

Pros and Cons of Using a Combination of Glucose-Lowering Drugs, In Particular Dpp-4 Inhibitors and Metformin in Patients with Type 2 Diabetes and Overweight

Kurbanova Nozima Sobirdjanovna

Assistant of the Department of Endocrinology, Samarkand State Medical University

Sa'dinov Siyovush, Turdialiyev Mirkomil, Toshqulov Zoyirjon, Omonova Dilorom

Students of the Samarkand state Medical University

Abstract: Relevance. In practice, when prescribing therapy, it is important to find a balance between the optimal glucose-lowering activity of the drug and a favorable safety profile in relation to body weight. In recent decades, new classes of drugs have emerged for the treatment of T2DM that do not affect body weight or even reduce it. Also, the arsenal of therapy for the treatment of obesity has been replenished with drugs that combine the ability to reduce body weight and compensate for carbohydrate metabolism. The article presents data on modern therapy for obesity and T2DM and options for optimal therapeutic combinations. The beginning of the new millennium was marked by an epidemic of non-communicable diseases. Since the 1980s The prevalence of obesity has doubled, and type 2 diabetes mellitus (T2DM) has increased by almost 2.5 times. The number of people with metabolic disorders continues to progressively increase, significantly exceeding all existing expert forecasts [1]. There are several possible explanations for this: first, increased food availability has led to a significant increase in average daily caloric intake (in the United States, this indicator increased by 24.5%, or ~530 calories between 1970 and 2000) [2]; secondly, a change in diet with an increase in the consumption of refined carbohydrates, sugar, animal and vegetable fats and a decrease in the consumption of fruits, vegetables and legumes; thirdly, due to the mechanization of labor and the development of transport, energy costs have significantly decreased; fourthly, thanks to the improvement of clothing and heating systems, the importance of adaptive thermogenesis has decreased [3]. At the same time, the contribution of genetic factors to the development of obesity should not be overestimated: it is only about 20%; the development of the pandemic of metabolic disorders is mainly due to environmental factors [4]. About 80% of patients with T2DM are overweight or obese. It has been proven that obesity and T2DM are closely related pathogenetically. Data from extensive epidemiological studies confirm the role of excess body weight in the development of carbohydrate metabolism disorders [10]. Timely weight loss not only slows the progression of prediabetes to diabetes, but also leads to improved glycemic control and a reduced need for glucose-lowering drugs in T2DM. Weight loss is most effective in the early stages of T2DM, when β -cell dysfunction is still reversible [5].

Key points: DPP-4, metformin, type 2 diabetes mellitus, GFR, overweight, obesity.

Introduction. Obesity and type 2 diabetes mellitus (T2DM) are epidemics of the 21st century. Obesity is one of the main risk factors for developing T2DM, so it is often possible to diagnose both diseases in the same patient. The presence of both diseases in a patient creates difficulties both in normalizing carbohydrate metabolism and in achieving normal body weight. Many glucose-lowering drugs lead to weight gain, which, in turn, contributes to an increase in insulin resistance and requires further intensification of glucose-lowering therapy.

Target– to evaluate the effect of sitagliptin in combination with metformin on glucotoxicity and lipotoxicity in patients with type 2 diabetes mellitus (T2DM) and overweight.

Material and methods. The study involved 82 patients (55 women, 27 men, mean age 56.1 ± 5.47 years) who did not achieve target HbA1c levels (mean HbA1c level $8.3 \pm 1.6\%$) on metformin monotherapy and on diet therapy. having excess weight, lipid metabolism disorders. Group 1 of patients (42 people) received a combination of sitagliptin and metformin; Group 2 (control) patients (40 people) – metformin 1.5–2.0 g/day. All patients at baseline and after 6 months were assessed over time the level of fasting glycemia, postprandial glycemia, glyated hemoglobin, weight, BMI, WC, WC/TB, insulin, leptin, adiponectin, insulin resistance using the HOMA-IR index, functional activity of β -cells by HOMA- β index.

