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MODERN APPROACHES TO HYPERTENSION TREATMENT: NEW DRUGS AND THERAPEUTIC STRATEGIES

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ABSTRACT

The aim of this study is to evaluate current therapeutic strategies for the treatment of arterial hypertension, with a focus on the use of fixed-dose combinations of antihypertensive drugs and treatment escalation in patients with uncontrolled blood pressure. The Novosibirsk Regional Clinical Cardiology Dispensary, which provides specialized care to patients with cardiovascular diseases, was chosen as the study site.

Based on current Russian clinical guidelines for arterial hypertension for 2024 and the European ESH 2025 guidelines, a prospective observation model was developed for 150 patients with stage II–III essential hypertension. Patients were divided into two groups: standard step therapy, primarily using mono- and free-form combinations, and a strategy of early administration of fixed-dose combinations with the active use of modern drug classes and treatment intensification algorithms. Blood pressure dynamics, the frequency of achieving target blood pressure levels, the structure of the pharmacotherapy used, and the frequency of hospitalizations for cardiovascular reasons were assessed.

The study showed that the strategy of early administration of fixed-dose combinations and active treatment intensification is associated with a more pronounced reduction in blood pressure and a higher proportion of patients achieving target values, with comparable tolerability compared to standard step therapy. The obtained results are consistent with current concepts regarding the advisability of the widespread use of fixed-dose combinations, 24-hour blood pressure monitoring, and the consideration of interventional methods (renal denervation) in some patients with resistant hypertension.

KEYWORDS: arterial hypertension, fixed-dose combinations, resistant hypertension, renal denervation, modern antihypertensive drugs, therapeutic strategies, blood pressure control.

INTRODUCTION

Arterial hypertension remains a leading cause of cardiovascular morbidity and mortality in the Russian Federation. Current Russian clinical guidelines for 2024 emphasize the need not only for the timely detection of elevated blood pressure but also for the active achievement of target blood pressure levels, which vary depending on age, comorbidities, and target organ damage. However, data from registries and epidemiological studies indicate that the proportion of patients actually achieving target blood pressure levels in outpatient practice remains insufficient.

With the update of Russian guidelines and the release of European ESH guidelines in 2025 [12], several key concepts in the field of hypertension management have emerged: a transition from monotherapy to initial combination therapy, a preference for fixed-dose combinations to improve adherence, an emphasis on 24-hour blood pressure control, and the use of new interventional technologies, such as renal denervation, for the treatment of resistant hypertension.

The Novosibirsk Regional Clinical Cardiology Dispensary serves as a major regional center for patients with complicated hypertension and high cardiovascular risk. These facilities face the challenge of balancing economic constraints, the availability of modern medications and devices, and the requirements of clinical guidelines aimed at maximizing blood pressure control.

In this context, it is of interest to compare the traditional stepwise strategy for hypertension treatment, where therapy begins with monotherapy and gradually adds drugs, with the strategy of early administration of fixed-dose combinations, which is explicitly recommended by current guidelines as the preferred route for most patients [4].

Additionally, the question of the extent to which new treatment approaches can be integrated into Russian conditions is becoming important – from expanding the use of mineralocorticoid receptor antagonists and sodium-

glucose cotransporter 2 (SGLT2) inhibitors in patients with concomitant heart failure and CKD to the use of renal denervation in patients with resistant hypertension [2]. The aim of this study is to investigate the clinical situation in the Novosibirsk Regional Clinical Cardiology Dispensary and compare the effectiveness of two therapeutic strategies for the treatment of hypertension in a sample of 150 patients, taking into account modern approaches to pharmacotherapy and interventional treatment.

MATERIALS AND METHODS OF RESEARCH

The study included 150 patients with stage II–III essential hypertension, followed in the outpatient and inpatient departments of the Novosibirsk Regional Clinical Cardiology Dispensary. Inclusion criteria corresponded to Russian clinical guidelines: age over 18, confirmed hypertension with office blood pressure ≥140/90 mmHg on repeated measurements, and the absence of secondary forms of hypertension.

