World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-30, January 2024
ISSN: 2749-3644

DIABETES MELLITUS AND ARTERIAL HYPERTENSION

Raza Muhammad Kalim
Resident Master's student
Samarkand State Medical University

Article history:

Received: November 26th 2023
Accepted: December 24th 2023
Published: January 28th 2024

Abstract:

Numerous studies have shown that diabetes mellitus and arterial hypertension are similarly associated with increased cardiovascular mortality. The presence of both diseases increases the risk of death by 2-fold. In 80% of cases diabetes mellitus is accompanied by arterial hypertension [1, 2]. The close relationship between these diseases is based on the unity of pathogenetic links, in particular, insulin resistance and hypersympathicotonia.

Keywords: arterial hypertension, type 2 diabetes mellitus, macro-microangiopathy, cardiovascular complications

INTRODUCTION: Type 2 diabetes mellitus arterial hypertension self-control of glycemia blood pressure control

It is known that insulin resistance even before the development of clinical manifestations of diabetes mellitus and hypertension leads to vascular wall damage. According to the Atherosclerosis Rise in Communities (ARIC) study, the stiffness of the vascular wall was a predictor of arterial hypertension: if the elasticity of the vascular wall decreased by one standard deviation, the risk of arterial hypertension increased by 15% [3].

To understand the relationship between insulin resistance and vascular wall damage, let us recall the mechanism of insulin action. Normally, insulin activates phosphatidylinositol-3-kinase, protein kinase B, via vascular wall receptor IRS-1, which finally initiates endothelial NO synthase and leads to NO synthesis and, consequently, vasodilation. On the other hand, insulin stimulates endothelin-1 synthesis through its effect on mitogen-activated protein kinase MAPK, i.e., it causes vasoconstriction.

Selective resistance to leptin is thought to develop in obesity. For some reason, which has not been established at present, there is an impairment of sensitivity to leptin in the arcuate nuclei of the hypothalamus (STAT 3 receptor), as a result of which the anorexigenic effect of leptin is blocked. However, sensitivity in ventromedial and dorsal hypothalamic nuclei is preserved, and leptin exposure to them leads to the activation of sympathetic influence [4].

Hypersympathicotonia leads to increased expression of the gene responsible for angiotensinogen synthesis in adipose tissue, which activates the renin-angiotensin system in the kidneys. The resulting angiotensin II, in turn, is a potent vasoconstrictor peptide and additionally, through its effect on AT1 receptors, increases SGLT2 receptor expression in the kidneys. Accordingly, glucose reabsorption increases and sodium retention occurs [5]. This may explain the ability of SGLT2 receptor inhibitors to exert a moderate hypotensive effect, reducing the risk of cardiovascular complications.

Insulin resistance provokes an increase in the stiffness and rigidity of the vascular wall, which leads to the development of arterial hypertension. In addition, angiotensin II stimulates the production of aldosterone in the adrenal glands. At the same time, it is known that there is a direct link between increased aldosterone levels and cardiovascular complications. It was also found that patients with diabetes mellitus and elevated aldosterone levels had a 10% higher risk of cardiovascular mortality compared to patients with normal aldosterone levels [6, 8]. The pathogenetic mechanism of this relationship is explained by the effects of aldosterone on blood vessels. Aldosterone through activation of NADPH-oxidase and lipid peroxidation leads to a decrease in NO bioavailability; additionally, it modulates the expression of sodium channels on the surface of endothelial cells [7]. In addition, aldosterone promotes further pro-gression of insulin resistance because it activates serine kinase, which causes degradation of IRS-1 .

Further, as diabetes progresses, all parts of the autonomic nervous system are affected, which was confirmed in a study conducted at our department. The study involved 86 patients with established diagnosis of type 2 diabetes mellitus and concomitant arterial hypertension. Daily BP monitoring was performed in all patients. In parallel, parameters of carbohydrate metabolism were determined by capillary blood glycemia and glycated hemoglobin level (HvA1c) with the help of continuous glycemia monitoring device CGMS (Continuous GLucose Monitoring System) by CGMS System Gold device of Medtronic MiniMed company. It should be reminded that for calibration of this device it is necessary to determine glycemia in capillary blood at least four times using a portable glucometer. The glucometer was selected based on the American Diabetes Association recommendations from 2011. [2, 9] on the quality of test strips, in which at a glycemia of £100 mg/dL (5.5 mmol/L) the measurement

