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Poltava State Medical University, Poltava, Ukraine

Optimized treatment of elderly patients with type 2 diabetes mellitus and hypertension in general practice

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Abstract. Background. Population aging has become a leading demographic feature of Ukraine. According to the World Health Organization, the number of elderly and senile people will increase to almost 40 % in the coming decades. Hypertension and type 2 diabetes mellitus (DM) are among the leading factors of cardiovascular risk. It is known that excessive oxidant stress and low-grade subclinical chronic systemic inflammation are determining factors of endothelial dysfunction, vascular reactivity disorders, increased peripheral vascular resistance, carbohydrate, and lipid metabolism disorders, which leads to increased blood pressure and plasma glucose levels. Hypertension and type 2 DM are among the leading cardiovascular risk factors. The purpose of the study was to increase the effectiveness of treatment and improve the quality of life of elderly patients with combined pathology of hypertension and type 2 DM by additional inclusion of empagliflozin and L-arginine in the basic therapy. **Materials and methods.** Fifty elderly patients with comorbid pathology were under our observation for second stage hypertension, coronary heart disease (functional class II) and type 2 DM in the stage of subcompensation. Participants were divided into two groups: the first one, controls (n = 25), received generally accepted basic therapy. In the second group (n = 25), the following drugs were added to the basic therapy: empagliflozin 10 mg/day, L-arginine 300 mg/day. **Results.** Clinical observation in outpatient conditions lasted for 3 months. Comprehensive therapy in the elderly patients with comorbid pathology of hypertension and type 2 diabetes, with the additional inclusion of empagliflozin and L-arginine to the basic therapy, contributes to a significant positive effect on the clinical course, reduces the risk of progression of this constellation. **Conclusions.** The application of the proposed comprehensive therapy in outpatient conditions under the control of a family doctor will significantly improve the quality of life of patients and prevent the development of complications.

Keywords: hypertension; type 2 diabetes mellitus; elderly patients; empagliflozin; L-arginine

Introduction

Population aging has become a leading demographic feature of Ukraine. According to the World Health Organization, the number of elderly and senile people will increase to almost 40 % in the coming decades [1, 2]. Hypertension and diabetes mellitus (DM) type 2 are among the leading factors of cardiovascular risk [3]. It is known that excessive oxidant stress and low-grade subclinical chronic systemic inflammation are determining factors of endothelial dysfunction, vascular reactivity disorders, increased peripheral vascular resistance, carbohydrate and lipid metabolism disorders, which leads to increased blood pressure (BP) and plasma glucose levels [4]. With the growing burden of metabolic

disease, cardiovascular disease, and diabetes mellitus, there is an implication for new pharmacological intervention. Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a class of drugs that work on SGLT2 receptors in the kidneys to decrease glucose reabsorption. Lowering glucose levels mainly aids those with type 2 DM, but they also have many other effects on the body [5].

L-arginine, an endogenous amino acid, is a safe substance that can be found in food. The compound is involved in synthesis of various products responsible for regulatory functions in the body. Among others, nitric oxide, a signaling molecule regulating carbohydrate and lipid metabolism, is particularly noteworthy. The increasing experimental and



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Для кореспонденції: Муравльова Оксана Василівна, кандидат медичних наук, доцент, завідувач кафедри ендокринології з дитячими інфекційними хворобами, Полтавський державний медичний університет, вул. Шевченка, 23, м. Полтава, 36011, Україна; e-mail: endocrinology@pdmu.edu.ua, o.muravlova@pdmu.edu.ua, mur_ov_pdmu@ukr.net; тел.: +380(50)7619084

For correspondence: Oksana Muravlova, PhD, Associate Professor, Head of the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Shevchenko Street, 23, Poltava, 36011, Ukraine; e-mail: endocrinology@pdmu.edu.ua, o.muravlova@pdmu.edu.ua, mur_ov_pdmu@ukr.net; phone: +380(50)7619084

Full list of authors' information is available at the end of the article.

