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V.F. Shatornaya, O.O. Nefyodova, O.O. Nefyodov, I.I. Kolosova, V.V. Major, O.V. Kuznetsova, Yu.V. Demidenko, G.A. Yeroshenko
SI "Dnipropetrovsk Medical Academy of the MOH of Ukraine", Dnipro

CARDIOGENESIS CHANGES AFTER THE PLUMBIC ACETATE IMPACT IN RATS UNDER THE CORRECTION CONDITIONS IN THE EXPERIMENT

e-mail: verashatornaya67@gmail.com

The purpose of the study was to determine the morphogenetic patterns of forming the effects of isolated plumbic acetate impact and the combined action of plumbic acetate with metal citrates on the development of the rat embryo's heart in the experiment. With isolated plumbic acetate administering to pregnant females in a dose of 0.05 mg/kg, the thickness reduction of the compact myocardium, walls of the right and the left ventricles in the embryo's heart occurs. The most sensitive to the plumbic acetate impact is the heart right ventricle wall, where not only the compact myocardium thinning, but also the increased number and diameter of the functioning vessels are observed. The combined administration of plumbic acetate with the gold citrate solution (or iron citrate/silver citrate) prevents the negative effect of plumbic acetate on the overall course of cardiogenesis in rat embryos under the experimental conditions and indicates their bioanagonism.

Key words: embryogenesis, cardiogenesis, plumbic acetate, gold citrate, silver citrate, iron citrate.

В.Ф. Шаторна, О.О. Нефьодова, О.О. Нефьодов, І.І. Колосова, В.В. Майор, О.В. Кузнєцова, Ю.В. Демиденко, Г.А. Єрошенко

ЗМІНИ КАРДІОГЕНЕЗУ ПІД ВПЛИВОМ ВАЖКИХ МЕТАЛІВ ТА ЗА УМОВ КОРЕКЦІЇ В ЕКСПЕРИМЕНТІ У ЩУРІВ

Метою дослідження було визначення морфогенетичних закономірностей формування ефектів ізольованого впливу ацетату свинцю та комбінованої дії ацетату свинцю з цитратами металів на розвиток серця зародків щурів в експерименті. При ізольованому введенні вагітним самицям ацетату свинцю в дозі 0,05мг/кг відбувається зменшення товщини компактного міокарду стінки правого та лівого шлуночків серця ембріонів. Найбільш чутливою до дії ацетату свинцю виявляється стінка правого шлуночку серця, де спостерігається не тільки витончення компактного міокарду, а й збільшення кількості та діаметру функціонуючих судин. Комбіноване введення ацетату свинцю з розчином цитрату золота (або цитрату заліза/цитрату срібла) попереджує негативний вплив ацетату свинцю на загальний хід кардіогенезу ембріонів щурів в експериментальних умовах та свідчить про їх біоантагонізм.

Ключові слова: ембріогенез, кардіогенез, ацетат свинцю, цитрат золота, цитрат срібла, цитрат заліза.

The work is a fragment of the research project "Biological foundations of the organ and animal morphogenesis under the nanometals impact in the experiment", state registration No. 0118U006635.

Despite the significant achievements in the diagnosis and treatment of many cardiovascular system diseases, there is a tendency for their growth in Ukraine, both in adults and children [4, 5]. Over the past 25 years, the cardiovascular pathology among the population of Ukraine has grown thrice, and according to the World Heart League, Ukraine occupies one of the first places among the European states in terms of mortality from blood diseases and strokes; in 2009, deaths from cardiovascular diseases amounted to 65.2% of the total number of deaths [2]. The results of numerous studies confirm that one of the etiopathogenetic causes of

cardiovascular diseases may be the impact of environmental factors: emissions from industrial enterprises and vehicles and agricultural chemistry [2].

Among many negative environmental factors affecting the health of the population, one of the most important places is occupied by the chemical pollution with heavy metals, among which the most widespread are lead and its salts. In the latest century, the accumulation of lead in soil, atmospheric air and water is progressing, which can have irreversible consequences for humanity. A number of experimental works by modern Ukrainian scholars, such as Trakhtenberg I.M., Skalny V.A. and Zerbin DD, it has been shown that lead has a high tropism to the vessels endothelium, causing structural changes in it due to lead's straight effect directly on the intracellular ultrastructure.

