Introduction. Obesity becomes one of the most common pathologies, which is accompanied by a violation of energy metabolism in the body, increased accumulation of fat in tissues. The development of visceral obesity can develop against the background of a high calorie diet that is unbalanced in terms of carbohydrates and fats.

The aim of the research: study of the hormonal-metabolic profile, structural-functional peculiarities of the liver and pancreas under the conditions of animals’ receiving high-carbohydrate or high-fat diets in dynamics.

Research methods. The study was performed using sexually mature male rats receiving a standard food diet (control group) and received the high-carbohydrate or high-fat diets. Animals were removed out of the experiment during the 21st, 35th, 46th and 56th days of the study. Metabolic indices and functional markers of the hepatopancreatic system were determined in the blood serum of experimental rats. Structural peculiarities of the liver and pancreas were studied using optical microscopy.

Results and discussion. As a result of the study, in animals that were on high calorie diet, a significant increase in the content of leptin and insulin was observed against the background of a decrease in the level of ghrelin in the blood serum of experimental rats during the 35th day of the experiment with the progression of the identified dys hormonal disorders until the 56th day. Such changes in the hormonal profile occurred against the background of an increase in the concentration of glucose in the blood serum, an increase in the content of glycosylated hemoglobin (HbA1c), an increase in the HOMA-IR insulin resistance index and body mass index (BMI). During the 21st day of the research, the activation of cytolytic processes (increased activity of alanine aminotransferase – ALT, aspartate aminotransferase – AST, gamma-glutamyl transpeptidase – GGT, α-amylase, alkaline phosphatase – AF) was revealed; they progressed until the end of the experiment. During the morphological examination of the liver and pancreas in animals under the conditions of a high-fat diet, pronounced fatty infiltration was observed. In the pancreas of animals receiving the high calorie diet, morphological changes are manifested by edematous processes and disruption of the vascular component, with greater dominance in the case of a high-fat diet.

Conclusions. The animals’ being on high-carbohydrate and high-fat diets leads to the development of metabolic disorders, functional and structural changes in the liver and pancreas, which characterize the development of insulin resistance, obesity, and metabolic syndrome.

Key words: insulin resistance, carbohydrate metabolism, body mass index, obesity, metabolic syndrome, liver, pancreas, hepatosis, dystrophic changes.

Introduction. Metabolism is one of the most important processes of the body’s homeostasis and maintenance of its vital activity. Disorder of metabolic processes leads to the occurrence of hyperlipidemia, diabetes mellitus, obesity, which are predictors of the development of a number of cardiovascular system diseases, diseases of the hepatobiliary system, tumors of various localizations, diseases of the musculoskeletal system, and premature death [1].

In recent years, the intensity of the development of abdominal obesity has attracted special attention. Visceral adipose tissue, as a key regulator of energy balance, has a pronounced innervation, a wide network of capillaries, high sensitivity to the lipolytic action of catecholamines and reduced sensitivity to the antilipolytic action of insulin. In the presence of excess weight, there are structural changes in adipocytes, the intensive lipolysis of which leads to the release of a large amount of free fatty acids mainly into the portal circulation of the liver and causes the development of systemic hyperinsulinemia [2]. Such changes in the hormonal profile can be accompanied by a violation of the permeability of cell membranes, lead to their destruction, destabilization of organelles, which negatively affects the metabolic and functional capabilities of the organs, in particular, the liver and pancreas.

A biomarker of obesity is the peptide hormone leptin, which is synthesized in adipose tissue and takes part in the regulation of hunger and satiety processes, as well as in maintaining the body’s energy balance. In particular, leptin stimulates the satiety center and suppresses the hunger center in the hypothalamus. In hyperleptinemia, there is a feeling of satiety while eating. Hyperleptinemia is observed in people with metabolic syndrome. Under physiological conditions, insulin supports the proper accumulation and use of energy, and leptin reduces constant energy consumption [3]. In general, these hormones play a key role in the central mechanisms of regulation of energy expenditure and homeostasis of carbohydrate metabolism.
metabolism. Ghrelin acts as a modulator of energy supply, the secretion of which significantly increases under the conditions of prolonged fasting, at the beginning of a meal [4].

