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Pathomorphology Of Coronary Arteries In Various Dysfunctional Cases Of Calcitonimon

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Abstract:

The problem of studying the metabolism of calcium and glucose remains relevant and not fully investigated. Calcium ion plays an important role in many vital processes of the body, including the conjugation of the processes of excitation and secretion. Indisputable evidence has been obtained confirming the importance of calcium ions in the secretion of hormones that regulate carbohydrate metabolism (insulin and glucagon). There are few data indicating the effect of pancreatic hormones on tissue and cellular calcium metabolism. Thus, the effect of glucagon and insulin on calcium metabolism is similar to that of calcitonin (Hollo et.al., 1979). Insulin, like calcitonin, increases the transport of calcium into cells [Etsuko et. al, 2009]. In this regard, it can be assumed that the functional state of the islet apparatus of the pancreas can be significantly influenced by hormones that regulate calcium metabolism in the body.

Key words: hyperparathyroidism, vitamin D intoxication, calcitonin, hypocalcemia, hypercalcinemia, isoptin, nifedipine, calcium-regulating hormone, chemosensitive.

Introduction

Among the latter, the thyroid hormone calcitonin attracts special attention, the main effect of which is to lower the concentration of calcium in the blood plasma, mainly due to the deposition of calcium in the bones and a decrease in bone resorption. Along with this, it has been established that calcitonin is a broad-spectrum hormone that affects the permeability of cell membranes to calcium and its intracellular distribution. In addition, at present, calcitonin preparations are effectively used to treat hypercalcemic conditions (hyperparathyroidism, vitamin D intoxication) and osteoporosis, to accelerate the healing of bone fractures, and in the treatment of gastric and duodenal ulcers. It is believed that a lack of calcitonin may be a factor in the development of osteoporosis (Mc Dermott, 1983). The widespread introduction of calcitonin into medical practice [Vik, 1998; Wall, 1999; Chestnut, 2000; Lee, 2009; Villa, 2009; Villalon, 2009] dictates the need for a detailed study of not only the specific action of this hormone, but also its nonspecific effects outside the target organs. Based on these data, it is permissible to assume that calcitonin, acting on the transmembrane current of calcium ions, can have a definite effect on the calcium-dependent mechanisms of the functioning of the islet apparatus of the pancreas. In the available literature there are only a few indications of the effect of calcitonin on glucose metabolism. The role of the effect of calcitonin on the

endocrine pancreas and the main stages of carbohydrate metabolism also remains unclear. The effect of the antagonist of calcitonin, the hormone of the parathyroid glands, parathyrin, on glucose homeostasis has not been studied either. Parathyrin preparations are proposed to be used for the treatment of osteoporosis [Cesario R. et.al, 2009]. The age-related aspects of the relationship between the neuroendocrine regulation of calcium and carbohydrate metabolism have not been studied at all.

The object of research in the article: Wistar rats of different age and sex (immature - 1-2 months, sexually mature - 5-7 months, old - 20-24 months), mice, rabbits.

Purpose of the article: to study in an experiment on animals the relationship of the mechanisms of regulation of calcium and carbohydrate metabolism.

Research objectives:

1. to study the physiological mechanisms of calcitonin secretion in insulin hypoglycemia.
2. to study the effect of calcitonin on the main stages of carbohydrate metabolism.
3. to study the effect of calcitonin on the level of glucose and calcium in rats of different age groups.
4. to study the effect of parathyrin on glucose and calcium levels, the nature of alimentary hyperglycemia and glucose consumption by muscle and adipose tissue.
5. to investigate the plasma calcitonin activity and the calcium content in it during changes in glucose metabolism in rats of different age groups.
6. to investigate the effect of calcium channel blockers on the hyperglycemic action of calcitonin.

Main solution: An increase in the secretion of calcitonin and hypocalcemia were shown in various states of carbohydrate metabolism (hypo- and hyperglycemia) and for the first time it was revealed that immature animals are characterized by more pronounced hypocalcemia and hypercalcinemia than sexually mature and old ones. It has been shown for the first time that adrenal cortex hormones (glucocorticoids), pancreatic glucagon, and the sympathetic and parasympathetic divisions are involved in the activation of calcitonin secretion during insulin hypoglycemia by means of the M-cholinergic, a- and 13-adrenergic receptor structures of the autonomic nervous system.

