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Contents

SITAGLIPTIN IN THE TREATMENT OF PATIENTS WITH DIABETES 2ND TYPE WITH CONCOMITANT CHRONIC RENAL DISEASE

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Abstract: *diabetic nephropathy (DN) – specific kidney damage in diabetes (D), accompanied by the formation of nodular or diffuse glomerulosclerosis and a progressive decrease in renal function. Currently, DN is one of the most common and severe complications of diabetes. According to epidemiological studies, DN develops in 20-40% of patients with D, being the only cause of end-stage CRF. Clinically significant renal disease occurs in every third patient with type 1 diabetes and six with type 2 diabetes. In the United States and Western Europe, DN ranks 1-3 among the diseases in which extracorporeal renal replacement therapy is carried out. Until recently, DN was presented as a process manifesting microalbuminuria and then progressing to proteinuria, which leads to end-stage renal failure. Studies in the last decade have shown that the progression of albuminuria and decreased renal function are rather two different manifestations of DN than successive stages of the same process.*

Keywords: *type 2 diabetes, diabetic nephropathy, glomerulosclerosis.*

СИТАГЛИПТИН В ТЕРАПИИ БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ 2-ГО ТИПА И С ХРОНИЧЕСКОЙ БОЛЕЗНЬЮ ПОЧЕК

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Аннотация: *диабетическая нефропатия (ДН) – специфическое поражение почек при сахарном диабете (СД), сопровождающееся формированием узелкового или диффузного гломерулосклероза и прогрессирующим снижением функции почек. В настоящее время ДН – одно из наиболее распространенных и тяжелых осложнений СД. По данным эпидемиологических исследований, ДН развивается у 20–40% пациентов с СД, являясь единственной причиной терминальной стадии ХПН. Клинически выраженное поражение почек развивается у каждого третьего больного с СД 1 типа и каждого*

шестого – с СД 2 типа. В США и странах Западной Европы ДН занимает 1-3 место среди заболеваний, при которых проводится экстракорпоральная заместительная почечная терапия. До недавнего времени ДН представлялась как процесс, манифестирующий микроальбуминурией и затем прогрессирующий до протеинурии, которая приводит к терминальной стадии почечной недостаточности. Исследования последнего десятилетия показали, что прогрессирование альбуминурии и снижение функции почек – скорее два разных проявления ДН, чем последовательные стадии одного процесса.
Ключевые слова: *сахарный диабет 2 типа, диабетическая нефропатия, гломерулосклероз.*

Diabetes (D) for the last 10-15 years has consistently occupied a leading position in the developed world among the causes of end-stage renal disease (ESRD) and the need for dialysis treatment [1, c.1-120].

The aim of our study was to study the effect of sitagliptin in patients with type 2 diabetes with concomitant chronic renal disease

Materials and methods of research. The study involved 42 people with type 2 diabetes complicated by CKD stage 3A, 24 women and 18 men. The duration of the disease ranged from 1 year to 7 years, the average age was 56.6±9.8 years. Also, 10 healthy individuals were studied. 53.5% of this group suffered from coronary artery disease, 88.4% - arterial hypertension. Most patients received aspirin, b-adrenoblockers and angiotensin converting enzyme inhibitors, B-adrenoblockers, calcium antagonists, statins. All patients were overweight – a body mass index (BMI) over 25 kg/m2. 32 (71.2%) patients were obese (BMI ≥30 kg/m2), 10 (28.8%) were overweight. The average waist circumference was 105.1±8.0 cm in men and 108.3±9.0 cm in women. Selection was carried out taking into account the state of carbohydrate metabolism, i.e. the study included only patients with poor carbohydrate metabolism, but glycated hemoglobin (HbA1c) did not exceed 9%. Before inclusion in the study, patients with the purpose of hypoglycemic therapy took only Metformin at a dose of 500-2000 mg / day. Male smokers were not included in the study. At the same time, patients were divided into 2 groups: 1 group - 18 patient, to Metformin at a dose of 1500-2500 mg/day added sulfanyl urea drug – glyclazide at a dose of 60 mg/day, 2 group - 24 patients, to Metformin was added sitagliptin at a dose of 50-100 mg/day for 12 weeks.

Immediately after randomization, patients were analyzed for the main diagnosis, gender, age and experience of the disease, achievement of target blood pressure levels. At the beginning of the course of therapy and after 12 weeks, laboratory control was carried out, which included the study of General blood analysis (hemoglobin, erythrocyte sedimentation rate), biochemical blood parameters (urea and blood creatinine with the calculation of GFR according to the formula CKD-EPI), General urine analysis (proteinuria, hematuria).

