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CERTAIN INDICATORS OF CARBOHYDRATE METABOLISM IN KIDNEYS AND LIVER OF PREGNANT FEMALE RATS UNDER THE EFFECT OF VANADIUM CITRATE

Halyna Klymets[1,*], Ruslana Iskra[1,2], Iryna Kovalchuk [3,4], Oksana Svarchevska[5]

[1]*Laboratory of Biochemistry of Adaptation and Ontogenesis of Animals, Institute of Animal Biology NAAS, Lviv, 79034, Ukraine*
[2]*Department of Human and Animals Physiology, Biology Faculty of Ivan Franko National University of Lviv, Ukraine*
[3]*Laboratory of Environmental Physiology and Product Quality, Institute of Animal Biology NAAS, Lviv, 79034, Ukraine*
[4] *Department of Normal and Pathological Physiology Named After S.V. Stoyanovsky, Veterinary Faculty, Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies, Lviv, Ukraine*
[5]*Department of Biotechnology and Radiology, Faculty of Food Technologies and Biotechnology, Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies, Lviv, Ukraine*

*Corresponding Author: klimets.halyna@gmail.com

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Abstract

The aim of the research was to investigate the effect of vanadium citrate in different concentrations on glucose and insulin contents in blood plasma, as well as the activity of enzymes of carbohydrate metabolism - lactate dehydrogenase and glucose-6-phosphate dehydrogenase and metabolites of L-lactate and pyruvate in the tissues of kidneys and liver of pregnant rats. The study of the effect of vanadium citrate is relevant since vanadium as an insulin-mimetic can adjust certain links of carbohydrate metabolism in pregnant women. Increased glucose and decreased insulin were detected in the blood plasma of pregnant rats. The findings also revealed the decrease in glucose-6-phosphate dehydrogenase activity and the increase in lactate dehydrogenase activity, along with the increase in pyruvate and L-lactate contents in the kidneys of pregnant animals. In the liver, glucose-6-phosphate dehydrogenase and lactate dehydrogenase activity rose, pyruvate content increased, and L-lactate content decreased. Under the effect of vanadium citrate at a concentration of 0.5 μg V/ml of water, the glucose content decreased, while the insulin content increased at concentrations of 0.03-0.125 μg V/ml of water. In the kidneys and liver, vanadium citrate effectively normalized carbohydrate metabolism at concentrations of 0.125-0.5 μg V/ml of water. According to the findings, vanadium citrate can be considered as a potential dietary drug to maintain the homeostasis of carbohydrate metabolism in pregnant rats. Its effect lies in a dose-dependent regulation of the activity of enzymes and metabolites of carbohydrate metabolism.

INTRODUCTION

Pregnancy is associated with physiological adaptations of the mother's body, which affects every organ system. Compensatory changes in the organs of the pregnant woman's body bring homeostasis into a state of unstable tension balance. Violation of this balance can lead to changes in homeostasis and the emergence of pathologies. It is necessary to determine the regulatory mechanisms for ensuring homeostasis in the organs of the pregnant woman. It is important to establish a certain framework for these physiological changes and adjust them if necessary [1]. Prevention aimed at preventing the occurrence of pathologies during pregnancy is the most effective. However, in the presence of clinically developed obstetric complications during pregnancy, it is possible to slow down

the development of the pathological process. Therefore, timely prevention and correction of disorders during pregnancy should be pathogenetically and clinically justified.

During pregnancy, changes in intra-abdominal pressure and hemodynamics occur in the maternal body [2]. The kidneys are especially sensitive to hormonal changes during pregnancy. The functional impact of pregnancy on the physiology of the kidneys covers almost all aspects of their functions [3]. During pregnancy, the filtration capacity of the kidneys and renal blood flow change. In particular, glomerular filtration decreases, and tubular re-absorption remains unchanged, which leads to an increase in the total amount of fluid in the body of the pregnant woman. Sometimes this state is accompanied by physiological albuminuria and glucosuria, which is associated with increased capillary permeability. Kidney failure may occur during pregnancy, which can lead to an increased risk of perinatal morbidity and even mortality [4, 5].

