EFFECTS OF POLYCHLOROCAMPHENE ON SOME ORGANS AND THEIR NERVOUS STRUCTURES IN PREGNANT ANIMALS

L. N. Badaeva

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Experiments on pregnant albino rats showed that after daily oral administration of polychlorocamphene (an organochlorine compound widely used in agriculture) in a dose of 12 mg/kg (0.05 LD_{50}) interconnected structural and enzymic changes take place in the nervous structures of the organs studied. The changes consisted of focal injury to nervous structures of the cerebral cortex, and progressive development of destructive processes in the nervous structures of the heart, uterus, and spinal cord toward the end of pregnancy. Against the background of a fall in cholinesterase (CE) activity in the cytoplasm of the neurons, distinctive changes occurred in the enzyme spectrum with preservation of activity in CE-positive pericellular structures, the number of which was considerably smaller than in the control. Predominance of destructive processes toward the end of pregnancy was due to marked accumulation of the compound in the heart, uterus, and brain, as shown by thin-layer chromatography. The presence of polychlorocamphene in the fetal organs indicates a disturbance of permeability of the transplacental barrier and a possible effect of the compound on the development of the fetal nervous system.

KEY WORDS: *Polychlorocamphene; cholinesterase; synapse; myelinated axon; transplacental barrier.*

Cases of onset of intrauterine pathology in pregnant women exposed to pesticides have been described [1, 4]. Since normal embryogenesis depends on the state of the nervous system, which integrates and regulates morphogenetic processes, it is essential to study the effect of pesticides on the nervous system under experimental conditions.

The compound chosen was polychlorocamphene (PCC), an organochlorine compound widely used in agriculture and whose neurotoxic action has been demonstrated by experimental studies and clinical observations [3, 6]. Morphological data on its neurotoxic action has not been described.

The object of this investigation was to study changes in nervous structures following exposure to PCC during pregnancy in order to decide whether it can influence the onset of intrauterine pathology.

EXPERIMENTAL METHOD

Experiments were carried out on 85 pregnant albino rats weighing 180-200 g, 20 of which acted as the control. PCC was given by mouth to the experimental animals in a dose of 12 mg/kg (0.05 LD_{50}) daily from the first day of pregnancy. The animals were decapitated on the seventh, 11th, 14th, 16th, and 20th days. Material (cerebral cortex, cervical and thoracic segments of the spinal cord, heart, and uterus) was studied by neurohistological (Bielschowsky–Gros, Spielmeyer) and histochemical (chromatophilic substance after Nissl, cholinesterase – CE – after Karnovsky) method. Electronmicroscopic investigations were carried out in the laboratory of Physiology of the Nervous System, Institute of Physiology, Academy of Sciences of the Ukrainian SSR (jointly with G. G. Skibo). The accumulation of PCC in the organs studied was determined (jointly with N. I. Kiseleva) by thin-layer chromatography.

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EXPERIMENTAL RESULTS AND DISCUSSION

After administration of PCC for 7 days, focal lesions were found in the brain, spinal cord, heart, and uterus, together with destructive changes in neurons, nerve fibers, and nerve endings. CE activity in the nervous structures was lower than in the control animals.

On the 14th day of the experiments hypertrophy of cells of the macro- and microglia, tortuosity and minute fragmentation of nerve fibers, and a decrease in the number of intact nervous structures were observed in the cerebral cortex. Myelinated fibers with an irregular outline on account of edema and vacuolation of the axoplasm could be distinguished. The myelin sheath of the nerve fibers lost its pattern and the Schmidt—Lantermann segments were widened. Some myelinated fibers underwent varicose changes and disintegration. Electron-microscopic investigation revealed degenerating myelinated axons among unchanged myelinated fibers. In some cases degeneration took place with separation of the axoplasm from the myelin sheath, shrinking of the axons, and irregular thickening of the myelin sheath, whereas in other cases the myelin laminae were swollen and loose in texture. Because of edema, separation of the myelin membranes into layers was observed, with vacuoles between them, leading to a disturbance of the relief of the myelinated axons.

Finally, myelinated fibers with periaxonal degeneration (demyelination) were found. In the nervous system of the heart and uterus single neurons died, fibers were destroyed, and Schwann cells proliferated. Individual nerve cells and fibers were almost completely devoid of enzyme activity.

On the 14th day of pregnancy accompanied by administration of the pesticide, thin-layer chromatography revealed PCC in the heart (2.5 μg/g), uterus (1.9 μg/g), and brain and spinal cord (1.2 μg/g). The low level of PCC in the brain and spinal cord despite considerable morphological changes and reduced CE activity could be evidence of the high sensitivity of the nervous (cholinergic) structures to the action of the compound.

After administration of PCC daily for 20 days, neurons continued to die in the cerebral cortex, the anterior horns of the spinal cord, and in the heart and uterus, and cell ghosts appeared in place of the nerve cells. A characteristic feature was increased CE activity in the glial cells. The enzymic reaction spread to the walls of the small vessels. In the organs studied, by contrast with the reduced CE activity in the nerve fibers, the cytoplasm of neurons, and also in certain areas of the myocardium, activity of the enzyme was found in residual hypertrophied synaptic structures. Electronmicroscopic investigation showed foci of destruction of muscle fibers in the myocardium, manifested by swelling and homogenization of the sarcoplasm and by fading and sometimes disappearance of the cross striation. Edema between the muscle bundles and individual myofibrils was a characteristic feature. Among unchanged mitochondria there were others which were swollen and contained either deformed cristae or no cristae at all. Invaginations of the nuclear membrane and focal edema between the membranes of the endoplasmic reticulum with dilatation of its cisterns were found in spinal motoneurons. Swelling and deformation of the mitochondria and disappearance of their cristae took place.

On the 20th day of the experiment, thin-layer chromatography revealed an increase in the PCC content in the heart (17 μg/g), gravid uterus (9.7 μg/g), and brain and spinal cord (4.3 μg/g). This deposition of the chemical evidently was responsible for the increased direct toxic action of PCC on the organs studied and on their nervous structures. Structural changes in the organs were accompanied by depression of their function and also by pathological phenomena (myocardial degeneration, disturbances of the menstrual cycle and pregnancy, development of neuritis), as detailed in the literature [2, 5, 7]. The presence of PCC in the fetal organs (brain and spinal cord, heart) despite a lower concentration of it in the placenta, may indicate the transplacental passage of the compound as a result of disturbance of permeability and relaxation of the barrier function of the placenta. Postimplantation death of fetuses and still birth must be assumed to be the result of the direct toxic action of PCC on the various systems of the fetus, including its nervous system.

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