The study included 42 patients with diabetic nephropathy with GFR from 45 to 59ml/min / 1,73m2. The exclusion criterion was severe decompensation of diabetes (HbA1c≥9%) and severe damage to other target organs. All patients received standard therapy for diabetes mellitus and diabetic nephropathy. Patients with satisfactory carbohydrate metabolism were selected in both groups to study the nephroprotective effect of sitagliptin for 12 weeks.

The age and duration of the disease, as well as biochemical parameters of patients of both groups are comparable. Patients complained of increased blood pressure, periodic frequent urination, pain in the heart, headaches, excess weight.

Discussion. Analysis of carbohydrate metabolism data showed that all patients had unsatisfactory values of carbohydrate metabolism, while there was an increase in lean, postprandial glycemia and HbA1c in group 1 by 39.2, 39.0 and 37.4%, in 2 – by 39.4; 40.5 and 36.5%, respectively. On the background of treatment there was an improvement in carbohydrate metabolism. Thus, groups 1 and 2 showed a decrease in HbA1c by 19 and 21% ($P<0.05$), respectively.

Table 1. Biochemical blood parameters in patients with type 2 diabetes before and during treatment

Indicators	Control n-10	1-group n-18	After treatment 1-group n-18	2-group n-24	After treatment 1-group n-24
Lean glycemia, mmol / l	4,2±0,48	7,91±2,3*	6,1±1,3*	7,8±2,5*	6,0±0,5*
Postprandial glycemia, mmol\l	5,8±0,67	11,5±4,3*	10,3±2,6*	11,9±3,9*	9,1±1,1*
HbA1c, %	4,5±0,5	8,1±0,6*	6,6±0,3*	8,2±0,8	6,5±0,3
TC mg\ DL	3,7±1,0	5,9±1,2*	4,7±1,0*	6,0±0,9	4,9±1,0
ALT	16,5±3,2	27,6±6,9	29,6±3,2	27,9±4,9	26,1±3,9
α-amylase	39,9±9,2	45,1±9,0	43,2±5,9	53,6±4,1	50,2±7,9

Note: n- number of examined patients;

* -- availability of reliability ($p<0.05$) in relation to the control group.

In the analysis of the lipid spectrum in patients with type 2 D, hypercholesterolemia was observed-a significant increase in cholesterol compared to the control group. At the same time, the blood level of TC in both groups was significantly increased by 35.0 and 37%, respectively, compared with the control group. During 12 weeks of treatment on the background of standard therapy, the content of TC in group 1 decreased to 4.2±0.4 mmol/l (29.3%) ($p<0.05$), in group 2 – to 4.4±0.8 mmol/l (27.0%), ($P<0.05$). In this case, the hepatic enzyme ALT and α-amylase did not significantly change.

When analyzing the dynamics of proteinuria after 12 weeks (table chart 2) protein loss decreased in both groups, but in patients of the second group the decrease was more significant. There was a decrease in protein loss by 327.4 mg/l, (37.3%), while in the first group this figure was only 121.3 mg/l, by 13.8%.

Table 2. Dynamics of the main indicators during treatment

Indicators	Control n-10	1-group n-18	After treatment 1-group n-18	2-group n-24
Blood urea, mol / l	9,7±3,8	8,9±1,8*	9,5±2,7	8,3±2,8*
Blood creatinine, μmol / l	132±6,3	110±6,3	135±7,0	109±6,3
GFR by CKD-EPI, ml/min/1,73m2	52,2±7,8	60,8±13,1*	51,9±7,4	66,9±7,4*
Proteinuria, mg / l	248,6±44,7	207,9±17,8*	251,3±37,7	197,3±45,0

Note: n- number of examined patients;

* -- availability of reliability ($p<0.05$) in relation to the control group.

The same changes can be seen in the biochemical parameters of blood, so creatinine in group 1 decreased by 17.6%, in 2 - by 20.3% ($P<0.05$), respectively. GFR increased by 14 and 24.7% in both groups ($P<0.05$), respectively. At the same time, 2 patients of group 1 (11%) and 6 patients of group 2 (25%) were diagnosed with CKD of stage 2 according to GFR.

Thus, in addition to standard therapy of antidiabetic drug, sitagliptin patients with diabetic nephropathy with CKD stage 3A, it is safe; according to our research there were no complications registered.

In addition, it should be noted a greater adherence of patients to treatment in group 2, as patients took the combined drug – sitagliptin/Metformin, compared with group 1, where patients took glyclazide in the morning, as well as 2 times a day Metformin. It was found that the use of the drug sitagliptin has a positive effect on renal function, as evidenced by an increase in GFR by 24.7% ($P<0.05$), compared with the study group of 11%.