Besides, changes in liver function and biochemical profile also occur, which have an important impact on nutrient metabolism, protein synthesis and biotransformation of substances in preparation for excretion [6]. In 3-5% of cases among the total number of pregnancies, complications of liver functions occur. Early diagnosis of abnormalities can lead to reduced morbidity and mortality for a mother and a fetus [7]. During pregnancy, blood circulation in the liver rises, the synthetic function of the liver (lipidemia with high levels of cholesterol and its esters) increases, and the antitoxic function decreases. The liver acts as a depot for metabolic fuel to keep the fetus during periods of starvation or malnutrition. Carbohydrate metabolism in the liver during pregnancy changes due to alterations in the activity of its enzymes, glycolysis metabolites and pyridine nucleotides [8]. The liver also plays a unique role in controlling carbohydrate metabolism by maintaining glucose levels within normal ranges for both short and long periods of time [9].

Vanadium is an element that has the ability to regulate carbohydrate metabolism in the human body. Most often, its compounds are used as anticancer and antidiabetic drugs. One of the largest places of accumulation of vanadium in the body is the parenchymal tissues of the liver and kidneys, so this trace element affects their functioning and the intensity of metabolic processes in them. The study of vanadium compounds is relevant as the findings may be extrapolated in the future to adjust certain metabolic parameters in pregnant women. In the form of vanadate, this trace element increases the excretion of soluble substances and water by the kidneys in the urine of rats, inhibits the accumulation of organic ions and increases the efficiency of renal Na^+-K^+-ATPase [10; 11]. Renal excretion of vanadium by urine occurs within 20-40 hours [12]. Compounds of this trace element play a significant role in carbohydrate metabolism, as indicated by *in vitro* animal studies in which vanadate and other vanadium compounds increase the activity of glucose transport, as well as improve glucose metabolism and oxidation [12]. Vanadium (IV) oxide regulates osteoblast differentiation through extracellular signal-regulatory kinase (ERK) and nuclear factor kappa B (NFκB) pathways. Together with other compounds, this trace element forms complexes that strengthen bone structure. Primary osteoblasts increased expressions of glycolysis-related enzymes such as GLUT1, hexokinase 1 and 2, lactate dehydrogenase A and pyruvate kinase M2 during their differentiation [13; 14]. Therefore, vanadium citrate can be used as an agent for the formation of fetal bones, which is important in the development of the organism. The vanadium compound VOdipic-Cl *in vivo* attenuated the increase in triglycerol level in the blood serum and liver of mice, enhancing autophagy and activating signaling pathways in the liver associated with liver kinase B-1 and adenosine monophosphate-activated protein kinase (LKB1/AMPK) [15]. This microelement is able to penetrate through the placental barrier and, thus, is metabolized in the fetus. Its high concentrations were found in the liver, intestines, and kidneys of the fetus [16]. It is known that the compounds containing this trace element are safe; their side effect is weak, which was tested on rat liver cells [17]. However, the amount of data on the effect of vanadium compounds on carbohydrate metabolism during pregnancy is limited.

The aim of the study was to investigate the effect of the organic compound vanadium citrate in different concentrations on the content of glucose and insulin in blood plasma, the activity of carbohydrate metabolism enzymes - lactate dehydrogenase and glucose-6-phosphate dehydrogenase and metabolites of L-lactate and pyruvate in the tissues of the kidneys and liver of pregnant female rats.

MATERIALS AND METHODS

The studies were performed on Wistar female white laboratory rats weighing 140-160 g, which were divided into five groups of 5 animals each. Group I - non-pregnant females (control), II - pregnant females which consumed pure water without additives, animals of groups III, IV, V - during mating and pregnancy received a solution of vanadium citrate in concentrations of 0.03, 0.125 and 0.5 μg V/ml of water, respectively, which in terms of animal body weight was 3.75, 15.63 and 62.5 μg V/kg of body weight, respectively. Females were kept in vivarium on a standard diet for laboratory animals [18]. Consuming water (in groups I and II) and vanadium citrate solution (in groups III, IV and V) was performed *per os* at the rate of 20 ml per animal. The behavior and mobility of all animals involved in the study met the physiological norms for pregnant Wistar rats. It should be noted that females gave birth to healthy offspring, the minimum mortality rate of pups (3%) [18].

