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The influence of fructose on structural and metabolic features of the tooth-jaw system of rats under conditions of iodine deficiency

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The aim of the study was to investigate an oxidative processes intensity and structural organisation of hard and soft periodontal tissues in rats under conditions of high-fructose diet against the background of iodine deficiency (research group) and standard diet and drinking regime (intact animals). It was found that carbohydrate metabolism was impaired in rats of the research group (glucose content increased by 63.3%, insulin – by 48.2% in blood serum, glycated haemoglobin of whole blood – by 2.1 time, HOMA-IR index – by 2.1 times compared to the data in intact rats) and thyroid status (free triiodothyronine and thyroxine content in blood serum decreased by 46.8 and 42.7%, respectively, compared to the control). Under such conditions, the intensity of lipid and protein peroxidation processes in periodontal tissues increases. In particular, the accumulation of diene conjugates and products that react to thiobarbituric acid in the mucous membrane of the alveolar process (by 19.0 and 7.1 times), in the teeth pulp (by 2.2 and 6.3 times) compared to the values in intact animals was found. The activation of peroxidative destruction of proteins is confirmed by an increase in the content of all fractions of their oxidative modification in the studied tissues by 2.8-8.4 times compared to the control values. The results of the histological examination of the alveolar process indicate thinning of the periosteum, disruption of the structural organisation of osteon, reduction in the thickness of bone trabeculae (by 21.8%), optical density of the osteogenic matrix (by 8.9%), area of intertrabecular connective tissue (by 61.0%). Mucosal edema of connective tissue, accumulation of glycosaminoglycans, hypertrophy of all epithelial layers (basal, prickle, keratinized layers – by 25.5-55.9%, granular layer – by 2.3 times), changes of the microcirculatory net were observed in the mucous membrane of the alveolar process. Thus, the combination of high-fructose and iodine-deficient diets causes the development of oxidative stress and destructive changes of the dentoalveolar complex of research animals, which characterises an increase of the risks of dental pathology development.
Key words: dentoalveolar complex, periodontal tissues, prooxidant system, structural changes, high-fructose loading, iodine deficiency.

INTRODUCTION

Humoral regulation of the body provides the stability of internal environment and the normal course of all physiological processes. Pancreatic and thyroid hormones are powerful regulators of key metabolic links, and violation of their hormonal activity leads to the pathological changes in the whole organism [1, 2]. According to the International Diabetes Federation prognosis, the number of patients with diabetes and insulin resistance tends to increase. It is important to emphasise that the percentage of multisystem manifestations of the disease increases [3]. At the same time, according to the World Health Organization data, thyroid dysfunction takes a second place among the most common endocrine diseases, and iodine deficiency is considered as a dominant factor in their development [2]. Cases of combined effects of impaired glucose tolerance and iodine deprivation are of a particular interest, because their pathogenetic mechanisms have common links and exert a double loading on the target cells [4, 5].

A wide range of biological effects of insulin and thyroid hormones explains the variety of clinical manifestations of combined endocrinopathy, among which the most of systemic changes are well known [4]. The examination of dental status under such conditions attracts a considerable attention, as oral manifestations are becoming more frequent, but their pathogenesis remains poorly studied [5-7]. It is worth noting that insulin resistance leads to the changes of all components of tooth-jaw system, affecting both hard and soft tissues. This is due to the fact that insulin regulates key aspects of not only carbohydrate, but also protein and lipid metabolism, as well as mitogenic processes [8]. The main role is assigned to the toxic effect of glucose excess, which is not assimilated by cells, but accumulates also in the structures of the tooth-jaw system. Chronic hyperglycaemia promotes non-enzymatic glycosylation of proteins with the subsequent formation of end products that stimulate macrophages to express proinflammatory cytokines. It is believed that cytokines induce immune cells of periodontium tissues to produce metalloproteinases, substances of protein nature, that cause destruction of alveolar bone by mediating connective tissue breakdown and inducing osteoclast differentiation and activity. Against the background of activation of pathogenic microflora in the oral cavity, a systemic immunological response of organism occurs [5, 9, 10]. Multifactorial mechanisms of pathological changes of the tooth-jaw segment also develop under conditions of hypothyroid dysfunction [11]. In particular, the processes of physiological demineralisation/remineralisation of bones are disrupted due to reduced osteoblasts activity. Potentiates the development of pathological processes the accumulation of excessive amount of mucopolysaccharides and inflammatory mediators [12].

Dental manifestations of hyperglycaemia are characterised by pathological changes of the oral mucosa (OM). Normally, maintaining the integrity of the epithelial layer depends on the continuous processes of cytodifferentiation and maturation, which are directly affected by carbohydrate homeostasis [13]. Given that these processes are also regulated by thyroid hormones, disorders of their synthesis reduce the intensity of regenerative and reparative phenomena. Due to the accumulation of glycosaminoglycans in the connective tissue, the hydrophilicity of its components increases, the colloidal structure of tissues is disturbed, which ultimately leads to swelling, structural disorganisation of elastic and collagen fibres as a result of their replacement by mucous-like masses. The microcirculatory system also undergoes changes, as the blood supply to soft tissues decreases, which worsens their trophism and resistance [14, 15].

