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ASSESSMENT OF NANOCHROMIUM CITRATE EFFECT ON THE CARDIAC FUNCTION AND HEMODYNAMIC STATE IN RABBITS

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Abstract

Chromium as a trace element is known to play an important role in carbohydrate, lipid and protein metabolism, and participates in regulation of functioning of the cardiovascular activity. Chromium protects vessels against cholesterol deposits, normalizes arterial blood pressure and heart rate, prevents development of atherosclerosis, occurrence of heart attacks, strokes etc. In terms of studying toxicological characteristics of nanochromium citrate (NCC) in an acute experiment conducted on rabbits the effect of NCC produced on the cardiac function and the state of cardio- and hemodynamics were investigated with a fractional intravenous introduction of NCC in increasing doses. With a fractional introduction in the cumulative dose and underlying urethane anesthesia NCC is not found to cause reliable changes in the parameters of the systemic and cardiac dynamics in rabbits in comparison with both their initial level and appropriate parameters in the control anesthetized animals.

Keywords: *nanochromium citrate, cardiac and hemodynamics, acute experiment*

Introduction

The interest to nanotechnology including nanobiology and nanomedicine is increasing in different fields of human activity [1-3]. Special attention is paid to the exploration of nanostructures of biometals regulating important biochemical and physiological functions in the body [4]. In Ukraine researches on studying toxicological and pharmacological properties of biometal nanoparticles such as silica, silver, copper, zinc etc. have been actively conducted Nanoparticles and nanostructured materials are already used as new medicinal agents, biosensors and devices for visualization and diagnostics [5]. Chromium nanoparticles can be promising structures used in nanomedicine [6]. The studies of the recent 50 years have shown that chromium is an important trace element essential for normal vital functions of the man and animals. Chromium is known to play an important role in carbohydrate, lipid, protein, nucleic acids metabolism, and together with iodine it provides functioning of the thyroid gland, regulates production and metabolism of insulin [7]. Everyday need for chromium for the man is 50-200 mcg. Its deficiency causes disorders of vitally important processes in the body and symptoms similar to those occurring during diabetes mellitus and cardiovascular diseases [8]. The body is supplied with chromium through the intake of foods rich in this trace element (fish, beef liver, poultry, eggs, beer yeast), which are recommended to normalize protein, lipid and carbohydrate metabolism in case of type 2 diabetes mellitus, obesity, hypertension etc. [9].

Ukrainian Scientific-Research Institute of Nanobiotechnologies and Resource-Saving (Kyiv) received a new chromium compound – nanochromium citrate (NCC) by means of electric pulse aquananotechnology [10]. Today NCC is found to produce a positive effect on biochemical processes in the body, and it is recommended to be used as a food additive in veterinary practice [11]. Meanwhile, NCC effect on the function of the cardiovascular system is not studied, which is especially important in case of its parenteral use. Objective of the research is to study NCC effect on the cardiac function and hemodynamic state in animals under conditions of an acute experiment.

Methods

The study was carried out on 12 chinchillas with the body weight of 3.0-4.5 kg. The animals were divided into two groups. The experimental animals (7 rabbits) were given intravenous NCC solution injections, the control ones (5 rabbits) received the equivalent by its volume 0.9% sodium chloride solution. Cardio- and hemodynamic parameters were examined with underlying urethane anesthesia (1 g/kg, 50% solution, intramuscularly). The left heart ventricle and femoral artery were catheterized in both the control and experimental animals, the electrodes were applied in three standard leads, and in the acute experiment by means of the device HP Viridia Component Monitoring System produced by «Hewlett Packard» (USA) electrocardiogram and cardiohemodynamic parameters were registered: maximal pressure in the left ventricle (Pmax LV, mm Hg), systolic arterial pressure (APs, mm Hg), heart rate (HR, bpm). Blood minute volume (BMV, ml/min) was identified by means of thermodilution method. The following parameters were calculated on the basis of the data obtained by the formulas: cardiac index (CI, ml/(m2•min), heart discharge (HD, ml/sec), the left ventricular work index (LVWI, kgm/(m2•min), the left ventricular stroke work index (LVSWI, kgm/m2).

