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CORTICOSTERONE LEVELS AND SPECIFIC IMMUNE FACTORS IN CHRONIC PESTICIDE POISONING

Khaydarova Dilorom Safoevna
Department of Pathophysiology, Samarkand
State Medical Universiti, Samarkand, Republic of Uzbekistan
e-mail: dilsaf63@mail.ru

ABSTRACT
In experiments on male Wistar rats during chronic poisoning with organophosphate pesticide antio at a dose of 1/100 LD50, a decrease in immunity parameters was revealed with a concomitant (simultaneous) increase corticosterone levels in the blood, which may be one of the mechanisms for reducing the organizm's resistance and increasing the number of morbidity in the regions heavy use of pesticides.

Keywords: organophosphate pesticides, chronic poisoning, neuroendocrine regulation, immunity parameters, corticosterone.

Introduction

It is known that pesticides are chemicals that are used to increase crop yields by destroying weeds, pests, various fungi, ectoparasites of pets, carriers of dangerous human and animal diseases. However, at the same time, they are toxic not only for harmful organisms, but also for humans and animals (Prozorovskiy V. B. et al., 1997; Lujnikov E. A., 1999; Sirempilov P. B., 2002; Chepur S. V., 2010; Vorobeva V. V. et al., 2017; Anuchina A.V., 2019). Organophosphorus compounds (OC) cause up to 3 million poisonings worldwide every year (Prozorovskiy V. B. et al., 1997; 2001). Organophosphate poisonings (OP) occupy one of the leading places in the total number of exotoxicoses. Despite recent progress in the treatment of OC poisoning, they usually occur with a predominance of severe forms (up to 55%) and in 10–15% of cases end in the death of the victims (Fergsheng H., 1996; Lujnikov E. A., 1999; Prozorovskiy V. B. et al., 2001). The danger of pesticides for human health lies not only in the possibility of acute poisoning, but mainly in long-term exposure to their small amounts, which can accumulate in the body and adversely affect it (Wang X. et al., 2018). Long-term consumption of food products contaminated with pesticides causes chronic poisoning, often accompanied by various diseases (Prozorovskiy V. B. et al., 1997; 2001; Chepur S. V., 2010). It is possible that this is based on a decrease in the body's resistance, in particular immunity. A number of works of domestic and foreign authors are devoted to this problem (Nikolaev A. I., 1988; Repetto R., Yafarova I. H., 1996; 2010; Zabrodskiy P. F., 2016; Korneva E. A. et al., 2017). However, the issues of neuroendocrine regulation of immunogenesis in chronic pesticide poisoning remain poorly understood. At the same time, literature data indicate their negative effect on

immunity factors, including long-term intoxication of the organism with small doses of pesticides (Yafarova I. H., 1996; Sirempilov P. B., 2002).

The purpose of this work was a comparative study of the effect of chronic poisoning with OC antio on the state of specific immunity factors and the blood level of one of the glucocorticoid hormones, corticosterone (CS).

Material and Research Methods

The experiments were carried out on male Wistar rats weighing 160-220 g, which were administered daily oral antio at a dose of 1/100 LD_{50} (3.5 mg/kg) for 2 months. Animals in the control group received an equal volume of solvent.

The functional state of the immune system was assessed by the intensity of the humoral immune response, for which hemagglutinin (HA) titers were determined in the blood serum of rats immunized intraperitoneally with sheep erythrocytes (ShE) at a dose of 1-5x10^9 cells in 1.0 ml of physiological solution on the 23rd and 53rd th days of antio poisoning. The intensity of cellular immunity was assessed in animals according to the delayed-type hypersensitivity reaction (DTHR), which was reproduced on the 21st day after sensitization by introducing EB at a dose of 10^8 cells in a volume of 0.1 ml of saline into the paw pads and measuring the difference in paw diameter before and after 24 and 48 hours after antigen injection. Plasma corticosterone (CS) concentration was determined by direct radioimmunoassay using standard RIN-B-3N kits. Blood for the study was obtained by simultaneous decapitation of animals.

Results were statistically processed using Student's t-test.

Research Results. The results obtained are presented in tables.

Table 1. The content of corticosterone (ng/mL) in the blood plasma of Wistar rats with chronic poisoning with organophosphate pesticides antio

Observation time (days)	Corticosterone (ng/mL) (basal level – 222,7+9,0 (9))	
	Control	Antio 1/100 LD_{50}
30	240,0+30,0 (5)	408,3+86,9 (6)
60	286,2+62,0 (5)	673,3+56,7 (6)*

Note: * - statistically significant ($p<0.001$) difference from control; figures in brackets - number of animals

As can be seen from Table 1, an increase in the level of corticosterone in poisoned animals compared with the data of the control group was noted on the 30th and 60th days of observation ($p<0.001$).

Determination of the HA titers (Table 2) revealed their decrease on the 30th and 60th ($p<0.02$) days in the animals of the experimental group in relation to the control.

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Table 2. Hemagglutinin titers (-log2) in the blood plasma of Wistar rats in chronic poisoning with organophosphate pesticides antio

Observation time (days)	**Hemagglutinin titers** (M+m)	
	Control	Antio 1/100 LD_{50}
30	4,20+0,43 (5)	3,50+0,20 (8)
60	4,20+0,53 (5)	3,06+0,26 (8)*

Note: * - statistically significant ($p<0.001$) difference from control; figures in brackets - number of animals

With regard to DTHR (Table 3), there was a decrease in its intensity compared to the control in the group of animals exposed to antio poisoning for 60 days ($p<0.02$ and $p<0.01$).

Table 3. Intensity of DTHR (mm) in Wistar rats with chronic poisoning with organophosphate pesticides antio

Obser vation time (days)	Rat paw diameter difference (M+m)			
	Control		Antio 1/100 LD_{50}	
	24 h	48 h	24 h	48 h
30	0,364+0,049 (5)	0,390+0,035 (5)	0,266+0,040 (5)	0,290+0,058 (5)
60	0,374+0,070 (5)	0,406+0,062 (5)	0,170+0,034*(5)	0,185+0,039**(5)

Note: * - ($p<0.02$), ** - ($p<0.01$) - statistically significant difference from control; numbers in parentheses are the number of animals; 24 hours and 48 hours - the time after the introduction of the resolving dose of antigen (ShE)

Discussion

According to the literature, it is known that large pharmacological doses of glucocorticoids, especially with their long-term use, inhibit the humoral and cellular immune response (Korneva E. A., 1988). These data make it possible to classify glucocorticoid hormones as inhibitors of the metabolism of lymphoid cells. The inhibitory effect of glucocorticoids is determined primarily by binding to specific cytoplasmic receptors; their further translocation to the nucleus, where the transformation of the hormonal signal into the biochemical response of the cell occurs due to changes in the function of its nuclear apparatus (Rozen V. B. et al., 1981).

In our studies, in case of OP poisoning, an increase in the concentration of CS in the blood, as a rule, coincided with a decrease in the parameters of humoral and cellular immunity, which indicates a suppression of the immune response, apparently associated with an increase in the secretion of CS.

Conclusion

Thus, the results of this work, taking into account the data of previous studies (Kurambaev Ya. K., 1986) suggest that an increase in the functional activity of the hypothalamic-pituitary neurosecretory and hypothalamic-pituitary adrenocortical systems, as well as the level of glucocorticoid hormones in chronic poisoning with organophosphorus pesticides (in particular, antio), coinciding in time with the suppression of the immune response, may be one of the mechanisms for reducing specific resistance and increasing the incidence of the organism in areas with long-term and intensive use of pesticides.

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