The synthesis of vanadium citrate by aquananotechnology takes place in two stages. At the first

stage, an aqueous colloidal solution of vanadium nanoparticles is obtained by dispersing high-purity granules of the corresponding metals by pulses of electric current in deionized water. At the second stage, the actual carboxylates of biogenic metals are obtained by the reaction of direct interaction of highly reactive nanoparticles with citric acid. Since no other substances are included in the number of reagents, and nanoparticles are fully involved in the chemical reaction of citric acid salt synthesis, the result is a product of high chemical purity, and most importantly, this compound does not contain nanoparticles [19]. Decapitation was conducted on days 22-24 using thiopental anesthesia [20]. Therefore, the animals did not experience pain during the study.

The material for the study was blood plasma and homogenates of the kidneys and liver of animals. Blood plasma was obtained by centrifugation of whole blood at 1000 g for 15 minutes. Ten percent homogenates from animal kidney and liver samples were prepared for the study. Homogenization of the samples was performed in Tris-HCl buffer (pH 7.4; 5 mm) with the help of the Homogenizer type 302 device (Warsaw, Poland), using tissue samples weighing 1 g. The tissue sample was placed in a refrigerated vessel and homogenized until uniformity and maximum comminution were obtained. The determination of glucose level was carried out by the glucose oxidase method [21]. An analytical kit, "CHROMGLUKOSA^{+}" (Ukraine) was used for enzymatic determination of glucose in serum and plasma. Insulin content was determined by enzyme-linked immunosorbent assay (ELISA) using the DRG Insulin ELISA kit (DRG International, Inc., USA) according to the instructions. The determination of glucose-6-phosphate dehydrogenase (G-6-PDH) and lactate dehydrogenase (LDH) activity was made using spectrophotometric methods based on the regeneration of conjugated nicotinamide coenzymes according to [22]. Spectrophotometric measurements were performed on a UNICO 1205 spectrophotometer (USA) at t + 37ºC, at the wavelength of λ = 340 nm, in 5-minute intervals. Measuring the activity of the studied enzymes was performed in 0.2 M Tris-HCl buffer, pH 7.5 ("Khimlaborreaktiv", Ukraine). The total volume of the reaction mixture was 3 ml. The preparation of concentrations of substrate mixture constituents:

- To identify G-6-PDH activity the following is needed: 1×10^{-3} M glucose-6-phosphate ("ACROS Organics", Belgium), 5×10^{-3} M $MgCl_2$ ("Khimlaborreaktiv", Ukraine); 0.5×10^{-4} M $NADP^{+}$ ("ACROS Organics", Belgium);
- To identify LDH activity the following is needed: 1×10^{-3} M sodium pyruvate ("ACROS Organics", Belgium), 5×10^{-5} NADH ("ACROS Organics", Belgium), 3×10^{-3} M $MgCl_2$ ("Khimlaborreaktiv", Ukraine).

The method for determining L-lactate content was measured as described previously [23] is based on the dehydrogenation reaction of lactate by lactate dehydrogenase ("ACROS Organics", Belgium) in the presence of nicotinamide adenine dinucleotide (NAD) ("ACROS Organics", Belgium) with the formation of pyruvic acid.

The pyruvate content was determined by Friedman and Haugen [24]. Pyruvic acid, when 2,4-dinitrophenylhydrazine ("Khimlaborreaktiv", Ukraine) is added to it, converts into 2,4-dinitrophenylhydrazone of pyruvic acid, which forms a brown-red compound with the acid. The color intensity was determined on a UNICO 1205 spectrophotometer (USA) at a wavelength of 465 nm.

Laboratory animals were treated in accordance with the standards of the European Convention for the Protection of Vertebrate Animals, used for research and scientific purposes (Strasbourg, 1986). Protocol of the Bioethics Committee meeting at the Institute of Animal Biology No. 89 dated July 8, 2020.

