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*O.A. Olenovych, N.V. Pashkovska***CARBOHYDRATE METABOLISM PARAMETERS IN CASE OF ADMINISTRATION OF ZINC-CONTAINING MEDICATIONS IN COMPLEX TREATMENT OF DIABETES MELLITUS**

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**Abstract.** In order to improve treatment efficacy for patients with diabetes mellitus the possibility of administration of Zinkit (Woerwag Pharma, Germany) in a complex treatment program was studied. According to the results of a complex assessment of glycemia control indices in patients with diabetes mellitus 3 weeks after the enrollment to the study it was revealed, that additional to hypoglycemic therapy administration of zinc-containing medication not

only promoted reliable decrease of fasting and 2-hours postprandial blood glucose level, but also approached glycemia indices to the goal levels of a satisfactory control of diabetes, provided significant reduction of HbA<sub>1c</sub> level by 6,8 % of its initial level.

**Key words:** diabetes mellitus, carbohydrate metabolism, zinc-containing medications.

**Introduction.** Diabetes mellitus (DM) – one of the most widely spread form of disturbance of all the types of metabolism and, furthermore, the acknowledged microelementosis, since is accompanied by metabolic disorders of trace elements [3, 6]. Disorganization of metabolic processes, developing in case of DM, is followed by the insufficiency of trace elements, responsible for numerous physiological functions of the organs and systems, that, in its turn, determines the severity and prognosis of the disease [12].

Among trace elements, most important for the pathogenesis of diabetes, zinc (Zn) is of a special attention. Zinc is known to play a significant role in the pancreas activity, implicated in the processes of synthesis, deposition, release of insulin from  $\beta$ -cells of Langerhans' islets. Considering the participation in the process of formation of zinc-containing proinsulin hexamer, Zn promotes insulin crystallization, storage of insulin granules, and its adequate secretion as the response on high glucose concentration [9, 10, 11]. With Zn ions participation the insertion of insulin into the blood transport systems takes place, providing its delivery to the cells [2], and the improvement of insulin receptors phosphorylation as well, activating the a signaling cascade of insulin cellular action [8].

An important role of zinc as secondary cellular messenger in the control of insulin activity and glucose homeostasis has been postulated [6, 13]. Thus, Zn ions are known to imitate series of insulin effects: they stimulate glucose transport and oxidation, cellular intake of glucose, promote conversion of the latter to triacylglycerols, that inhibits the process of lipolysis [4, 5, 6]. Meantime, Zn is found to have an independent, additional to insulin action, a strong stimulating effect on lipogenesis in the adipocytes [11]. Moreover, the ability of Zn to inhibit the action of insulinase is known.

Zn is acknowledged to have an antioxidant action as well. The cation protects insulin and  $\beta$ -cells from free radicals harmful influence, since it's a structural part of antioxidant enzymes, such as Cu-Zn-superoxide dismutase, and a competitor of oxida-

tion-reduction metals, such as iron [7]. Other mechanism of antioxidant action of Zn ions is related to their ability to stimulate the expression of pancreatic metalloproteins, known to accumulate hydroxide radicals and prevent the destruction of  $\beta$ -cells [11].

All the mentioned above enables to suggest, that deviations of physiological concentrations of Zn in human body may be one of the reasons of glucose intolerance, disturbance of insulin secretion, reduction of its biologic activity and transportation to the tissues, that is – formation of absolute or relative insulin insufficiency, which is pathogenetical base-ment of DM. Furthermore, deficiency of the trace element in patients with DM worsens excessively the period of wound healing and increased sensitivity to infectious complications, leads to the disorder of collagen synthesis, reduction of protective body abilities [1].

At the same time, the development of DM is characterized by loss of the ability to accumulate Zn by insulocytes, is followed by the intensive renal excretion of Zn (loss of the trace element reach double, and sometimes even triple norm level not depending on the type of diabetes or hypoglycemic therapy) and its poor intestinal absorption, then stipulating pre-conditions for the development of its deficiency in the body [6]. Considering the known participation of Zn in pathogenesis of numerous pathologies, the question of administration of zinc replacement therapy requires a special attention in case if DM – the diseases, dangerous due to its numerous multiorganic complications.

**Objective of the research** – the improvement of treatment efficacy for patients with DM by administration of Zinkit (consists of 10 mg of zinc sulphate per tablet) in a complex treatment program.

**Material and methods.** 33 patients with DM (16 women and 17 men – 48 % and 52 % respectively), aged between 19 and 78 years (mean age – 50,7 $\pm$ 2,27 years) and 10 healthy individuals, who constituted the control group, participated in the study.

