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Сборник содержит научные статьи отечественных и зарубежных авторов по экономическим, техническим, философским, юридическим и другим наукам.

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ANNOTATSIYA

Гипертония касаллиги-асосан юрак –кон томирлар системаси патологияси,артериал босимнинг баркарор ва авж олиб ошиши,кейин эса орган-морфологик узгаришлар билан кечадиган мураккаб бирламчи –функционал касаллигидир. Қандли диабет асосан 40 ёшдан ошган аҳоли қатламида учрайди. Касалликнинг асосий сабаби ортиқча тана вазни ва қонда холестерин хамда паст зичликдаги липопротеидларнинг миқдорининг ошишидир Ҳозирги кунда дунё аҳолисининг 392 милион яъни 6% га яқин қисми ушбу хасталикдан аъзият чекмоқда. Касалликнинг инсон организмида юзага келтириши мумкин булган асосий узгаришлардан бири бу қон босимининг кутарилиши ҳисобланади. Юқори қон босимидан шикоят қилувчи беморларнинг 20-60% қисмида қандли диабет хасталиги мавжуд.

КАЛИТ СУЗЛАР: Юкори кон босими, Кандли диабет, Нормоалбуминурия, Уртача ошган албуминурия, Жадал албуминурия, Ангиотензин айлантирувчи фермент ингибиторлари, Ангиотензин рецептор антагонистлари.

АННОТАЦИЯ

Гипертоническая болезнь –сложное первично-функциональное заболевание,характеризующееся в основном патологией сердечно –сосудистой системы,стабильным и стремительным повышением артериального давления с последующим органоморфологическими изменениями. Сахарный диабет встречается в основном среди населения старше 40 лет. Основной причиной заболевания является избыточная масса тела и повышенный уровень липопротеидов низкой плотности в крови. В настоящее время 6% из 393 миллионов человек в мире страдают от этой болезни. Одним из основных изменений, которые может вызвать заболевание в организме человека, является повышение артериального давления. Сахарный диабет выявляется у 20-60% больных, которые жалуются на повышение артериального давления.

КЛЮЧЕВЫЕ СЛОВА: ВЫСОКОЕ ДАВЛЕНИЕ, САХАРНЫЙ ДИАБЕТ, НОРМОАЛЬБУМИНУРИЯ, УМЕРЕННО ПОВЫШЕННАЯ АЛЬБУМИНУРИЯ, ИНТЕНСИВНАЯ АЛЬБУМИНУРИЯ, ИНГИБ ИТОРЫ АНГИОТЕНЗИН ПРЕВРАЩАЮЩЕГО ФЕРМЕНТА,АНТАГОНИСТЫ АНГИОТЕНЗИНОВЫХ РЕЦЕПТОРОВ.

ANNOTATION

Hypertension is a complex primary functional disease characterized mainly by pathology of the cardiovascular system, stable and rapid increase in blood pressure with subsequent organomorphological changes. Diabetes mellitus occurs mainly among the population over 40 years of age. The main cause of the disease is overweight and elevated levels of low-density lipoproteins in the blood. Currently, 6% of the 393 million people in the world suffer from this disease. One of the main changes that can cause a disease in the human body is an increase in blood pressure. Diabetes mellitus is detected in 20-60% of patients who complain of an increase in blood pressure.

KEYWORDS: *HIGH BLOOD PRESSURE, DIABETES MELLITUS,*

NORMOALBUMINURIA,MODERATELY ELEVATED ALBUMINURIA, SEVERE ALBUMINURIA, ANGIOTENSIN CONVERTING ENZYME INHIBITORS, ANGIOTENSIN RECEPTOR ANTAGONISTS.