The survey results were statistically processed using the computer software package Statistica 8 (StatSoft Inc., USA, 2014). The arithmetic mean value and the standard deviation of the arithmetic mean (M±SD) were determined. Statistical significance was determined by one-way analysis of variance (ANOVA) with calculating the Student's t test. Significance is defined as P-value less than 0.05.

RESULTS

According to the results of the study, it was found that the bodyweight of pregnant female rats in group II decreased by 7.48% in comparison with non-pregnant females of group I. Under the effect of vanadium citrate, animals of groups III, IV and V showed an increase in body weight by 15.13, 14.03 and 37.13%, compared with pregnant females of group II (Table 1).

Table 1. Changes in body weight of pregnant female rats under the effect of vanadium citrate in concentrations of 0.03 (III), 0.125 (IV) and 0.5 (V) μg V/ml of water (M ± SD, n = 5)

Groups of animals	Body weight of female rats, g
I	181.75±15.31
II	168.16±8.54 [a]
III	193.6±14.53 [ab]
IV	191.75±14.05 [ab]
V	230.6±6.47 [ab]

Note: [a] - probably relative to group I of non-pregnant rats ($P < 0.05$); [b] - probably relative to group II of pregnant rats ($P < 0.05$)

The study found that the glucose content in the blood plasma of pregnant rats of group II increased by 41.25%, and the insulin content decreased by 42.05%, as compared with group I of non-pregnant females (control group) (Table 2).

By watering vanadium citrate, the glucose content reduced significantly in females of group IV and V by 13.33 and 27.46%, as compared with pregnant rats of group II. The insulin content increased in groups III and IV by 92.0 and 33.54%, respectively, as compared with group II of the animals.

Table 2. Glucose and insulin content in blood plasma of pregnant female rats under the effect of vanadium citrate in concentrations of 0.03 (III), 0.125 (IV) and 0.5 (V) μg V/ml of water (M ± SD, n = 5)

Groups of animals	Glucose, mmol/l	Insulin, μO/ml
I	4.46 ± 0.18	2.83 ± 0.19
II	6.30 ± 0.27[a]	1.64 ± 0.2[a]
III	5.90 ± 0.60[a]	3.15 ± 0.25[ab]
IV	5.46 ± 0.30[ab]	2.19 ± 0.12[ab]
V	4.57 ± 0.12[ab]	1.69 ± 0.17[a]

Note: [a] - probably relative to group I of non-pregnant rats (P < 0.05); [b] - probably relative to group II of pregnant rats (P < 0.05).

In the kidneys of pregnant female rats of group II, there was a decrease in G-6-PDH activity by 53.61%, compared with group I of non-pregnant animals. However, there was an increase in LDH-activity by 50.79% and pyruvate content by 57.89%, the content of L-lactate increased by 1.5 times, compared with group I of non-pregnant animals (Table 3).

Table 3. Indicators of carbohydrate metabolism in the kidneys of pregnant female rats under the effect of vanadium citrate in concentrations of 0.03 (III), 0.125 (IV) and 0.5 (V) μg V/ml of water (M ± SD, n = 5)

Groups of animals	G-6-PDH, μmol/min × mg protein	LDH, μmol/min × mg protein	Pyruvate, mM	L-lactate, mM
I	41.84 ± 4.2	241.5 ± 17.3	0.038 ± 0.002	0.002 ± 0.0001
II	19.41 ± 1.8[a]	364.2 ± 29.2[a]	0.060 ± 0.002[a]	0.005 ± 0.0005[a]
III	20.43 ± 2.0[a]	224.7 ± 29.0[b]	0.069 ± 0.007[ab]	0.002 ± 0.0003[ab]
IV	30.37 ± 2.9[ab]	259.2 ± 28.1[ab]	0.0522 ± 0.001[ab]	0.004 ± 0.0006[ab]
V	63.40 ± 5.8[ab]	314.3 ± 42.5[a]	0.046 ± 0.003[ab]	0.002 ± 0.0004[ab]

Note: [a] - probably relative to group I of non-pregnant rats (P < 0.05); [b] - probably relative to group II of pregnant rats (P < 0.05)

Under the effect of vanadium citrate, G-6-PDH activity increased in the kidneys of pregnant animals of groups IV and V by 56.46 and 226.63%, respectively, as compared with pregnant females of group II.