clinical data indicate that L-arginine supplementation may be helpful in managing metabolic disorders in obesity, regulating blood pressure or alleviating type 2 DM symptoms, but the mechanisms underlying these effects have not been sufficiently elucidated [6]. Any improvement in endothelial function contributes to the prevention of cardiovascular diseases. As a functional amino acid, L-arginine serves not only as a building block of protein but also as an essential substrate for the synthesis of nitric oxide (NO), creatine, polyamines, homoarginine. NO (a major vasodilator) increases blood flow to tissues and contributes to a moderate reduction of systolic (SBP) and diastolic blood pressure (DBP) [7, 8].

Psychosocial stress has been long known to have deleterious effects on health and is considered a modifiable risk factor for stroke. Given the prevalence of chronic and acute exposure to stress, it represents a potentially attractive target for population-health interventions [9]. It is also known that with age, there is an increase in sensitivity to humoral influences (in particular, adrenaline), which leads to increased sensitivity of the myocardium of older people to stressors [10]. Also, improvements in the circadian rhythm of blood pressure under the influence of treatment that improve the quality of sleep have been noted [11].

The aim of the study was to increase the effectiveness of treatment and to improve the quality of life of elderly patients with combined pathology of hypertension and type 2 DM with the help of additional therapy with empagliflozin and L-arginine.

Materials and methods

We monitored 50 elderly patients with comorbid pathology of second-stage hypertension, coronary heart disease: functional class II angina pectoris and type 2 DM in the subcompensation stage. Duration of disease was more than 10 years. Patients gave informed consent in compliance with the principles of bioethics and deontology during the study in accordance with the principles of the Declaration of Helsinki.

The average age of the patients was 66.8 ± 2.3 years. Clinical diagnoses were determined in accordance with the Order of the Ministry of Health of Ukraine dated May 24, 2012 No. 384 and the current Unified Clinical Protocols “Hypertension” of 2016, Order of the Ministry of Health of Ukraine dated December 23, 2021 No. 2857 “Stable Ischemic Heart Disease” and Order of the Ministry of Health of Ukraine of December 21, 2012 No. 1118 “Unified Clinical Protocol of Primary and Secondary (Specialized) Medical Care for Type 2 Diabetes”, as well as new 2023 European Society of Cardiology guidelines [12]. Patients were examined using general clinical, laboratory and instrumental methods.

BP measurement in the elderly patients with hypertension and diabetes was carried out after 5 minutes at rest on both arms. To rule out possible orthostatic hypertension, BP was measured after 1 and 3 minutes in a standing position. Thickening of the common and internal carotid artery walls, or the presence of atherosclerotic plaques, as well as intima-media thickness (IMT) were determined using duplex scanning on an ultrasound scanner ACCUVIX A30 (Sam-

sung Medison, South Korea) with a linear sensor in B-mode in three places on distance of 1.5 cm from the bifurcation of the distal part of the right and left common carotid artery, internal carotid artery along the anterior wall.

The diagnostic criterion for increased IMT was considered to be ≥ 0.9 mm, the presence of an atherosclerotic plaque was noted with local thickening of $IMT \geq 1.5$ mm or thickening of more than 50 % of the lumen of the vessel, or 0.5 mm according to other areas of IMT. Endothelium-dependent vasodilation (EDV) was calculated using the formula: $EDV = (d60 - d0) \times 100 \% / d0$, where $d60$ is the diameter of the brachial artery (BA) 60 seconds after the restoration of blood circulation, $d0$ is the initial diameter of the brachial artery. Endothelium-dependent vasodilation is calculated by the difference in the diameter of the artery. Endothelial dysfunction was considered to be at $< 10 \%$ EDV BA [13].

Parameters of plasma hemostasis were determined: levels of fibrinogen, activated partial thromboplastin time (aPTT). Blood lipids were studied: the levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein (LDL-C) cholesterol. Careful monitoring of the following indicators was carried out: glycated hemoglobin (HbA1c), BP and body mass index (BMI). The psychological state of the patients was determined using Spielberger-Khanin questionnaire. The results were evaluated in points: less than 30 points — low anxiety; 31–45 — moderate anxiety; 46 or more points — high anxiety [14].