For the first time, the hyperglycemic effect of the domestic calcium-regulating hormone - calcitrin - has been shown. A high degree of correlation was revealed between the glucose level and the total calcium content in the blood plasma under the influence of calcitrin. The age and sex characteristics of the hyperglycemic action of calcitrin were revealed for the first time. The hyperglycemic action of calcitrin was demonstrated in rats of all age groups, and the efficiency of the hyperglycemic action of calcitrin was more pronounced in immature and old animals. It was shown for the first time that under the influence of calcitrin, rats of all age groups and sex develop a diabetoid character of glucose tolerance; in sexually mature and old males, the deterioration of glucose torlerance is more pronounced than in females.

Deceleration of insulin secretion stimulated by glucose, a decrease in the basal level of glucagon was shown, and for the first time an increase in glucagon secretion in insulin hypoglycemia under the influence of calcitrin was established. It was shown for the first time that calcitrin has no effect on the absorption of glucose in the small intestine, on the transfer of glucose from the blood to the tissues, but it

affects the main stages of the interstitial metabolism of carbohydrates, enhancing glycogenolysis and insulin resistance of peripheral tissues. For the first time, an experimental and theoretical substantiation of the action of calcitonin as a counterinsular hormone is given.

For the first time, data were obtained on the inhibitory effect of calcium channel blockers - isoptin and nifedipine on the hyperglycemic effect of calcitrin. For the first time, isoptin suppression and enhancement of Bau-K 8644 of the inhibitory effect of calcitrin on insulin-stimulated glucose consumption by muscle and adipose tissue in vivo and in vitro have been shown.

For the first time, data were obtained on a decrease in the basal glucose level, the degree of hyperglycemia during the glucose tolerance test under the influence of parathyroidin. exhibits the opposite effect of calcitonin on glucose homeostasis.

The theoretical and practical significance of the work. The results of this study form new ideas about the calcium-regulating hormone calcitonin as a counterinsular hormone.

Data on the suppression of the hyperglycemic action of calcitrin by calcium channel blockers expand the existing understanding of the role of calcium in the regulation of glucose metabolism.

The scientific significance of the work lies in the fact that the calcium mechanisms of the hyperglycemic action of calcitrin with the participation of slow voltage-gated L-type and chemosensitive calcium channels are shown and an improvement in insulin resistance against the background of calcium channel blockers, caused by the introduction of calcitrin, is revealed, which makes it possible to suggest a new method for correcting hyperglycemia and insulin resistance. fabrics.

The data obtained make it possible to develop a new approach to the study of the mechanisms of action of calcitonin, parathyrin and calcium channel blockers from the standpoint of their effect on ion channels.

The data of the analysis of the calcium mechanisms of action of the regulators of calcium metabolism - calcitrin, parathyrin and calcium channel blockers are the rationale for their further targeted study.

The main provisions for the defense:

1. Calcium-regulating hormone - calcitrin has a hyperglycemic effect, in the manifestation of which slow voltage-gated L-type and chemosensitive calcium channels take part. The mechanism of the hyperglycemic action of calcitrin is mediated by its inhibitory effect on insulin secretion, a decrease in glucose uptake by peripheral tissues and an increase in glycogenolysis processes.
2. Calcitrin has a contrainsular effect on glucose metabolism. Under unfavorable conditions (obesity, age, burdened heredity, stress, etc.), calcitrin can contribute to the development of metabolic syndrome and diabetes mellitus.
3. Blockers of calcium channels do not have a negative effect on glucose metabolism, reduce the hyperglycemic effect of calcitrin and improve tissue insulin resistance.
4. Calcium-regulating hormone - parathyroidin has the opposite effect of calcitrin on glucose metabolism, increasing glucose tolerance.

5. Between the neuroendocrine regulation of calcium and glucose metabolism, an interaction is established, the severity of which depends on the ontogenetic characteristics of the organism.