These changes lead to disorders of transport, metabolic, synthesizing, adhesive functions of cells and promote development of vascular pathology, which is accompanied by disorders of hemorheology and microcirculation [3]. The modern theory of the environmental heavy metals impact on the state of the cardiovascular system and heart diseases is being widely developed both by doctors [1, 8] and by experimental studies of morphologists, biologists and hygienists [9, 10, 11]. At the same time, some scholars do not consider lead and heavy metal compounds as etiological factors stimulating disorders in the cardiovascular system, but only evaluate them as a risk factor [6, 7].

Physiological lead antagonists are zinc, iron, calcium and selenium, which weaken the toxic effect of lead compounds and reduce its content in the body. The reduction of the toxic action of lead by a number of trace elements is due to their ability to induce the synthesis of a metallothionein protein that binds excess lead, which contributes to detoxification.

Today, nanomaterial engineering develops very rapidly and forms an important class of new materials with special physico-chemical properties differing from the materials of the same group. The unique properties of nanomaterials make them very attractive to the pharmaceutical industry, agriculture, and the technical industry. The issue of the nanoparticles impact on the body, on the process of embryonic development and cardiogenesis remains insufficiently studied. The issues of possible antagonism or synergism of nanosized metals as trace elements remain undetermined today. Therefore, studying these problems is expedient and relevant. Direct observation of the human developmental disorders is impossible, therefore, using the induced experimental models permits to analyze morphogenetic changes during embryogenesis.

The purpose of the study was to determine morphogenetic regularities of forming the outcomes of the isolated impact of lead acetate and the combined action of lead acetate with metal citrates on the development of the rat embryo's heart in the experiment.

Materials and methods. Experimental studies were conducted on female Wistar rats. The experimental animals management was carried out in accordance with the sanitary-hygienic norms in the vivarium SI "DMA". All experiments were carried out in accordance with the Ukrainian legislation, the European Convention on the protection of vertebrate animals used in experimental studies. The choice of these particular laboratory animals as the study object is due to the low level of spontaneous developmental defects compared to mice and rabbits. In experimental models, solutions of silver, gold, and iron citrates were obtained by aquananotechnology. Bimetal citrates are safe, moreover, they demonstrate antioxidant and radioprotective effects, have a positive effect on the cardiovascular and immune systems of the body.

All rats were divided into 5 groups: group 1 included animals fed a solution of plumbic acetate in the dose of 0.05 mg/kg; group 2 – animals fed a solution of plumbic acetate in the dose of 0.05 mg/kg and a solution of gold citrate in the dose of 1.5 μg/kg; group 3 – animals administered a solution of plumbic acetate in the dose of 0.05 mg/kg and a solution of silver citrate in the dose of 2 μg/kg; group 4 – those administered a solution of plumbic acetate in the dose of 0.05 mg/kg and a solution of iron citrate at the dose of 1.5 μg/kg; group 5 animals constituted the control group.

Female rats were subjected to these factors impact from the 1st to the 19th day of pregnancy, the test substances were administered intragastrically once a day. On the 20th day, the female slaughtering was carried out and embryos removed, being afterwards fixed in 10% neutral formalin. To determine the effect of microelements on the course of cardiogenesis, the heart removal was carried out in the fixed embryos of the control and experimental rat groups, serial histological sections were made for further histological and morphometric analysis.

Results of the study and their discussion. Analysis of the study results has demonstrated the negative effect of plumbic acetate low doses on the development of the heart, which was manifested in reducing not only the embryo mass, but also the heart: if in the control group the heart weight was - 35.3 mg, whereas in the group subjected to plumbic acetate it decreased to 8% (fig. 1).

In the combined impact groups, the heart rate was restored: in the plumbic acetate group and silver citrate, and in gold citrate and iron citrate, this index even unreliably exceeded the control one. Such indices testify to the modifying effect of metal citrates on the of plumbic acetate embryotoxicity.

Even at the macro level in the lead intoxication group, thinness of myocardium, walls of the heart chambers and disorders of the internal ventricular relief under the impact of plumbic acetate were observed.