Statistical processing of the results was carried out using Prism5 (version 5/03) Microsoft Excel 2010 software packages, methods of descriptive statistics and statistical analysis. The probability of the obtained results was determined using the Student's t-test of reliability. Differences were considered insignificant at the probability of error $P < 0.05$ generally accepted in medical and biological research. Correlation between quantitative indicators was assessed using the Pearson correlation coefficient (r). All patients were given personalized motivational recommendations for lifestyle changes: a rational diet with a restriction of salt (up to 5 g per day) and simple carbohydrates, a decrease in the consumption of saturated fats and trans fats, and an increase in polyunsaturated fatty acids and dosed fiber; dosed physical activity: slow walking for 40 minutes 4 times a week; careful control of glycemia, monitoring of BP and body weight at home.

The patients were divided into two groups. The first one (controls, $n = 25$) received the generally accepted basic therapy: angiotensin-converting enzyme inhibitor — perindopril, calcium antagonist — amlodipine, antiplatelet agent — acetylsalicylic acid, statin — rosuvastatin, glucose-lowering therapy — metformin. The second (main) group ($n = 25$) had the following drugs added to the basic therapy: SGLT2 inhibitor empagliflozin 10 mg/day and L-arginine 300 mg/day. Clinical observation in outpatient conditions lasted for 3 months.

Results

Before the beginning of treatment, all elderly patients with comorbid pathology of hypertension and type 2 DM had complaints of headache, dizziness was noted in 43

(86 %) cases, sleep disorders in 48 (96 %), periodic pain in the lower limbs when walking in 46 (92 %), periodic seizures in 26 (52 %), weakness in the legs in 36 (72 %), nervous tension, or irritability and restlessness were noted by all patients (100 %). The listed complaints testified to characteristic clinically significant symptoms of macroangiopathy and psychopathological disorders, which significantly worsen the prognosis and the process of social adaptation of the elderly.

The average duration of reduction of the main clinical symptoms (headache) in the main group was 4.30 ± 0.33 days, while in the comparison group 5.90 ± 0.41 days ($P < 0.05$); normalization of sleep — 5.10 ± 0.44 days, and 6.40 ± 0.38 days in the controls ($P < 0.05$). The obtained results show that in patients of the main group, the normalization of sleep, reduction of clinical symptoms such as headache occurred in a shorter time.

The average level of reactive anxiety (RA) in patients of the main group before treatment was 47.8 ± 2.2 points, which indicates its high level. Clinically, this was manifested by a feeling of mildly and moderately expressed anxiety, worry, sleep disturbances. After treatment, the anxiety was 40.10 ± 2.94 points, decreased by 16.1 % ($P < 0.05$). The average level of personal anxiety (PA) before treatment in the comparison group was 47.20 ± 3.12 points, after treatment, it decreased not significantly, by 9.1 %, and was 42.9 ± 2.5 points ($P > 0.05$). There were no significant differences in the level of PA after the course of therapy. The obtained results allow us to state that comprehensive therapy significantly reduces the level of RA, contributes to the normalization of sleep and improves the quality of life of patients.

The comparative evaluation of the integral standard indicator of carbohydrate metabolism in patients of the main group demonstrated a significant decrease in the average level of HbA1c by 14.1 % (before treatment, it was 7.70 ± 0.33 %, after treatment — 6.52 ± 0.41 %) ($p < 0.05$), while in the controls, HbA1c decreased not significantly, by 9 %, from 7.45 ± 0.65 % to 6.78 ± 0.51 ($P > 0.05$). It can be assumed that the hypoglycemic effect of empagliflozin and

L-arginine is due to a positive impact on the regulation of insulin synthesis and release, an increase in its content in the blood, a decrease in insulin resistance and an increase in the sensitivity of tissues to insulin, an increase in the utilization of glucose, which coincides with the opinion of scientists [15, 16].