Approbation of the work: the results of the work were presented in the form of oral and poster presentations - at the conference of young scientists of the North Caucasus "Mechanisms for the integration of biological systems" (Rostov-on-Don, 1982, 1983); All-Union conference "Problems of general and developmental physiology in pedagogical universities of the country" (Stavropol, 1983); XIV Congress of the All-Union Physiological Society. I.P. Pavlova (Baku, 1983); 37th and 38th Herzen Readings (Leningrad, 1985, 1986); Leningrad Society of Physiologists, Biochemists and Pharmacologists. I.M.Sechenov (Leningrad, 1986); Leningrad City Conference of Young Scientists and Specialists "Mechanisms of regulation of physiological functions" (Leningrad, 1988); VII All-Russian conference "Neuroendocrinology -2005" (St. Petersburg, 2005); All-Russian symposium with international participation "Hormonal mechanisms of adaptation", dedicated to the memory of prof.A.A. Filaretova (St. Petersburg, 2007); V All-Russian conference with international participation, dedicated to the 100th anniversary of the birth of V. N. Chernigovsky, "Mechanisms of the functioning of visceral systems" (St. Petersburg, 2007); VI All-Russian conference with international participation, dedicated to the 50th anniversary of the discovery of membrane digestion by A.M. Ugolev, "Mechanisms of the functioning of visceral systems" (St. Petersburg, 2008); VII All-Russian conference with international participation, dedicated to the 160th anniversary of the birth of IP Pavlov, "Mechanisms of the functioning of visceral systems" (St. Petersburg, 2009); V All-Russian Symposium with international participation "Problems of human adaptation to the ecological and social conditions of the North" (Syktyvkar, 2010); XXI Congress of the Physiological Society. I.P. Pavlova (Kaluga, 2010), the All- Russian scientific-practical conference "High technologies, fundamental and applied research in medicine and physiology" (St. Petersburg, 2010), the All-Russian conference with international participation "Mechanisms of regulation of physiological systems of the environmental conditions ", dedicated to the 85th anniversary of the founding of the Institute of Physiology named. I.P. PavlovaRAS, (SaintPetersburg, 2010).

The results of our studies on the influence of the autonomic nervous system on the secretion of calcitonin in insulin hypoglycemia allowed us to conclude that the regulation of calcitonin secretion in insulin hypoglycemia involves the sympathetic and parasympathetic divisions, as well as the peripheral M-cholinergic, a- and 13-adrenergic receptor nervous systems of the vegetation. We have not come across similar data in the literature. There are publications showing that, under conditions of normoglycemia, B-adrenergic agonists and a-adrenergic antagonists stimulate the secretion of calcitonin, while B-adrenergic antagonists, a-adrenergic agonists and dopamine inhibit it [13, 2]. The mechanism of the influence of these structures on the secretion of calcitonin is not clear. Woga N. [4] believes that B- adrenergic influences stimulate adenylate cyclase, which leads to the formation of cAMP, and, possibly, the latter increases the secretion of calcitonin. In addition, the possibility of an indirect effect of antiadrenergic substances on the secretion of calcitonin cannot be ruled out, in particular, their possible inhibition of the secretion of glucagon, a hormone that not only counteracts hypoglycemia, but also activates the production of calcitonin

[2]. It can be assumed that in our studies the injection of the ganglion blocker pentamine, the M-anticholinergic blocker atropine, the a-blocker tropaphen and the B- blocker obzidan against the background of insulin hypoglycemia causes inhibition of the functional activity of thyroid C-cells producing calcitonin, and therefore a decrease in CT rat blood plasma activity. This is confirmed by the results of studies on changes in the activity of C-cells of the thyroid gland in rats with experimental hyperthyroidism upon administration of the B-blocker propranolol [7].

When assessing changes in the total calcium content in plasma under the influence of the applied neurotropic agents, it should be noted that the latter can affect both the production of calcitonin and parathyrin [19]. Therefore, there is no clear correlation between changes in plasma calcium concentration and its CT activity.

Increased secretion of calcitonin is a nonspecific response to the action of a stressor (insulin hypoglycemia), the biological significance of which is determined as follows: 1. calcitonin and a decrease in the concentration of extracellular calcium inhibit the secretion of endogenous insulin, the main sugar-lowering hormone, and thereby protect the body from an excessive decrease in blood glucose [4]; 2. increase the secretion of endogenous glucagon (as established by us); 3. Under the influence of calcitonin, the processes of gluconeogenesis [6] and glycogenolysis are stimulated; 4. under the influence of calcitonin, the secretion of sugar-increasing hormones - catecholamines and cortisol increases [3]; 5. calcitonin has a hyperglycemic effect [12]; 6. calcitonin increases the concentration of free fatty acids in the blood [11].

