



RESISTANT ARTERIAL HYPERTENSION: CONTEMPORARY CONCEPTS OF DIAGNOSIS, PSEUDORESISTANCE, AND THERAPEUTIC STRATEGIES

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Abstract. Arterial hypertension remains one of the leading global health problems due to its high prevalence, chronic course, and major contribution to cardiovascular morbidity and mortality. Resistant arterial hypertension represents a particularly challenging clinical phenotype, characterized by the failure to achieve target blood pressure levels despite the use of combination antihypertensive therapy. This article reviews current concepts regarding the epidemiology, pathophysiology, clinical manifestations, and diagnostic criteria of resistant hypertension. Special emphasis is placed on the phenomenon of pseudoresistance, including improper blood pressure measurement, white-coat hypertension, poor medication adherence, and the influence of concomitant drugs. Approaches to the differential diagnosis of secondary hypertension and principles of rational pharmacological management are discussed. The importance of ambulatory blood pressure monitoring and patient engagement in long-term disease control is highlighted.

Key words: arterial hypertension, resistant hypertension, pseudoresistance, ambulatory blood pressure monitoring, antihypertensive therapy.

РЕЗИСТЕНТНАЯ АРТЕРИАЛЬНАЯ ГИПЕРТЕНЗИЯ: СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О ДИАГНОСТИКЕ, ПСЕВДОРЕЗИСТЕНТНОСТИ И ТЕРАПЕВТИЧЕСКИХ СТРАТЕГИЯХ

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Аннотация. Артериальная гипертензия остается одной из ведущих медико-социальных проблем современного здравоохранения вследствие высокой распространенности, хронического течения и значительного вклада в структуру сердечно-сосудистой заболеваемости и смертности. Особое место занимает резистентная артериальная гипертензия, при которой не удается достичь целевых уровней артериального давления несмотря на применение комбинированной антигипертензивной терапии. В статье рассмотрены современные представления о патогенезе резистентной гипертензии, ее эпидемиологии, клинических проявлениях и диагностических критериях. Особое внимание уделено феномену псевдорезистентности, включая ошибки измерения артериального давления, гипертензию «белого халата», низкую приверженность пациентов к лечению и влияние сопутствующих медикаментов. Освещены подходы к дифференциальной диагностике вторичных форм гипертензии и принципы рациональной фармакотерапии. Подчеркивается значение суточного мониторирования артериального давления и активного участия пациента в контроле заболевания.

Ключевые слова: артериальная гипертензия, резистентная гипертензия, псевдорезистентность, суточное мониторирование АД, антигипертензивная терапия

REZISTENT ARTERIAL GIPERTENZIYA: DIAGNOSTIKA, PSEVDOREZISTENTLIK VA DAVOLASH STRATEGIYALARIGA ZAMONAVIY YONDASHUVLAR

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Annotatsiya. Arterial gipertenziya yuqori tarqalganligi, surunkali kechishi hamda yurak-qon tomir kasalliklari va o'lim ko'rsatkichlariga sezilarli ta'siri tufayli zamonaviy sog'liqni saqlash tizimining muhim muammolaridan biri hisoblanadi. Rezistent arterial gipertenziya esa kombinatsiyalangan antigipertenziv terapiyaga qaramay, arterial bosimning maqsadli darajalariga erishib bo'lmazligi bilan tavsiflanadi. Ushbu maqolada rezistent gipertenziyaning epidemiologiyasi, patogenezi, klinik belgilari va diagnostik mezonlari yoritilgan. Psevdohezistentlik omillari, jumladan arterial bosimni noto'g'ri o'lchash, "oq xalat" gipertenziyasi, davolanishga past rioya qilish va ayrim dori vositalarining ta'siri batafsil tahlil qilingan. Shuningdek, ikkilamchi gipertenziya shakllarini aniqlash va samarali farmakoterapiya tamoyillari muhokama qilinadi. Arterial bosimni sutkalik monitoring qilish va bemorning faol ishtiroki kasallik nazoratida muhim ahamiyat kasb etishi ta'kidlanadi.