Trabecules were disorientated, uterine muscle was not expressive (about 23%), tendons of atrial-ventricular valves were shortened (18%), and the cusps themselves showed polymorphism. Such morphological changes undeniably influenced the contractile function of the heart and disrupted hemodynamics. In the group of the combined lead and iron citrate administration, the heart wall of the embryo was well-formed, the compact myocardium was sufficiently developed, the mucosal muscles, the atrial-ventricular valve cusps and the internal relief of the heart ventricles corresponded to the stage of the embryo development, although in 63% of cases, a significant thickening of the interventricular septum was observed.

In the combined lead with silver citrate impact group, the hypertrophic growth of the atrial volume by almost 28% was detected. Such extension of the atrial testifies to the formation of a compensatory mechanism during cardiogenesis, with the expansion of the aorta and pulmonary trunk in the places of their outlet from the heart.

In the study of embryonic heart sections in the group of the combined plumbic acetate and gold citrate impact, thickening of the ventricles, atrium walls and interventricular septum was determined. In general, the embryo heart wall was well-formed, the compact myocardium was sufficiently developed, the fossilized muscles and the internal heart ventricular relief corresponded to the embryo's development stage. The heart chambers cavities were not enlarged, the aorta and the pulmonary trunk had no obvious developmental defects.

When evaluating the course of cardiogenesis, one of the indices of heart forming processes is the process of the ventricular myocardium compactation. One of the main stages in the myocardium formation is the spatial change in the direction of the ventricle myocardium layers. In the control group, we determined the well-developed layers of the myocardium and the vessels formed at the histological level. Studies have shown that the thickness of the compact myocardium ventricular wall after exposure to plumbic acetate reduces, and this reduction is not unequivocal for the right and left ventricular myocardium. More damage is caused to the right ventricular myocardium.

Namely, we observed a reduction in the thickness of the wall due to the compact layer thinness by 11%. As the results of the right ventricle wall's compact myocardium thickness measurement with the combined administration of plumbic acetate and iron citrate, it recovered to normal, and in the groups of silver or gold citrate combination it even exceeded that of the control group (fig. 2).

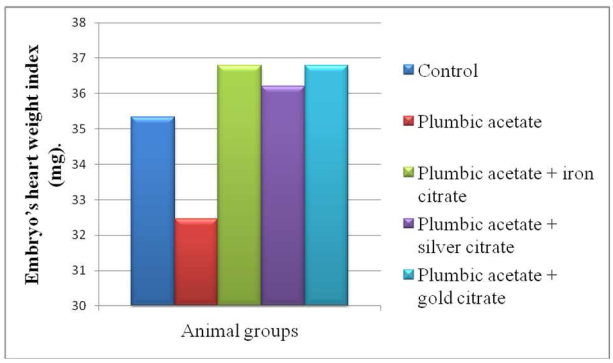

Fig. 1. Indices of the embryos heart weight in the control and experimental groups (mg).

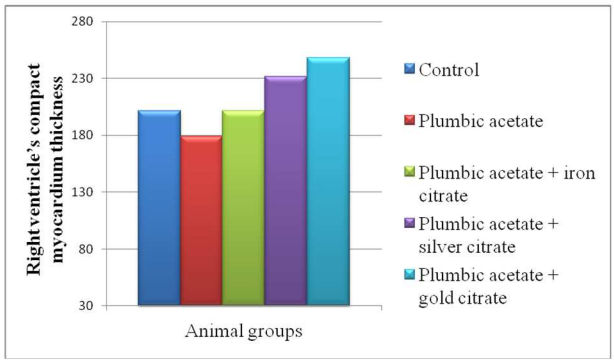

Fig. 2. Thickness of the embryo heart right ventricle's compact myocardium in the control and experimental groups (μm).

The process of cardiac myocardial compaction occurs in parallel with angiogenesis, changes in cardiogenesis in the ventricular compartment of the embryonic heart in the plumbic acetate exposure group was determined not only at the wall thickness level, but also a disorder in the vasculogenesis of a compact myocardium was observed.

We determined an increase in the number of functioning vessels and their diameter growth in the right ventricle myocardium of the heart. Such a fact of morphological adaptation by the vascular system suggests the hypoxic state of the myocardium under the plumbic acetate impact, which is confirmed by the scientific data of other researchers [1, 3] (fig. 3).