Research results. After 6 months, patients in both groups showed significant positive dynamics in the levels of fasting glucose, postprandial glycemia and glyated hemoglobin. In group 1, there was a decrease in HbA1c levels from 8.3 ± 1.6 to $6.6 \pm 1.24\%$ ($p < 0.01$), in group 2 – from 8.35 ± 1.75 to $7.62 \pm 1.39\%$ ($p < 0.01$). FPG and PPG levels in group 1 decreased by an average of 2.67 and 3.3 mmol/l, respectively, in group 2 – by 2.1 and 1.8 mmol/l. IRI in group 1 decreased by 3.45 μ U/ml, in group 2 – by 1.63 μ U/ml ($p = 0.05$). HOMA – increased in the 1st group by 23.4 conventional units, in the 2nd group – by 4.8 conventional units. ($p < 0.005$). There are no significant differences between the groups in the dynamics of HOMA-IR; positive dynamics are observed in both groups. There was a significant difference in the dynamics of adiponectin levels between the groups; in group 1 there was an increase of 1.9 ng/ml, in group 2 – by 0.49 ng/ml ($p < 0.01$). Leptin in group 1 decreased by 7.37 ng/ml, in group 2 – by 1.21 ng/ml ($p < 0.01$). There are significant differences in the dynamics between groups in anthropometric indicators ($p < 0.001$). Weight loss in group 1 was by 4.9 ± 3.2 kg, in group 2 – by 2.0 ± 0.94 kg on average. BMI in group 1 decreased by 1.8 ± 1.3 , in group 2 – by 0.68 ± 0.3 . WC in group 1 decreased by 6.5 ± 4.7 cm, in group 2 – by 2.42 ± 1.02 cm. WC/TB in group 1 decreased from 0.95 ± 0.06 to 0.91 ± 0.05 cm, in group 2 – from 0.94 ± 0.03 to 0.93 ± 0.03 cm. During treatment, no episodes of hypoglycemia were recorded in any of the groups.

Conclusions. Combination therapy with sitagliptin and metformin resulted in a decrease in glucotoxicity and lipotoxicity, which overall led to improved glycemic control.

References:

1. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamurodova NN, Daminov AT. TIME-RESTRICTED NUTRITION AS A NEW STRATEGY FOR THE THERAPY OF OBESITY AND COMORBID CONDITIONS. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):660-667.
2. Takhirovič DA, Nasimova D, Xushvaqtova B, Aliyeva N, Mirabrór B. QUALITY OF MEDICAL CARE PROVIDED TO CHILDREN WITH TYPE 1 DIABETES MELLITUS. *PEDAGOG*. 2024;7(3):16-22.
3. Xoldorov X, Omonov F, Jumayev I, Daminov AT. TYPE 1 DIABETES AS A RISK FACTOR FOR BONE HEALTH IN CHILDHOOD. *Results of National Scientific Research International Journal*. 2023;2(8):131-135.
4. Daminov AT, Xurramova S, Islomov A, Ulashev M, Ikramov R, Mirzakhakimov P. Type 2 diabetes and bone mineral density in postmenopausal women. *Science and Education*. 2023;4(11).
5. Berkinov A, Safarov F, Tursunova S, Daminov AT. VITAMIN D STATUS IN SENIOR RESIDENTS OF SAMARKAND REGION. *Results of National Scientific Research International Journal*. 2023;2(8):136-140.
6. Taxirovič DA, Ulugbekovna RN, Abduxalimova YJ. STATUS AND PROSPECTS FOR THE FIGHT AGAINST DIABETES MELLITUS. *Educational Research in Universal Sciences*. 2024;3(1):4-9.