It is worth noting that OM cells are particularly vulnerable to the damaging effects of free radicals. This is due to the fact that reactive oxygen species have the ability not only to interact with cell membrane components, but also diffuse easily directly into epithelial cells and destroy intracellular structures [16]. Activation of peroxidation processes can also affect the structure and function of periodontal hard tissue elements, which in combination worsens the dental status under the conditions of insulin resistance against the background of iodine deficiency.

The aim of the study was to investigate the intensity of oxidative processes and structural organisation of hard and soft periodontal tissues in rats under conditions of high-fructose diet against the background of iodine deficiency and normal diet and drinking regime.

METHODS

The study was carried on 60 sexually mature male rats weighing 150-180 g. The research group consisted of animals (n = 30) that received a 10 % fructose solution instead of a drinking water for two months, and that were on a diet with a limited iodine content [17]. The control group included intact rats (n = 30), which were

kept under the conditions of a standard diet and drinking regime of the vivarium.

To assess the effect of fructose loading on experimental animals, the markers of carbohydrate metabolism were analysed: insulin and glucose content in the blood serum, glycosylated haemoglobin (HbA1c) in whole blood. To confirm the state of insulin resistance, the HOMA-IR (Homeostasis Model Assessment Insulin Resistance) index was determined [17]. Thyroid status was characterised by quantifying thyroid-stimulating hormone of adenohypophysis (TSH), free triiodothyronine (fT_3) and thyroxine (fT_4) in the blood serum by the enzyme immunoassay method, followed by calculation of fT_3/fT_4, TSH/fT_4 indices [17]. The state of iodine supply in rats was determined by the concentration of iodine in urine, which was collected by using metabolic cages.

The examination of prooxidant system of periodontal tissues was carried out on the basis of determining the products of lipid and protein peroxidation in the homogenates of the OM and teeth pulp. The state of free radical lipid oxidation was assessed by the accumulation of diene conjugates (DC) of polyunsaturated fatty acids and products that react to thiobarbituric acid (TBA-AP) [18]. The level of protein peroxidation (PP) was determined by the number of products of their oxidative modifications (OMP) [19].

Features of structural organisation of hard and soft periodontal tissues were studied by the histological structure of the alveolar process and its mucous membrane (MMAP), as well as tooth root cementum. For this purpose, the pieces of the alveolar process and the tooth root cement were subjected to acid decalcification for two days [20]. The MMAP was fixed in a 10 % solution of neutral formalin for 24 hours. Serial paraffin sections of the studied tissues were performed on a sledge microtome, followed by staining with haematoxylin and eosin, alcian blue by Stidman (to identify non-sulfated glycosaminoglycans), and PAS staining (Periodic Acid Schiff Reaction) for verification of glycoproteins [20].

Histological studies were performed in a light microscope Leica DME (Germany). Objectification of quantitative studies was made using computer morphometry and densitometry of objects in histological preparations using a Nikon Coolpix 4500 digital camera. Subsequently, digital copies of the image were analysed using the computer software ImageTool 3.0 for Windows (free licence). In order to assess the accumulation of glycosaminoglycans and glycoproteins, a densitometric study of previously obtained micrographs of histological sections was performed.

Morphometric parameters were calculated in at least 10 digital copies of the optical image of microscopic sections in each animal. The morphometric analysis of the alveolar process included the determination of the thickness of bone trabeculae; the area of intertrabecular bone connective tissue per cell; the optical density of the osteogenic bone matrix. The morphometric analysis of the MMAP was performed taking into account the thickness of the epithelium; depth and width of acanthosis; thickness of the basal, prickle, granular, and keratinized epithelial layers; perimeter and area of cells of all epithelial layers; perimeter and area of the cell's nucleus of all epithelial layers; optical density of the ground substance of connective tissue.

Animals were euthanized by decapitation under ketamine anaesthesia (100 mg/kg body weight). Material for examination was collected immediately after the decapitation of rats. The keeping, feeding, and euthanasia of animals were in accordance with the current legislation of Ukraine (Law of Ukraine No. 3447-IV "About the protection of animals from cruelty", 2006), the rules of the European Convention for the Protection of Vertebrate Animals Used for Experimental Research and Other Scientific Purposes (European convention for the protection of vertebrate animals used for experimental and other scientific purposes, Strasbourg, 1986).

Statistical data processing was performed using the computer program Excel package

Microsoft Office 365 ProPlus. For each of the samples, checked whether the distribution of the studied index was normal using the Shapiro-Wilk test. This criterion was used to determine whether the distribution of the samples corresponds to the Gauss's distribution. In the case of two normal distributions, the equality of the general variances was checked using the Levene's test, and then the samples were compared using the Student's t-test. The difference at $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

In rats that were under the influence of high fructose loading and iodine deficiency, the disorders of carbohydrate metabolism were observed (Table 1). In particular, in the blood serum of animals of the research group increased the glucose content by 63.3% ($P < 0.001$) and insulin level by 48.2% ($P < 0.001$) compared to the control values. According to the excessive accumulation of glucose in the blood under such experimental conditions, an increase of HbA1c level by 2.1 times ($P < 0.02$) was observed compared to the data of intact rats. A reliable criterion for the development of insulin resistance in animals with combined endocrinopathy was a 2.1-fold increase of HOMA-IR index ($P < 0.001$) compared with similar values in rats of control group.