After the treatment, SBP and DBP decreased significantly in patients of the main group. SBP reduced in them by 25.5 % (from 175.2 ± 4.1 mmHg before treatment to 131.40 ± 3.63 mmHg after it) ($p < 0.05$), while in the controls — by 19.1 % (from 172.80 ± 4.52 mmHg to 137.4 ± 3.5 mmHg) ($P < 0.05$). DBP in the research group decreased by 25.2 % (from 96.4 ± 4.2 mmHg to 73.2 ± 6.1 mmHg) ($p < 0.05$), in the control group, a non-significant decrease in diastolic blood pressure by 16.4 % was noted (from 94.7 ± 5.9 to 79.2 ± 6.8) ($P > 0.05$). The obtained results convincingly prove the positive therapeutic effect of comprehensive therapy with the use of empagliflozin and L-arginine, which contributes to increasing the effectiveness of antihypertensive drugs.

After the course of therapy, an improvement in the blood lipids was noted. A more significant positive trend was observed in the level of TG ($p < 0.05$): in the main group, it decreased by 25.7 % (from 1.91 ± 0.12 mmol/l to 1.42 ± 0.18 mmol/l) ($p < 0.05$), while in the controls by 17.1 % (from 1.88 ± 0.20 mmol/l to 1.56 ± 0.13 mmol/l) ($p > 0.05$). Under the influence of comprehensive therapy, there was a significant decrease in the level of fibrinogen by 12.1 % (before treatment, it was 4.53 ± 0.16 , after treatment 4.01 ± 0.21 g/l) ($p < 0.05$) in the main group, while in the comparison group, it reduced only by 7.2 % (from 4.41 ± 0.34 to 4.14 ± 0.29 mmol/l) ($p > 0.05$).

After the course of therapy, the patients of the main group reported an increase in the level of aPTT to 23.70 ± 0.55 seconds, while in the controls, this indicator did not increase significantly and was 21.8 ± 0.8 seconds ($p < 0.05$). An increase in the level of fibrinogen and a decrease in aPTT indicates the activation of coagulation hemostasis in the elderly with comorbid pathology of hypertension and type 2 DM. After a course of comprehensive therapy, a decrease in

Table 1. The results of laboratory-instrumental studies in the elderly patients with comorbid pathology of hypertension and type 2 DM

Indicators	Main group (n = 25)		Comparison group (n = 25)	
	Before treatment	After treatment	Before treatment	After treatment
TC, mmol/l	5.57 ± 0.64	4.13 ± 0.51	5.42 ± 0.59	4.60 ± 0.72
LDL-C, mmol/l	0.95 ± 0.13	1.12 ± 0.22	0.99 ± 0.28	1.08 ± 0.21
HDL-C, mmol/l	3.82 ± 0.23	2.90 ± 0.26	3.91 ± 0.32	3.24 ± 0.29
TG, mmol/l	$1.91 \pm 0.12^*$	1.42 ± 0.18	1.88 ± 0.20	1.56 ± 0.13
Fibrinogen, g/l	$4.53 \pm 0.16^*$	4.01 ± 0.21	4.41 ± 0.34	4.14 ± 0.26
aPTT, sec	21.3 ± 0.8	$23.70 \pm 0.55^{**}$	20.10 ± 0.76	21.80 ± 0.80
AI	$4.89 \pm 0.54^*$	2.98 ± 0.31	4.47 ± 0.42	$3.25 \pm 0.23^*$
IMT CA	$1.28 \pm 0.06^*$	1.04 ± 0.08	1.22 ± 0.09	1.130 ± 0.076
EDV BA	6.48 ± 0.31	$7.85 \pm 0.44^*$	6.31 ± 0.33	7.02 ± 0.51

Notes: * — differences before and after treatment are reliable; ** — differences are reliable between patients of the main and control groups after treatment.

the content of fibrinogen, an increase in aPTT was noted in patients of the main group, which indicates a decrease in coagulation properties and an improvement in blood rheology that coincides with the results of researchers [17].