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-30, January 2024
ISSN: 2749-3644

error should not exceed 15%, and at glycemia less than this figure the error should not exceed 15 mg/dL (0.83 mmol/L). ISO (International Organization for Standardization) recommendations of 2003 were also taken into account. [3], according to which the discrepancy at glycemia >75 mg/dL (4.2 mmol/L) should not exceed 20% and 15 mg/dL (0.83 mmol/L) at glycemia ^ 75 mg/dL. Given that most patients were from the older age group (mean age was 67.5 ± 8.4), the choice was based on the ease of use of the glucometer. It is known that many glucometer models require coding, which complicates their operation. At the same time, a study by Raine et al. revealed that up to 16% of patients incorrectly code their glucometers [1]. Currently, the easiest glucometer to use is the glucometer with the "no coding" system, which was chosen for the study.

Arterial hypertension is about twice as common in patients with diabetes mellitus as in the general population. The incidence of arterial hypertension among patients with diabetes mellitus ranges from 20 to 60% depending on the criteria used for elevated blood pressure (BP) and the type of diabetes mellitus. Arterial hypertension has a significant impact on the fate of diabetic patients, significantly increasing the risk of cardiovascular and renal complications, which are the main causes of their premature death. Thus, according to the data of the Framingham study, arterial hypertension increases mortality 5 times among patients with diabetes mellitus [1]. In patients with diabetes mellitus with arterial hypertension, effective drug therapy significantly prevents the development of cardiovascular complications and renal failure. Antihypertensive drugs are recommended to be prescribed to all adult patients with diabetes mellitus with BP 130/85 mm Hg or more [2]. In individualized doses, drugs belonging to different pharmacological groups have the same effect on BP, but they differ in their effect on carbohydrate metabolism, urinary albumin excretion and renal function.

Antihypertensive drugs can be divided into three main groups depending on their effect on carbohydrate metabolism:

1. Drugs that have an unfavorable effect on carbohydrate metabolism (diuretics, except indapamide, and b-adrenoblockers).
2. Drugs with no significant effect on carbohydrate metabolism (indapamide, b-adrenoblockers with vasodilating properties, calcium antagonists, AT1-angiotensin receptor blockers, central a2-adrenoreceptor agonists).
3. Drugs that have some favorable effect on carbohydrate metabolism (ACE inhibitors, a1-adrenoblockers and I1-imidazoline receptor agonists).

Thiazide diuretics and b-adrenoblockers, usually recommended for use in patients with uncomplicated hypertension, are not entirely appropriate in the treatment of arterial hypertension in patients with diabetes mellitus. First, thiazide diuretics and b-adrenoblockers may impair glucose tolerance. Secondly, according to some observations, they predispose to the occurrence and, possibly, progression of diabetes mellitus in hypertensive patients.

Thiazide diuretics in high doses (50 mg of hydrochlorthiazide or equivalent doses of other diuretics) increase fasting glucose levels and glycosylated hemoglobin concentration, as well as impair tolerance to oral and intravenous glucose load. Cases of development of non-ketonemic hypersmolar coma during treatment with thiazide diuretics in diabetic patients have been described. Suggested mechanisms of impaired glucose tolerance during treatment with thiazide diuretics include decreased insulin secretion and decreased tissue sensitivity to the action of insulin (insulin resistance) [3].

b-Adrenoblockers impair glucose tolerance. In diabetic patients they aggravate hyperglycemia and in some cases may cause the development of non-ketonemic hypersmolar coma. The most unfavorable effect on glucose metabolism has non-selective b-adrenoblockers (propranolol, nadolol, timolol) and b1-selective blockers (atenolol, metoprolol, etc.) in high doses. On the other hand, b-adrenoblockers with intrinsic sympathomimetic activity (oxprenolol, pindolol, etc.) have little effect on carbohydrate metabolism.

The suggested mechanisms of impaired glucose tolerance during treatment with b-adrenoblockers include inhibition of insulin secretion, decreased tissue sensitivity to insulin action (insulin resistance), inhibition of glucose utilization in peripheral tissues and increased secretion of growth hormone [3].