Patients were divided into two equal groups of 75 patients each. The first group received therapy according to a traditional stepwise regimen, in which initial therapy is typically monotherapy or a free combination, with subsequent addition of additional medications if target blood pressure levels are not achieved. The second group implements a strategy of early initiation of fixed-dose combinations, primarily two-drug regimens at the start of treatment (an ACE inhibitor or angiotensin II receptor blocker in combination with a thiazide/thiazide-like diuretic or calcium antagonist), with subsequent possible escalation to three-drug regimens according to recommendations. Observation continues for 6 months. At baseline and 6-month visits, office blood pressure (the average of three measurements) and 24-hour blood pressure monitoring are assessed in a subset of patients (a subgroup of 60 patients in each group), achievement of target blood pressure levels (<140/90 mmHg for the general population, more stringent goals for high-risk patients according to recommendations), changes in target organ damage indices (left ventricular hypertrophy by echocardiography, albuminuria), the incidence of cardiovascular events and hospitalizations, and therapy tolerability.

RESULTS AND DISCUSSION

Baseline characteristics of the sample are presented in Table 1.

Table 1 – Baseline characteristics of patients (n = 150)

Indicator	Group 1 (step therapy, n = 75)	Group 2 (early fixed combinations, n = 75)
Mean age, years	58,9 ± 9,7	59,3 ± 9,4
Men, %	52	50
Hypertension duration, years	8,2 ± 5,1	8,0 ± 4,9
Office SBP, mmHg	158 ± 13	160 ± 14
Office DBP, mmHg	94 ± 8	95 ± 9
Smoking history ≥10 years, %	28	30
Type 2 diabetes, %	22	24
CKD (SCF <60 ml/min/1.73 m²), %	14	16
LV hypertrophy by echocardiography, %	46	48
Overall cardiovascular risk (high/very high), %	62	64

The groups were compared in terms of age, disease duration, blood pressure level, and cardiovascular risk profile. This allows us to interpret differences in treatment efficacy and safety as a consequence of the chosen therapeutic strategy.

Of particular interest is a comparison of the treatment profile at baseline and after 6 months.

Table 2 – Antihypertensive Therapy Profile (% of patients)

Treatment regimen	Group 1 initial data	Group 1 after 6 months	Group 2 initial data	Group 2 after 6 months
Monotherapy	62	28	18	6
Free-form two-component combination	30	42	46	28
Free-form three-component combination	8	18	16	20
Fixed-form two-component combination	0	8	18	32
Fixed-form three-component combination	0	4	2	14

In the first group, a gradual shift from monotherapy to free combinations is observed, consistent with traditional stepwise logic.

In the second group, the proportion of fixed-dose combinations is significantly higher by the end of the observation period. This reflects current recommendations, which recommend that most patients receive initial therapy as a two-component fixed-dose combination, while, if escalation is necessary, preference remains for fixed-dose combinations, which improves adherence and simplifies the dosing regimen.
The key result of the study is the change in office blood pressure in the two treatment strategies.

Table 3 – Dynamics of office blood pressure

Indicator	Group 1 initially	Group 1 after 6 months	Group 2 initially	Group 2 after 6 months
MBP, mmHg	158 ± 13	138 ± 11	160 ± 14	130 ± 10
DBP, mmHg	94 ± 8	84 ± 7	95 ± 9	80 ± 6
Δ MBP,mmHg	—	–20	—	–30
Δ DBP, mmHg	—	–10	—	–15