Along with the changes of carbohydrate metabolism markers, an imbalance of thyroid homeostasis was observed in rats of the research group (Table 1). Thus, the levels of fT_3 and fT_4 in the blood serum decreased by 46.8% ($P < 0.001$) and 42.7% ($P < 0.001$), respectively, compared with similar values in intact animals. The disruption of synthesis of iodine-containing hormones is confirmed by a decrease of the fT_3/fT_4 index by 21.1% ($P < 0.05$) compared to the control. Such changes of thyroid balance are consistent with the literature data [4, 5] and indicate a decrease of functionally active T_3 under conditions of insulin resistance. The criterion for the development of iodine deficiency in animals with combined endocrinopathy was a decrease in the concentration of iodine in the daily urine portion by 44.2% ($P < 0.001$) compared with similar values in rats of the control group.

Metabolic disorders under conditions of impaired glucose tolerance against the background of iodine deficiency were accompanied by intensification of lipoperoxidation in the studied tissues. Thus, in the teeth pulp homogenate, the content of intermediate and end products of lipid peroxidation increased by 2.2 times ($P < 0.001$) and 6.3 times ($P < 0.001$), respectively,

Table 1. Indexes of carbohydrate metabolism and thyroid status of intact animals and rats with insulin resistance against the background of iodine deficiency (M ± m; n = 30)

Indexes	Intact animals (control group)	Insulin resistance against the background of iodine deficiency (research group)
Glucose, mmol/l	4.22 ± 0.14	6.89 ± 0.58****
Immunoreactive Insulin, μU/l	13.31 ± 0.43	19.73 ± 0.44****
Glycosylated Hb, μmol of fructose/g Hb	3.65 ± 0.41	7.58 ± 1.03**
HOMA-IR index	2.63 ± 0.12	5.48 ± 0.56****
Free triiodothyronine, pmol/l	6.54 ± 0.41	3.48 ± 0.63****
Free thyroxine, pmol/l	29.84 ± 1.26	17.11 ± 1.64****
Thyroid stimulating hormone, mU/l	0.13 ± 0.02	0.15 ± 0.01
Iodine in urine, μg/l	105.17 ± 4.92	58.64 ± 0.65****

Note: Here and in the following tables *P < 0.05; **P < 0.02; ****P < 0.001 – a reliable difference between the indexes for similar values in intact animals.

compared with similar indicators in intact rats. It is worth noting, that lipid complexes of MMAP underwent more pronounced destruction by oxygen radicals. This was confirmed by an increase in the content of DC and TBA-AP in the MMAP homogenate by 19.0 times ($P < 0.001$) and 7.1 times ($P < 0.001$), respectively, compared to the values in animals, which were kept on a normal diet and drinking regimen (Fig. 1).

It is believed that one of the main reasons for the development of free radical reactions in case of impaired glucose tolerance is persistent hyperglycaemia [21]. Under such conditions, the intensity of glucose autooxidation and non-enzymatic glycosylation processes increases, and protein kinase-C is activated, which causes peroxidative destruction of protein and lipid biomolecules [22].

In addition to lipoperoxidation, the changes of biological activity of protein complexes due to oxidative stress are also a molecular mechanism of periodontal tissue damage [23]. This disrupts the structure of nucleic acids, which can trigger