Significantly lowering blood glucose levels is known to be a powerful stressor. The development of stress is accompanied by increased secretion of calcitonin and hypocalcemia [4]. Therefore, an increase in the secretion of calcitonin in insulin hypoglycemia is a protective mechanism that limits the severity of the stress response, and is an adaptive response of the body aimed at saving calcium. Thus, inhibition of insulin secretion, increased secretion of glucagon and the processes of glycogenolysis and gluconeogenesis under the influence of calcitonin, on the one hand, causes, together with other sugar- increasing hormones, the release of glucose, thus providing the brain with the energy material it needs. On the other hand, it should be especially noted that to compensate for the energy costs associated with "acute stress", calcitonin (along with glucagon, adrenaline, glucocorticoids, growth hormone) causes the release of free fatty acids. As is known, stress is phylogenetically related to muscle activity; therefore, data on an increase in CT activity and a decrease in the level of calcium in the blood plasma of humans and laboratory animals under muscular load are of interest [18, 19,8]. Glucose levels during muscle work soon drop as a result of their rapid consumption and the released fatty acids can be used by the muscles as a source of energy.

The magnitude of CT activity and the degree of hypocalcemia in insulin hypoglycemia are more pronounced in immature rats than in sexually mature and old ones. This circumstance can be explained by the increased energy requirements of a growing organism and is important in the adaptation of an organism, especially a growing one, for which a significant decrease in the level of glucose - the main energy source - is the most dangerous.

When conducting a glucose tolerance test in rats of all age groups, we found an increase in CT activity and a decrease in the concentration of total calcium in plasma. The data of other researchers indicate a decrease in the calcium content and an increase in the concentration of calcitonin in the blood plasma in response to glucose intake. It can be assumed that hypocalcemia is associated with the ability of glucose to influence calcium metabolism, increasing its accumulation in tissues by increasing calcium entry into cells [22] or the ability of insulin to reduce calcium concentration [2] and increase calcium transport into cells [19]. The accumulation of intracellular calcium in the thyroid tissue leads to an increase in the secretion of calcitonin [16], which contributes to the further progression of hypocalcemia. The direct effect of increased glucose concentration on thyroid C-cells is also possible, since it was shown that the administration of glucose to thyroidectomized rat pups did not change the calcium concentration in the blood [15].

A decrease in the concentration of calcium in the blood plasma, as well as a change in the functional activity of C-cells of the thyroid gland, according to Zoloev G.K. [9] may have some biological significance. The author believes that an increase in blood glucose concentration contributes to an increase in insulin levels in it and a simultaneous decrease in calcium content. In turn, hypocalcemia weakens the effect of glucose on pancreatic B cells [6], while insulin contributes to a decrease in glycemic levels. As a result of both processes, the excess secretory activity of B-cells of the pancreas is reduced and thus a feedback mechanism between glucose, calcium and insulin secretion is realized in a peculiar form. In addition, we believe that the increased secretion of calcitonin in hyperglycemia caused by oral glucose load is important in maintaining calcium for the body. Exhibiting its main hypocalcemic effect, calcitonin blocks bone resorption and enhances calcium absorption by bone tissue, thereby reducing urinary calcium excretion. Considering the fact that patients with newly diagnosed overt diabetes mellitus have an increased level of calcitonin in the blood plasma [5] and a relationship has been established between the rate of urinary calcium excretion and the degree of hyperglycemia [9], the data obtained deserve close attention and give grounds for further research. the role of hormonal homeostasis in the regulation of calcium and carbohydrate metabolism.

Age-related differences in the diamics of hypocalcemia and calcitonin secretion after glucose loading are possibly related to the fact that parafolicular cells of the thyroid gland in immature rats are more sensitive to the action of increased glucose concentration than in sexually mature and old ones. Since the depletion of calcium reserves is most significant for the growth and development of a young organism, this age-related feature is of general biological significance for the preservation of plastic resources.

Thus, under various states of carbohydrate metabolism (hypo- and hyperglycemia), there is an increase in the level of calcitonin and a decrease in the concentration of total calcium, the main significance of which is to preserve calcium for the body, which is realized through an increase in the secretion of calcitonin. Moreover, the specific gravity of neuroendocrine regulation of calcium homeostasis in adaptation to changes in blood glucose levels is not the same in different age periods and is characterized by age and sex characteristics.

The existence of a large number of points of application of the action of calcitonin on glucose metabolism determines the complexity and variety of metabolic disorders that can occur in conditions of hypercalcitoninemia. The combination of these changes is expressed in impaired glucose tolerance. In turn, impaired glucose tolerance stands out as a separate form of the pathology of carbohydrate metabolism, which can be the stage of diabetes mellitus and under unfavorable conditions can develop into overt diabetes mellitus. In other words, as evidenced by the above data, calcitonin exhibits an anti- insular effect on glucose metabolism.