Hypertension occurs frequently in patients with diabetes and, together, diabetes and hypertension substantially increase the risk of cardiovascular and kidney disease. Effective treatment of hypertension in such patients reduces cardiovascular risk. In addition to the development of kidney disease, at least two other factors have been proposed to contribute to hypertension in diabetes: extracellular fluid volume expansion and increased arterial stiffness [1]. Sodium retention and volume expansion may be induced both by insulin and the hyperglycemia-induced increase in the filtered glucose load [2,3]. The excess filtered glucose is reabsorbed in the proximal tubule via a sodium-glucose cotransporter, resulting in a parallel rise in sodium reabsorption [3]. Thus, salt loading tends to raise the blood pressure, an effect that can be reversed by salt restriction. Patients with diabetes have increased vascular stiffness [1], which is thought to be a consequence of increased protein glycation and, at a later stage, atheromatous disease. The reduction in arterial distensibility, which is seen with both impaired glucose tolerance and overt diabetes, can contribute to the rise in systolic pressure disproportionately to diastolic pressure and is associated with increased blood pressure variability and mortality risk [4,5]. Hypertension is a common problem in patients with both type 1 and type 2 diabetes, but the time course in relation to the duration of diabetes is different [2,6-9].

The findings are different in patients with type 2 diabetes [11-13]. In a series of over 3500 newly diagnosed patients, 39 percent were already hypertensive [11]. In approximately one-half of these patients, the elevation in blood pressure occurred before the onset of moderately increased albuminuria. Hypertension was strongly associated with obesity, and not surprisingly, the hypertensive patients were at increased risk for cardiovascular morbidity and mortality. Among patients with diabetes in general

(regardless of vintage) in the United States, the prevalence of hypertension is nearly 70 percent.

2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guidelines [14], as well as the American Diabetes Association (ADA) guidelines that suggest a goal blood pressure of less than 130/80 mmHg in patients with diabetes mellitus who have greater than a 10 percent 10-year cardiovascular risk [15,16]. Since hypertension magnifies cardiovascular risk among those with diabetes, all patients with diabetes and persistently elevated blood pressure should be started on antihypertensive drug therapy [16,22-25]. Drug therapy in patients with diabetes and hypertension is unequivocally protective [17,26-32]. In addition, all patients with diabetes and elevated blood pressure should be counseled on lifestyle modification to reduce blood pressure. Successful implementation of nonpharmacologic therapy may permit later reduction in the dose or number of antihypertensive agents.

Nonpharmacologic therapy (lifestyle modification) — Nonpharmacologic interventions to prevent and treat hypertension include lifestyle modifications such as:

Salt restriction, Weight reduction, Increased consumption of fresh fruits, vegetables, and low-fat dairy products, Increased exercise, Avoidance of smoking and excess alcohol ingestion.

American Diabetes Association (ADA) 2020 guidelines, which advise that, among patients with a systolic blood pressure ≥120 mmHg or a diastolic pressure ≥80 mmHg, such nonpharmacologic methods should be used to reduce blood pressure [33]. When to initiate antihypertensive drug therapy — The decision to initiate drug therapy should be individualized and involve shared decision-making between patient and provider. In general, however, we suggest that antihypertensive drug therapy be initiated in the following hypertensive patients (2017 American College of Cardiology/American Heart Association [ACC/AHA] guidelines and by the 2020 ADA guidelines) [14,15,33]

- Patients with out-of-office daytime blood pressure ≥135 mmHg systolic or ≥85 mmHg diastolic (or an average office blood pressure ≥140/90 mmHg if out-of-office readings are not available)

- Patients with an out-of-office daytime blood pressure ≥130 mmHg systolic or ≥80 mmHg diastolic (or an average of appropriately measured office blood pressures ≥130/80 mmHg if out-of-office readings are not available) who, in addition, have one or more of the following:
- Established clinical cardiovascular disease (eg, chronic coronary syndrome [stable ischemic heart disease], heart failure, carotid disease, previous stroke, or peripheral arterial disease)
- Type 2 diabetes mellitus
- Chronic kidney disease
- Age 65 years or older
- An estimated 10-year risk of atherosclerotic cardiovascular disease of at least 10 percent

Early treatment of hypertension is particularly important in patients with diabetes both to prevent cardiovascular disease and to minimize progression of kidney disease and diabetic retinopathy [34]. This is exemplified by the 21-year follow-up of the Steno diabetes study; specifically, appropriate management of systolic blood pressure, glycated hemoglobin (A1C), and low-density lipid (LDL) cholesterol resulted in a 20 percent absolute risk reduction at 13 years, a benefit that was persistent at 21 years [35,36].