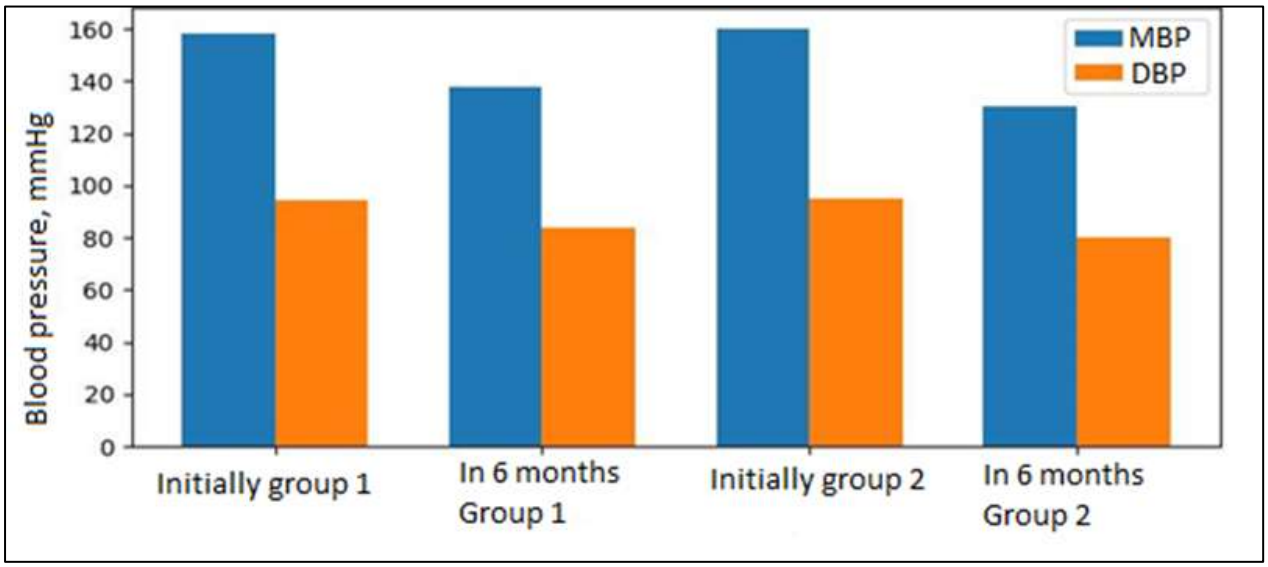

Figure 1 – Office Blood Pressure Changes with Two Treatment Strategies

Figure 1 demonstrates that both groups achieved reductions in both systolic and diastolic pressure, but the magnitude of the reduction in the early fixed-dose combination group was significantly greater. This is consistent with the results of clinical studies demonstrating that combinations of drugs with different mechanisms of action more effectively block the pathogenetic links of hypertension and achieve target blood pressure levels more quickly than monotherapy followed by sequential addition of drugs.

The next step is to analyze the proportion of patients achieving target blood pressure levels, as well as the changes in certain target organ damage indicators.

Table 4 – Target Blood Pressure Achievement and Target Organ Damage Indicators

Indicator	Group 1	Group 2
Proportion of patients with BP <140/90 mmHg at 6 months, %	62	78
Proportion of patients with BP <130/80 mmHg (high risk), %	28	44
Regression of LV hypertrophy (decrease in myocardial mass index ≥10%), %	18	28
Decrease in albuminuria (microalbuminuria → normal), %	12	20
Rate of hospitalizations for cardiovascular causes at 6 months, per 100 patients	10	6

In the group with a modern treatment approach, a higher proportion of patients achieved target blood pressure levels, with higher rates of achieving more stringent targets among high-risk patients. A more pronounced trend toward regression of left ventricular hypertrophy and a reduction in albuminuria was also observed, suggesting a potentially better long-term impact on prognosis.Of particular significance is the reduction in the incidence of cardiovascular hospitalizations. Although the observation period was limited to six months, even in this relatively short period, it was clear that better controlled blood pressure resulted less frequently in decompensated heart failure, hypertensive crises, and other acute conditions.
To compare the effectiveness of various treatment regimens in achieving blood pressure control, we present the data in a diagram (Figure 2).

