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The influence of phosphorus complex organic mixtures on the content of sexual hormones and gonadotropins in the serum with violations in the reproductive system

Abstract: At 100 Wistar rat population in subacute experiment the effect of small doses of subtoxic phosphorus detergents (Efasol, Polifos, Syntaf) on the level of sex hormones in the blood serum of females - estrogen and gonadotropins was investigated by radioimmunoassay. There were 9 research groups and one control, 10 animals in each (N=100). Estrogen and gonadotropins were studied in rat serum. Significant inhibition of gonadotropin secretion may be combined with the permeability of the haemato-encephalic barrier for phosphorus complex organic compounds and their direct influence on the hypothalamic-pituitary neuroendocrine complex.

Keywords: xenobiotics, progesterone, prolactin, luteotropin, follicle-stimulating hormone, estradiol, serum, rats.

Introduction

In recent decades, accumulated a lot of data on the impact of harmful factors and the environment on production and reproductive function of women of childbearing age in contact with chemicals. Studies have shown that some chemicals can affect on the formation of defective gametes, the development of embryos and fetuses, gestation, lactation [1,2,3]. The analysis of scientific literature suggests that reducing the number of zygotes can be combined with the induction of dominant lethal mutations, and by reducing the number of fertilized eggs and therefore a violation of the fertilizing capacity of sperm as well as eggs. It is known that the frequency of ovulation, death of embryos before and after implantation controlled by independent genetic systems and genes that control death for implantation, exhibit

high level of domination.

The increase amount of stillborn and abortions was repeatedly educed for women that work on chemical productions. Next to that, at the analysis of questionnaires, that characterize psychical and physical development and general of descendants status, attract attention on itself frequent complaints of workers of chemical industry on lag of the children in early development of cognitive function, subzero success with studies at school, excited, irritate, nervousness, increase morbidity of the nervous, cardiovascular, respiratory system, perverted of immune-biological reactivity etc. [3, 4, 5]. There are violation of the endocrine system and immunological insufficiency in many cases [5-7]. Researches specify on the wide use of phosphorus complex organic mixtures of difficult organic mixtures in different industries of national economy and on their contact with a population both on a production and in the way of life.

The absence of prognostic description of potential safety for warm-blooded animals and man, large production volumes and assortment of products on their basis, dictate the necessity of study of physiopathology and pathochemical mechanisms of forming of reproductive function in the conditions of the protracted subtoxic operating on an organism. Our previous researches showed that phosphorus organic mixtures that have the commodity name as Efasol, Polifos, Syntaf 10-18 in doses 1/10 and 1/100 LD₅₀ at the protracted subtoxic action in a toxicological experiment diminished the amount of living embryos, mass and sizes of garden-stuffs, promoted preimplantic and postimplantic death of the embryos [8, 9].

Above-mentioned, the **purpose** is to study the contents of serum levels of sexual hormones - estrogen and gonadotropins in the conditions of prolonged subtoxic action of phosphorus detergents.

Materials and methods

The choosing of organic phosphorus compound mixtures was justified by the necessity of opening the pathophysiological mechanisms of action and long subtoxic formation of reproductive disorders in rats in subacute experiment. The study subjected the following phosphorus detergents: Efasol - mix based on and secondary alcohols fraction C10-C20; Polifos - a mixture of synthetic primary alcohols fractions C7-C12 and phosphoric anhydride; Syntaf 10-18 - a mixture of mono- and diephirs alkilphosphats' acid based on primary fatty acid fraction C10-C18.

The program included the study of subacute experiment on mature rats (female) population Wistar, weighing 210-220 grams. The animals were fed for 45 days by a metal probe daily morning fasting intragastric administered aqueous solutions of phosphorus detergents at a rate of 1/10, 1/100, 1/1000 LD₅₀.

The control group of females received the appropriate volume of drinking water. In each group, both in experimental and in the control group were 10 animals (N=100). During the all phases of scientific experiment we observed the rules of humane treatment of animals and requirements of the European Convention for the Protection of vertebrate animals used in scientific experiments and other purposes (Strasbourg, 1986).