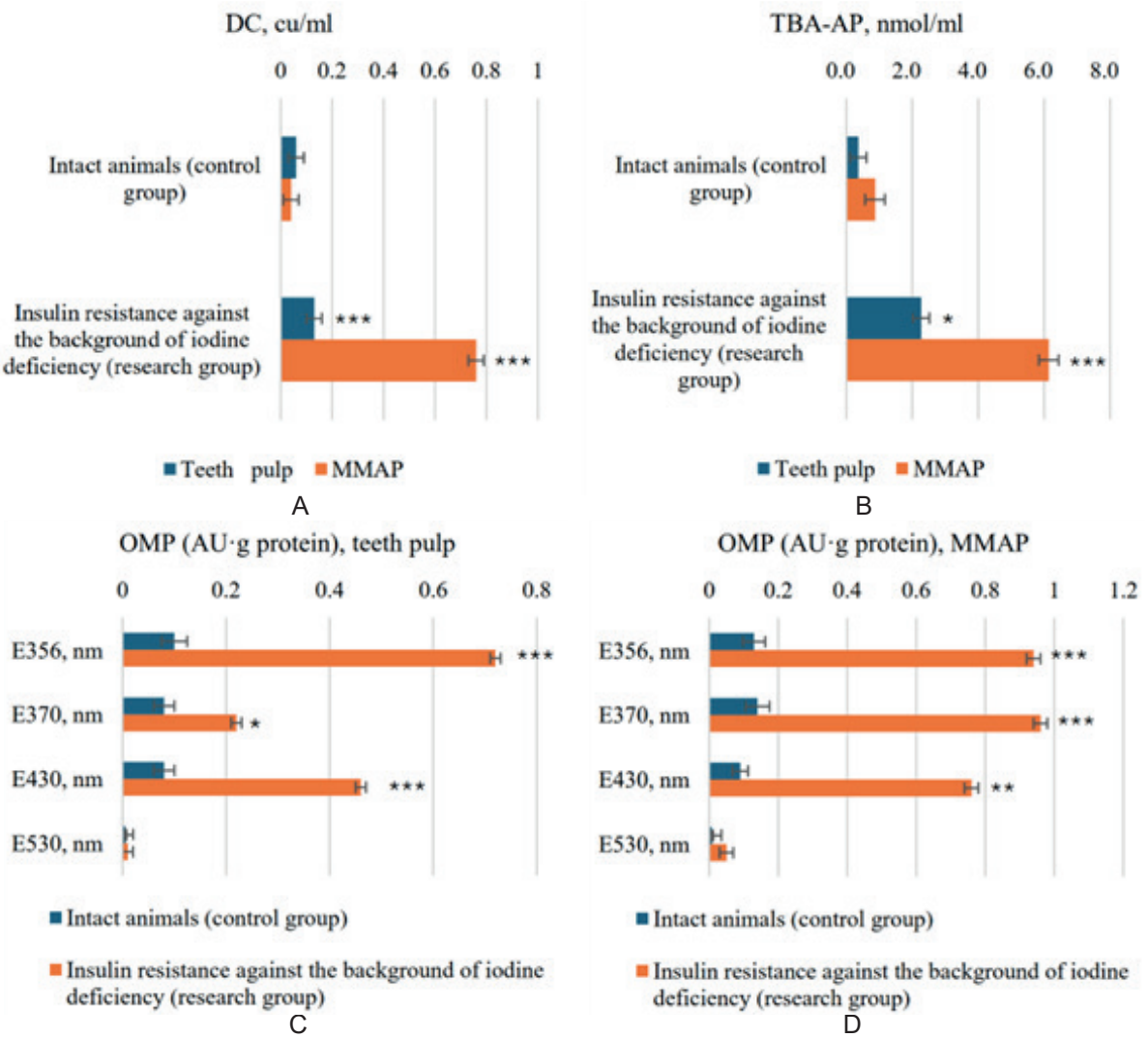

Fig.1. Changes in the content of lipid (DC – A, TBA-AP – B) and protein (OMP – C, D) peroxidation products in homogenates of the teeth pulp and mucous membrane of alveolar process in intact animals and rats with insulin resistance against the background of iodine deficiency (M ± m). *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$ – a reliable difference between the indexes for similar values in intact animals

a cascade of structural and functional changes in the elements of dentoalveolar system. In general, the intensity of peroxidative destruction of proteins was consistent with the activation of peroxidation of lipid bioelements. Thus, the development of combined endocrine pathology led to a co-directional intensification of PP in the homogenates of the studied tissues (Fig. 1).

In particular, in the homogenates of teeth pulp and MMAP of animals with impaired glucose tolerance against the background of iodine deficiency, an reliable increase in the content of all fractions of OMP was noted: E_{356} – by 7.2 times and 7.1 times, E_{370} – by 2.8 times and 6.9 times, E_{430} – by 5.8 times and 8.4 times, E_{530} – by 4.3 times and 5.2 times, respectively, compared to the control values.

It is known that oxidative stress is a trigger for the formation of proinflammatory cytokines, which are directly involved in the pathogenetic mechanisms of osteogenic matrix and mucous membrane damage. The development of hyperglycaemia promotes the cooperation of glycosylated molecules with the receptor apparatus of immunocompetent cells. That's why, the disturbances in the activity of monocytes and macrophages occurs as a result of changes in their phenotype [3, 10]. Therefore, the progression of inflammatory changes under conditions of combined endocrine pathology potentiates the damage of the entire dentoalveolar complex.

Hyperglycaemia against the background of hypothyroid dysfunction caused not only functional metabolic disorders, but also structural alteration of hard and soft periodontal tissues. Thus, the results of histological examination of the alveolar process and tooth root cementum indicate their structural changes. In particular, there was a thinning of the periosteum covering the outer part of the bone of the alveolar process, with connective tissue and osteogenic layers. The last was represented by a zone with a small number of osteocytes. In turn, the adhesion lines of the bone trabeculae of the outer surface of the bone were also predominantly thin, basophilic. Their uneven distribution and blurring were noted locally. In some areas, the boundaries of the osteocyte nuclei were unclear, and in some places only fragments of karyolema were visualised (Fig. 2).

Changes of the deeper layers of bone tissue were also typical, which was shown by data of densitometry. Thus, trabeculae of various shapes and sizes were formed in the depth of the bone, the thickness of which was 21.8% ($P < 0.001$) less than in the control group (Table 2). A slight, homogeneous, but increased accumulation of non-sulfated glycosaminoglycans in the bone matrix was also observed (Fig. 2), which is one of the pathogenetic mechanisms of osteon structural disorders under conditions of iodine deficiency.

These histological violations were confirmed by the results of a densitometric examination of the osteogenic matrix optical density, which in animals with combined endocrinopathy was by 8.9% lower ($P < 0.01$) compared with the corresponding indexes of intact animals (Table 2).

The structural changes in the connective tissue of the alveolar process, which was located between the bone girders of individual areas also attracted attention. An expansion and full bloodedness of its vessels, the presence of neutrophilic leukocytes in their lumen, and single, extravascular leukocytes was noticed. The dominant majority of connective tissue cells were macrophages (see Fig. 2). It can be assumed that the structural changes of bone matrix are based on disorders of haemocirculation and trophism of these structures.