LDH activity decreased in the kidneys of pregnant rats of groups III and IV by 38.29 and 28.81%, respectively, compared with group II of pregnant females which consumed pure water. The pyruvate content decreased in groups III, IV and V by 15.0, 15.0 and 23.0%, respectively, and the L-lactate content decreased in groups III, IV and V by 47.92, 20.0 and 58.33%, respectively, as compared with pregnant females in group II.

It was found that in the liver of pregnant females of group II, there was an increase in G-6-PDH and LDH activity by 11.25 and 49.30%, respectively, as compared with non-pregnant animals in group I (Table 4).

Table 4. Indicators of carbohydrate metabolism in the liver of pregnant female rats under the effect of vanadium citrate in concentrations of 0.03 (III), 0.125 (IV) and 0.5 (V) μg V/ml of water (M ± SD, n = 5)

Groups of animals	G-6-PDH, μmol/min × mg protein	LDH, μmol/min × mg protein	Pyruvate, mM	L-lactate, mM
I	3.82 ± 0.13	5.70 ± 0.32	0.024 ± 0.002	1.060 ± 0.10
II	4.25 ± 0.05[a]	8.51 ± 0.19[a]	0.044 ± 0.002[a]	0.587 ± 0.02[a]
III	3.67 ± 0.34[ab]	4.87 ± 0.39[ab]	0.047 ± 0.007[a]	0.510 ± 0.02[ab]
IV	4.57 ± 0.1[ab]	6.57 ± 0.49[ab]	0.062 ± 0.005[ab]	0.610 ± 0.01[a]
V	3.25 ± 0.34[ab]	6.93 ± 0.32[ab]	0.039 ± 0.006[a]	0.820 ± 0.03[ab]

Note: [a] – probably relative to group I of non-pregnant rats (P < 0.05); [b] - probably relative to group II of pregnant rats (P < 0.05)

The pyruvate content in the liver of pregnant female rats increased by 83.33%, while the content of L-lactate decreased by 13.12%, compared with non-pregnant females of group I.

Under the effect of vanadium citrate, G-6-PDH activity in the liver of pregnant females of group IV increased by 7.0% and decreased in groups III and V by 13.64 and 28.88%, compared with pregnant animals of group II.

LDH activity in the liver of females of the experimental groups decreased: in group III - by 42.77%, IV - by 22.8% and V - by 18.57%, compared with group II.

The pyruvate content in the liver of pregnant animals, which were given vanadium citrate solutions, significantly increased in all experimental groups, as compared with the control one, by 40.91% in group IV, compared with group II. The content of L-lactate decreased in the liver of animals of group III by 13.12% and increased in group V by 39.69%, compared with group II of pregnant females.

DISCUSSION

Moderate vanadium addition can improve glucose utilization and feeding efficiency in animals [25]. The weight increase of female rats of III, IV and V groups, which received solutions of vanadium citrate, is obviously due to the intensification of lipid and protein metabolism. Studies by other authors found that some diabetic rats treated with vanadyl sulfate had normalized hyperlipidemia [26]. Thus, there is a correlation between the weight of pregnant females and the total protein content [27] (Table 1). According to the research by Shafrir E. et al., *in vivo* vanadyl treatment restored the total protein content. This element influences the growth of the total protein content, which is the reason for the weight changes of female rats under the effect of vanadium citrate [28; 29].

The progressive change in glucose homeostasis in the maternal body develops throughout pregnancy, with its peak at the end of the term. The rise in glucose content at the end of pregnancy is a common occurrence (Table 2). Insulin controls the production of hepatic glucose and maintains its homeostasis due to direct action on hepatic insulin receptors and indirectly through the influence on adipose tissue, pancreas, and indirect action of insulin receptors on the central nervous system [30]. The main function of insulin is to inhibit gluconeogenesis in the liver and reduce the release of glucose into the blood. It is known that some vanadium compounds act as insulin simulators [31].