It is known that insulin antagonists are substances that are capable of either directly suppressing the action of insulin or destroying its molecule, or having a metabolic effect opposite to insulin. Based on these ideas, we will try to briefly substantiate the antagonism of the action of calcitonin in relation to insulin using the example of target tissues for insulin: liver, muscle and adipose tissue, since, as is known [1], impaired glucose homeostasis can occur at the following levels: prereceptor (change structure and function of the pancreas and / or insulin), cellular (impaired insulin sensitivity of adipose and muscle tissue) and at the liver level (increased glucose production).

So, in contrast to insulin, which enhances the processes of glycogenesis and reduces the processes of gluconeogenesis, calcitonin stimulates glycogenolysis and gluconeogenesis [6, 7, 8, 3]. Antagonism of the action of calcitonin is also manifested in relation to its effect on the activity of key glycolysis enzymes in liver cells. Thus, after intravenous administration of insulin to intact rabbits and rats, a decrease in glucose-6-phosphatase activity of the liver was observed simultaneously with a decrease in the level of glycemia [8], while calcitonin caused a significant increase in glucose-6-phosphatase activity in liver microsomes of adult rats [6]. Calcitonin has a hyperglycemic effect opposite to insulin on blood glucose.

Under the action of insulin on the cells of muscle and adipose tissue, a distinct and rapid increase in the penetration of glucose through the plasma membrane into the cell is observed. Calcitonin completely suppresses insulin-stimulated glucose uptake by muscle and adipose tissue. The data on the inhibition of glucose uptake in muscle and adipose tissues by calcitonin, stimulated by insulin, indicates an antagonistic relationship between insulin and calcitonin in the action of these hormones on peripheral tissues. However, we cannot assume that calcitonin is a hyperglycemic hormone such as, for example, hydrocortisone, since the administration of calcitonin alone did not alter the spontaneous absorption of glucose by muscle and adipose tissues. Finally, the significant inhibition of insulin secretion under the influence of calcitonin should be noted [4, 19, 8].

Thus, calcitonin has the opposite effect of insulin on glucose homeostasis at the prereceptor level (inhibits the secretion and biological effect of insulin), at the cellular level (reduces insulin sensitivity of muscle and adipose tissue) and at the liver level (enhances glycogenolysis and gluconeogenesis), resulting in hyperglycemia, insulin resistance and impaired glucose tolerance are. As you know, in accordance with Leauep's concept. [7] insulin resistance is a basic component of metabolic syndrome [1] along with obesity, arterial hypertension, dyslipidemia (elevated triglycerides and low HDL cholesterol), and carbohydrate metabolic disorders (high fasting glycemia, impaired glucose tolerance). The progression of metabolic

syndrome leads to the development of prediabetes, diabetes, cardiovascular disease, non- alcoholic fatty liver disease, gout, hyperandrogenism syndrome (polycystic ovary disease), and cancer. According to some authors [13, 6], a decrease in tissue sensitivity to insulin is an important link in the pathogenesis of diabetes mellitus, and the factors causing a decrease in insulin sensitivity can be considered as risk factors for the incidence of diabetes mellitus. Therefore, in our opinion, it can be assumed that with respect to glucose homeostasis, calcitonin under certain conditions can contribute to the development of metabolic syndrome and diabetes mellitus.

One of the reasons for prereceptor-type insulin resistance is the presence in the circulation of insulin antagonists, which can be hormonal and non-hormonal in nature. Hormonal antagonists include glucagon, corticosteroids, catecholamines, growth hormone and other factors, they are counterinsular in their mechanism of action on some metabolic processes. Their antagonism in relation to the action of insulin is also manifested at the level of the insulin-receptor system. In this regard, it should be noted that calcitonin increases the content of insulin inhibitors, leading to a decrease in its biological activity. Thus, under the influence of calcitonin, the level of STH, catecholamines and cortisol in the blood increases [22]. Non-hormonal insulin antagonists include antibodies to insulin and antibodies to insulin receptors, ketone bodies, free fatty acids, sinalbumin. Calcitonin significantly increases the concentration of free fatty acids in the blood serum and in the liver cytosol [11], lowers the level of C-peptide in the blood [3], which indicates an increase in the concentration of proinsulin, a less active form of insulin.