Evaluation of the results of a carotid artery duplex scan confirmed the thickening of the intima-media of the common carotid artery. After the course of therapy, the carotid artery IMT in the main group decreased by 18.7 % (from 1.28 ± 0.06 to 1.04 ± 0.08 ($p < 0.05$)), while in the comparison group, the reduction of 7.4 % (from 1.22 ± 0.09 to 1.130 ± 0.076) was insignificant ($p > 0.05$).

In the patients of the main group, a significant increase in the absolute index of the artery diameter was noted. The EDV in patients of the main group increased by 17.9 %, from 6.48 ± 0.31 to 7.85 ± 0.44 ($p < 0.05$), while in the controls, an insignificant increase was noted — by 11.4 % (from 6.31 ± 0.33 to 7.02 ± 0.51) ($p > 0.05$). Thus, the use of L-arginine in the comprehensive treatment of elderly patients with hypertension and type 2 DM contributes to the improvement of endothelium-dependent vasodilation.

BMI showed a significant decrease in the main group after the course of therapy, by 5.7 % (from 29.9 ± 0.7 kg/m² to 28.1 ± 0.4 kg/m²) ($p < 0.05$), while in the controls, an insignificant decrease by 1.4 % was noted (from 30.1 ± 0.9 kg/m² to 29.7 ± 0.6 kg/m²). It can be assumed that comprehensive therapy with the use of empagliflozin contributes to the reduction of insulin resistance and the activation of catabolic processes such as increased lipolysis and fat oxidation, which contributes to weight loss.

After the course of therapy, 13 (52 %) patients of the main group and 5 (21 %) patients of the control group noted a reduction in the symptoms of macroangiopathy of the lower extremities ($p < 0.05$), which suggested a positive effect and the effectiveness of the proposed comprehensive therapy in the elderly.

Discussion

The pandemic of type 2 DM has become a serious public health threat [18]. A consistent downward trend in the age of type 2 DM onset even worsens the situation [19]. Mounting evidence has demonstrated that the younger the age at diabetes onset, the greater the risk of diabetes-related comorbidities, e.g., cardiovascular diseases and premature mortality [20]. The existence of “metabolic memory”, when the influence of an early glycemic exposure environment is imprinted in target cells and organs and leads to prolonged impairments even after optimal glucose control [21], emphasizes the need for the clinical priority of early identification and intervention against risk factors for type 2 DM [22].

Our study found a significant interaction between cumulative inflammation and atherogenic dyslipidemia associated with type 2 DM onset among the general population.

Endothelial dysfunction contributes to the development and progression of atherosclerosis, which leads to cardiovascular complications [23]. Among the most significant mechanisms of endothelial dysfunction, there is a disruption of the metabolism of L-arginine — NO, which is the main effector molecule produced by endotheliocytes [24]. The

results of the study indicate that the use of L-arginine in the comprehensive treatment of elderly patients with hypertension and diabetes can be successfully combined with standard hypotensive therapy and can contribute to the additional reduction of systolic and diastolic blood pressure; it also prevents the progression of the atherosclerotic process. Additional use of empagliflozin in the comprehensive therapy contributes to the blood glucose reduction through an insulin-independent mode of action, namely, increasing the excretion of glucose in the urine [5]. In addition, empagliflozin enhances the fractional excretion of sodium and has a moderate diuretic and natriuretic effect, which also helps reduce blood pressure and uric acid levels and is appropriate in the comprehensive treatment of patients prone to hypertension and type 2 DM [5].

Elderly patients with hypertension and type 2 DM have a high level of RA, poor sleep, which justifies the need to use comprehensive therapy. A reliable positive correlation found between the level of RA and blood pressure before treatment in the main ($r = 0.448$; $p < 0.005$) and comparison groups ($r = 0.385$; $p < 0.005$), between the level of HbA1c and total cholesterol before treatment in both groups ($r = 0.158$; $p < 0.005$ and $r = 0.472$; $p < 0.005$, respectively) proves that a controlled decrease in the level of HbA1c prevents the progression of atherosclerosis, long-term micro- and macrovascular events.