The same changes can be seen in the biochemical parameters of blood, so creatinine in group 1 decreased by 17.6%, in 2 - by 22.3% ($P<0.05$), respectively. The safety of the drug in patients of this group is evidenced by the absence of significant differences in the main clinical and laboratory parameters. There was no increase in Alt and α-amylase in blood in patients of group 2.

The analysis of the frequency of hypoglycemia in both groups revealed: in group 1, 7 (38%) patients had mild hypoglycemia, which were observed at the beginning of treatment, 2 patients glyclazide dose was reduced to 30 mg/day. In patients of the 2nd group, only the 1st patient was noted as hypoglycemia at the beginning of treatment, dose sitagliptin was reduced to 50 mg/da

Conclusion. Thus, the combined administration of sitagliptin and Metformin (in the form of a single tablet) is recommended as the first line of treatment of type 2 diabetes. Sitagliptin also reduces timakovoy postprandialnoy and hyperglycemia, as well as the content of glycated hemoglobin in the blood. The effectiveness of the use of DPP-4 inhibitors is confirmed by a significant decrease in proteinuria and the rise of GFR in its use, which contributes to slowing the progression of renal dysfunction. Given the good tolerability of the drug, its nephroprotective effect sitagliptin can be used in a wide group of patients-against the background of diseases of the cardiovascular system, chronic kidney disease, etc.

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SIBUTRAMINE IN THE TREATMENT OF OBESITY IN WOMEN

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Abstract: *we studied 30 obese women aged 43.5±3.2 years. All patients, depending on the received therapy, were divided into two groups: 1 group consisted of 15 patients receiving sibutramine, 2 group consisted of women receiving sibutramine and Metformin. All women were measured weight, height, then calculated body mass index, waist (W) and hip (H), also fasting blood sugar and 2 hours after eating, lipid spectrum, to eliminate hypothyroidism hormones TSH, free T3, free T4, antibodies to TPO. During the treatment of sibutramine with Metformin in combination led to a decrease in body weight in 15% of patients, sibutramine monotherapy was observed in 10%.*
Keywords: *obesity, body mass index, sibutramine, total cholesterol, triglycerides.*

ПРИМЕНЕНИЕ СИБУТРАМИНА В ЛЕЧЕНИИ ОЖИРЕНИЯ У ЖЕНЩИН

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Аннотация: *нами были исследованы 30 женщин с ожирением в среднем возрасте 43,5±3,2 года. Все больные в зависимости от получаемой терапии были разделены на две группы: 1 группу составили 15 больных, получавших сибутрамин, 2 группу составили женщины, получающие сибутрамин и метформин. Всем женщинам измеряли вес, рост, затем вычисляли индекс массы тела, объем талии (ОТ) и объем бедер (ОБ), также сахар в крови натощак и через 2 часа после еды, липидный спектр, для исключения гипотиреоза, гормоны ТТГ, свободный Т3, свободный Т4, антитела к ТПО. Лечение сибутрамином с метформином в комбинации привело к снижению массы тела у 15% пациентов, на монотерапии сибутрамином - отмечалось у 10%.*
Ключевые слова: *ожирение, индекс массы тела, сибутрамин, общий холестерин, триглицериды.*

Obesity has become one of the most common chronic diseases of our time and is a serious medical and social problem. The high prevalence of this disease is due to urbanization, decreased physical activity and availability of high-calorie food [1, c. 58-61, 2, c. 758-769].

The aim of our study was to study the effectiveness of sibutramine in the treatment of obesity in women.

Materials and methods of research. We studied 30 women with obesity at the average age of 43.5±3.2 years, who applied to the consultative polyclinic of the 3-clinic of the Tashkent medical academy. All patients, depending on the received therapy, were divided into two groups: 1 group consisted of 15 patients receiving sibutramine at a dose of an average of 12.3±2.4 mg per day and dosed physical activity corresponding to the diet; 2 group consisted of women receiving sibutramine and Metformin at an average dose of 13.4 ±2.1 mg/day, 860.3±2.3 mg/day, also dosed physical activity and diet. All women were measured weight, height, then calculated body mass index (BMI), waist (W) and hip (H), also fasting blood sugar and 2 hours after eating, lipid spectrum, to eliminate hypothyroidism hormones TSH, free T3, free T 4, antibodies TPO. The examined patients underwent ultrasound examination of the abdominal cavity and thyroid gland. In order to monitor the safety of the drug to all women before and after taking sibutramine ALT and AST were investigated.