The data of histological structure of connective tissue elements are complemented by the results of morphometric studies. In particular, in animals of the research group, the area of intertrabecular connective tissue per cell decreased by 61.0% ($P < 0.001$) compared with the control (see Table 2). At the same time, the connective tissue contained mainly thin-walled vessels. However, in some areas, thickening of the wall of these vessels with accumulation of glycoproteins was verified, which was reliably

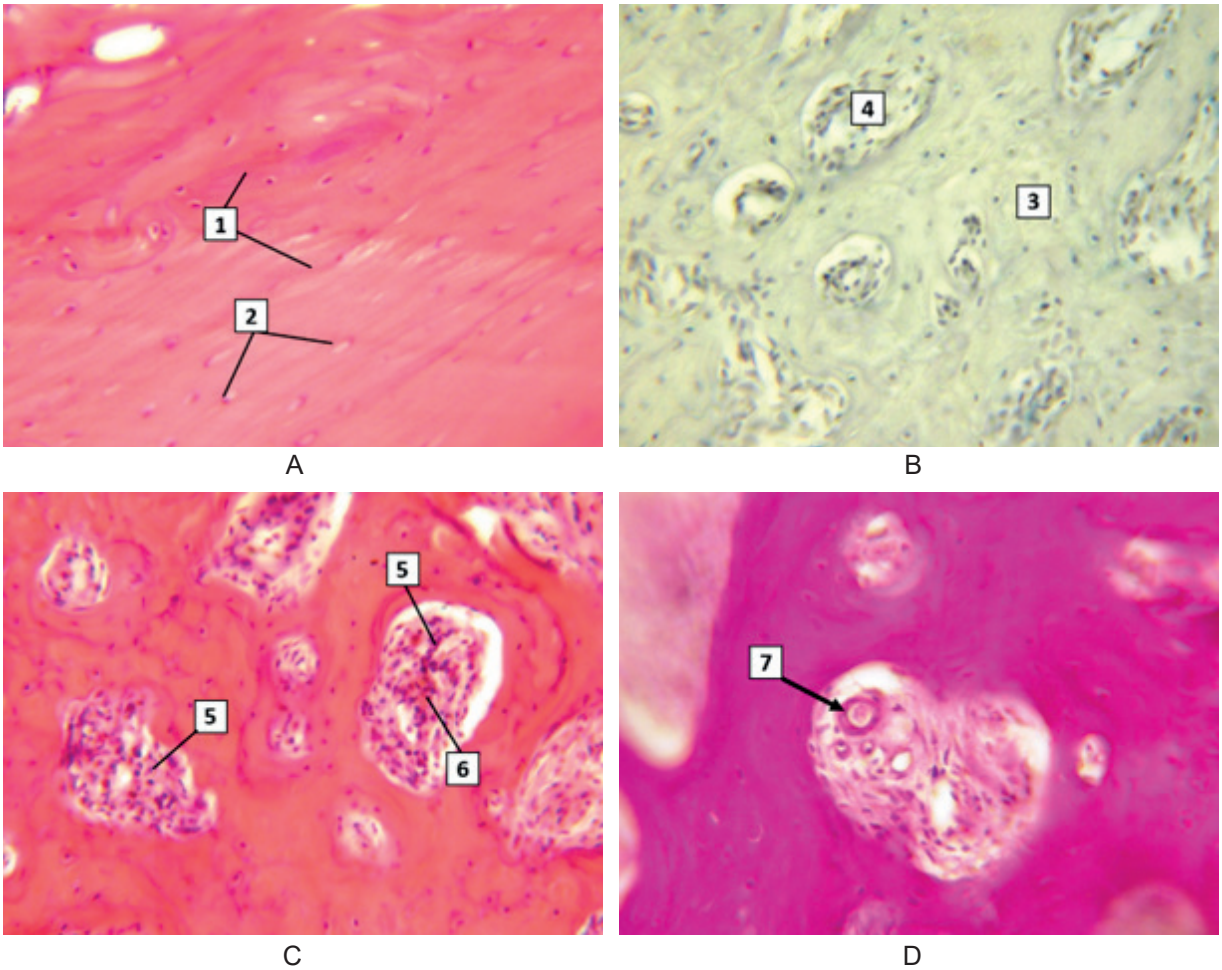

Fig. 2. Histological structure of the alveolar socket bone of insulin-resistant rat against the background of iodine deficiency (1 – irregularity of the adhesion lines of the bone trabeculae, 2 – degenerative changes of osteocytes, 3 – glycosaminoglycans in the osteogenic matrix, 4 – intertrabecular connective tissue, 5 – cellular infiltration of intertrabecular connective tissue, 6 – full-blooded vessels of the microcirculatory net, 7 – accumulation of glycoproteins in the wall of some vessels of intertrabecular connective tissue). Staining: haematoxylin and eosin (A, C), alcian blue by Steedman (B), PAS (D). 400×

visualised by PAS staining (see Fig. 2).