Choice of antihypertensive drug therapy — The choice of antihypertensive agents in patients with diabetes is based upon their ability to do the following:

●Prevent mortality

●Prevent adverse cardiovascular events, such as myocardial infarction, stroke, and heart failure

●Prevent the progression of kidney disease, if present

The choice is not based upon retinopathy endpoints, since comparative trials have not demonstrated superiority of one agent over another for retinopathy.

Major guidelines including the 2017 ACC/AHA, European Society of Hypertension/European Society of Cardiology (ESH/ESC), ADA, and Canadian guidelines all conclude that the degree of blood pressure reduction is the major determinant of reduction in cardiovascular risk in both younger and older patients with hypertension (including patients with diabetes), **not** the choice of antihypertensive drug; this is also true in patients with diabetes [37]. However, in patients with diabetic kidney disease, renin-angiotensin system inhibitors (angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs]) may slow kidney disease progression more effectively than other antihypertensive drugs. In addition to kidney disease, placebo-controlled trials of ACE inhibitors and ARBs in high-risk patients have led some experts to conclude that these agents have a unique cardiovascular benefit in this setting [38,39]. However, the available data are more consistent with the conclusion that the achieved blood pressure, rather than the specific drug or drug class used, is the principal determinant of cardiovascular benefit.

Based upon the effects of ACE inhibitors and ARBs on kidney disease progression, our overall approach in patients with diabetes who require antihypertensive therapy is as follows:

In patients with severely increased albuminuria, ≥300 mg/day (formerly called "macroalbuminuria" and sometimes called "very high albuminuria"), we treat with an ACE inhibitor or an ARB as part of the regimen to achieve the blood pressure goal.

Use these drugs in patients with moderately increased albuminuria (formerly called "microalbuminuria" and sometimes called "high albuminuria") who are hypertensive, even though the benefits of angiotensin inhibition on kidney disease progression in such patients are unproven.

In patients without increased albuminuria, initial monotherapy can consist of an ACE inhibitor, ARB, thiazide diuretic, or calcium channel blocker. However, because thiazide diuretics have the disadvantage of an adverse effect on glucose metabolism, many experts will choose an ACE inhibitor, ARB, or calcium antagonist as initial therapy.

•In patients whose blood pressure is >20/10 mmHg above their goal, initial combination therapy (with a single pill, if available) should be prescribed. In addition, among patients with diabetes initiated on monotherapy, a second agent will often be required to attain goal blood pressure. In these settings (ie, when two antihypertensive drugs are needed), we generally treat with an ACE inhibitor or ARB plus a long-acting dihydropyridine calcium channel blocker. The combination of an ACE inhibitor or ARB with a diuretic is an acceptable alternative, and may be preferred in patients with edema; however, the Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial suggested that combining an ACE inhibitor or ARB with a long-acting dihydropyridine calcium channel blocker was superior to the combination with a thiazide diuretic [40], including among patients with diabetes [41].

If an ACE inhibitor or ARB is indicated but cannot be used, alternative first-line agents include calcium channel blockers and diuretics. However, in patients with severely increased albuminuria, nondihydropyridine agents (eg, diltiazem, verapamil) are generally preferred over dihydropyridine drugs (eg, amlodipine, felodipine) since nondihydropyridine calcium channel blockers can reduce albuminuria [42,43].

Severely increased albuminuria (300 mg/day or higher) — In hypertensive patients with diabetes who have severely increased albuminuria, defined as a measured (eg, with a 24-hour urine collection) or estimated (eg, using a random urine albumin-to-creatinine ratio [ACR]) albumin excretion ≥300 mg/day, we recommend treatment with an ACE inhibitor or an ARB rather than other antihypertensive agents. Other drugs can be added, as needed, to attain the blood pressure goal.