Along with impaired glucose tolerance, the ability of b-adrenoblockers to mask the clinical manifestations of hypoglycemia and inhibit the mobilization of glucose from the liver in response to hypoglycemia is of clinical importance. Many of the signs and symptoms of hypoglycemia are known to be due to increased activity of the sympathetic-adrenal system. All b-adrenoblockers, by suppressing clinical manifestations of hypersympathicotonia, can complicate the diagnosis of hypoglycemic states in diabetic patients.

b-Adrenoblockers inhibit the mobilization of glucose from the liver in response to hypoglycemia, both spontaneous (e.g., after intense exercise or prolonged

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-30, January 2024
ISSN: 2749-3644

fasting) and induced by insulin or oral glucose-lowering drugs. Glucose mobilization from the liver is mediated by b2-adrenoreceptors. Therefore, hypoglycemic reactions to insulin and oral sugar-reducing drugs are more often observed during treatment with non-selective b-adrenoblockers.

Thus, in diabetes mellitus b-adrenoblockers (especially non-selective), on the one hand, impair glucose tolerance, and on the other hand, predispose to the development of hypoglycemia and complicate the timely diagnosis of hypoglycemic states.

Several population-based studies have shown that thiazide diuretics and b-adrenoblockers increase the likelihood of diabetes mellitus in middle-aged and elderly hypertensive patients. Thus, C. Bengtsson et al. [4] reported a 3.5-fold increase in the risk of diabetes mellitus in women with hypertension treated with thiazide diuretics compared to untreated patients. According to a 10-year study, thiazide diuretics increase the risk of developing type II diabetes mellitus independent of other risk factors [5]. In a comparative study, the incidence of diabetes mellitus was 2 to 3 times higher in elderly hypertensive patients treated with b-adrenoblockers or thiazide diuretics compared with untreated patients [6]. Finally, according to a retrospective study, thiazide diuretics accelerate the development of diabetic nephropathy in diabetic patients with hypertension [7].

The assumption of an adverse effect of thiazide diuretics and b-adrenoblockers on the occurrence and progression of diabetes mellitus in patients with arterial hypertension, based on the results of retrospective and uncontrolled prospective studies, was recently confirmed in the SARRP study (Captopril Prevention Project, 1998). In this controlled study, the incidence of diabetes mellitus during 6 years of follow-up was significantly higher in the group of hypertensive patients treated with diuretics and b-adrenoblockers compared with patients treated with the ACE inhibitor captopril.

Given the effect of antihypertensive drugs on carbohydrate metabolism, ACE inhibitors, a1-adrenoreceptor blockers and I1-imidazoline receptor agonists should be used primarily in the treatment of arterial hypertension in patients with diabetes mellitus without concomitant heart and kidney damage.

However, the ability of antihypertensive drugs to prevent cardiovascular and renal complications in diabetic patients is much more important than their effect on carbohydrate metabolism. Unfortunately, the preventive efficacy of various antihypertensive drugs in diabetic patients has not been sufficiently studied in long-term studies. In controlled studies, the ability of thiazide diuretics and b-adrenoblockers to prevent cardiovascular complications in diabetic patients with arterial hypertension, despite their adverse effects on glucose metabolism, has been proven [2]. Recently published results from the CARRP study (1998) suggest that in hypertensive patients with hypertension combined with diabetes mellitus, the ACE inhibitor captopril is more effective in preventing cardiovascular complications than diuretics and b-adrenoblockers. Two other controlled studies have shown the superiority of ACE inhibitors over "vasoselective" calcium antagonists in the prevention of cardiovascular complications in patients with hypertension combined with type II diabetes mellitus. Thus, in the controlled study ABCD (Appropriate Blood Pressure Control Diabetes) [8], myocardial infarction and other cardiovascular complications developed significantly less frequently in patients with type II diabetes mellitus with arterial hypertension treated with the ACE inhibitor enalapril than in the group of patients treated with the calcium antagonist nisoldipine..

In the FACET (Fosinopril versus Amlodipine Cardiovascular Events randomized Trial) [9] randomized trial, cardiovascular complications were significantly less likely to occur in the group of patients with hypertension combined with type II diabetes treated with the ACE inhibitor fosinopril compared with patients treated with the calcium antagonist amlodipine.

The ability of a1-adrenoblockers and I1-imidazoline receptor agonists to improve long-term prognosis in diabetic patients with arterial hypertension has not, to our knowledge, been investigated. Therefore, given the results of the controlled trials KAPPP, ABCD and FACET, ACE inhibitors can be considered the drugs of choice for the treatment of hypertension in patients with type II diabetes mellitus.

