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The choice of the antihypertensive drug in special conditions (part 4): evidence-based data in co-morbid kidney disease

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Abstract

The article reviews in brief the main approaches to the hypertension management in kidney damage based on the recommendations by the leading worldwide experts (the Joint National Committee of the USA, European Society of Cardiology/European Society of Hypertension, American Society of Hypertension/International Society of Hypertension) and national guidelines. Treatment algorithm is particularly relevant due to the high prevalence of chronic kidney disease and association between renal damage and persistent blood pressure elevation. The paper concerns treatment approaches in hypertension associated with chronic kidney disease, microalbuminuria, glomerulonephritis, atherosclerotic renal artery lesions, end-stage renal disease, hemodialysis etc.

Key words: kidney, chronic kidney disease, antihypertensive therapy, proteinuria

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Выбор антигипертензивного препарата в особых группах пациентов (часть 4): данные доказательной медицины при сопутствующей патологии почек

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Резюме

В представленном кратком сообщении приводятся основные позиции экспертов ведущих мировых кардиологических сообществ (Объединенного национального комитета США, Европейского общества кардиологов и Европейского общества по артериальной гипертензии, Американского и Международного обществ по артериальной гипертензии) по вопросам лечения артериальной гипертензии у пациентов с сопутствующей патологией почек с учетом Российских рекомендаций по сердечно-сосудистому риску и хронической болезни почек. Высокая распространенность хронической болезни почек и взаимосвязь поражения почек со стойким повышением артериального давления обусловливают актуальность и востребованность четких лечебных алгоритмов, особенно при начале терапии. В статье затрагиваются вопросы лечения артериальной гипертензии при хронической болезни почек, микроальбуминурии, гломерулонефритах, атеросклеротических окклюзионных поражениях почечных артерий, при терминальных стадиях хронической почечной недостаточности, на фоне проведения гемодиализа и других патологических состояниях.

Ключевые слова: почки, хроническая болезнь почек, антигипертензивные препараты, протеинурия

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Introduction

The link between elevated blood pressure (BP) and renal disease is evident in all groups of patients. Due to the high cardiovascular risk in renal disease, some experts (in particular, experts of the American and International Societies of Hypertension, ASH-ISH) state the need to maintain a stricter target level of BP (below 130/80 mm Hg), especially when microalbuminuria is verified [1]. Nevertheless, conventional target BP < 140/90 mm Hg is acceptable in these patients of any age [2, 3]. In case of concomitant diabetes mellitus target diastolic

BP is below 85 mm Hg. Glomerular filtration rate (estimated, eGFR) and microalbuminuria should be estimated before the administration of antihypertensive drugs. More precise monitoring may be required in the elderly subjects and in African patients, who are characterized by a significantly higher risk of kidney damage. Management of hypertension (HTN) in a patient with severe renal damage should be coordinated with the nephrologist, and if hemodialysis is required, a specialist in extracorporeal treatment methods should be invited.

Chronic kidney disease, microalbuminuria and proteinuria

All medical societies agree that nephroprotection is one of the most important goals of antihypertensive therapy, and the prevention and reduction of existing microalbuminuria and proteinuria is the top goal. Regarding this, the most effective drugs are renin-angiotensin-aldosterone system (RAAS) blockers, which are recommended as monotherapy or in combination with other drug classes, especially diuretics (loop and thiazide) and calcium antagonists [4]. Noteworthy, the maximal antiproteinuric effect is observed only 3–6 months after treatment initiation when medium and/or submaximal doses are prescribed. According to the guidelines of the European Society of Cardiology (ESC), a combination of two RAAS blockers (including renin inhibitor) is more effective for proteinuria reduction [5], but it is not recommended for wide use due to the increased risk of adverse cardiovascular events. At the same time, the experts of the Joint National Committee of the United States (JNC8), recommend angiotensin-converting enzyme (ACE) inhibitors or type 1 angiotensin II receptor blockers (ARBs) in chronic kidney disease (CKD), regardless of race or diabetes mellitus. ASH-ISH experts place ACE inhibitors in the first place for Afro-American patients [1]. As a second-line therapy, calcium channel blockers or thiazide/thiazide-like diuretics are recommended regardless of race. At later stages of CKD (starting from stage 3b according to the Russian guidelines [6], when eGFR is below 30 ml/min/1.73 m^2, or creatinine level is below 60 mcmol/l), loop diuretics are the most appropriate, while thiazide diuretics are not effective anymore. In CKD patients potassium-sparing drugs, especially aldosterone antagonists, should be avoided, in particular the combinations with RAAS blockers due to the high risk of hyperkalemia [7].