7. Davranova A. QALQONSIMON BEZ PATOLOGIYASI BO'LGAN O'SMIR QIZLARDA HAYZ DAVRINING BUZILISHINI O'ZIGA XOSLIGI. *Евразийский журнал медицинских и естественных наук*. 2022;2(8):113-115.
8. Хамраев Х, Содиков С, Хамраева Д, Собирова Д. Клинико-функциональное состояние печени у больных с сахарным диабетом. *ЖПБМ*. 2018;(1 (99)):189-191.
9. Содиков С, Каримова Н, Каримова З. Реабилитация больных пожилого возраста сахарным диабетом 2-типа. *ЖПБМ*. 2017;(4 (97)):105-106.
10. Хамидова МН, Исматова ИФ, Бердиев ЖШ, Негматова ГШ, Даминов АТ. САХАРНЫЙ ДИАБЕТ И COVID-19. *Eurasian Journal of Medical and Natural Sciences*. 2022;2(13):190-204.
11. Шухратовна СД, Кахрамонович ЮУ, Махмудович КТ. Структурные изменения сосудисто-стромального комплекса щитовидной железы при эутиреоидной и токсических формах зоба. *Научный журнал*. 2019;(10 (44)):67-69.
12. Собиржонова КН, Саллохидинович СС, Акбаровна ОМ. Эпидемиологический Статус И Факторы Риска Сахарного Диабета На Сегодняшний День. *Miasto Przyszłości*. 2023;32:212-219.
13. Salimova DE, Daminov AT. A CLINICAL CASE BASED ON THE EXPERIENCE OF TREATING HYPERTENSION IN A PATIENT WITH TYPE 2 DIABETES MELLITUS, OBESITY AND VITAMIN D DEFICIENCY. *Educational Research in Universal Sciences*. 2023;2(12):150-154.
14. Takhirovich DA. ASSESSMENT OF HEARING FUNCTION IN INDIVIDUALS WITH TYPE 2 DIABETES. *American Journal of Pediatric Medicine and Health Sciences (2993-2149)*. 2023;1(9):124-126.
15. Qahramonov FA, Amirov BY, Tursunboyeva LI, Daminov AT. Autoimmun tireoidit bilan kasallangan bemorlardagi funksional buzilishlarning differensial diagnostikasida qalqonsimon bez zichligini aniqlash. *Science and Education*. 2023;4(3):82-86.
16. Nazira K, Siddikovna TG, Davranovna DA, Takhirovich DA, Tulkinovich OS. Cardiovascular complications in patients who have had covid on the background of diabetes mellitus 2. *1*. 2021;2(3):37-41.
17. Choriyev S, Gadoeva Z, Mardonova F, Jurakulov F, Hafizov S, Daminov AT. Changes in the thyroid gland in the long period after a new coronavirus infection. *Science and Education*. 2023;4(12):102-106.
18. Kamalov T, Bahriev N, Yuldashev U, Sabirova D. CLINICAL AND HORMONAL CHARACTERISTICS OF PRIMARY HYPOGONADISM IN PRESCHOOL BOYS. *MedFarm*. 2019;10(9). doi:10.32743/2658-4093.2019.9.10.188
19. Daminov AT, Yuldoshev B, Murodullo I, Naimova N. CLINICAL CASE OF PRIMARY HYPOTHYROIDISM. *Educational Research in Universal Sciences*. 2024;3(3 SPECIAL):135-138.
20. Daminov AT, Norkulov A, Turamudov R, Zayniddinova D. CLINICAL OBSERVATION OF SEVERE ITSENKO-CUSHING DISEASE. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):549-556.
21. Daminov A, Khaydarov O, Hasanova M, Abdulkahorova R. COMPLICATIONS OF GLUCOCORTICOID THERAPY IN PATIENTS DIABETES SURVIVED COVID-19. *Евразийский журнал медицинских и естественных наук*. 2023;3(4):197-200.
22. Takhirovich DA, Corners SJA, Shukhratovna NG, Shukhratovna SG, Zaynuddinovna MG. COURSE OF COVID-19 IN PATIENTS WITH DIABETES MELLITUS. *Web of Scientist: International Scientific Research Journal*. 2022;3(02):73-76. doi:10.17605/OSF.IO/B6FU2