Kalit so'zlar: arterial gipertenziya, rezistent gipertenziya, psevdorezistentlik, arterial bosimning sutkalik monitoringi, antigipertenziv terapiya

Introduction. Arterial hypertension is one of the most prevalent chronic non-communicable diseases worldwide and affects approximately one quarter of the adult population. Despite the availability of modern, highly effective antihypertensive therapies, achievement of target blood pressure values remains suboptimal in a substantial proportion of patients. Large-scale clinical trials evaluating the efficacy of various antihypertensive regimens have convincingly demonstrated that in 20–60% of patients, target blood pressure levels cannot be achieved despite the use of three or more antihypertensive agents [1-4]. Hypertension in which blood pressure remains above recommended targets despite treatment with at least three antihypertensive drugs of different classes, including a diuretic, is defined as resistant hypertension. In addition, hypertension that is controlled only with the use of four or more antihypertensive medications is also classified as resistant. Both systolic and diastolic blood pressure may be elevated; however, isolated systolic hypertension is particularly common, especially in older patients.

Epidemiological data derived from relatively small observational studies indicate that the prevalence of resistant hypertension ranges from approximately 5% in general medical practice to as high as 45% among patients with nephrological disorders. The adoption of a so-called "civilized" lifestyle, characterized by physical inactivity, excess caloric intake, psychosocial stress, and aging of the population, has contributed to the widespread burden of hypertension. In Russia, elevated blood pressure has been reported in 38.9% of men and 42.1% of women. Importantly, although a significant proportion of individuals are aware of their diagnosis, only 5–10% receive effective treatment that achieves adequate blood pressure control [3,7,10].

Clinically, patients with arterial hypertension may present with a wide spectrum of nonspecific complaints. These commonly include recurrent dull headaches localized to the temporal, frontal, or occipital regions, a sensation of heaviness in the head or behind the eyes, increased fatigability, reduced exercise tolerance, and dyspnea on exertion. Many patients report discomfort in the precordial region, palpitations, excessive sweating, sleep disturbances, anxiety, tinnitus, visual disturbances such as blurred vision or the appearance of "floaters" and light flashes, dizziness, nausea, and a general feeling of weakness or malaise [4,6,9]. Although these symptoms are not pathognomonic, their presence often reflects chronic elevation of blood pressure and target organ involvement.

Even at early stages of arterial hypertension, cerebral blood flow may be compromised. Chronic hypoperfusion of the brain leads to the development of headaches, dizziness, tinnitus, and a decline in cognitive and occupational performance. With prolonged disease duration, particularly in inadequately controlled hypertension, small ischemic lesions known as lacunar infarctions may develop in deep brain structures as a consequence of sustained microvascular damage. Progressive loss of brain parenchymal volume may occur, manifesting clinically as cognitive decline, memory impairment, and, in advanced cases, vascular dementia. In addition to central nervous system involvement, chronic hypertension may result in progressive renal damage. Hypertensive nephropathy is characterized by impairment of renal excretory function, leading to increased levels

of nitrogenous waste products such as urea and creatinine in the blood, as well as the appearance of proteinuria, which reflects glomerular injury.

The diagnosis of arterial hypertension is often delayed because the disease may remain asymptomatic for many years. Currently, three principal diagnostic approaches are employed to identify hypertension: direct measurement of blood pressure, physical examination, and electrocardiography. Among these, noninvasive blood pressure measurement remains the simplest, most accessible, and most widely used method. The first noninvasive measurement of arterial pressure using an inflatable cuff applied to the upper arm was performed in 1895 by the pediatrician Scipione Riva-Rocci. In 1905, the Russian surgeon Nikolai Korotkoff described the auscultatory sounds that arise in an artery during gradual deflation of the cuff, forming the basis of the auscultatory method that remains the gold standard for blood pressure measurement today. Although this technique requires appropriate training and experience, the introduction of automated and electronic sphygmomanometers has greatly simplified the procedure and facilitated both clinical and home-based blood pressure monitoring [10].

In the evaluation of patients with apparent resistant hypertension, it is essential to consider the phenomenon of pseudoresistance. Pseudoresistant hypertension refers to the persistence of elevated blood pressure values due to factors other than true pharmacological resistance, such as improper measurement techniques, inadequate treatment regimens, or misdiagnosis. Importantly, the term “resistant hypertension” should not be regarded as synonymous with uncontrolled hypertension. Studies conducted in the United States have shown that only approximately 58% of patients diagnosed with resistant hypertension in a physician’s office truly have resistant disease. In the majority of cases, elevated blood pressure reflects pseudoresistant hypertension, and elimination of contributing factors often allows achievement of target blood pressure levels. True resistant hypertension, in contrast, is characterized by the inability to achieve adequate blood pressure control despite optimal pharmacological therapy and correction of all reversible causes of resistance.