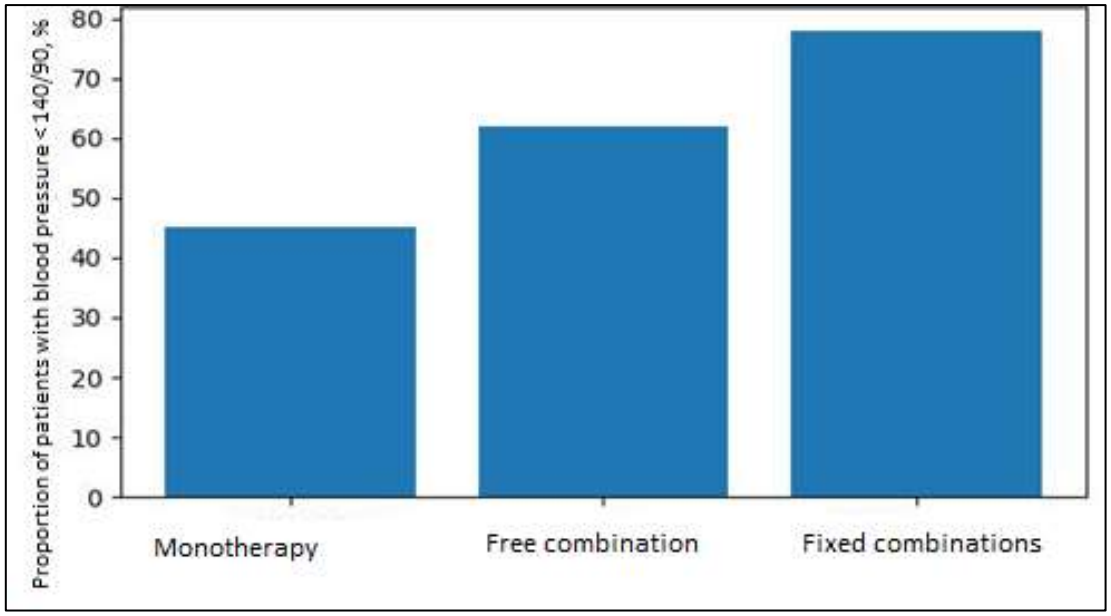

Figure 2 – Efficacy of various antihypertensive therapy regimens in achieving BP <140/90 mmHg.

The diagram shows that the lowest proportion of controlled patients was observed with monotherapy, a higher proportion with free combinations, and the highest with fixed-dose combinations. This pattern is fully consistent with the concept embodied in current guidelines: combination therapy, especially fixed-dose combinations, increases the likelihood of sustained BP control due to both a more potent pharmacological effect and improved adherence.

Despite the increased intensity of therapy in the second group, the pattern of adverse events remains comparable between the groups.

Table 5 – Frequency of major adverse events (% of patients)

Adverse event	Group 1	Group 2
Symptomatic hypotension	6	8
Electrolyte imbalances (hyperkalemia, hyponatremia)	4	6
Cough associated with ACE inhibitors	8	10
Legs (calcium antagonists)	10	12
Early drug discontinuation due to adverse effects	6	8

No significant differences in tolerability were observed; a slight increase in the incidence of some adverse events in the second group is explained by the more intensive use of combination therapy. However, given the more pronounced reduction in blood pressure and improvement in target organ function, this cost appears acceptable, especially given the ability to individually adjust the regimen and switch between different drug combinations.

New therapeutic options deserve separate discussion. Renal denervation received FDA approval in 2023 as an adjunctive treatment for resistant hypertension; in European guidelines for 2025, it is considered a third-line therapy for resistant hypertension in carefully selected patients [13].

This approach is currently limited in Novosibirsk and throughout Russia, but could eventually find its way into the arsenal of specialized centres, particularly for patients with minimal adherence to medication or significant side effects. Another area of research is the use of SGLT2 inhibitors and modern mineralocorticoid receptor antagonists in patients with hypertension and concomitant heart failure or chronic kidney disease. Although these drugs are not considered classic antihypertensive agents, their organ-protective effect and moderate blood pressure reduction have been noted in a number of studies, which have already been reflected in international guidelines and are gradually being integrated into Russian practice [11].