Describing the structural organisation of the periodontal ligament, it is necessary to point out the presence of ordered connective tissue fibres,

Table 2. Morphological characteristics of the bone tissue of the alveolar process of intact animals and rats with insulin resistance against the background of iodine deficiency (M ± m; n = 30)

Indexes	Intact animals (control group)	Insulin resistance against the background of iodine deficiency (research group)
Optical density of osteogenic matrix, units	165.58 ± 3.12	150.80 ± 1.55***
Thickness of bone trabeculae, μm	63.89 ± 1.30	49.97 ± 1.90****
Area of intertrabecular connective tissue/1 cell, μm^2/1 cell	283.19 ± 11.43	110.58 ± 16.34***

Notes: Here and in the following tables ***P < 0.01 – a reliable difference between the indexes for similar values in intact animals.

fibroblasts, fibrocytes, single macrophages, and the presence of thin-walled capillary-type vessels. It is important from the prognostic point of view, that redistribution of glycoproteins and non-sulfated glycosaminoglycans was not observed in it.

Along with the structural changes of the hard periodontal tissues of rats, that were under conditions of fructose loading and limited iodine intake, disorders of the histological structure of MMAP were also observed. Haematoxylin and eosin staining of the specimens allowed to trace the development of mucosal edema in the connective tissue in the form of blue areas, devoid of connective tissue fibres due to their separation. Mostly along the periphery of the areas of severe mucosal edema, there was a slight hypercellularity, caused mainly by macrophages (Fig. 3).

Densitometric examination of alcian blue-stained specimens showed a decrease in the optical density of connective tissue, contai-

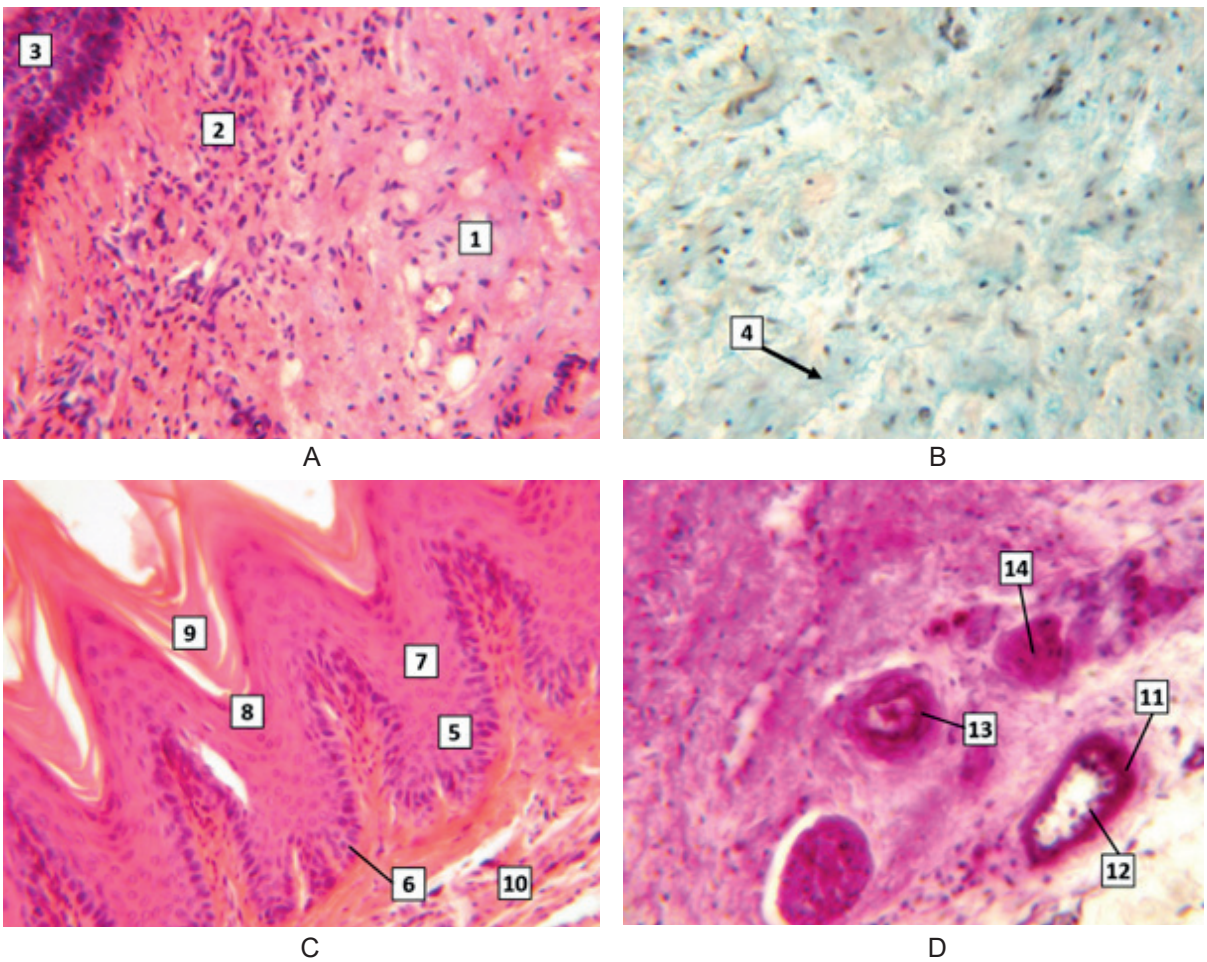

Fig. 3. Mucous membrane of the alveolar process of insulin-resistant rat against the background of iodine deficiency (1 – mucosal edema of the connective tissue of the mucous membrane, 2 – macrophage-leukocyte infiltration of connective tissue, 3 – intraepithelial macrophage-leukocyte infiltration, 4 – glycosaminoglycans in the ground substance of the mucosal connective tissue, 5 – severe acanthosis of the mucosal epithelium, 6 – basal layer of the epithelium, 7 – prickle layer of epithelial cells, 8 – granular layer of epithelial cells, 9 – keratinized layer of epithelial cells, 10 – subepithelial connective tissue, 11 – increase of glycoproteins in the venous wall, 12 – venous endotheliosis, 13 – uneven accumulation of glycoproteins along the internal elastic membrane of the small artery, 14 – narrowing of the lumen of the small artery). Staining: haematoxylin and eosin (A, C), alcian blue by Steedman (B), PAS (D). 400×

