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Influence Of Different Hypoglycemic Therapy Schemes On Carbohydrate Exchange Indicators In Type 2 Diabetes Mellitus

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ABSTRACT

Aim of the study: To study the effect of prescribing inhibitors of sodium glucose cotransporter type 2 (iSGLT-2) and inhibitors of dipeptidyl peptidase-4 (iDDP-4) on the parameters of carbohydrate metabolism in patients with type 2 diabetes.

Materials and methods: A prospective study included 80 patients with type 2 diabetes. The average age was 52.7 ± 3.78 years; diabetes experience - 8 years; BMI-30 ± 0.17; Hb1C-9.2 ± 0.4%; fasting glycemia –10.2 mmol/; eGFR-78 ml/min; TG-2.7 ± 0.44; total cholesterol-3.4 ± 0.72; MAU 32 ± 0.125. The patients were divided into 2 groups: group 1 - 30 patients with DN with impaired renal function and 30 patients with diabetic nephropathy without renal dysfunction in the presence of metformin + iSGLT- 2; 2 group of 30 patients with impaired renal function and 30 patients with diabetic nephropathy without impaired renal function on the background of metformin + iDPP-4.

Results: The study of the effect of the inclusion of drugs iSGLT-2 (group 1) and iDPP-4 (group 2) showed a positive dynamics of carbohydrate metabolism indicators in patients with type 2 diabetes. So if the initial indicators in the groups were comparable in terms of glycemic control indicators, then by the 3rd month of treatment there was a significant decrease in HbA1c in the 1st group of patients in relation to the 2nd group. The result of the correction performed within 3 months was the achievement of the state of compensation in the 1st group in 36.7%, and in the 2nd group in 28.3%, 48.3% of the patients of the 1st group were brought into the state of sub compensation and 31.7 % of patients of the 2nd group.

Conclusion: On the combination of metformin and INGLT-2, a larger number of patients managed to achieve the set goals of therapy with a lower risk of overt hypoglycemia, then this combination should be considered not only more effective.

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KEYWORDS

Diabetes mellitus, diabetic nephropaty, hypoglycemic therapy.

INTRODUCTION

Diabetes mellitus (DM) is a global medical and social problem of our time, which is faced by medical science and healthcare in almost all countries of the world. World health organization (WHO) for the first time recognized this disease as a new non-infectious epidemic of the 21st century in relation to a chronic degenerative disease, since in recent years the growth rate of patients has become threatening. The urgency of diabetes mellitus is determined by its progressive morbidity [1,2]. Correction and prevention of the main manifestations of the disease and its complications are priority areas of medicine. The study of the patterns of the epidemiological status The development of the diabetes process, the solution of problems related to the increase in the prevalence of diabetes are numerous studies that are currently becoming a priority. The situation in Uzbekistan follows the global trend. According to 2019 data, 230 610 patients with diabetes are registered in the country: 18 349 patients with type 1 diabetes and 212 261 - with type 2 diabetes. According to screening studies, the prevalence of type 2 diabetes in Uzbekistan over the past 14 years has increased 1.6 times and, according to the latest data (2015), is hypoglycemic therapy 7.9% among people over 35 years old [1,3]. Despite the variety of drugs, satisfactory glycemic control is achieved in no more than 40% of patients. The standard treatment regimen for type 2 diabetes, both in domestic and international recommendations, involves monotherapy with metformin at the onset of the disease (sometimes in combination with another drug for high hyperglycemia). The long-term management of type 2 diabetes was mainly aimed at glycemic control. A meta-analysis based on the results of 4 fundamental studies of diabetology (ACCORD, ADVANCE, UKPDS and VADT), which includes more than 27 thousand patients with type 2 diabetes, confirmed the primacy of intense glycemia for the prevention of chronic microvascular diseases of type 2 diabetes, including diabetic damage [4]. The pathogenetic multifactoriality and morphological heterogeneity of DN make one think about how universal the mechanisms of nephroprotection are. Taking into account the key role of hyperglycemia in the pathogenesis of DN, in recent years, the nephroprotective properties of hypoglycemic agents have been actively studied, since, apparently, any drug that corrects hyperglycemia can have a moderate beneficial effect on the development of DN. However, it is still unclear whether different hypoglycemic drugs are equally effective in slowing the progression of renal dysfunction in diabetes mellitus [5]. Treatment of patients with DN in type 2 diabetes with the appointment of iDPP-4 promotes an increase in the level of endogenous GLP-1, improvement of its functioning, which in turn leads to the restoration of the function of GLP-1 receptors in the structures of the kidneys and vascular endothelium [6], reducing the effect of oxidative stress and suppresses excessive proliferation [7,8]. In addition, the multiple nephroprotective effects of iDPP-4 may possibly have a relationship with metamorphoses of the profile of the substrates of iDPP-4 action [9]. The circulating