The development of visceral obesity and insulin resistance are most likely to develop against the background of a high calorie diet that is unbalanced in terms of carbohydrates and fats.

Therefore, the aim of the research was to study the hormonal-metabolic profile, structural-functional peculiarities of the liver and pancreas under the conditions of the animals’ being on high-carbohydrate or high-fat diet in dynamics.

Research materials and methods

The research was performed using sexually mature male rats, which were divided into the following groups: group I (control group) – animals that were on a standard diet (n=12); group II – animals receiving a high-carbohydrate diet (n=12); group III – animals receiving a high-fat diet (n=12). Rats of the group II (experimental) received 10% fructose solution instead of drinking water for 8 weeks [5]. The animals of the experimental group III were on a diet with a high content of fats and cholesterol throughout the study [6]. Animals were removed from the experiment during the 21st, 35th, 46th and 56th days of the study.

Changes in carbohydrate metabolism were characterized by the content of insulin and glucose in blood serum followed by the calculation of the HOMA-IR (Homeostasis Model Assessment Insulin Resistance) insulin resistance index, as well as the level of glycosylated hemoglobin (HbA1c) in whole blood was determined. Glucose concentration in blood serum and HbA1c content were determined using kits “Reahent” (Dnipro, Ukraine). Measurements were performed on a STAT FAX 2100 enzyme-linked immunosorbent assay tablet (China). The content of insulin was studied using Rat INS (Insulin) ELISA Kit reagents (Elabscience, USA). The content of leptin and ghrelin in blood serum was determined using the Rat Lpt (Leptin) ELISA Kit (Elabscience, USA) and Rat GHRL (Ghrelin) ELISA Kit (Elabscience, USA) reagents, respectively, using the ER-500 Microplate Reader device. Functional changes of the hepatopancreaticobiliary system were characterized by the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GHT), α-amylase, alkaline phosphatase (AL) and the content of uric acid (UA) in the blood serum of experimental rats.

The structural peculiarities of the liver and pancreas were studied by the light microscopy method. [7]. Photodocumentation of micropreparations was performed using a MICROS MC300 (XT) microscope (Austria), a ToupCam 5.1M UHCCD C-Mount Sony digital camera, an Adapter AMA075 in the ToupTek ToupView program (V3.7.1398).


Statistical data analysis was performed using the Excel computer program of the Microsoft Office 365 ProPlus package. For each of the samplings, it was checked whether the distribution of the studied index was normal, using the criterion of Kolmogorov-Smirnov, Lilliefors’ test. Since the obtained data followed a Gauss’ law, the results are represented by the M+m interval. The reliability of the data difference in the samplings was checked using the parametric Student’s t-test, the presence of a correlation relationship was assessed by calculating the Pearson correlation coefficient (r). A difference of p<0.05 was considered statistically significant.

Results and discussion

As a result of observation, changes in the parameters of the hormonal profile, markers of carbohydrate metabolism compared to the control data were found in the experimental animals, regardless of the composition of the high calorie diet. Significant changes in the studied parameters were observed during the 35th day of the experiment (increase in the level of leptin in rats of the groups II and III at 23.34 and 30.56%, p1-2.3<0.05, respectively, relative to the control). During the 66th day of the study, the level of leptin in the blood serum of experimental animals of the same groups increased at 41.78 and 48.84% (p1-2.3<0.01), respectively, and ghrelin decreased at 30.77 and 42.31% (p1-2.3<0.01) in relation to intact animals, while the insulin content exceeded the initial data at 34.98% (p1-2<0.05) only in rats of the experimental group II. During the 56th day, the concentration of leptin in blood serum increased at 52.38 and 68.62% (p1-2<0.01), insulin – at 47.95 and 38.47% (p1-2<0.05), and ghrelin decreased at 35.58 and 48.08% (p1-2<0.05), respectively, compared to the control (Fig. 1).