NCC solution was introduced slowly into the marginal auricular vein of the experimental animals, and 0.9% NaCl solution was introduced to the control animals according to the pattern (see Table 1). The initial NCC dose was 0,9 mg/kg [5]. Every two following 30 minute periods the animals received the compound in the dose three times higher (2.7 mg/kg), the final total dose of NCC with fractional introduction was 6.3 mg/kg. After NCC introduction hemodynamic parameters were registered in the animals 30 minutes later, and after the last one – in 15, 30 and 60 minutes. The animals from the control group which were under urethane anesthesia received 0.9% NaCl solution in the similar periods of time in the volume equivalent to that of the experimental animals. Changes of the cardio- and hemodynamic parameters in the experimental animals were compared with the initial level before NCC introduction and with the parameters of the control animals.

All studies were carried out in accordance with the criteria outlined in the European Union Directive 2010/63/EU "On the protection of animals used for scientific purposes".

Statistical processing of the obtained data was performed using the SPSS Statistics 17.0 software. All data are represented as a mean ± standard error of the mean (M±m). Estimation of the differences between the samples was conducted using a parametric Student's t-test and a nonparametric Mann-Whitney U test. The minimum significance level was $p<0.05$.

Results

In terms of studying toxicological characteristics of NCC in an acute experiment conducted on rabbits the effect of NCC produced on the cardiac function and the state of cardio- and hemodynamics were investigated with a fractional intravenous introduction of NCC in increasing doses. After the first single intravenous introduction of NCC in the dose of 0.9 mg/kg in the amount of 3.2 ml in 30 minutes changes in the registered parameters of the cardio- and hemodynamics were not registered. Repeated introduction of NCC in the dose three times as much (2.7 mg/kg) in the total dose of 3.6 mg/kg did not cause any considerable changes in the parameters either.

The next repeated NCC introduction in the dose of 2,7 mg/kg decreased APs from the beginning of the introduction in comparison with the initial value. In the following 15 minutes since the beginning of the introduction BMV decreased (see Table 2). With decreased APs the parameters of CI and HD decreased as well in comparison with the initial level of the parameters in the experimental animals. Decreased BMV in 15 and 60 minutes resulted in reduced parameters of LVWI and LVSWI (see Table 3).

At the same time, in the control group of animals which were under urethane anesthesia as well, decreased levels of APs, LVWI and LVSWI were found in comparison with the initial values and no changes in the parameters of HR, Pmax. of the LV, BMV, CI and HD were registered (see Table 2, 3).

Discussion

Literary data indicate that chromium as a trace element is known to play an important role in carbohydrate, lipid and protein metabolism, and participates in regulation of functioning of the cardiovascular activity [12]. Chromium normalizes arterial blood pressure and heart rate, prevents development of atherosclerosis, occurrence of heart attacks, strokes etc. We have examined NCC effect on the cardiac function and hemodynamic state not only in the aspect of learning its effect on the cardiovascular activity which functions are directed to homeostasis maintenance in the body, but from the point that in addition to other functions the circulatory system performs excretory function as well. The results obtained were indicative of the fact that primary single and repeated NCC introduction in the dose three times as much (2,7 mg/kg) did not cause any changes in the parameters of the cardio- and hemodynamics in animals. The next repeated NCC introduction in the similar dose resulted in reliable decrease of APs in comparison with the initial value. Decreased APs resulted in reduced parameters of CI and HD. Due to decreased BMV, LVWI and LVSWI reduced respectively, which is indicative of reduced pumping function of the heart occurring with an increased concentration of NCC in the blood. Though, it should be noted that the control animals also presented reliable decrease of APS, LVWI and LVSWI in comparison with the initial values and absent disorders of other parameters. Therefore, the changes of the cardio- and hemodynamics found under NCC effect might be caused by the action of anesthesia and are not associated with NCC toxic effect on the cardiovascular function in the examined doses. Moreover, our preliminary studies of the hydrostructure of the internal organs in the experiments on rats after repeated (14 days) NCC introductions in increasing doses did not find any pathomorphological changes in the cardiac muscle [13].

Conclusion. Under conditions of the acute experiment with underlying urethane anesthesia NCC effect on the parameters of the systemic and cardio-, hemodynamics in rabbits was not registered, since decreased pumping function of the heart found with an increased NCC dose did not

differ reliably from the appropriate parameters in the control animals.