As it is shown by the analysis of the data obtained, the left ventricle is less susceptible to lead intoxication, possibly due to its greater physical and hemodynamic load, which acts as a protective mechanism. In the lead impact group, we did not observe any growth in the number and diameter of the blood vessels in the left ventricle compacted myocardium of the embryo heart. The effect of plumbic acetate with isolated administration resulted in a reduction in the left ventricular myocardium thickness by 8% without concomitant vascular disorders. In the combined effects groups, recovery of the compact myocardium thickness parameters was observed, indicating a positive effect of metal citrates on the cardiotoxicity of plumbic acetate and on the cardiac wall formation (fig. 4).

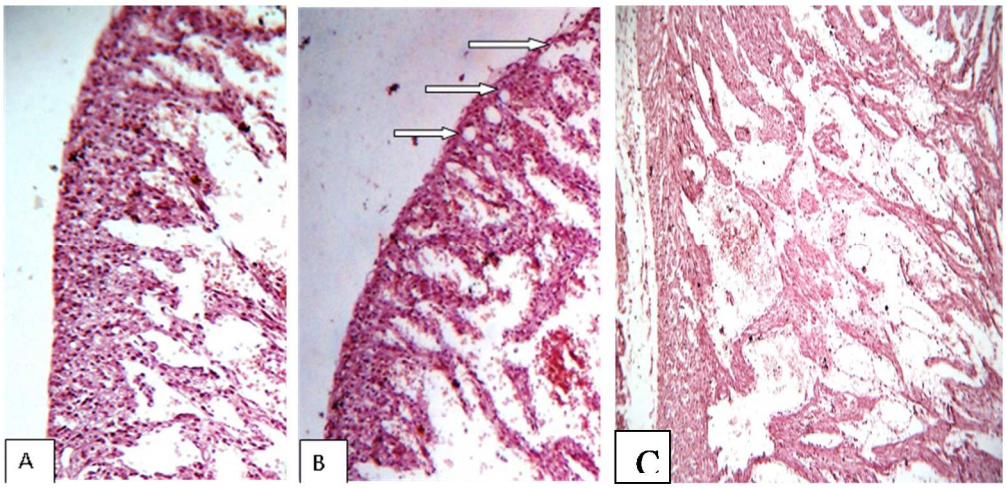

Fig. 3. Microphotography of the rat embryo heart right ventricle wall in the control group (A) and in the group of lead intoxication (B); C - in the group of the combined plumbic acetate + silver citrate impact. Arrows indicate a growth in the number and diameter of the compact myocardium functioning vessels in the group of lead intoxication. Staining: hematoxylin-eosin. Magnification: Oc. 8 x obj. 10.

In groups of the combined lead and metal citrates impact, not only the myocardium thickness restoring, but even its significant growth is observed compared with that in the control group: in the combination of lead acetate and iron citrate – by 9%, lead and silver citrate – by 29% and lead and gold citrate – by 31 %, which is a manifestation of cardiogenesis adaptive mechanisms effect on lead intoxication.

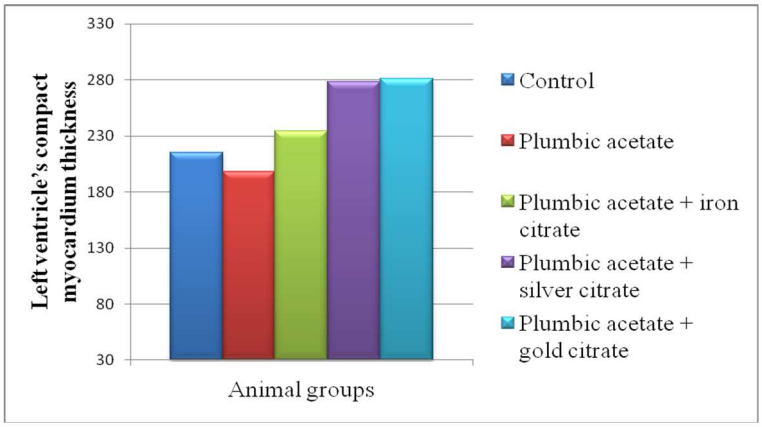

Fig. 4. Thickness of the left ventricle compact myocardium of the embryo's heart in the control and experimental groups (μm).

We have not met the results of the plumbic acetate and the above trace elements combined effects on the heart development in the scientific literature and it is not possible to draw parallels.