Attention-grabbing changes are in indices of carbohydrate metabolism in rats receiving high calorie diets. Namely, during the 35th day of the experiment, a significant increase in blood glucose content was observed in
Fig. 1. Changes in metabolic and functional indices of the hepatopancreatobiliary system of blood serum under the conditions of high-carbohydrate (HC) and high-fat (HF) diets in dynamics (M±m).
the blood serum of rats of the experimental group II at 29.53% (p<0.05) compared to the control. Under such conditions, in the animals of the research groups II and III, there was determined an increase in the content of HbA1c in whole blood at 54.48 and 29.81% (p<0.05), an increase in the HOMA-IR index at 55.21 and 42.33% (p<0.05) in relation to the control, which reflects the development of insulin resistance in animals [8]. At the same time, a significant increase in BMI (at 37.21%, p<0.05) compared to the values in intact animals was found only in rats of the experimental group III. During the 46th day of the experiment, in the rats of the experimental groups II and III, an increase in the glucose content in the blood serum was observed at 58.45 and 21.38% (p<0.05), the concentration of HbA1c in whole blood – at 80.76 and 57.05% (p<0.01), HOMA-IR index – at 90.18 and 63.80% (p<0.01), BMI – at 32.56 and 58.14% (p<0.05), respectively, in relation to data in animals receiving a standard diet. During the 56th day of the stay of the animals of the same research groups on the experimental diets, the glucose content in the blood serum increased at 76.57 and 27.69% (p<0.01), respectively, and the level of HbA1c in whole blood doubled and increased at 82.05% (p<0.01), HOMA-IR index – 2.30-fold and at 79.14% (p<0.01), BMI – at 51.16 and 74.42% (p<0.05) in relation to the initial data.

Close inverse relationships were found between the level of ghrelin and leptin (strong, r=-0.76), insulin (medium strength, r=-0.62) and BMI (strong, r=-0.83). Hypoglycemia caused by hyperinsulinemia and insulin resistance can cause and potentiate the development of metabolic disorders and obesity [9].

As the dyshormonal disorders developed, markers of the functional state of the hepatopancreatobiliary system changed compared to the values of the control group. Thus, in the early periods of being on diets (the 21st day) in the blood serum of rats of experimental groups II and III, there was found a significant increase in the activity of enzymes: ALT (at 67.14 and 84.28%, p<0.01), LF (at 16.67 and 48.28% p<0.05), respectively, relative to the control (see Fig. 1). During the 35th day, the same trend of changes was observed: the activity of ALT increased twice and 2.08-fold (p<0.01), LF – at 36.67% and 2.06-fold (p<0.01), uric acid – at 18.42 and 26.42% (p<0.05), respectively, compared to the control. In the same period, GGT activation was determined in the blood serum of rats of the experimental group III (at 67.70% p<0.01) against the background of inhibition of α-amylase (at 13.49%, p<0.05) compared to the control. Such biochemical changes in blood serum may indicate a decrease in liver and pancreas functioning, which can characterize the development of metabolic syndrome [10]. During the 46th day of the experiment, the direction of changes in the studied parameters was maintained. In particular, a significant increase in the activity of enzymes in the blood serum of rats of the experimental groups II and III was noted (ALT – 2.51-fold and 2.59-fold, p<0.01, AST – 2.06-fold and at 92.68%, p<0.01, GGT at 73.85 and 76.90%, p<0.01, LF at 71.98% and 2.88-fold, p<0.01), increase in uric acid content (at 24.30 and 54.49%, p<0.01) respectively regarding the control. Under these conditions, changes in α-amylase activity were multidirectional (increased at 15.21%, p<0.01 in rats of the experimental group II and decreased at 18.70% p<0.01 in animals of the group III regarding the control). During the 56th day of excessive loading of animal diets with carbohydrates and fats, the activity of ALT increased 3.24- and 3.47-fold, respectively (p<0.01), and AST increased 2.59- and 2.54-fold (p<0.01), GGT – at 87.69% and 2.03-fold (p<0.01), LF – 2.08- and 4.93-fold (p<0.05), the concentration of uric acid increased at 32.53 and 79.28% (p<0.05), respectively, compared to the control. The activity of α-amylase increased at 21.02% (p<0.05) in the blood serum of rats of the group II. Such dynamics of enzyme activity indicates the development of an inflammatory process in the pancreas [11]. In the blood serum of rats of the experimental group III, the activity of α-amylase decreased at 20.97% (p<0.05) compared to the data of the control group.