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form of DPP-4 is involved in the degradation of neuroregulatory peptides, hormones, intermediates, and growth factors. DPP-4 has natriuretic properties, has an anti-inflammatory effect, and also promotes vasodilation and direct protection of renal cells [10]. Over the past 2 decades, the pharmacotherapy of type 2 diabetes has been supplemented by several new classes of antihyperglycemic drugs (ADP) with different mechanisms of action. These classes of drugs, in addition to a positive effect on carbohydrate metabolism, have the ability to correct other metabolic disorders that are risk factors for the development and progression of type 2 diabetes [11,14]. Among them, inhibitors of sodium-glucose cotransporters type 2 (iSGLT-2), or gliflozins, are effective not only for their pronounced positive metabolic effects, but also for their ability to correct hemodynamic disorders, reducing intraglomerular hypertension and systemic arterial pressure, which can potentially have a nephroprotective effect. [12]. Thus, due to their unique mechanism of action, inhibitors of the sodium-glucose co-transporter type 2, in addition to glycemic and metabolic effects, have the ability to exert an inhibitory effect on various aspects of the pathogenesis of micro- and macro vascular complications of diabetes mellitus. Further large-scale clinical trials should provide information on which groups of patients with type 2 diabetes mellitus can benefit most from the prescription of gliflozin while minimizing the risk of adverse events[13,15].

OBJECTIVE

To study of the effect of prescribing inhibitors of sodium glucose cotransporter type 2 (iSGLT-2) and inhibitors of dipeptidyl peptidase-4 (iDDP-4) on the parameters of carbohydrate metabolism in patients with type 2 diabetes.

MATERIAL AND METHODS

A prospective study included 80 patients with type 2 diabetes the average age was 52.7 ± 3.78 years, diabetes experience - 8 years; BMI-30 ± 0.17; Hb1C-9.2 ± 0.4%; fasting glycemia – 10.2 mmol/; eGFR-78 ml/min; TG-2.7 ± 0.44; total cholesterol-3.4 ± 0.72; MAU 32 ± 0.125. To study the effect of various hypoglycemic therapy regimens on the functional state of the kidneys in type 2 diabetes mellitus, the patients were divided into 2 groups: group 1 - 30 patients with DN with impaired renal function and 30 patients with diabetic nephropathy without renal dysfunction in the presence of metformin + inhibitors. sodium-glucose cotransporter type 2 (iSGLT-2); 2 group of 30 patients with impaired renal function and 30 patients with diabetic nephropathy without impaired renal function on the background of metformin + dipeptidyl peptidase-4 inhibitors (iDPP-4). The diagnosis of diabetes and complications was confirmed by clinical and laboratory research methods and consultations of narrow specialists, according to the WHO classification. Clinical examination was carried out at the Republican Specialized Scientific-and-Practical Medical Centre of Endocrinology named after Academician Ya.Kh.Turakulov under the Ministry of Health of the Republic of Uzbekistan.. Clinical condition of patients - physical examination (BMI, BP, PS).Examination of patients included: collection of anamnesis, complaints, consideration of concomitant pathology, constancy of drug treatment. An assessment of the compensation of type 2 diabetes was carried out, taking into account the self-control of glycemia. The indicators of fasting glucose (after 8 hours of eating) and after 2 hours of starting to eat were taken into account.

Glycemia was determined on an automatic biochemical analyzer BS-380 "Mindray" by

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glucose oxidase method in venous blood on an empty stomach using HUMAN Glucose reagents (Germany). TSH) using kits from Cypress Diagnostics (Belgium). According to the WHO criteria (2003): Glycated hemoglobin (HbA1c) was determined by the using the HbA1c analyzer (automatic machine) Huma Nex A1c with HUMAN reagents (Germany).

RESEARCH RESULTS AND DISCUSSION

The study of the effect of the inclusion of drugs iSGLT-2 (group 1) and iDPP-4 (group 2) showed a positive dynamics of carbohydrate metabolism indicators in patients with type 2 diabetes. So if the initial indicators in the groups were comparable in terms of glycemic control indicators, then by the 3rd month of treatment there was a significant decrease in HbA1c in the 1st group of patients in relation to the 2nd group. The decrease in HbA1c in the 1st group occurred by 9.8% (9.2 ± 0.4% versus 8.3 ± 0.12%; P <0.05), while in the 2nd group by 7.9 % (8.8 ± 0.7% versus 8.1 ± 0.6%; P> 0.05) which is almost 2% lower.