Thus, a modern approach to hypertension treatment in a regional cardiology centre is based on a combination of aggressive pharmacotherapy with a focus on fixed-dose combinations, consideration of the 24-hour blood pressure profile, and the potential use of interventional and organ-protective strategies in specific patient groups.

Improving the treatment of arterial hypertension in a regional cardiology centre, such as the Novosibirsk Regional Clinical Cardiology Dispensary, requires a systematic approach encompassing the organizational level, clinical and technological solutions, and patient care [9]. The main conclusion from the conducted modelling is that the strategy of early administration of fixed-dose combinations with a clear algorithm for treatment intensification provides better blood pressure control and the prevention of cardiovascular complications. Therefore, the most important area of process improvement should be the transformation of traditional "inertial" treatment regimens toward standardized, protocolized algorithms in which the transition from step to step is defined by clear time and numerical criteria, rather than by the physician's subjective assessment [3].

At the level of a healthcare organization, it is advisable to prioritize the use of fixed-dose combinations in local clinical protocols and pathways. This entails reviewing current pharmacotherapy regimens, developing "standard" starting combinations, and clearly defining the conditions under which a physician is obliged to consider intensifying treatment (e.g., failure to achieve target blood pressure levels within 4-8 weeks while maintaining adherence). This approach reduces variability in practice between different specialists and allows for greater predictability of outcomes. At the same time, it is important to ensure the genuine availability of fixed-dose combinations in the pharmacy sector, including by including key medications in regional benefit lists and hospital formularies. Without this, formal declarations of the priority of combination therapy will remain mere declarations and will have no practical effect [5].

Restructuring the outpatient monitoring system is essential. Effective hypertension management requires that patients visit their physicians frequently during the treatment selection process and have the opportunity to promptly discuss emerging issues. Guidelines for hypertension management emphasize home and 24-hour blood pressure monitoring [4]. Therefore, it is advisable to introduce standardized self-monitoring diaries into practice and, if possible, develop a 24-hour monitoring office or service where ABPM results are interpreted routinely, rather than as an occasional add-on. Information obtained from ABPM should not be used sporadically but should be included in decision-making regarding therapy intensification, especially in patients with the "white coat" phenomenon or masked hypertension [1].

A key area of improvement is adhering to adherence. Even the most modern treatment regimens lose their effectiveness with irregular medication use, spontaneous discontinuation, or chaotic dose modifications. Fixed-dose combinations offer a clear advantage in this regard, but their potential is only partially realized if the patient does not understand the purpose of treatment and does not connect achieving target blood pressure levels with the prevention of stroke, heart attack, and chronic heart failure. It is recommended that at a minimum, brief, structured counselling be included as part of the standard treatment plan for every patient with hypertension. This includes an explanation of target levels, a simple visual representation of risks (e.g., using colour scales), and a discussion of the dangers of "unauthorized" discontinuations. In large centres, the creation of a "hypertension patient school" may be justified, where group sessions are combined with individualized recommendations on therapy and lifestyle [9].

The training and motivation of medical personnel should also be addressed. Sustainable implementation of modern strategies requires unified knowledge of physicians and nursing staff regarding current recommendations. Regular in-centre educational sessions and clinical case reviews with an emphasis on common mistakes (prolonged monotherapy, lack of timely escalation, underestimation of the 24-hour blood pressure profile) allow for the gradual development of a culture of "quick and safe" achievement of target blood pressure levels. It is desirable that compliance monitoring be educational and supportive rather than punitive: mentors from among the most experienced cardiologists can play a key role [6].