This approach is based upon high-quality, randomized trials demonstrating that these agents slow the progression of kidney disease compared with alternative therapy [44-47]. In addition, indirect evidence from trials of nondiabetic individuals supports the conclusion that ACE inhibitors and ARBs reduce the risk of kidney failure among those with severely increased albuminuria [48,49]. However, ACE inhibitors and ARBs do not

appear to decrease all-cause mortality or the incidence of major cardiovascular events compared with other antihypertensive drugs.

●Type 1 diabetes – The best data supporting angiotensin inhibition in patients with type 1 diabetes come from a trial of 409 adult participants who had urine protein excretion ≥500 mg/day and a serum creatinine ≤2.5 mg/dL (221 micromol/L) [44,45]. Patients were randomly assigned to captopril (25 mg three-times daily) or placebo; other antihypertensive drugs, except for calcium channel blockers, were added if needed. Captopril reduced the rate of death or end-stage kidney disease (ESKD; 11 versus 21 percent) at three years, reduced the likelihood of doubling of serum creatinine (12 versus 21 percent), and slowed the annual loss of creatinine clearance (11 versus 17 percent per year). Smaller trials similarly concluded that ACE inhibitor slow the progression of kidney disease in patients with type 1 diabetes [50,51].

●Type 2 diabetes – In type 2 diabetes, the best data comparing renin-angiotensin system inhibition with alternative therapy come from the Irbesartan Diabetic Nephropathy Trial (IDNT) and the Reduction of Endpoints in Non-Insulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL) trial [46,47]:

•In IDNT, 1715 participants aged 30 to 70 years with type 2 diabetes, hypertension, urine protein excretion ≥0.9 g/day, and mean serum creatinine of 1.7 mg/dL (150 micromol/L) were randomly assigned to irbesartan (75 to 300 mg once daily), amlodipine (2.5 to 10 mg once daily), or placebo [46]. Target systolic blood pressure was ≤135 mmHg, or 10 mmHg lower than the value at screening (if systolic blood pressure at screening ≥145 mmHg), and target diastolic blood pressure was ≤85 mmHg. At 2.6 years, the likelihood of a doubling of serum creatinine was lower with irbesartan (17 percent) compared with amlodipine (25 percent) and placebo (24 percent); in addition, irbesartan nonsignificantly reduced the incidence of ESKD (14 versus 18 percent with amlodipine and placebo). Patients assigned to placebo had a higher blood pressure throughout the trial than those assigned irbesartan; however, the blood pressure in the irbesartan and amlodipine groups

were similar, and therefore the benefits from irbesartan were independent of attained blood pressure [52,53].

•In RENAAL, 1513 adults with type 2 diabetes, albuminuria >300 mg/day (median urinary ACR of approximately 1250 mg/g), and mean serum creatinine 1.9 mg/dL (168 micromol/L) were randomly assigned to losartan (50 titrating up to 100 mg once daily) or placebo; additional drugs were added as need to attain goal blood pressure [47]. At 3.4 years, the incidence of ESKD was lower with losartan (20 versus 26 percent), as was doubling of serum creatinine (22 versus 26 percent). Unlike IDNT, there was no active comparator, and the mean blood pressure throughout the study was lower among those assigned losartan.

ACE inhibitors and ARBs have similar effects on patient-important outcomes among patients with diabetes as well as among broader populations [54-59]. Thus, in general, either agent can be used when treating patients with diabetes and albuminuria.

Some studies suggest that ACE inhibitors are superior to ARBs in preventing mortality and cardiovascular events in patients with diabetes. As an example, a meta-analysis of 48 trials that compared ACE inhibitors or ARBs with either placebo or another antihypertensive drug found that ACE inhibitors significantly reduced mortality compared with placebo (9.3 versus 10.5 percent) but that ARBs did not reduce mortality compared with placebo (5 versus 5 percent) [54]. However, both ACE inhibitors and ARBs had similar, nonsignificant benefits on mortality when compared with another antihypertensive drug (10.2 versus 11.9 percent and 8.5 versus 10.5 percent, respectively). The lack of benefit when ARBs were compared with placebo may be due to the fact that one-half of these trials included lower-risk patients (ie, normotensive and/or those with normoalbuminuria). In addition, both drugs had significant benefits on heart failure; ACE inhibitors significantly reduced the risk of myocardial infarction, and ARBs significantly reduced the risk of stroke. Other meta-analyses that included many of the same trials found that, in contrast to the study mentioned above, ARBs are equivalent to ACE inhibitors. One network meta-analysis, for example, used both direct