The use of the proposed comprehensive therapy in the elderly with hypertension and type 2 DM in the outpatient settings under the supervision of a family doctor will significantly improve the quality of life of patients and prevent the development of complications.

Conclusions

The conducted clinical observations and current laboratory-instrumental studies provide basis to claim that hypertension combined with type 2 diabetes in the elderly is a complex pathogenetic syntropy. Long-term course of combined pathology, insufficiently effective results of standard therapy, modern challenges (military actions) lead to the development of anxiety states, which significantly affects the course of comorbid pathology in the elderly patients and worsens the prognosis.

References

1. Potyazhenko MM, Nastroga TV, Sokolyuk NL, Kitura OY, Motorna NM, Korpan AS. Efficient comprehensive treatment of chronic obstructive pulmonary disease exacerbation and postcovid syndrome in elderly patients. *Wiad Lek.* 2022;75(6):1486–1491. doi: 10.36740/WLek202206111.
2. Kazakov YM, Potyazhenko MM, Nastroga TV. Treatment optimization in management of combined pathology - arterial hypertension and post-covid syndrome in elderly patients. *Wiad Lek.* 2023;76(7):1543–1548. doi: 10.36740/WLek202307105.
3. Serhiyenko V, Serhiyenko O. Diabetes Mellitus and Arterial Hypertension. *Mižnarodnij endokrinologičnij žurnal.* 2021;17(2):175–188. doi: 10.22141/2224-0721.17.2.2021.230573.
4. Pankiv V, Yuzvenko T. The Relationships Between Variables of Glycated Hemoglobin and Diabetes Distress in patients With Type 1 and Type 2 Diabetes Mellitus. *Mižnarodnij endokrinologičnij žur-*

nal 2023;19(6):424-427. doi: 10.22141/2224-0721.19.6.2023.1310.

5. Jasleen B, Vishal GK, Sameera M, et al. Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: Benefits Versus Risk. *Cureus*. 2023 Jan 18;15(1):e33939. doi: 10.7759/cureus.33939.

6. Szlas A, Kurek JM, Krejpcio Z. The Potential of L-Arginine in Prevention and Treatment of Disturbed Carbohydrate and Lipid Metabolism—A Review. *Nutrients*. 2022 Feb 24;14(5):961. doi: 10.3390/nu14050961.

7. Wu G, Meininger CJ, McNeal CJ, Bazer FW, Rhoads JM. Role of L-Arginine in Nitric Oxide Synthesis and Health in Humans. *Adv Exp Med Biol*. 2021;1332:167-187. doi: 10.1007/978-3-030-74180-8_10.

8. Kurhaluk N. The Effectiveness of L-arginine in Clinical Conditions Associated with Hypoxia. *Int J Mol Sci*. 2023 May 3;24(9):8205. doi: 10.3390/ijms24098205.

9. Reddin C, Murphy R, Hankey GJ, et al.; INTERSTROKE investigators. Association of Psychosocial Stress With Risk of Acute Stroke. *JAMA Netw Open*. 2022 Dec 1;5(12):e2244836. doi: 10.1001/jamanetworkopen.2022.44836.

10. Sirenko Y, Radchenko G, Rekovets O. Stress and hypertension: C and H type of hypertension and causes of resistance. *Міжнародний ендокринологічний журнал*. 2022;18(5):251-264. Ukrainian. doi: 10.22141/2224-0721.18.5.2022.1183.

11. Nelson KL, Davis JE, Corbett CF. Sleep quality: An evolutionary concept analysis. *Nurs Forum*. 2022 Jan;57(1):144-151. doi: 10.1111/nuf.12659.