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Table 1. The pattern of the experiment to determine NCC effect on the systemic and cardio-, hemodynamics in the acute experiment in rabbits

Time since the first introduction, min.	Nanochromium citrate, n=7		Control, n=5
	Single dose, mg/kg	Total dose, mg/kg	
0	0.9	0.9	0.9% NaCl
30	-	-	-
35	2.7	3.6	0.9% NaCl
65	-	-	-
70	2.7	6.3	0.9% NaCl
85	-	-	-
100	-	6.3	-
130	-	6.3	-

Single dose – one-time dose with i/v introduction; total dose – general dose, sum total of all the previous single doses, n – number of animals in the group.

Table 2. Dynamics of the cardiac function changes and hemodynamic state in rabbits with NCC introduction in increasing doses

Parameters	HR, bpm	$P_{max.}$ LV, mm Hg	APs, mm Hg	BMV, ml/min
Experiment (n=7)				
Initial level	290.9±5.2	111.0±4.2	123.9±2.3	970±30
NCC, 0.9 mg/kg				
in 30 min	293.8±7.39	110.0±1.97	118.0±3.2	950±30
NCC, 2.7 mg/kg				
in 30 min	295.0±4.8	112.1±4.5	119.9±2.8	940±30
NCC, 2.7 mg/kg				
in 15 min	294.0±6.2	105.9±3.4	116.3±3.7*	930±20
in the following 15 min (30 min)	294.0±8.4	104.9±6.6	114.1±6.0	900±30*
in the following 30 min (60 min)	289.7±6.8	106.3±5.8	111.4±4.6*	920±40
Control (n=5)				
Initial level	294.3±6.5	110.6±6.1	126.0±3.0	940±30
0.9 % NaCl				
in 30 min	296.6±4.37	110.7±1.91	123.9±2.1	920±50
0.9 % NaCl				
in 30 min	297.1±5.9	111.4±6.6	120.3±4.7	910±30
0.9 % NaCl				
in 15 min	298.3±9.2	105.3±5.2	117.1±6.0	880±10
in the following 15 min (30 min)	299.9±10.9	102.3±9.1	111.8±8.8	860±20
in the following 30 min (60 min)	296.1±6.6	104.0±8.0	108.1±5.8*	880±40

* – the difference reliable in comparison with the initial level of the parameters in the control and experimental animals ($p<0,05$), n – number of animals in the group.

Table 3. Dynamics of the cardiac function changes and hemodynamic state in rabbits with NCC introduction in increasing doses

Parameters	CI, ml/(m²•min)	HD, ml/sec	LVWI, kgm/(m²•min)	LVSWI, kgm /m²
Experiment (n=7)				
Initial level	4502.8±139.2	16.2±0.5	7434.8±207.7	25.9±1.1
NCC, 0.9 mg/kg				
in 30 min	4479.5±166.8	16.1±0.6	7149.9±238.5	25.6±1.2
NCC, 2.7 mg/kg				
in 30 min	4386.9±157.2	15.7±0.5	7110.0±345.9	24.2±1.5
NCC, 2.7 mg/kg				
in 15 min	4200.4±132.2	15.1±0.4	6578.4±233.0*	22.5±1.2*
in the following 15 min (30 min)	4198.4±169.0*	15.1±0.6*	6463.0±421.8	22.2±1.8
in the following 30 min (60 min)	4295.3±210,7	15.4±0.7	6442.3±381.4*	22.4±1.7*
Control (n=5)				
Initial level	4408.1±177.0	15.7±0.5	7408.1±319.6	25.6±1.5
0.9 % NaCl				
in 30 min	4312.1±184.1	15.3±0.4	7038.4±269.0	24.5±1.4
0.9 % NaCl				
in 30 min	4300.4±212.6	15.3±0.5	7031.6±517.4	23.6±2.0
0.9 % NaCl				
in 15 min	4139.2±178.5	14.7±0.3	6543.1±338.0	22.0±1.6
in the following 15 min (30 min)	4027.4±185.1	14.3±0.4	6074.9±488.2	20.4±2.0
in the following 30 min (60 min)	4136.0±262.3	14.7±0.7	6013.9±362.7*	20.3±1.4*

* – the difference reliable in comparison with the initial level of the parameters in the control and experimental animals ($p<0,05$), n – number of animals in the group.