The intergroup difference in the dynamics of treatment after 3 months was significant, as the percentage between the initial data and after 3 months in the 1st group was almost 2 times higher than the data of the 2nd group (24.9% and 19.8% versus 14, 1% vs. 16.8%; P <0.05). A similar trend was observed in the next 3 months. In the next 3 months, there is a decrease in fasting glycemia in the 1st group by 29.9%, while in the 2nd group by 19.8%, which is significantly low (P <0.05). The level of postprandial glycemia within 6 months in both the 1st and 2nd groups significantly decreases in relation to the initial data, however, in the 1st group it is significantly pronounced - by 25.6% and by 19.9% (P <0.05). The content of HbA1c after 6 months decreased by 25% in the 1st group of patients with diabetes mellitus 2 and by 10.2% in the 2nd group (P <0.05). The reason for these differences is nocturnal hypoglycemia. The lack of flexibility in titrating the dose and taking each of the components of the drug separately leads to the fact that, in parallel with an increase in the dosage of metformin, the dosage of iDPP-4 also increases, as a result of which the hypoglycemic effect of the combination increases significantly and the frequency of hypoglycemia increases. It is because of the lower frequency of hypoglycemia on therapy with metformin and iSGLT-2 that a larger number of patients managed to achieve the goals of therapy both in terms of the level of glycated hemoglobin, fasting glycemia and 2 hours after a meal, and in terms of three indicators simultaneously both after 3 months and after 6 months. therapy.

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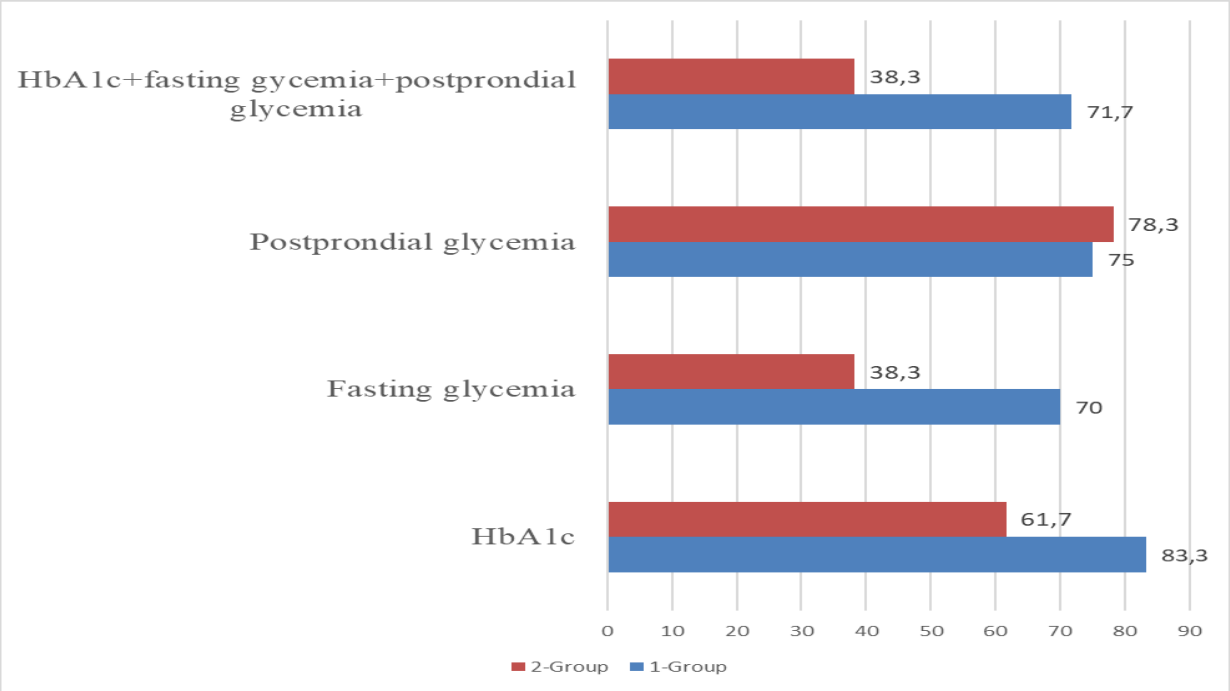
The proportion of patients (%) in the groups that achieved the goals of therapy for the level of HbAlc, fasting glycemia, 2 hours after a meal and three indicators of glycemic control simultaneously.



The result of the correction performed within 3 months was the achievement of the state of compensation in the 1st group in 36.7%, and in the 2nd group in 28.3%, 48.3% of the patients of the 1st group were brought into the state of subcompensation and 31.7 % of patients of the 2nd group. The percentage of the occurrence of decompensation was higher in the 2nd group (40%) in relation to the 1st group (30%). Over the next 3 months, the main indicators of carbohydrate metabolism continued to improve, which led to an increase in the number of patients who reached a state of compensation by the end of 6 months of the study in group 1 - in 60.0% of patients, and in the second group it was almost 2 times less - in 31.7% of patients (P <0.05).

CONCLUSION

On the combination of metformin and iSGLT-2, a larger number of patients managed to achieve the set goals of therapy with a lower risk of overt hypoglycemia, then this combination should be considered not only more effective. Compensation of carbohydrate metabolism plays a key role in preventing the development and slowing the progression of CKD in patients with type 2 diabetes. In the late stages of CKD, the compensation of carbohydrate metabolism is extremely difficult due to the high risk of hypoglycemia due to a decrease in renal

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gluconeogenesis, accumulation of insulin, hypoglycemic agents and their metabolites, and the unreliability of HbA1c values in developing anemia. Thus, great care and an individual approach is required when choosing and intensifying antihyperglycemic therapy in patients with DN.

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