ning an increased amount of non-sulfated glycosaminoglycans (see Fig. 3) – 160.3 ± 2.8 units versus 169.6 ± 3.8 units in the control group. It should be noted the diffuse nature of glycosaminoglycans augmentation, even in areas that did not show signs of mucosal edema after staining with haematoxylin and eosin.

The connective tissue of the MMAP was covered with multi-layered squamous epithelium, the thickness of which exceeded the indexes of the control group. This can be explained by the development of hyperplastic changes in the epithelium due to all layers, but mainly basal, granular and prickle (see Fig. 3). The appearance of acanthotic cords was a reflection of these changes in the epithelium of rats with insulin resistance against the background of iodine deficiency (Table 3).

The morphometric examination of all MMAP epithelium layers revealed the changes in the histological structure of each from them. In particular, it was found that the thickness of the basal layer was by 55.9% ($P < 0.01$) greater than the control indexes. The cells in it were arranged in five rows on average. Basal epithelial cells were compactly arranged, with rounded ovoid nuclei, finely dispersed chromatin, eosinophilic-basophilic cytoplasm. The area of their nuclei exceeded indexes of the control group of animals by 39.3% ($P < 0.05$), which led to an increase of the nuclear cytoplasmic index by 2.5 times ($P < 0.05$) compared to similar parameters of intact rats (Table 4).

Specific were the changes of structural organisation of the overlying prickle layer of MMAP epithelium in rats with endocrinopathies. A morphometric analysis showed a decrease of its thickness by 25.5% ($P < 0.02$) compared to the corresponding values of animals which were kept on a normal diet and drinking regime. In accordance with the above manifestations, a decrease in the size of the cells of this layer was observed. In particular, the perimeter of the prickle layer epithelial cells decreased by 13.6% ($P < 0.01$) compared to the control (see Tables 3; 4).

Morphological changes of the MMAP granular layer under conditions of combined endocrinopathy were characterised by an increase in its thickness, which was 2.3 times ($P < 0.02$) greater than the corresponding indexes in the rats of control group. However, there a decrease in the size of this layer cells was noticed. Thus, their area became smaller by 24.9% ($P < 0.02$) compared to the initial data. Similar changes were observed in the nuclei of granular layer cells, where the perimeter and area became smaller by 24.1% ($P < 0.01$) and

Table 3. Morphological characteristics of the mucous membrane of the alveolar process of intact animals and rats with insulin resistance against the background of iodine deficiency (M ± m; n = 30)

Morphometric indexes	Intact animals (control group)	Insulin resistance against the background of iodine deficiency (research group)
Thickness of the epithelium, μm	233.75 ± 10.35	251.15 ± 6.79
Depth of acanthosis, μm	–	199.26 ± 4.26
Width of acanthosis, μm	–	110.99 ± 5.08
Thickness of the basal layer, μm	42.64 ± 2.46	66.49 ± 5.91***
Thickness of the prickle layer, μm	93.77 ± 6.54	69.89 ± 3.33**
Thickness of the granular layer, μm	19.88 ± 3.05	45.05 ± 1.64**
Thickness of the keratinized layer, μm	41.83 ± 2.15	53.66 ± 2.59***
Optical content of glycosaminoglycans in connective tissue, units	169.56 ± 3.78	160.25 ± 2.84
Optical content of glycolsaminoglycans perivascularly, units	167.33 ± 2.34	161.83 ± 3.69

43.6% ($P < 0.01$), respectively, compared to the similar indicators of intact animals. This resulted in a decrease of the nuclear cytoplasmic index of rats of the research group by 70.6% ($P < 0.05$) compared with the control. Epithelial cells were covered with a layer of keratin, which by 28.3% ($P < 0.01$) exceeded the thickness of keratinized layer in the animals of control group (see Tables 3; 4).

It is worth noting that under conditions of humoral imbalance, the haemocirculatory system of the mucous membrane underwent marked changes. For the most part, the lumens of the vessels remained open. However, in some vessels of the microcirculatory net, as well as in some small veins and arteries of the MMAP, there was an increase in the content of glycoproteins and connective tissue edema, which was possible to verified by PAS staining. In some vessels, there was a slightly pronounced endothelial hypercellularity. The nuclei of such endothelial cells acquired an irregular rounded shape and penetrated into the lumen (see Fig. 3).

CONCLUSIONS

The keeping of animals on a high-fructose and iodine-deficient diet leads to the development of insulin resistance and hypothyroid dysfunction. The accumulation of excessive glucose amount can be considered as a key pathogenetic trigger for the initiation of metabolic disorders in hard and soft periodontal tissues. An additional aggressive factor, that has a damaging effect on the cells of the osteogenic matrix and mucous membrane is oxidative stress. Activation of peroxidation of lipid and protein biocomponents is the result of excessive formation of oxygen radicals in rats with hormonal imbalance.