and indirect comparisons to evaluate trials of antihypertensive therapy in patients with diabetes and found that ACE inhibitors and ARBs had identical effects on mortality and ESKD [55]. In addition, a meta-analysis that included patients with and without diabetes found that ACE inhibitors and ARBs reduced mortality and cardiovascular events to a similar degree [56].

Moderately increased albuminuria (30 to 299 mg/day) — In hypertensive patients with diabetes who have moderately increased albuminuria, defined as a measured (eg, with a 24-hour urine collection) or estimated (eg, using a random urine ACR) albumin excretion 30 to 299 mg/day, we suggest treatment with an ACE inhibitor or ARB rather than other antihypertensive drugs. Additional agents are added, as needed, to attain the blood pressure goal.

The rationale for this approach comes from evidence that ACE inhibitors and ARBs, compared with other antihypertensive agents, can prevent the progression from moderately increased albuminuria to severely increased albuminuria in patients with diabetes [60-62].

SUMMARY

Contributors to hypertension in patients with diabetes include kidney disease, extracellular fluid volume expansion, and increased arterial stiffness. Hypertension is common problem in patients with both type 1 and type 2 diabetes, but the time course in relation to the duration of diabetes is different. In type 1 diabetes, the prevalence of hypertension at the time of diagnosis is low, increasing subsequently over several decades. In type 2 diabetes, a substantial proportion of patients already have hypertension at the time of diabetes diagnosis

- In general, patients with diabetes are at higher cardiovascular risk compared with the general population, and therefore we target more intensive, rather than less intensive, blood pressure control. Our recommendations on goal blood pressure in hypertensive

patients with diabetes mellitus are presented in detail elsewhere. Goal blood pressure also depends upon the method by which it is measured.

●Nonpharmacologic interventions should be prescribed, as appropriate, to all patients with hypertension. These include salt restriction; weight reduction; increased consumption of fresh fruits, vegetables, and low-fat dairy products; increased exercise; and avoidance of smoking and excess alcohol ingestion.

●The decision to initiate drug therapy should be individualized and involve shared decision-making between patient and provider. In general, however, we initiate antihypertensive drug therapy in patients with diabetes who have an out-of-office daytime blood pressure ≥130 mmHg systolic or ≥80 mmHg diastolic (or an average of appropriately measured office blood pressures ≥130/80 mmHg if out-of-office readings are not available).

●Our approach to the choice of antihypertensive therapy depends in part upon the degree of the patient's urine albumin excretion

•In patients with severely increased albuminuria, ≥300 mg/day (formerly called "macroalbuminuria" and sometimes called "very high albuminuria"), we treat with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) as part of the regimen to achieve the blood pressure goal

•Use these drugs in patients with moderately increased albuminuria (formerly called "microalbuminuria" and sometimes called "high albuminuria") who are hypertensive, even though the benefits of angiotensin inhibition on kidney disease progression in such patients are unproven.

•In patients without increased albuminuria, initial monotherapy can consist of an ACE inhibitor, ARB, thiazide diuretic, or calcium channel blocker. However, because thiazide diuretics have the disadvantage of an adverse effect on glucose metabolism, albeit minor, many experts will choose an ACE inhibitor, ARB, or calcium antagonist as initial therapy.

•In patients whose blood pressure is >20/10 mmHg above their goal, initial combination therapy (with a single pill, if available) should be prescribed. In addition, among patients with diabetes initiated on monotherapy, a second agent will often be required to attain goal blood pressure. In these settings (ie, when two antihypertensive drugs are needed), we generally treat with an ACE inhibitor or ARB plus a long-acting dihydropyridine calcium channel blocker.

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