Experimental results showed cardiotoxicity of lead acetate, which was determined to reduce the thickness of the compact myocardium wall ventricle of the heart, reducing thickness fibrillation, ventricular septal thinning. Violation of delamination processes and ventricular myocardium compaction under the influence isolated lead acetate manifest violation of the trabecular layer formation and the formation of ventricular myocardium atrioventricular valve holes: shortening valves, change the content and scope of the atrioventricular valves accompanied by the formation of additional anomalous tendon strings [1, 3]. The influence on the course of cardiogenesis in groups with combined effects of lead acetate and silver or gold citrate showed recovery of myocardial thickness and ventricular fibrillation, no violations in the formation of valvular heart rat embryos, indicating a decrease in cardiac toxicity of lead acetate citrate metals during combined administration [9, 11].

Conclusion

With the isolated administration of plumbic acetate in the indicated dose, there is a decrease in the thickness of the right and left ventricles wall's compact myocardium of the heart. The most sensitive to the action of plumbic acetate is the wall of the heart right ventricle, where not only the compact myocardium thinness, but also a growth in the number and diameter of functioning vessels are observed.

Combined administration of gold citrate, iron citrate, silver citrate solutions prevents the negative influence of plumbic acetate on the overall course of rat embryo cardiogenesis under the experimental conditions and indicates their bioantagonism.

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O.V. Sheshukova, K.S. Kazakova, G.A. Yeroshenko, V.P. Trufanova, T.V. Polishchuk, K.V. Shevchenko, A.V. Solod
Ukrainian Medical Stomatological Academy, Poltava

DYNAMICS OF EXPRESSION OF CARBOHYDRATE DETERMINANTS OF MANNOSE-SPECIFIC LECTINS IN THE MUCOUS MEMBRANE OF THE RAT ATTACHED GINGIVA IN CHRONIC ETHANOL INTOXICATION

e-mail: grem23062017@gmail.com

The study found that concanavalin A lectin is specific to the horny scales of the mucous membrane of the attached part of the gums. On day 5 and day 12 of the experiment the ethanol effect showed weakening of the intensity of marking on the keratinocytes, which was morphologically manifested by the phenomena of hyperkeratosis. The expression of receptors on fibroblasts and collagen fibers to the resident structural components of the lamina propria was reduced at all times of observation. The mast cells were characterized by an increase in degree on day 5 and day 12 of the experiment.

Key words: attached part of gums, rats, lectin concanavalin A, sounding.

О.В. Шешукова, К.С. Казакова, Г.А. Єрошенко, В.П. Труфанова, Т.В. Поліщук, К.В. Шевченко, А.В. Солод

ДИНАМІКА ЕКСПРЕСІЇ ВУГЛЕВОДНИХ ДЕТЕРМІНАНТ МАНОЗОСПЕЦИФІЧНИХ ЛЕКТИНІВ У СЛИЗОВІЙ ОБОЛОНЦІ ПРИКРІПЛЕНОЇ ЧАСТИНИ ЯСЕН ЩУРІВ ПРИ ХРОНІЧНІЙ ІНТОКСИКАЦІЇ ЕТАНОЛОМ

У роботі встановлено, що лектин конканаваліну А є специфічними до рогових лусочок слизової оболонки прикріпленої частини ясен. При дії етанолу на п’яту та дванадцяту доби встановлено зниження інтенсивності маркування на кератиноцитах, що морфологічно проявлялось явищами гіперкератозу. До резидентних структурних компонентів власної пластинки експресія рецепторів на фібробластах і колагенових волокнах зменшилася на всіх термінах спостереження. Мастоцити характеризувалися збільшенням ступеня на 5-у та 12-ту доби.

Ключові слова: прикріплена частина ясен, щури, лектин конканаваліну А, зондування.

The work is a fragment of the research project “Experimental morphological study of the effect of cryopreserved cord blood products and embriofetoplacental complex (EFPC), diphereline, ethanol and 1 % methacrylate on the morphofunctional condition of several internal organs”, state registration No. 0119U102925.

The problem of alcohol use is extremely relevant to date: the global consumption of alcoholic beverages is accounted for huge numbers. Alcoholism is a severe chronic disease, in most cases it is difficult to cure. The disease occurs due to regular and prolonged alcohol consumption and is characterized by a special pathological condition of the body: uncontrollable craving for alcohol, changes in its tolerability and personality degradation [15].