The verification of the diagnosis and disease severity was based on the acting national and inter-

national regulating documents. According to the results of a complex patients' examination DM type 1 was found in 10 patients – 30 % (mean age –  $36,5 \pm 3,83$  years), whereas in 23 patients (70 %) DM type 2 was diagnosed (mean age –  $56,9 \pm 1,55$  years). Moderate severity of DM was identified in 17 (52 %) enrolled patients with overwhelming majority of DM type 2 patients (82 %); severe form of the disease was observed in 16 (48 %) examined patients, represented by 44 % of type 1 diabetics and 56 % of type 2 diabetics. In 12 of the enrolled patients the duration of diabetes was less than 5 years ( $3,4 \pm 0,56$  years), in 11 participating individuals diabetes lasted for 6-10 years ( $7,8 \pm 0,56$  years), 10 of participants had diabetes longer than 10 years ( $15,1 \pm 1,11$  years). It should be noted, that the cohort of patients with DM type 1 in severe form was equally represented by cases of its duration less than 5 and more than 10 years, whereas in patients with DM type 2 severe form of the disease was mostly observed at the duration more than 10 years.

At the moment of enrolment to the investigation patients' condition was stable and didn't require additional measures, except those provided by the National medical care protocols for patients with diabetes mellitus. All the enrolled patients have been trying to keep diet recommendations and received hypoglycemic therapy – «basis-bolus» insulin therapy in case of DM type 1 and oral hypoglycemic agents (4 % individuals), combined hypoglycemic therapy (52 % individuals), insulin preparations (44 % individuals) – in case of DM type 2.

Examined patients were divided in two groups: group 1 (control) – patients with DM under standard treatment program (18 individuals); group 2 (basic) – patients with DM under a complex treatment with additional administration of Zinkit (Woerwag Pharma, Germany), 1 effervescent tablet twice a day dur-

ing meals (previously dissolved in 100-200 ml of water) for 3 weeks (15 individuals). It should be noted, that all the enrolled patients were rather tolerant to the administered treatment, nobody developed allergic reactions or withdrew the research.

All patients underwent standard general clinical and laboratory-instrumental examination. Glucose blood concentration was determined by glucose oxidase method before and 2 hours after meal (pre- and postprandial glycemia) at the beginning of the study and 2 weeks after treatment to assess carbohydrate metabolism. Detection of glycated haemoglobin ( $HbA_{1C}$ ) 2 months after treatment was used as informative criterion of continuous glycemic control (by colorimetric method).

Statistical processing of the obtained data was performed with the establishment of mean values, standard errors, confidence intervals. To estimate the probability of differences in comparison of studied groups, Student's coefficient (t) was used. The difference between groups was considered to be significant at the level of  $P < 0,05$ .

#### Results of the research and their discussion.

The analysis of carbohydrate metabolism parameters revealed no significant difference concerning the comparison of investigation results in patients of the control and basic groups (Table) and evidenced a poor compensation of the disease in patients of the examined cohort. Average two-fold elevation of fasting glycemia was registered in all the patients as compared to the group of healthy individuals: in diabetic patients of the control group fasting glycemia was found to be increased by 2,1 times ( $P < 0,001$ ), in the examined patients of the basic group – by 2,3 times ( $P < 0,001$ ). Postprandial glycemia 1,8-fold ( $P < 0,001$ ) exceeded the level of that of the control in both groups, and a relative content of  $HbA_{1C}$  reliably

Table

Carbohydrate metabolism indices in the studied groups ( $\bar{X} \pm S_x$ )

Indices	Group, number of examined patients with DM				
	Healthy individuals, n=10	Control group, n=18		Basic group, n=15	
		before treatment	after treatment	before treatment	after treatment
Fasting glycemia, mmol/L	$4,43 \pm 0,25$	$9,48 \pm 0,18$ $P < 0,001$	$7,78 \pm 0,20$ $P < 0,001$ $P_2 < 0,001$	$10,01 \pm 0,24$ $P < 0,001$ $P_1 > 0,05$	$6,51 \pm 0,15$ $P < 0,001$ $P_1 < 0,001$ $P_2 < 0,001$
Postprandial gly- cemia, mmol/L	$6,14 \pm 0,30$	$10,95 \pm 0,11$ $P < 0,001$	$10,05 \pm 0,17$ $P < 0,001$ $P_2 < 0,001$	$11,01 \pm 0,13$ $P < 0,001$ $P_1 > 0,05$	$9,15 \pm 0,21$ $P < 0,001$ $P_1 < 0,01$ $P_2 < 0,001$
$HbA_{1C}$ , %	$4,95 \pm 0,17$	$7,22 \pm 0,04$ $P < 0,001$	$7,02 \pm 0,17$ $P < 0,001$ $P_2 > 0,05$	$7,19 \pm 0,06$ $P < 0,001$ $P_1 > 0,05$	$6,70 \pm 0,10$ $P < 0,001$ $P_1 > 0,05$ $P_2 < 0,001$