Table 1. Differential Characteristics of True Resistant and Pseudoresistant Arterial Hypertension

Parameter	True Resistant Hypertension	Pseudoresistant Hypertension
Blood pressure control	Persistent elevation above target values	Apparent elevation, often situational
Number of antihypertensive drugs	≥3 drugs including a diuretic (or ≥4 drugs)	Often inadequate or irrational regimen
Adherence to therapy	High or confirmed	Low or inconsistent
Blood pressure measurement	Correct technique confirmed	Errors in cuff size, positioning, or rest
White-coat effect	Usually absent	Frequently present
Ambulatory BP monitoring	Confirms sustained hypertension	Normal or near-normal BP profile
Secondary hypertension	Excluded by diagnostic work-up	Often undiagnosed or suspected
Vascular stiffness (elderly)	May contribute but not primary	Common cause of pseudohypertension
Response to optimization	Minimal or absent	Significant improvement after correction
Therapeutic implications	Requires advanced combination therapy	Controlled by correcting reversible factors

Several factors contribute to pseudoresistant hypertension. These include errors in blood pressure measurement, such as inappropriate cuff size, insufficient rest before measurement, or incorrect patient positioning. The “white-coat” effect, defined as elevated blood pressure in the

clinical setting with normal values outside the physician's office, is another frequent cause. Pseudohypertension, particularly in elderly patients, may result from marked arterial calcification that prevents complete compression of atherosclerotic vessels, leading to falsely elevated readings. Poor adherence to prescribed therapy remains one of the most significant contributors to pseudoresistance. Nonadherence may be intentional or unintentional and is influenced by lifestyle factors, socioeconomic conditions, cultural beliefs, inadequate patient education, and insufficient understanding of the long-term risks and complications associated with hypertension [5]. Furthermore, inappropriate selection or dosing of antihypertensive medications, as well as the use of substances that increase blood pressure—such as corticosteroids, anabolic steroids, and nonsteroidal anti-inflammatory drugs—may compromise treatment efficacy.

Secondary hypertension, defined as elevated blood pressure resulting from an identifiable underlying condition, is also frequently implicated in cases of apparent resistance. Although secondary hypertension is often categorized as a cause of pseudoresistance, it may in fact represent a true cause of resistant hypertension if left undiagnosed and untreated. Epidemiological data suggest that 7–12% of patients with resistant hypertension have an unrecognized secondary etiology. The most common causes include renal parenchymal disease and endocrine disorders. Consequently, patients with persistent hypertension should undergo targeted evaluation, including urinalysis, assessment of serum creatinine and potassium levels, and renal ultrasonography, to exclude secondary causes.

The management of arterial hypertension relies on both pharmacological and nonpharmacological interventions. Currently, the main classes of antihypertensive drugs used worldwide include diuretics, beta-adrenergic blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and alpha-adrenergic blockers. Diuretics enhance renal excretion of sodium and water and are particularly effective when used in combination with other antihypertensive agents. However, their use may be associated with adverse metabolic effects such as hyperuricemia and impaired glucose tolerance. Beta-blockers are effective as monotherapy in selected patient populations and are also commonly combined with diuretics, although they may cause side effects including fatigue and sexual dysfunction. Calcium channel blockers are generally well tolerated, provide potent blood pressure reduction, and exert favorable effects in patients with concomitant heart failure, but may induce tachycardia, facial flushing, or constipation [6].

Although many antihypertensive agents are effective when used alone, combination therapy is often required to achieve target blood pressure levels, particularly in patients with moderate to severe hypertension or resistant disease. To minimize the risk of pseudoresistance and to improve long-term blood pressure control, regular home blood pressure monitoring and maintenance of a self-control diary are strongly recommended. Such strategies enhance patient engagement, facilitate early detection of inadequate control, and allow timely adjustment of therapy, ultimately improving cardiovascular and renal outcomes.

Conclusion. Resistant arterial hypertension represents a complex and multifactorial clinical condition that requires a comprehensive and individualized diagnostic and therapeutic approach. A substantial proportion of patients initially classified as having resistant hypertension actually exhibit pseudoresistance, which may be corrected through proper blood pressure measurement, optimization of pharmacological regimens, identification of secondary causes, and improvement of patient adherence. Failure to recognize these factors may lead to unnecessary escalation of therapy and increased risk of adverse effects. The integration of ambulatory blood pressure monitoring, rational combination pharmacotherapy, and patient-centered education is essential for achieving optimal blood pressure control. Early identification and effective management of resistant hypertension may significantly reduce target organ damage and improve long-term cardiovascular and renal outcomes.

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