12. Marx N, Federici M, Schüt K, et al; ESC Scientific Document Group. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. *Eur Heart J*. 2023 Oct 14;44(39):4043-4140. doi: 10.1093/eurheartj/ehad192.

13. Poredos P, Poredos AV, Gregoric I. Endothelial Dysfunction and Its Clinical Implications. *Angiology*. 2021 Aug;72(7):604-615. doi: 10.1177/0003319720987752.

14. Shpakou A, Sokotowska D, Krajewska-Kułak E, et al. The impact of the COVID-19 pandemic on physical activity, life satisfaction, anxiety, stress perception and coping strategies in student-athletes: A comparison between countries with a different approach of anti-pandemic measures. *Front Public Health*. 2022 Dec 2;10:1052744. doi: 10.3389/fpubh.2022.1052744.

15. Savchenko LG, Digtar NI, Selikhova LG, et al. Liraglutide exerts an anti-inflammatory action in obese patients with type 2 diabetes. *Rom J Intern Med*. 2019 Sep 1;57(3):233-240. doi: 10.2478/rjim-2019-0003.

16. Fortin E, Lundin M, Mellbin L, et al. Empagliflozin improves

insulin sensitivity in patients with recent acute coronary syndrome and newly detected dysglycaemia : Experiences from the randomized, controlled SOCOGAMI trial. *Cardiovasc Diabetol*. 2023 Aug 11;22(1):208. doi: 10.1186/s12933-023-01950-0.

17. Santoro RC, Molinari AC, Leotta M, Martini T. Isolated Prolongation of Activated Partial Thromboplastin Time: Not Just Bleeding Risk! *Medicina (Kaunas)*. 2023 Jun 17;59(6):1169. doi: 10.3390/medicina59061169.

18. Standl E, Khunti K, Hansen TB, Schnell O. The global epidemics of diabetes in the 21st century: Current situation and perspectives. *Eur J Prev Cardiol*. 2019 Dec;26(2_suppl):7-14. doi: 10.1177/2047487319881021.

19. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. *Diabetologia*. 2019 Jan;62(1):3-16. doi: 10.1007/s00125-018-4711-2.

20. Tomic D, Shaw JE, Magliano DJ. The burden and risks of emerging complications of diabetes mellitus. *Nat Rev Endocrinol*. 2022 Sep;18(9):525-539. doi: 10.1038/s41574-022-00690-7.

21. Miller RG, Orchard TJ. Understanding Metabolic Memory: A Tale of Two Studies. *Diabetes*. 2020 Mar;69(3):291-299. doi: 10.2337/db19-0514.

22. Testa R, Bonfigli AR, Praticchizzo F, La Sala L, De Nigris V, Ceriello A. The "Metabolic Memory" Theory and the Early Treatment of Hyperglycemia in Prevention of Diabetic Complications. *Nutrients*. 2017 Apr 28;9(5):437. doi: 10.3390/nu9050437.

23. Maruhashi T, Higashi Y. Pathophysiological Association between Diabetes Mellitus and Endothelial Dysfunction. *Antioxidants (Basel)*. 2021 Aug 18;10(8):1306. doi: 10.3390/antiox10081306.

24. Skrypnyk I, Maslova G, Lymanets T, Gusachenko I. How to improve quality of life in patients with acute leukemia and comorbid ischemic heart disease treated with anthracycline-based induction chemotherapy. *Exp Oncol*. 2019 Dec;41(4):353-356. doi: 10.32471/exp-oncology.2312-8852.vol-41-no-4.13906.

25. Higashi Y. Endothelial Function in Dyslipidemia: Roles of LDL-Cholesterol, HDL-Cholesterol and Triglycerides. *Cells*. 2023 May 1;12(9):1293. doi: 10.3390/cells12091293.