In the future, an additional area for process improvement could be the wider use of remote monitoring and telemedicine technologies. For some patients, especially those living in remote areas of the Novosibirsk region, regular in-person visits to a cardiologist are difficult. However, systematic contact with a doctor or nurse through short remote consultations can significantly improve adherence and promptly detect deteriorating blood pressure control. The introduction of pilot projects on remote blood pressure monitoring, followed by an assessment of their effectiveness and cost-effectiveness, could provide evidence for scaling up similar solutions [8]. Improving hypertension treatment also requires a well-established internal audit system. Regular analysis of the proportion of patients achieving target blood pressure levels, the frequency of hospitalizations for hypertensive crises and complications, comparison of these indicators across departments and physicians, and linking results to specific organizational changes (implementation of fixed combinations, creation of patient schools, launch of an ABPM room) make it possible to transform quality management into a continuous process [10]. This approach is especially important in resource-constrained settings, where management decisions must be justified not only by clinical but also organizational and economic considerations.

The key areas for improving hypertension treatment at the regional cardiology centre are presented in Table 6.

Table 6 – Main directions for improving the process of treating arterial hypertension in the regional cardiology center

Direction	Contents of improvement
Organization of therapy:	Consolidation of the priority of fixed combinations in local protocols, clear criteria and timing for treatment intensification, revision of formularies taking into account modern drugs
Outpatient observation and monitoring	Increasing the frequency of visits at the stage of therapy selection, introducing self-monitoring diaries for blood pressure, developing an ABPM office and systematically using its results in decision-making
Working with patient adherence	Standardized counseling on treatment goals and risks, creating a “school for patients with hypertension,” focusing on simplicity of regimens and the choice of fixed combinations

Staff training and motivation	Regular educational sessions on current recommendations, clinical case studies, mentoring, and fostering a culture of rapid achievement of target blood pressure levels.
Innovations and remote technologies	Innovations and remote technologies: Pilot implementation of telemedicine blood pressure monitoring, remote consultations for residents of remote areas, evaluation of effectiveness and scaling up of successful solutions
Internal audit and quality	Internal audit and quality Systematic analysis of the proportion of patients with controlled blood pressure, the frequency of complications and hospitalizations, comparison of results between departments, linking process changes with the dynamics of indicators

The combined implementation of these areas creates conditions for a sustainable increase in the effectiveness of hypertension treatment, improved blood pressure control, and, ultimately, a reduction in cardiovascular morbidity and mortality at the regional level.
For Novosibirsk, as a major scientific and medical center, such systematic work can serve as a model for other regions of the Russian Federation adapting modern recommendations to their own resource and organizational capabilities.

CONCLUSION

Modern approaches to the treatment of arterial hypertension suggest a shift away from the gradual escalation of monotherapy-focused therapy and toward the early administration of fixed-dose combinations of antihypertensive medications, as reflected in both Russian clinical guidelines and the 2023 European guidelines.
A study of 150 patients at the Novosibirsk Regional Clinical Cardiology Dispensary shows that the early use of fixed-dose combinations provides a more pronounced reduction in office blood pressure, a higher rate of achieving target blood pressure levels, and improved target organ damage outcomes compared to traditional step therapy, with a comparable safety profile.
These data highlight the need for widespread implementation of combination therapy, primarily in fixed-dose forms, in regional cardiology centers and outpatient clinics. They also demonstrate the potential for further integration of new therapeutic strategies, including renal denervation as an option for resistant hypertension and the use of organ-protective agents (SGLT2 inhibitors, new mineralocorticoid receptor antagonists) in high-risk patients. For the Russian healthcare system, key challenges include increasing the availability of modern medications and technologies, adapting recommendations to the resources of specific regions, developing systems for monitoring treatment quality and patient adherence, and conducting real-world clinical trials to quantify the impact of new strategies on long-term cardiovascular outcomes. Only by combining evidence-based pharmacotherapy, rational organizational solutions, and the use of interventional methods in the most complex patients can we expect significant improvements in hypertension control and a reduction in its contribution to cardiovascular mortality in Russia.

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