiological mechanisms of generative dysfunction in their long-term effects on the body in sub-toxic doses.

The study subjected the following phosphorus detergents: Efasol, Polifos-72 Syntaf 10-18. Efasol is a mix based on alkyl phosphates and secondary alcohols fraction C10-C20; Polifos-72 is a mixture of synthetic primary alcohols fractions C7-C12 and phosphoric anhydride; Syntaf 10-18 is a mixture of mono- and diephirs alkilphosphats' acid based on primary fatty acid fraction C10-C18. Xenobiotics in aggregate state represent as viscous liquid, readily soluble in water and organic solvents - alcohols, ether, benzene, and toluene.

Average lethal dose (LD_{50}) to white Wistar rats were set at $6,9 \pm 1,2$; $8,2 \pm 0,4$ and $11,7 \pm 0,9$ g/kg of the animal, according to Efasol, Polifos-72 and Syntaf - 10-18. Translation dose shows that current concentrations for Efasol are 690.0 and

69.0 mg/kg; for Polifos-72 - 820.0 and 82.0 mg/kg; Syntaf 10-18 - 1170.0 and 117.0 mg/kg body weight, according to the doses of 1/10 and 1/100 LD₅₀.

The program included a study of the effect of long sub-toxic action of xenobiotics on the level of chromosomal aberrations and cells' mitotic activity of red bone marrow. The paper used generally accepted guidelines [6].

In the scientific experiment male white rats of Wistar population weighing 180-200 g (N=100) were involved, which were exposed to toxification for 2.5 months, daily, in the morning on an empty stomach treated orally with aqueous solutions of xenobiotics calculate 1/10, 1/100, 1/1000 LD₅₀. The control group of rats received corresponding amounts of drinking water. There were 100 rats. 2 hours before the decapitation 2.5 mg/kg body weight colchicine was introduced intraperitoneally. Preparations were prepared by conventional method, followed by painting by Romanovsky-Himza.

100 metaphases from each animal were analyzed, single and paired fragments, translocations, ditsentryks, deletions, ring chromosomes were taken into account, spaces were not taken into account. In red marrow cells counted cells that divide at 1500 cells for each animal. All stages of the scientific experiment were carried out while respecting bioethics rules of humane treatment of animals, and the requirements of "the European Convention for the Protection of vertebrate animals used in scientific experiments" (Strasbourg, 1986). The results worked out methods of variation statistics and probability assessment by Student-Fisher.

Results and discussion

Our results showed that phosphorus-containing organic mixtures significantly increased the frequency of cells with rearrangement in chromosomal system (Table 1).

Table 1

The impact of phosphorus-containing organic compounds during prolonged sub-toxic action on the frequency of chromosomal aberrations and cells' mitotic activity of red bone marrow (M ± m)

Xenobiotics	The dose, LD ₅₀	Number of cells with the restructuring	Mitotic index
Efasol	1/10 (n=10)	8,3±0,57*	2,4±0,33*
	1/100 (n=10)	6,2±0,44*	2,9±0,27*

	1/1000 (n=10)	0,81±0,14	6,6±0,29
Polifos-72	1/10 (n=10)	9,4±0,63*	2,2±0,25*
	1/100 (n=10)	7,5±0,58*	3,1±0,32*
	1/1000 (n=10)	0,84±0,16	6,7±0,53
Syntaf 10-18	1/10 (n=10)	7,95±0,31*	2,6±0,24*
	1/100 (n=10)	6,34±0,27*	2,98±0,26*
	1/1000 (n=10)	0,76±0,14	6,6±0,37
Control	n=10	0,78±0,12	6,8±0,46

Note: * - the difference is likely to control, $r \leq 0,05$

Among them translocation disjunctions, deletions, single and paired fragments were met. Circular chromosome was met more rarely. Clear relationship between dose intensity and toxic effects and the restructuring in chromosomal apparatus were checked. The number of cells with chromosomal aberrations in a dose-dependent (1/10, 1/100 LD₅₀) increased from 5 to 10 times. The study of cells' mitotic activity of red bone marrow identified the reducing mitotic index, which may indicate the cytostatic effect of phosphorus detergents in appropriate doses 1/10 and 1/100 LD₅₀. All xenobiotics in 1/1000 LD₅₀ dose did not affect on the genetic apparatus.

Our previous study of pathophysiological mechanisms of structural and metabolic disorders under the action of these xenobiotics in the body 1/1000 LD₅₀ dose didn't find no changes in homeostatic functions neither. These data suggests that phosphorus detergent is not characteristic of a specific effect on the genetic apparatus, and identified chromosomal aberrations are the result of toxic action, the ability to penetrate biological membranes, having surface active properties.

Conclusion

Thus, phosphorus detergents with trade names Efasol, Polifos-72 Syntaf 10-18 at doses of 1/10 and 1/100 LD₅₀ are able to lead to the emergence reduce of chromosomal aberrations and cells' mitotic activity of red bone marrow in male rats. In 1/1000 LD₅₀ phosphorus complex organic mixtures do not affect the genetic apparatus and its mitotic activity. The study has found that phosphorus detergents do not have specific mutagenic effect.

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