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ON THE PATHOGENESIS OF CARDIOVASCULAR DYSFUNCTION IN THE PRESENCE OF CHRONIC VINYL CHLORIDE INTOXICATION

The study was performed on outbred male white rats with an initial weight of 160-180 g. The animals were exposed to vinyl chloride (VC) intoxication for 7 months for 4 1/2 hours per day at concentrations of 20 mg/m^3 (group 1) and 300 mg/m^3 (group 2); the third group of animals was the control group. The seven month duration was due to the attempt to determine possible delayed functional changes under the influence of VC at a level below the present limiting allowable concentration (LAC).

The condition of the cardiovascular system was determined from changes in the bioelectric activity of the heart and in the arterial pressure. An ECG recording was made on an ELKAR-4 instrument in standard lead II. The systolic and diastolic arterial pressure and pulse were determined photoplethysmographically. The factors studied were recorded in months 1, 3, 5 and 7 of the test.

The animals exposed to the effect of VC in a concentration of 20 mg/m^3 received adrenaline and Pituitrin subcutaneously in doses at the threshold level for the given factors, 0.3 mg and one unit per kg of weight of the animal, respectively. The effect of the preparations was evaluated by the change in the ECG readings and the blood sugar level.

In the experimentals, VC poisoning at concentrations of 300 mg/m^3 from the third to the fifth months of the test caused a decrease in the $R - R$ interval (third month - experimentals: 0.140 $\pm$ 0.001; controls: 0.153 $\pm$ 0.005 sec; $P \leq 0.05$; fifth month - experimentals: 0.134 $\pm$ 0.006 sec; controls: 0.160 $\pm$ 0.004 sec; $P \leq 0.05$), changing in the 7th month to a clearly expressed lengthening of the $R - R$ interval (experimentals: 0.172 $\pm$ 0.008; controls: 0.158 $\pm$ 0.007; $P \leq 0.05$); at a VC concentration of 20 mg/m^3 the $R - R$ interval increased by the 7th month (experimentals: 0.180 $\pm$ 0.008; controls: 0.158 $\pm$ 0.007 sec; $P \leq 0.05$).

In the first 5 months of exposure the systolic arterial pressure in animals of the second group was characterized by a tendency to increase with development of hypotension in the 7th month. The diastolic pressure increased in the animals of both experimental groups, but more slowly in the animals of the first group. Subsequently the diastolic pressure decreased. In the animals of the 2nd group the pulse pressure was characterized by significant variations throughout the period of exposure, and in animals of the 1st group it decreased throughout the exposure period.

The use of a functional pharmacologic load of Pituitrin showed that the sensitivity of animals, poisoned with VC at a concentration of 20 mg/m^3, to this preparation differs significantly from the sensitivity of the controls. After the first month of intoxication the experimental animals showed a retardation of the rate of heart activity greater than that of the control in response to the load. The interval increased in the experimentals from 0.150 ± 0.002 to 0.177 ± 0.007 sec, $P \leq 0.05$; in the controls from 0.150 ± 0.003 sec to 0.167 ± 0.007 sec, $P \leq 0.05$). In 4 of the 12 experimental animals, after introduction of Pituitrin, we observed phenomena of coronary insufficiency (rise of the ST segment above the isoelectric line, increase of the T voltage, in the first case a negative T wave). In the control rats these phenomena were not noted. In the third month of intoxication no statistically significant change in the rhythm of cardiac activity was noted in the experimental animals under the influence of Pituitrin. A different reaction, more pronounced than in the control rats, increase of the $R - R$ interval, was noted in the fifth month of exposure. Subsequently, in the seventh month of exposure, the cardiac sensitivity of the experimental rats to Pituitrin increased still more. This caused a sharp increase in the $R - R$ interval and, against this background, appearance of clearly expressed sinusal arrythmia (difference of $R - R_{max}$ and $R - R_{min}$ in the controls: 0.12 ± 0.002 sec; in the experimentals: 0.040 ± 0.003 sec; $P \leq 0.05$), appearance of individual ventricular [illegible; extra-?]-systoles and signs of impairment of the atrioventricular conduction.

Adrenaline caused more clearly expressed tachycardia in the experimentals in the first and fifth months than in the controls. In the third and seventh months of exposure no changes were noted in the rhythm of cardiac activity due to introduction of adrenaline to the experimentals.

The hyperglycemic effect of adrenaline was more clearly expressed in the experimental animals in the first and especially in the fifth months of exposure. The level of hyperglycemia was the same in the experimental and control rats in the third month of exposure. In the seventh month of the study the hyperglycemic reaction to the introduction of adrenaline was more clearly expressed in the experimentals than in the controls.

The studies showed that chronic VC intoxication leads to impairment of the neurohumoral regulation of the activity of the cardiovascular system. VC vapor at a concentration of 300 mg/m^3 causes initial activation of the sympathetic part of the autonomic nervous system, which subsequently is replaced by intensification of parasympathetic effects. Under the influence of VC at a concentration of 20 mg/m^3 only in the 7th month was the hyperglycemic reaction to the introduction of adrenaline more clearly expressed in the experimentals than in the controls.

[Part of the next paragraph is a repetition of the paragraph above. This is probably due to a composing error of some kind in the original. -- Translator].

The studies showed that chronic VC intoxication leads to impariment of the neurohumoral regulation of cardiovascular system activity. VC vapor at a concentration of 300 mg/m^3 causes initial activation of the sympathetic part of the autonomic nervous system, which is subsequently replaced by intensification of parasympathetic effects. Under the influence of VC at a concentration of 20 mg/m^3, only in the 7th month of exposure did we succeed, without use of loads, in determining differences in the state of the autonomic/endocrine regulation of the cardiovascular system. These were shown by arterial hypotonicity and retardation of the cardiac

activity rhythm, showing intensification of the tonus of the parasympathetic part of the autonomic nervous system. The use of a pharmacologic load of adrenaline revealed an increase in the sensitivity of the peripheral adrenoreceptors even in the first months of exposure. Subsequently the periods of increased sensitivity of the adrenoreceptors are replaced by periods of reduced sensitivity, as shown by the change in the rhythm of cardiac activity and the blood sugar level.

The use of a Pituitrin load also showed that VC intoxication is characterized by a change in the reaction of the myocardium.

The study results show that chronic intoxication by low concentrations of VC lead to neurovegetative and cardiovascular dysfunctions, initially appearing as compensated impairments of the neurohumoral equilibrium, and then as impairment of vegetative regulation with predominant parasympathetic effects. The central nature of these changes is also shown by the synchronous phase dynamics of the reactions of the effector organs.