If the antihypertensive efficacy of ACE inhibitors is insufficient, calcium antagonists and/or diuretics are added. Recent studies have demonstrated the cardioprotective effect of the combination of an ACE inhibitor and dihydropyridine calcium antagonists such as amlodipine and felodipine-retard.

b1-Selective b-adrenoblockers (atenolol, betaxolol, bisoprolol, metoprolol, etc.) still play an important role in the treatment of arterial hypertension in patients with diabetes mellitus combined with CHD. After all, IBS patients have a particularly high risk of sudden death and development of myocardial infarction, which are prevented by b-adrenoblockers

CONCLUSIONS: Thus, the effect of insulin on the endothelium creates a balance between vasodilatory, antithrombotic and anti-inflammatory effects and vasoconstrictor, inflammatory and thrombotic effects.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-30, January 2024
ISSN: 2749-3644

In insulin resistance due to phosphorylation of IRS-1, NO synthesis decreases, i.e. vasodilation is impaired. At the same time vasoconstrictor effects of insulin are preserved. Thus, insulin resistance provokes an increase in the stiffness and rigidity of the vascular wall, which leads to the development of arterial hypertension.

Another trigger mechanism for the development of hypertension and diabetes mellitus is the imbalance of the autonomic nervous system, manifested by hypersympathicotonia. At the heart of this phenomenon, among other causes, there are hyperleptinemia and hyperinsulinemia.

LITERATURE:

1. Wilson PW, Cupples CF, Kannel WB. Is hyperglycemia associated with cardiovascular disease? The Framingham Study. - Amer. Heart J 1991;121:586-90.
2. The sixth report of the Joint National Committee on prevention, detection, evaluation abd treatment of high blood pressure - Arch. Intern. Med 1997;157 (11):2413-46.
3. Houston MC. The effects of antihypertensive drugs on glucose intolerance in hypertensive nondiabetic and diabetics -Amer Heart J 1988;115(3):640-56.
4. Bengtsson C, Blohme G, Lapidus L, Lundgren H. Diabetes in hypertensive women: an effect of antihypertensive drugs or the hypertensive state per se? - Diabetes Med. 1988;5:261-4.
5. Skarfors ET, Selinus KI, Lithell HO. Risk factors for development of noninsulin-dependent diabetes in middle-aged men - Brit. Med. J 1991;303:755-60.
6. Mykkanen L, Kuusisto J, Pyorala K. et al. Increased risk of non-insulin-dependent diabetes mellitus in elderly hypertensive subjects - J. Hypertens 1994;12:1425-32.
7. Walker WG, Herman J, Yin DP. et al. Diuretics accelerate diabetic nephropathy in hypertensive insulin-dependent and non-insulin-dependent subjects - Trans. Amer. Assoc. Phys. 1987;100:305-15.
8. Estacio RO, Jeffers BW, Hatt WR. et al. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension - New Engl. J. Med. 1998;338 (10):645-52.
9. Tatti P, Guarisco R, Pahor M. et al. Outcome results of the fosinipril versus amlodipine cardiovascular events randomized trial (FACET) in patients with hypertension and NIDDM - Diabetes Care 1998;21 (4):597-603.
10. Lewis EJ, Hunsicker LO, Baix R. et al. The effects of angiotensin-converting enzyme inhibition on diabetic nephropathy - New Engl. J. Med 1993;329 (20):1456-62.
11. Parving HH, Rossing P. The use of antihypertensive agents in prevention and treatment of diabetic nephropathy - Curr. Opin. Nephrol. Hypertrytens. 1994;3:292-300.
12. Ravid M, Brosh D, Levi Z. et al. Use of enalapril to attenuate decline in renal function in normotensive normoalbuminuric patients with type 2 diabetes mellitus - Ann. Intern, Med 1998;128 (12):982-8.
13. Hansson L, Zanchetti A, Carruthers SG. et al. Effects of intensive blood pressure-lowering and low-dose aspirin in patients with hypertension: principle results of the Hypertension Optimal Treatment (HOT) randomised trial - Lancet 1998;351 (9118):1755-62.
14. Peterson JC, Adler S, Burkart JM. et al. Blood pressure control, proteinuria, and the progression of renal disease - Ann. Intern. Med. 1995;123 (10):754-62.