23. Shukhratovna NG, Erkinovna SD, Suxrobovna XM, Ikromovna AZ. DIABETES MELLITUS, ISCHEMIC HEART DISEASE AND ARTERIAL HYPERTENSION. *PEDAGOG*. 2022;5(5):381-386.
24. O'g'li SOS, O'g'li RSO, Taxirovich DA. DIFFUZ TOKSIK BUQOQ. *Личные интеллектуальные исследования*. 2023;4(1):131-133.
25. Negmatova GS, Toshimova GT qizi, Abdiyev LS o'g'li, Daminov AT. EFFECTIVENESS OF CORRECTION OF DYSLIPIDEMIA IN ELDERLY PATIENTS WITH TYPE 2 DIABETES MELLITUS. *Educational Research in Universal Sciences*. 2024;3(1 SPECIAL):269-274.
26. G.Sh N, D.e S, Oybekovna XS, Qamariddinovna XA, O'g'li BJA. ENDOCRINE GLANDS, STRUCTURE, AGE FEATURES, FUNCTIONS. *PEDAGOG*. 2022;5(5):341-345.
27. Sobirjonovna KN. FACTORS DETERMINING THE CLINICAL SIGNIFICANCE OF DEPIPTIDYL PEPTIDASE 4 INHIBITORS IN THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS. *World Bulletin of Public Health*. 2022;8:67-72.
28. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamuradova NN, Daminov AT. FAMILY FORM OF NEPHROGENIC X-LINKED DIABETES INSUPLIUS. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):703-710.
29. Daminov AT, Djabbarova D, Abduvohidova N, Furkatova D, Farxodova S, Ibragimova P. Features of bone tissue remodeling in patients with type 2 diabetes mellitus. *Science and Education*. 2023;4(11).
30. Daminov Abdurasul Takhirovich RSU. FEATURES OF THE CLINIC, REHABILITATION, TREATMENT OF AUTOIMMUNE THYROIDITIS IN THE CONDITIONS OF THE IODINE-DEFICIENCY REGION. Published online April 12, 2023. doi:10.5281/ZENODO.7820412
31. Shuhratovna NG, Shukhratovna SD. Features of the course of autoimmune hepatitis in children as a variant of autoimmune polyglandular syndrome. *Asia Journ of Multidimensi Resear (AJMR)*. 2020;9(7):89. doi:10.5958/2278-4853.2020.00228.1
32. Erkinovna SD. Features of the Course of Diabetes Mellitus Type 2 with Arterial Hypertension. *JournalNX*. Published online 2020:460-461.
33. Negmatova GS, Xakimova GD qizi, Abdiyev LS o'g'li, Daminov AT. FEATURES OF THE RULES FOR INSULIN INJECTION TECHNIQUES IN ELDERLY AND SENILE PATIENTS WITH DIABETES MELLITUS. *Educational Research in Universal Sciences*. 2024;3(1 SPECIAL):259-264.
34. Takhirovich DA, Zafarovna KM, Isroilovna IS. FEATURES OF TYPE 1 DIABETES IN CHILDREN WHO HAVE COVID-19. *American Journal of Pediatric Medicine and Health Sciences (2993-2149)*. 2023;1(9):121-123.
35. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamuradova NN, Daminov AT. FEATURES OF VITAMIN-D METABOLISM IN PATIENTS WITH DIABETIC NEPHROPATHY. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):681-689.
36. Xudoyorov S, Mirkomilova M, Burxonov U, Sayfieva G, Sheralieva N, Daminov AT. Fourniers gangrene in modern conditions. *Science and Education*. 2023;4(12):107-117.
37. Alimovna KN, Sobirjanovna KN, Abdurasul D, Tulkinovich OS. GROWTH HORMONE FOR THE TREATMENT OF HEREDITARY DISEASES IN CHILDREN. 10.
38. Negmatova .G.Sh, D.e S, Qizi MZO, Mannobovich MS, Orifjonovich MM. HERPETIC MENINGITIS. *PEDAGOG*. 2022;5(5):346-348.
39. Ahrorbek N, Myungjae L, Jungjae L, et al. Hormonal Regulation. *Texa Jour of Mutl Stud*. 2023;25:39-43.