According to our findings, the concentration of glucose in the blood plasma of the animals in group V decreased after adding the vanadium compound. Similar results were found in the studies by A. Zarqami et al. The more vanadium got into the blood, the lower the glucose level was observed [25]. The increased insulin content against the background of reduced glucose indicates the ability of vanadium citrate to enhance the influence of insulin [31]. An increase in insulin content was detected in pregnant females that consumed vanadium citrate at concentrations of 0.03-0.125 μg V/ml of water, which is caused by the insulin-mimetic and insulin-enhancing effects of vanadium. The effect of vanadium, as well as insulin, stops the development of inflammatory processes in animals due to a decrease in pro-inflammatory cytokines, adhesion molecules and an increase in adiponectin [32].

Pregnant women often have carbohydrate metabolism disorders that significantly affect kidney function. After all, the kidneys play an important role in regulating insulin metabolism. According to Sweazea et al. [33], insulin, modulating the glomerular filtration rate, lowers glucose in blood plasma and promotes its entry into tissues. This hormone can also cause hypertension in rats, the development of which begins inside the kidneys [34].

The decreased G-6-PDH activity in the kidneys of pregnant females of group II indicates the inhibition of the pentose phosphate pathway (PPP) (Table 3). The increase in pyruvate content against the background of increased LDH activity suggests wider use of energy substrates by the kidneys during pregnancy [35]. The accumulation of pyruvate in the kidneys during female pregnancy is due to the generation of ATP mainly by aerobic glycolysis [36].

The trace element vanadium in the form of vanadate is activated by catalyzing G-6-PDH activity as a result of oxidation of glucose by $NADP^+$. This is due to the fact that vanadate forms a substrate for G-6-PDH - glucose-6-vanadate, which is an analogue of glucose-6-phosphate. Therefore, the possibility for the rise in G-6-PDH activity in the kidneys of pregnant animals with the use of vanadium citrate at concentrations of 0.125-0.5 μg V/ml of water is due to the ability of vanadium citrate to form substrates for this enzyme. However, with the rise in G-6-PDH activity, the content of activated vanadate due to glucose oxidation reduces sensitivity to the increase in enzyme activity. Vanadium compounds were found to increase the dose-dependent activity of G-6-PDH [37].

LDH activity decreased in the kidneys of pregnant rats which consumed vanadium citrate at concentrations of 0.03-0.125 μg V/ml of water. Compounds containing vanadium stimulate glucose oxidation. Moreover, they are able to act as highly efficient and recycling catalysts for the conversion of L-lactate to pyruvate, which takes place as a result of direct oxidative dehydrogenation. This may be proved by decreased L-lactate content in the kidneys of three experimental groups [38]. A decrease in pyruvate content along with a decrease in L-lactate content in pregnant females may indicate immediate glucose regeneration by conversion to oxaloacetate. In addition, pyruvate can be converted to alanine [39].

The increase in liver size, which is caused by pregnancy, precedes the increase in hepatocyte proliferation. Such functional changes are likely to affect changes in the activity of enzymes in this organ, in

particular carbohydrate metabolism enzymes (Table 4) [40].

The increased activity of the enzymes of PPP and glycolysis indicates an elevated need for energy expenditure in the liver during pregnancy. The rise in G-6-PDH activity occurs due to the active use of NADPH by hepatocytes. Besides, the level of $NADP^+$ increases and allosterically activates the enzyme. NADPH, which is synthesized in the G-6-PDH reaction, takes an active part in the processes of reductive biosynthesis and helps to overcome the harmful effects of reactive oxygen species. In addition, PPP enzymes are very common in the liver because an intensive biosynthesis of fatty acids, cholesterol and other steroids occurs there. An increase in LDH activity and pyruvate content in the liver indicates the activation of aerobic glycolysis during pregnancy in this tissue.