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Information about authors

Yurii Kazakov, MD, DSc, PhD, Professor, Head of the Department of Propaedeutics of Internal Medicine, Poltava State Medical University, Poltava, Ukraine; e-mail: kazakov.med.ua@gmail.com; <https://orcid.org/0000-0003-2224-851X>

Oksana Muravlova, PhD, Associate Professor, Head of the Department of Endocrinology with Pediatric Infectious Diseases, Poltava State Medical University, Poltava, Ukraine; e-mail: endocrinology@pdmu.edu.ua, o.muravlova@pdmu.edu.ua, mur_ov_pdmu@ukr.net; phone: +380(50)7619084; <https://orcid.org/0000-0002-5319-7092>

Tetiana Nastroga, PhD, Associate Professor at the Department of Internal Diseases and Emergency Medicine, Poltava State Medical University, Poltava, Ukraine; e-mail: t.nastroha@pdmu.edu.ua; <https://orcid.org/0000-0001-5347-6094>

Oksana Kitura, PhD, Associate Professor at the Department of Internal Diseases and Emergency Medicine, Poltava State Medical University, Poltava, Ukraine; e-mail: o.kitura@pdmu.edu.ua; <https://orcid.org/0000-0001-5319-5831>

S.V. Shut, PhD, Associate Professor at the Department of Propaedeutics of Internal Medicine, Poltava State Medical University, Poltava, Ukraine; e-mail: svetaumsa57@gmail.com; <https://orcid.org/0000-0003-0336-1891>

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Authors' contribution. Yu.M. Kazakov — study concept and design; O.V. Muravlova — final approval of the article, material processing; T.V. Nastroga — text writing, data analysis; O.E. Kitura — data analysis and interpretation; S.V. Shut — collection of material.

Казаков Ю.М., Муравльова О.В., Настрога Т.В., Кітура О.Є., Шуть С.В.
Полтавський державний медичний університет, м. Полтава, Україна

Оптимізація лікування пацієнтів похилого віку з цукровим діабетом та артеріальною гіпертензією в загальній практиці

Резюме. Актуальність. Старіння населення стало провідною демографічною ознакою України. За прогнозами Всесвітньої організації охорони здоров'я, кількість людей похилого та старечого віку в найближчі десятиліття зросте майже до 40 %. Артеріальна гіпертензія (АГ) і цукровий діабет (ЦД) 2-го типу є одними з головних факторів серцево-судинного ризику. Відомо, що оксидантний стрес і субклінічне хронічне системне запалення низької інтенсивності є визначальними факторами ендотеліальної дисфункції, порушень реактивності судин, підвищення периферичного судинного опору, порушень вуглеводного і ліпідного обміну, що призводить до зростання артеріального тиску і рівня глюкози в плазмі крові. **Мета:** підвищити ефективність лікування та покращити якість життя пацієнтів похилого віку з поєднаною патологією (ЦД 2-го типу та АГ) за допомогою включення емпагліфлозину та L-аргініну до базисної терапії. **Матеріали та методи.** Під нашим спостереженням перебувало 50 осіб похилого віку з коморбідною патологією: АГ II ст., ішемічна

хвороба серця (функціональний клас II) та ЦД 2-го типу в стані субкомпенсації. Хворі були розподілені на дві групи. Першій (контрольній) групі (n = 25) призначали загальноприйнятну базисну терапію. У другій (основній) групі (n = 25) до базисної терапії додавали емпагліфлозин 10 мг/добу, L-аргінін 300 мг/добу. **Результати.** Клінічне спостереження в амбулаторних умовах тривало протягом трьох місяців. Комплексне лікування хворих похилого віку з коморбідною патологією (АГ та ЦД 2-го типу) з додатковим включенням емпагліфлозину та L-аргініну до базисної терапії сприяє суттєвому позитивному впливу на клінічний перебіг, знижує ризик прогресування цієї констеляції. **Висновки.** Застосування запропонованої комплексної терапії в амбулаторно-поліклінічних умовах під контролем сімейного лікаря дозволить суттєво покращити якість життя пацієнтів, попередити розвиток ускладнень.

Ключові слова: артеріальна гіпертензія; цукровий діабет 2-го типу; хворі похилого віку; емпагліфлозин; L-аргінін