The detected changes in the functional indices of the hepatopancreatobiliary system confirm the role of insulin resistance in the progression of liver steatosis against the background of metabolic syndrome and may act as predictors of the development of mesenchymal-inflammatory syndrome with a decrease in the detoxification and protein-synthetic function of hepatocytes [12].

During the light-optical examination of the liver and pancreas of animals receiving a standard food diet, the orderliness of the structural elements was confirmed in all investigated terms of the experiment. Under the conditions of a high-carbohydrate diet, disassembly of liver plates, sludge in the vessels of the portal triad, and disseminated lymphocytic infiltration were observed during the 21st day. During the 35th day, stasis in the central veins, deformation of the vessel wall of the portal triad was found. The cytoplasm of hepatocytes is illuminated, with loci of granularity. Hepatocyte nuclei are round, basophilic. Perisinusoidal and interlobular spaces are expanded. During the 46th day of the study, disassembly of trabecularity was expressed in all zones of the lobule (central, intermediate, peripheral). The central vein is deformed, its wall is swollen, there are stasis phenomena in the lumen of the vessel. During the 56th day of observation, structural changes in the liver are progressing (Figs. 2, 3). Lymphocytic infiltration is observed peripherally, pericentrally. Stasis is found in the central veins and triads. The wall of blood vessels is deformed, diapedesis is fixed. Hepatic plates are deformed, surrounded by optical lucidification. The cytoplasm of hepatocytes is weakly eosinophilic, the granularity is un-
even. Destructured hepatocytes are visible in all fields of view, however, binucleate cells are also found in the array of mononuclear cells.

The histostructure of the pancreas in the animals of the experimental group II during the 21st day was not changed, but a slight lightening of the cytoplasm in the intralobular duct epitheliocytes was visualized. During the 35th day of the study, slight lightening of the cytoplasm in acinocytes and blurring of the contours of endocrinocytes of islets is revealed. Duct epitheliocytes are swollen. Fine vesicularity of the cytoplasm of acinus cells is visible on semi-thin sections. During the 46th day of the experiment, the luminosity of the cytoplasm of epitheliocytes of acinus cells and endocrinocytes of islets increases. Connective tissue layers are expanded, swollen. There is a pronounced injectability of blood vessels (Fig. 4). During the 56th day of a high-carbohydrate diet, vacuoles are found in the cytoplasm of epitheliocytes of the acinus cells, which causes its optical lucency (Fig. 5). Centroacinous cells of interstitial ducts also undergo edematous changes.

The animals’ receiving a high-fat diet was accompanied by the following structural changes in the liver. Thus, during the 21st day of the experiment, small lipid inclusions are found in the cytoplasm of hepatocytes, and lipid droplets of various sizes are found extracellularly. Trabecularity of hepatocytes is disturbed. Pronounced lymphocytic infiltration attracts attention. During the 35th day of the study, dystrophic changes are observed in hepatocytes. In the nuclei of liver cells, chromatin is condensed under the nuclear membrane. Cytoplasm is lucid, with variously shaped lipid inclusions. Destructured hepatocytes are visible in the field of vision. The vascular wall is disorganized, the lumen is deformed, sludge is marked. During the 46th day of the study, fatty infiltration of the liver progresses (Figs. 6, 7). The cytoplasm of hepatocytes is filled with fat droplets that mask the nucleus. On semi-thin sections, the nuclei are illuminated, with a narrow rim of chromatin under the nuclear membrane. Lipid droplets of various sizes are also found extracellularly. Interlobular connective tissue layers are expanded and deformed. During the 56th day, the pronounced fatty dystrophy of the liver is observed. Trabecular orderliness is lost. Lipid inclusions deform hepatocytes, nuclei are difficult to visualize. Extracellular fat droplets of various shapes and sizes are chaotically placed in all fields of vision.