The increase in pyruvate content, accompanied by its transport across the inner mitochondrial membrane, is a necessary condition for gluconeogenesis in hepatocytes. This is important for maintaining normoglycemia in pregnant women because, during this period, intensive use of energy resources of the body takes place. During pregnancy, the lactate formed in the tissues is transported by the blood to the liver, converted into pyruvate. Therefore, the increase in pyruvate content in the liver of group II animals can be considered a compensatory mechanism to ensure the physiological course of pregnancy [41].

The main mechanism of vanadium action is a cofactor that enhances or inhibits enzymatic activity. Therefore, one of the possible factors for reducing G-6-PDH activity in the liver of animals of group V may be the inhibition of this enzyme by vanadium citrate [42]. Such a decrease in the activity of the enzyme in group V may indicate its saturation with the substrate - glucose-6-vanadate and the loss of sensitivity of the enzyme to this substrate. Some vanadium compounds are similar in structure and phosphate charge [43]. They, by analogy with phosphate, form ester bonds, which cause dose-dependent activation or inhibition of G-6-PDH activity in the liver of pregnant animals.

Vanadium affects the reduction of glucose levels in the blood due to improved glycolysis metabolism and increased activity of insulin receptors in tissues, particularly in the liver. LDH activity is one of the important diagnostic enzymes in the liver test and one of the key glycolysis enzymes [44]. Normalization of the activity of this enzyme under the effect of vanadium citrate during pregnancy may indicate normoglycemia and the physiological course of pregnancy.

The increased pyruvate content in the liver during pregnancy and under the influence of vanadium citrate in all doses indicates a rise in the intensity of aerobic glycolysis. However, these changes indicate insufficient doses of vanadium citrate to normalize the pyruvate content during pregnancy. The increase in the lactate content in the liver of animals of group V, compared with group II, and its approaching the level of control group indicates the normalisation of anaerobic glycolysis during pregnancy under the action of vanadium citrate at a dose of 0.5 μg V/ml of water.

CONCLUSION

The findings revealed an increase in glucose content against the background of a decrease in insulin content in the blood plasma of pregnant female rats. In the kidneys of pregnant animals, there was a decrease in G-6-PDH activity and an increase in LDH activity, with the increased level of pyruvate and L-lactate. In the liver, G-6-PDH and LDH activity increased, the pyruvate level rose and L-lactate content decreased.

Under the effect of vanadium citrate at a concentration of 0.125 and 0.5 μg V/ml of water, the glucose content in the blood plasma of pregnant rats decreased, while the insulin content increased at 0.03 and 0.125 μg V/ml of water. G-6-PDH activity in the kidneys of animals increased at concentrations of 0.125-0.5 μg V/ml of water, while LDH activity decreased at 0.03-0.5 μg V/ml of water, the pyruvate and L-lactate content decreased at all concentrations of vanadium citrate (0.03-0.5 μg V/ml of water). In the liver of pregnant rats there was an increase in G-6-PDH activity at 0.125 μg V/ml of water and a decrease at 0.03 and 0.5 μg V/ml of water. In contrast, LDH activity decreased in rats of all three experimental groups, the pyruvate content increased at 0.125 μg V/ml of water, and the L-lactate content decreased at 0.03 μg V/ml of water and increased at 0.5 μg V/ml of water. According to the results of our study, it was determined that vanadium citrate most effectively normalizes carbohydrate metabolism indicators at concentrations of 0.125-0.5 μg V/ml of water.

Vanadium citrate can be considered as a potential dietary drug to maintain homeostasis of carbohydrate metabolism in pregnant rats. Its effect lies in dose-dependent regulation of the activity of enzymes of carbohydrate metabolism. At concentrations of 0.125 and 0.5 μg V/ml of water, it has a more pronounced corrective effect on carbohydrate metabolism indicators in blood plasma, kidneys, and liver of pregnant female rats. The action of this compound is tissue-specific. According to our findings, the concentrations of 0.125-0.5 μg V/ml of water in the liver of pregnant animals are insufficient to normalize carbohydrate metabolism in pregnant rats.

Prospects. The results of the study can potentially be extrapolated to pregnant women in medical practice.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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