SUMMARY

Bubalo N.M. Lesions of the hepatobiliary system, metabolic disorders and obesogenic effects in patients who suffered acute and chronic intoxication with pesticides. – Manuscript.

Dissertation for a scientific degree of candidate of medical sciences in speciality 14.03.06 – toxicology (222 – medicine). – State Institution "Y.I. Kundiev Institute of Occupational Medicine of the National Academy of Medical Sciences of Ukraine", Kyiv, 2020.

The dissertation is dedicated to the study of the features of toxic damage to the hepatobiliary system (HBS), metabolic disorders, an imbalance of adipose tissue hormones in patients who underwent acute and chronic pesticide intoxication and obesogenic effects, as a consequence of these intoxications and to substantiate informative biomarkers for their diagnosticity and optimization of prevention.

The study examined the main syndromes of acute pesticide poisoning from the class of organophosphorus pesticides (OPP), 2,4-Dichlorophenoxyacetic acid (2,4-D), synthetic pyrethroids (SP), as well as chronic intoxications with pesticides (CIP), long-term effects of damage to the hepatobiliary system, features of the formation of intrahepatic cholestasis syndrome, the role of oxidative stress and endotoxicosis in the development and progression of toxic lesions systems, the potential risk of the formation of liver steatosis, metabolic disorders and obesity in patients with proved acute and chronic pesticides intoxication.

Based on clinical, biochemical and clinical-instrumental studies, it has been established that, in addition to the prevalence of neurological disorders in patients with acute and chronic pesticide intoxication, toxic damage to hepatobiliary system develops in acute pesticide intoxications based on 2,4-D – in 35,8% cases, in case of OPP intoxication – in 53,3% of cases, in case of SP intoxication – in 64,2% of cases and CIP – in 84% of cases.

Cytolytic syndrome predominated in the structure of clinical syndromes of toxic lesions of HBS: in acute intoxication with 2,4-D based pesticide – in 89,6% of cases mainly with the first degree of cytolysis, in acute OPP intoxication – in 93,7% of cases the second degree of cytolysis prevailed, in acute intoxication of SP – 88,9% of cases and in CIP - in all cases of toxic hepatitis – II degree of cytolysis.

Hepatodepressive syndrome was less frequently found in the structure of clinical syndromes of toxic lesions of HBS: with 2,4-D intoxication in 10,3 % of cases, with OPP intoxication in 25,0% of cases, with acute SP intoxication – 22,2 % and with CIP – in 25.4% of cases. Intrahepatic cholestasis syndrome was found almost equally in patients with lesion of HBS (17.3 – 27.1 %) and in patients without lesion of HBS (15,4 – 27.3 %), but in patients with lesion of HBS hepatocellular form of intrahepatic cholestasis syndrome prevailed, and in patients without signs lesion of HBS – canalicular.

In a distant period after 15 years, patients with 2,4-D-toxic pesticide with lesion of HBS showed metabolic disorders with dyslipoproteinemia (significant

increase in levels of total cholesterol, triglycerides, cholesterol), as well as obesity mainly grade II-III with a significant increase in body mass index (BMI) to an average of (42,75±2,39) kg/(m)2 and waist size to an average of (116,9±5,95) cm ($p<0,05$).

It was defined increased levels of fatty tissue hormones in the blood – leptin 2,5 times ($p<0.05$), resistin – 2 times ($p<0.05$), TNF-α – 10 times ($p <0.05$). A moderate decrease in adiponectin levels in patients with long-term checkup who have undergone acute 2,4-D intoxication can predict an increased risk of progressive liver steatosis, metabolic disorders, and obesity. Increased secretion of leptin, resistin, and TNF-α not only supports metabolic disorders and decontamination effects but also contribute to their progression.

The first time the feasibility of studies of adipose tissue hormones (leptin, resistin, adiponectin, TNF-α) for patients undergoing acute 2,4-D herbicide intoxication as diagnostic biomarkers of lesion of HBS and liver steatosis was substantiated.

The theoretical significance of the results obtained and their analysis is that metabolic disorders and obesogenic effects are considered as a consequence of acute P intoxication, 2,4-D, OPP, SP, as well as CIP, mainly in patients with toxic damage to HBS.

The diagnostic significance of these hormones (leptin, resistin, TNF-α, and adiponectin) as biomarkers of toxic lesions of the hepatobiliary system, hepatosteatosis and obesity have been determined. Available data suggest a higher risk of gradient steatohepatitis and obesity in the long term.

Keywords: pesticides, synthetic pyrethroids, 2,4-D, acute poisoning, chronic intoxication, oxidative stress, metabolic disorders, obesogenic effects, leptin, resistin, adiponectin, TNF-α.