Under such conditions, the animals of the group III during the 21st day show “translucency” of the histostructure of the pancreas – optical voids are visualized in the parenchyma. The connective tissue layers are swollen. During the 35th day, the unevenness of the color of the acinus cells is noticeable (there are light and dark fields of vision). Duct epitheliocytes are enlightened. Optical voids are visualized periductally. On semi-thin sections in the acini, fat drops of various sizes are found, which diffusely fill the cytoplasm. During the 46th day, the same structural changes are observed (swelling of the duct wall, connective tissue layers). Fat droplets are diffusely distributed in the cytoplasm of acinocytes (Fig. 8). During the 56th day, the connective tissue layers are swollen, phenomena of stasis are visualized in blood vessels. The nuclei of acinocytes are rounded, located near the basal pole, surrounded by small fatty inclusions. Granules of the zymogenic area are also surrounded by lipid droplets (Fig. 9).

Thus, a qualitative assessment of the histostructure of the liver and pancreas under the conditions of high caloric carbohydrate and fat diets indicates the progression of dystrophic changes over time. In particular, during the 56th day of the experiment, changes in the liver are pronounced, however, binucleated hepatocytes are often found in the animals of the group II, which indicates the possibility of regression and regenerative potential. At the same time, the animals of the experimental group III have total fatty infiltration. In the pancreas of animals of the groups II and III, structural changes are manifested by edematous processes and disorder of the vascular component with greater dominance in a high-fat diet.

**Conclusion:**
1. The animals’ receiving high-carbohydrate or high-fat diets is accompanied by hormonal and metabolic changes, the formation of insulin resistance and obesity, which are predictors of the development of diabetes mellitus and diseases of the cardiovascular system.
2. An increase in the activity of functional indices of the liver and pancreas, characterizes the activation of cytolytic processes and reflects the growth of hepatopancreatico-biliary risks.
3. Biochemical changes are consistent with structural disorders, in particular, fatty dystrophy of hepatocytes, edematous and degenerative changes of the liver and pancreas, which are more pronounced under the conditions of a high-fat diet.

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**References**
**Fig. 2.** Histostructure of the liver of a rat receiving a high-carbohydrate diet. 56th day. Designation: 1 – stasis in the central vein; 2 – lymphocytic infiltration; 3 – optical lucidity. Staining: hematoxylin and eosin. Magnification: x200.

**Fig. 3.** Histostructure of the liver of a rat receiving a high-carbohydrate diet. 56th day. Designation: 1 – binucleated hepatocyte; 2 – boundaries between hepatocytes; 3 – sinusoidal hemocapillaries. Semi-thin section. Staining: methylene blue. Magnification: x1000.

**Fig. 4.** Histostructure of the pancreas of a rat receiving a high-carbohydrate diet. 46th day. Designation: 1 – acinus; 2 – intercalated duct; 3 – islet; 4 – connective tissue layers; 5 – blood vessels. Staining: hematoxylin and eosin. Magnification: x400.

**Fig. 5.** Histostructure of the pancreas of a rat receiving a high-carbohydrate diet. 56th day. Designation: 1 – acinus; 2 – zymogenic area; 3 – vacuoles; 4 – nuclei of centroacinous cells of the intercalated duct. Semi-thin section. Staining: methylene blue. Magnification: x1000.

**Fig. 6.** Histostructure of the liver of a rat receiving a high-fat diet. 46th day. Designation: 1 – lipid droplets; 2 – interlobar connective tissue layers; 3 – dystrophically changed hepatocytes. Staining: hematoxylin and eosin. Magnification: x200.

**Fig. 7.** Histostructure of the liver of a rat receiving a high-fat diet. 46th day. Designation: 1 – sinusoidal hemocapillary with formed elements; 2 – hepatocytes with preserved structure; 3 – hepatocytes with enlarged organelles; 4 – dystrophically changed hepatocytes. Semi-thin section. Staining: methylene blue. Magnification: x1000.


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