Prognostically unfavourable changes of dental status under the studied conditions is a glycation of periodontal hard tissues, which

Table 4. Morphometric parameters of epithelial cells of the mucous membrane of alveolar process of intact animals and rats with insulin resistance against the background of iodine deficiency (M ± m; n = 30)

Indexes	Intact animals (control group)	Insulin resistance against the background of iodine deficiency (research group)
Basal layer of epithelium		
Perimeter of the cell nucleus, μm	28.99 ± 1.52	32.67 ± 3.15
Area of the cell nucleus, μm^2	47.45 ± 6.95	66.12 ± 3.07*
Perimeter of the cell, μm	48.52 ± 1.89	47.86 ± 3.05
Cell area, μm^2	137.38 ± 10.46	143.44 ± 5.72
Nuclear cytoplasmic index	0.35 ± 0.10	0.86 ± 0.18*
Prickle layer of epithelium		
Perimeter of the cell nucleus, μm	36.22 ± 0.46	37.98 ± 1.38
Area of the cell nucleus, μm^2	82.78 ± 3.65	76.13 ± 4.57
Perimeter of the cell, μm	78.17 ± 2.65	67.51 ± 1.07***
Cell area, μm^2	393.95 ± 26.87	271.57 ± 12.40
Nuclear cytoplasmic index	0.27 ± 0.13	0.39 ± 0.10
Granular layer of epithelium		
Perimeter of the cell nucleus, μm	34.17 ± 1.85	25.92 ± 1.45***
Area of the cell nucleus, μm^2	63.89 ± 4.86	36.04 ± 2.79***
Perimeter of the cell, μm	81.41 ± 2.21	78.83 ± 5.84
Cell area, μm^2	263.70 ± 17.44	197.98 ± 9.13**
Nuclear cytoplasmic index	0.34 ± 0.10	0.10 ± 0.01*

leads to a decrease in the thickness of bone trabeculae and a decrease in the optical density of the bone matrix, reflecting the development of demineralisation processes in the bone bed of the jaw. The trophic disorders of MMAP are mainly associated with the development of oxidative stress, increase of mucosal edema of connective tissue, accumulation of non-sulfated glycosaminoglycans and haemocirculatory disorders at the level of microcirculatory net.

The identified metabolic and structural changes of periodontal tissues characterise an increase the risks of dental pathology development under conditions of excessive fructose consumption against the background of iodine deficiency, which are a risk factor for residents of endemic regions.

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of co-authors of the article.

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ВПЛИВ ФРУКТОЗИ НА СТРУКТУРНО-МЕТАБОЛІЧНІ ОСОБЛИВОСТІ ЗУБО-ЩЕЛЕПНОЇ СИСТЕМИ ЩУРІВ ЗА УМОВ ЙОДОДЕФІЦИТУ

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Метою дослідження було вивчення інтенсивності оксидативних процесів та структурної організації твердих і м'яких тканин пародонта щурів за умов високофруктозної дієти на тлі йододефіциту (дослідна група) та стандартного харчового раціону й питного режиму (інтактні тварини). Установили, що у щурів дослідної групи порушується вуглеводний обмін (збільшується вміст глюкози на 63.3%, інсуліну – на 48.2%, у сироватці крові, глікованого гемоглобіну цільної крові – у 2,1 раза, індекс HOMA-IR – у 2,1 раза щодо значень у інтактних щурів) та тиреоїдний статус (знижується вміст вільних трийодтироніну і тироксину у сироватці крові на 46,8 і 42,7% відповідно щодо контролю). За таких умов зростає інтенсивність процесів ліпідної і білкової пероксидації у тканинах пародонта. Зокрема зростала акумуляція дієнових кон'югатів та продуктів, що реагують на тіобарбітурову кислоту у слизовій оболонці альвеолярного відростка (у 19,0 і 7,1 раза), у пульпі зубів (у 2,2 і 6,3 раза) щодо значень у інтактних тварин. Активацію перекисної деструкції білків підтверджує збільшення вмісту всіх фракцій їх окисної модифікації у досліджуваних тканинах у 2,8–8,4 раза щодо контролю. Результати гістологічного дослідження альвеолярного відростка вказують на стоншення окістя, порушення структурної організації остеона, зменшення товщини кісткових трабекул (на 21,8%), оптичної щільності остеогенного матриксу (на 8,9%), площі міжтрабекулярної сполучної тканини (на 61,0%). У слизовій оболонці коміркового відростка спостерігали слизовий набряк сполучної тканини, накопичення глікозаміногліканів, гіпертрофію всіх шарів епітелію (базального, шипуватого, рогового – на 25,5–55,9%, зернистого – у 2,3 раза), зміни мікроциркуляторного русла. Отже, поєднання високофруктозної та йододефіцитної дієт зумовлює розвиток оксидативного стресу та деструктивні зміни зубоальвеолярного комплексу дослідних тварин, що характеризує зростання ризиків розвитку стоматологічної патології.

Ключові слова: зубоальвеолярний комплекс; тканини пародонта; прооксидантна система; структурні зміни; високофруктозне навантаження; йододефіцит.

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