Based on the parameters of acute toxicity the chemical mixtures belong to low-toxic compounds that do not have the species and gender sensitivity, but have distinct cumulative properties. All these xenobiotics on aggregate state are viscous liquids that are readily soluble in water and organic solvents - alcohols, ether, toluene, benzene and others. Average lethal dose (LD₅₀) 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. According to the purpose of the study serum gonadotropin and estrogen level in female were studied by radioimmunoassay using appropriate test systems. The content of serum progesterone was determined using reagents Institute of Bioorganic Chemistry of Belarus; Prolactin (PL), luteotropin (LH), follicle-stimulating hormone (FSH), estradiol (ED) were determined using test systems of Oris Industrie SA (France) [8, 9]. Statistical analysis of the results was carried out by methods of variation statistics estimate the probability for the Student-Fisher.

Results and discussion

Results of assessment of the impact of phosphorus compounds in ovarian hormones in rats have shown that doses of xenobiotics in 1/10 and 1/100 LD₅₀ reduce the level of serum estradiol. Efasol doses 1/10 and 1/100 LD₅₀ reduced rates of estradiol to 60.28% and 38.72%, Polifos-72 -to 57.51% and 35.69%, Syntaf 10-18 – to 56, 63% and 37.33% respectively. These results indicate that phosphorus complex organic mixtures in appropriate doses can inhibit folliculogenesis and the formation of female secondary sexual characteristics.

Against this background the inhibition of secretion of progesterone (the pregnancy hormone) in yellow bodies was marked. Influenced by Efasol the

progesterone levels decreased to 48.60% and 35.57%, by Polifos-72 - to 42.96% and 30,64%, by Syntaf 10-18 - to 38.74% and 16.91%, respectively to groups of animals which were toxicated by 1/10 and 1/100 LD₅₀.

Analysis showed that the decrease in progesterone production may interfere with implantation of a fertilized egg and development of pregnancy. Content of the gonadotropins in serum revealed lower levels of luteinizing hormone, follicle stimulating hormone and prolactin influenced by 1/10 and 1/100 LD₅₀.

During the research it was found that phosphorus detergents can inhibit luteotropins content in blood serum for 50.18% and 37.55% influenced by Efasol. Similar dynamics was typical to others detergents: Polifos-72 reduced the level at luteotropin to 44.57% and 42.11%, Syntaf 10-18 - to 48.25% and 35.09%, respectively, in groups of animals which were toxicated by 1/10 and 1/100 LD₅₀. Reduced levels of luteinizing hormone can be combined in violation of ovulation, pregnancy formation of corpora lutea in the ovaries, inhibition of secretion of estradiol and progesterone that occur during prolonged subacute experiments in animals [7].

Follicle stimulating hormone decreased under the influence by Efasol to 51.60% and 34.28%, Polifos-72 reduced the level to 47.71% and 32.16%, Syntaf 10-18 – to 41.70% and 24.74%, according to the groups of which were toxicated by 1/10 and 1/100 LD₅₀. Reduced levels of this hormone can affect the growth and maturation of follicles in the ovaries and disrupt the secretion of estrogen and cooperative action of luteotropin and the process of ovulation. It was found the reduction of lactotropic hormone in serum influenced by Efasol to 47.05% and 33.82%, Polifos-72 reduced the level at 40.48% and 42.82%, Syntaf 10-18 – at 33.83% and 30.46%, respectively, in groups of animals which were toxicated by 1/10 and 1/100 LD₅₀.

Analysis shows that phosphorus detergents are able to disrupt lactation, the differentiation of various tissues, growth and metabolism [7-9]. At the same time, it should be noted that a dose of xenobiotics 1/1000 LD₅₀ do not influence on the content of sexual hormones and gonadotropins in the serum.

Conclusion

Thus, complex organic phosphorus compounds - Efasol, Polifos-72, Syntaf 10-18 at doses of 1/10 and 1/100 LD₅₀ at long subtoxic action can inhibit the synthesis and secretion of gonadotropins (FSH, LH, PL) and hormones (ED, PG). Under such circumstances the genital dysfunction, disorders of the formation of secondary sexual characteristics, violation of ovarian-menstrual cycle and lactation should be expected.

Thus, in terms of working environment and a significant burden on the body of phosphorus compounds the formation of dysfunction in sexual instinct and mental status in women may be expected.

The analysis shows that a significant inhibition of gonadotropin secretion may be combined with the permeability of the haemato-encephalic barrier for phosphorus complex organic compounds and their direct impact on the hypothalamic-pituitary neuroendocrine complex.

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