Ca2 + plays a role not only in secretion, but also in the implementation of the action of insulin. According to the data obtained in vitro, Ca2 + increases the activity of insulin receptors in rat adipocytes, as a result of which the dissociation of the hormone from the membrane of these cells decreases and, therefore, the effectiveness of the hormone action increases [4]. It can be indirectly assumed that calcitonin, by lowering the level of Ca2 +, can reduce the activity of insulin receptors.

Conclusion

These data suggest that calcitonin is a contrainsular hormone. In addition to the hypocalcemic effect, calcitonin also exhibits an anti-insular effect, participating in the regulation of glucose metabolism. It is interesting to note that such sugar-increasing counterinsular hormones as glucagon, ACTH, STH, glucocorticoids, thyroxine also have a hypocalcemic effect, i.e. as well as calcitonin, they take part in the regulation of calcium and glucose metabolism, which is an additional confirmation of the functional relationship of calcium and carbohydrate metabolism.

Of particular note is the fact that metabolic disturbances caused by the administration of calcitonin are also observed in diabetes mellitus. Thus, a significant increase in LDH activity was found in diabetes [7] and in the pre-diabetic state and susceptibility to diabetes [1], as well as in our studies after the administration of calcitonin to rats. An increase in the level of free fatty acids is observed during the injection of calcitonin [11] and in patients with insulin-dependent diabetes on an empty stomach and after meals [11]. Free fatty acids are believed to play an important role in the early stages of insulin resistance [18, 152], and elevated triglyceride levels contribute to the development of insulin resistance [3]. A clear

positive correlation was found between an increase in the concentration of free fatty acids and triglycerides in the blood and the degree of insulin resistance in muscles and adipose tissue [19, 152]. Free fatty acids are considered a new marker of insulin resistance [22]. Recent studies have shown that fatty acids in muscle cells inhibit insulin-stimulated glucose transport [13].

It should also be noted that antibodies to calcitonin appear in the blood of rats with alloxan diabetes, which is noted only at high blood sugar levels. A relationship was found between the blood sugar level and antibodies to calcitonin [17]. The authors believe that the appearance of autoantibodies to calcitonin is a pathogenetic factor in the development of hyperglycemia in alloxan diabetes.

Analysis of data on the antagonistic action of calcitonin in relation to insulin suggests that this hormone is diabetogenic.

Many drugs impair insulin secretion, and some cause toxic damage (3-cells of the pancreas. Thus, it has been established that thyroxine in high doses causes apoptosis of B-cells of the rat pancreas and that the action of thyroxin is reversible. In this regard, it is believed that hyperthyroidism can be accompanied by increased apoptosis of B cells, leading to a decrease in the basal level of insulin and its secretion under the influence of glucose [5]. It is interesting to note that the administration of calcitonin for 20 days causes an increase in the concentration of thyroid hormones in the blood [8]. With this, it is possible to assume another mechanism by which calcitonin can impair the functional state of pancreatic B cells. Apparently, it consists in the fact that calcitonin, by increasing the concentration of thyroid hormones that can induce apoptosis of B cells, can indirectly reduce the activity of B cells.

There are cases of disorders associated with excessive secretion or exogenous administration of insulin antagonist hormones, leading to the development of diabetes mellitus. Thus, steroid diabetes can occur with hypersecretion of glucocorticoids or their prolonged use as a therapeutic agent, and does not occur in the case of hypersecretion of other steroid hormones, such as mineralocorticoids or sex hormones, which have little effect on carbohydrate metabolism. As for calcitonin, there is no consensus in the literature on the diabetogenicity of its action, and the evidence is very contradictory [15, 10]. Clinical observations of patients with Paget's disease who have received calcitonin for a long time are ambiguous. Some authors [15] describe the hyperglycemic effect of synthetic salmon calcitonin and the presence of a strict inverse correlation between the plasma calcium level and glucose content in it, while others [10] did not find signs of diabetes mellitus in patients with this disease even after 8 years of calcitonin use. These data suggest that the diabetogenic effect of calcitonin is not always manifested, but, apparently, with changes in the initial state (3 cells of the pancreas. It is possible to assume that calcitonin, which has been present in the blood for a long time in high concentrations, and, especially, with unfavorable conditions (obesity, age, burdened heredity, stress, etc.) can act on insulin receptors indirectly through metabolic processes and cause the development of relative insulin deficiency due to a decrease in the biological activity of insulin. In our previous studies [22] showed impaired glucose tolerance in children 10-14 years old with 1st degree obesity, as well as more pronounced impaired glucose tolerance in sexually mature and old rats when performing a glucose tolerance test against the background of calcitonin administration.

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