The combination of RAAS blockers with calcium antagonists is beneficial for the prevention and/or delaying the progression of kidney damage and creatinine increase [8].

Glomerulonephritis and other renal disease

The sparse available data support the use of low-dose RAAS blockers (under the control of eGFR) in glomerulonephritis and other nephropathies associated by BP elevation [9–11]. In particular, ACE inhibitors were shown to be effective and safe in children with acute post-streptococcal glomerulonephritis and BP elevation [12].

Hemodialysis and renal transplantation

Patients undergoing hemodialysis are commonly characterized by the volume-dependent HTN, although other factors (high renin HTN, increased cardiac output due to arteriovenous anastomosis, changes in osmotic pressure, etc.) are also important. A close cooperation with nephrologists and specialists in extracorporeal treatment methods is of high importance. All classes of antihypertensive drugs, except diuretics, can be used, and BP monitoring should be carried out continuously before, during and after hemodialysis, as well as at home. Electrolyte monitoring should be also regularly performed.

Currently, recommendations for management of hypertensive patients after kidney transplantation have not been developed yet. Therefore, standard approaches applied for high risk patients should be implemented [13]. European and American experts suggest that any drug class can be used in order to reduce BP after renal transplantation. At the same time, RAAS blockers are considered to be the most effective for the prevention and reduction of proteinuria (albuminuria). However, they require careful monitoring, especially in the first 3 months after surgery [14, 15].

Urolithiasis

Conventional approaches for HTN management are used in urolithiasis (the CKD manifestations should be controlled). In case of hypercalciuria and presence of calcium oxalate renal calculus thiazide and thiazide-like diuretics are beneficial

due to their anticalciuric effect. However, it is proven for the high-dose hydrochlorothiazide, while effectiveness of low-dose thiazide diuretics the prevention of calcium oxalate nephrolithiasis has not been studied. Loop diuretics should be avoided in hypercalciuria [16, 17].

Chronic pyelonephritis

Randomized clinical trials provide insufficient data on the use of antihypertensive therapy in chronic pyelonephritis; generally, any drug class can be used, and the restrictions would depend on the renal function and CKD manifestations.

Renal artery stenosis

Atherosclerotic renal artery

The atherosclerotic lesions of renal arteries require combination and complex treatment, including antihypertensive drugs, as well as lifestyle changes, control of lipid and carbohydrate metabolism. RAAS blockers (ACE inhibitors, ARB) are contraindicated in renal artery stenosis of the sole kidney, and in bilateral renal artery stenosis due to the high risk of acute renal failure. In unilateral stenosis RAAS blockers can be prescribed, but a careful control of renal function (GFR) is required [18].

Hemodynamically significant renal artery stenosis (defined by ACC/AHA as either a 50–70 % stenosis by visual assessment with a peak pressure gradient at narrowing site of at least 20 mm Hg, or an average pressure gradient of 10 mm Hg; or stenosis at least 70 % assessed by angiography, or a stenosis more than 70 % evaluated by intravascular ultrasound) is a potentially modifiable cause of secondary HTN. However, the efficiency and suitability of revascularization remain controversial. Thus, conventional approach is reasonable in patients with renal artery stenosis and severe renal dysfunction (proteinuria > 1 g/day, kidney length at least 10 cm, renal resistive index > 0.8, severe nephropathy verified by kidney biopsy). Surgery can be considered in uncontrolled HTN, concomitant coronary heart disease (unstable angina), severe heart failure involving pulmonary circulation, and in acute deterioration of renal function. Angioplasty with stenting is the preferred approach in these cases, as it is characterized by better morbidity and mortality compared to open renal revascularization [19].

Radiofrequency ablation of renal sympathetic nerves (renal denervation)

Any antihypertensive drugs can be used in patients with persistent elevated BP after radiofrequency ablation of renal sympathetic nerves, and the recommendations for the management of high-risk patients should be implemented. However, an abrupt BP decrease is commonly observed requiring treatment correction and drug dose reduction.

Conclusions

An early detection of kidney damage is highly relevant in hypertensive patients considering high cardiovascular risk associated with renal disease. The preventive measures include timely and correct administration of antihypertensive therapy. The drug choice for a patient with renal dysfunction should be based on both drug class and the characteristics of the individual medications, such as route of elimination of the drug and/or its metabolites. The preferred medications will be those with the non-renal elimination route (those eliminated through the gastrointestinal tract). In case of renal dysfunction (low eGFR) the drug clearance should be assessed, and the doses should be recalculated. The correct choice of the antihypertensive drug would allow the best nephroprotection and the improvement cardiovascular prognosis.

Conflict of interest

Authors declare no conflict of interest.

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