Research result. In women in the first group BMI averaged 37.2±2.3, W was 108.3±2.3 cm, H 124.3±2.3 cm, after observation in the dynamics of a decrease in BMI, W, H 5.7;4.9; 5.0%, respectively. Before treatment in women of the second group BMI, W, H was 36,5±3,4; 110.1±3,4; 118,4±2,3 accordingly, after treatment with sibutramine and Metformin, there was a decrease in BMI, W, H by 16.0; 9.0; 5.0%, respectively. (Table.1). The first group of patients noted a decrease in body weight in 10% of women, in the second group of patients in 15% of women.

Table 1. Changes in anthropometric parameters during treatment with sibutramine

Indicators	Initially		8 weeks		12 weeks	
	1st group	2nd group	1st group	2nd group	1st group	2nd group
Body weight, kg	104,2±2,3	102,2±2,7	96,4±3,2	94,6±2,4	92,1±3,2	85,5±2,1
BMI, kg/m²	37,2±2,3	36,5±3,4	36,3±1,4	33,4±1,3	35,3±2,1	31,2±1,2
W, sm	108,3±2,3	110,1±3,4	106,2±2,1	104,2±2,3	103,2±3,6	101,2±1,2
H, sm	124,3±3,2	118,4±2,3	121,4±1,2	121,3±1,5	118,4±2,1	114,2±2,6

We have also made all of the women have lipid profile. As shown, our results on the background of treatment with sibutramine showed a decrease in the concentration of total cholesterol, LDL, triglycerides by 5.6; 3.5; 16.6%, respectively. HDL increased by 33%. In the second group of patients on the background of therapy with Metformin sibutramine total cholesterol, LDL, triglycerides decreased by 16.7; 6.7; 37.5 %. (Table chart 2).

Table 2. Changes in biochemical parameters in women during treatment with sibutramine

Indicators	Initially		12 weeks	
	1st group	2nd group	1st group	2nd group
Total cholesterol, mmol / l	5,6±1,2	5,6±1,2	5,3±1,5	4,8±1,3
HDL, mmol/l	1,2±0,2	1,1±0,3	1,8±0,4	1,4±0,3
LDL, mmol/l	3,15±1,4	3,2±1,5	3,0±1,3	3,1±1,2
TG, mmol/l	2,1±1,4	2,2±1,6	1,8±1,4	1,6±1,3
Glucose, mmol / l	5,6±0,8	5,7±0,6	5,4±0,2	5,2±0,2

To study hemodynamics in patients, we measured SBP and DBP before sibutramine treatment. In the first group of patients with SBP was an average of 135.5±5.3 mm Hg, DBP 90.4±4.3 mm Hg, in the second group SBP 135,2±3,2 mm Hg, DBP 85,3±3,1 mm Hg. Against the background of the dynamics did not change as a SBP, as well DBP. (Table chart 3).

Table 3. Change in hemodynamic parameters during therapy with sibutramine

Indicators	Initially		12 weeks	
	1st group	2nd group	1st group	2nd group
SBP (mm Hg)	135,4 ± 5,4	135±4,7	130,1±3,2	125±5,3
DBP (mm Hg)	90,2 ± 3,2	90,3±10,3	85,2±5,6	80,0±4,1
PS (bpm)	80,4 ± 4,2	80,8±4,5	78,5±4,3	76,2±6,3

To study the safety of the drug, we tested ALT and AST in the blood. After the use of sibutramine and in combination with Metformin, there were no changes in the liver enzymes within 12 weeks.

Numerous literature data indicate a favorable effect of sibutramine on carbohydrate and lipid metabolism. In most studies, treatment with sibutramine was accompanied by a significant decrease in serum glucose and triglycerides levels, as well as an increase in HDL cholesterol [4, 5, 6].There are studies that show a decrease in the levels of TC and LDL-C in the treatment of sibutramine [1]. Our results correspond to the changes described in the literature data.

Conclusion

1. During the treatment of sibutramine with Metformin in combination led to a decrease in body weight in 15% of patients, sibutramine monotherapy was observed in 10%.
2. Therapy with sibutramine and Metformin led to a decrease in total cholesterol, triglycerides by 16.7; 37.5%, against the background of monotherapy there was a decrease in total cholesterol, triglyceride by 5.6; 16.6%.
3. The use of sibutramine for the treatment of obesity in women has not led to an increase in heart rate and blood pressure.
4. Sibutramine is a safe drug for the treatment of obesity in women, as there was no increase in ALT and AST during therapy.

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