Note. P – statistically significant difference in comparison with healthy individuals;  $P_1$  – statistically significant difference in comparison with corresponding indices of the control group;  $P_2$  – statistically significant difference in comparison with the data before treatment; n – number of patients

enhanced in patients with DM of both groups – by 1,5 times ( $P < 0,001$ ).

The investigation of glycemia control indices in patients with DM 3 weeks after the enrollment to the study revealed the substantial reduction of pre- and postprandial glycemia in both groups of the examined patients. Meantime, additional to hypoglycemic therapy administration of zinc-containing medication not only promoted reliable decrease of fasting blood glucose level (by 1,5 times,  $P_2 < 0,001$ ) and 2 hours after meal (by 1,2 times,  $P_2 < 0,001$ ), but also approached glycemia indices to the goal levels of a satisfactory control of DM. Improved glucose utilization and elimination of continuous hyperglycemia episodes is evidenced by significant reduction of HbA<sub>1C</sub> level in patients of the basic group as well (by 6,8 % of initial level,  $P_2 < 0,001$ , as compared to only 2,8 % decrease from the level before treatment,  $P_2 > 0,2$ , in patients of the control group).

The obtained data are reliably indicative of expediency of additional administration of zinc-containing medications in a complex treatment of DM not only for the management of corresponding microelementosis and, thus, normalizing influence on numerous physiological functions of the organs and systems, but also for the control on glycemia, carbohydrate metabolism parameters and the intensity of diabetes complications progressing.

### Conclusion

The administration of three-weeks course of Zinkit in a complex treatment of diabetes mellitus improves glycemic control, promotes normalization of carbohydrate metabolism parameters. The obtained results are indicative of further perspective investigations concerning the efficacy of zinc-containing medications influence on different pathogenic chains of diabetes mellitus and its complications.

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## ПОКАЗАТЕЛИ УГЛЕВОДНОГО ОБМЕНА НА ФОНЕ ПРИМЕНЕНИЯ ПРЕПАРАТОВ ЦИНКА В КОМПЛЕКСНОМ ЛЕЧЕНИИ САХАРНОГО ДИАБЕТА

*О.А. Оленович, Н.В. Пашковская*

**Резюме.** С целью повышения эффективности лечения больных сахарным диабетом изучена возможность применения в комплексе лечебных мероприятий препарата Цинкит (Woerwag Pharma, Германия). По результатам комплексной оценки показателей контроля гликемии у больных сахарным диабетом через три недели с момента привлечения к исследованию установлено, что дополнительное к гипогликемизирующей терапии применение цинксодержащего препарата не только способствовало достоверному понижению уровня глюкозы крови натощак и через 2 часа после приема пищи, но и приближало показатели гликемии к целевым уровням удовлетворительного контроля диабета, обеспечивало достоверное снижение уровня HbA<sub>1C</sub> на 6,8 % от исходного.

**Ключевые слова:** сахарный диабет, углеводный обмен, цинксодержащие препараты.

**ПОКАЗНИКИ ВУГЛЕВОДНОГО ОБМІНУ НА ТЛІ ЗАСТОСУВАННЯ ПРЕПАРАТІВ ЦИНКУ  
В КОМПЛЕКСНОМУ ЛІКУВАННІ ЦУКРОВОГО ДІАБЕТУ***О.А. Оленович, Н.В. Пашковська*

**Резюме.** З метою підвищення ефективності лікування хворих на цукровий діабет вивчено можливість застосування в комплексі лікувальних заходів препарату Цинкіт (Woerwag Pharma, Німеччина). За результатами комплексної оцінки показників контролю глікемії у хворих на цукровий діабет через три тижні з моменту залучення до дослідження встановлено, що додаткове до гіпоглікемізувальної терапії застосування цинковмісного препарату не лише сприяло достовірному зниженню рівня глюкози крові натще та через 2 години після прийому їжі, а й наблизило показники глікемії до цільових рівнів задовільного контролю діабету, забезпечувало вірогідне зниження рівня HbA<sub>1C</sub> на 6,8 % від початкового.

**Ключові слова:** цукровий діабет, вуглеводний обмін, цинковмісні препарати.

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