Edited by
Sofiia Sokolova

PEDAGOGY AND EDUCATION MANAGEMENT IN MEDICAL UNIVERSITY

Alcide De Gasperi University
of Euroregional Economy in Józefów

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Scientific monograph

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COMPARATIVE CHARACTERISTICS OF THE STUDY SAMPLE OF PATIENTS AND FREQUENCY OF APPOINTMENTS OF DIFFERENT VARIANTS OF ANTIHYPERTENSIVE THERAPY

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Cardiovascular disease is a top socio-medical problem in all industrialized countries. One of the most important conditions for increasing life expectancy, as well as maintaining viability and quality of life, is to address the issue of proper treatment of cardiovascular disease, as well as their timely prevention. One of the most effective ways to achieve this goal is the timely detection and proper treatment of hypertension. Experts note that in diseases such as stroke, coronary heart disease, including myocardial infarction, heart and renal failure can be reduced their level as a result of adequate antihypertensive therapy. This is especially important in Ukraine, where mortality rates from cardiovascular disease are gaining in importance every year. In recent years, along with the expansion of opportunities in the treatment of hypertension, there has been sufficient information on the effectiveness of drugs that reduce blood pressure.

Purpose of our study was to perform a comparative analysis of the prescriptions of different variants of antihypertensive drugs by doctors of Kyiv for 2019.

Methods: physician questionnaire and comparative analysis of primary documents (content analysis of medical histories). At the first stage of the study, conducted jointly with the staff of the Institute

of Cardiology. A survey of 153 doctors was conducted by the Strazheska Institute of Cardiology of Ukraine (Kyiv), Department of propedeutics of internal diseases No. 1, Department of propedeutics of internal diseases No. 2, Department of internal diseases of the Bogomolets National Medical University (Kyiv).

Results: certain patterns of blood pressure lowering were found in patients on the background of hypertension monotherapy, in the treatment of two antihypertensive drugs, and in patients who received two or more drugs.

Keywords: arterialhypertension, antihypertensive drugs, pharmacoepidemiological study.

Introduction

The number of people with cardiovascular disease has increased significantly in recent years, it can be said that diseases of the cardiovascular system occupy one of the first places among other diseases. One of the major pathologies in cardiology is arterial hypertension (AH). According to WHO statistics, the number of people suffering from hypertension has increased. Treatment with antihypertensive drugs is one of the most costly, and therefore raises the question of economically sound therapy.

The rapid development of the pharmaceutical market in our country has led to the emergence of a large number of generic drugs on it. Today, according to various authors, their number reaches 80% (Borovikov 2003; Brown 2007; Shalnova, 2001).

Main purpose of drug use research is to determine whether drug therapy is rational. To solve this problem, appropriate methods of assessing the rationality of drug treatment are needed.

Methods. In the first stage of our study, a pharmacoepidemiological study was performed to obtain the data needed to plan and conduct a clinical and economic analysis (Borovikov 2003; Brown 2007; Gavorník 2015; Jelínek 2018; Kornatskyi 2006). Its main objectives were to study the practice of prescribing antihypertensive drugs by physicians (Nussbaumerová 2011; Widimský 2011; Yavorskaya 2006), as well as the manifestation of the antihypertensive effect of these drugs, in accordance with the data of primary medical records.

Treatment of hypertension with antihypertensive drugs of patients of different age categories

The analysis of the sample studied showed that 41,7% of patients were male, 58,3% were female. The mean age of the study group of patients was in the range of 19-86 years, and the average age was 55,8+0,3 years. The average duration of hypertension recorded in the documentation was 5,3 ± 0,5 years. The duration of antihypertensive therapy averaged 9,3 ± 5 months. Only 3,1% of them, according to medical records, did not have concomitant pathology, while at the same time, the majority of patients with arterial hypertension revealed the presence of comorbidities, the structure is presented in Figure 1.

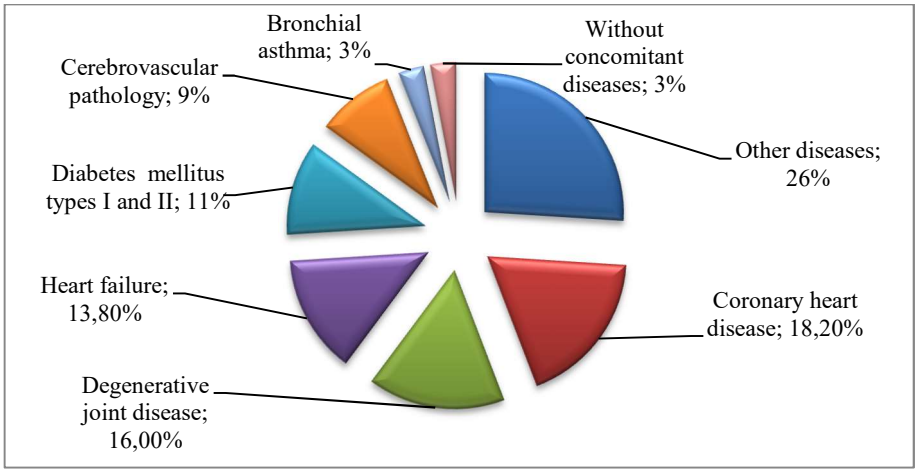
The distribution of patients by the number of prescribed antihypertensive drugs was as follows: one drug was prescribed in 32% (group 1), treatment with two drugs was carried out in 35,5% (group 2), administration of three or more drugs was recommended in 32,5% (group 3).

In the overall sample, men made up 41,7%, women 58,3%, in group 1– 46,6 and 53,4%, in group 2 – 42,1 and 57,9%, in the third group – 36,4 and 63,6%, respectively. The mean age in the groups was: 52,6 ± 0,5; 59,1 ± 0,5 and 59,1 ± 0,7 years, respectively. By age, patients in group 1 were significantly ($p<0,05$) younger than patients in other groups. Analysis of the initial level of blood pressure showed that it was 167,4 ± 1,1 / 98,5 ± 0,5 mmHg among patients in group 1, in patients in group 2 – 174,1 ± 1,5 / 99,6 ± 0,8 mm Hg and 189,0 ± 2,2 / 108,4 ± 1,3 mm Hg in patients of group 3. Thus, baseline blood pressure ($p<0,01$) differed in these groups and was minimal in patients in group1 and maximum in patients in group 3. No significant differences were observed only in diastolic blood pressure (DBP) levels among patients in groups 1 and 2.

Fixed combination of two antihypertensive agents is useful alternative approach on start of pharmacological therapy of hypertension. Current data indicate, that use of fixed combination improves adherence, persistence and compliance to antihypertensive therapy (Kovalenko 2014; Mancia 2013; Metelitsa et al. 1995; Shvarts et al. 2000; Vachulová, 2019). Analysis of the frequency of appointments of antihypertensive drugs from different clinical and pharmacological groups showed that the major share of appointments falls on angiotensin-converting enzyme (ACE) inhibitors – 39,8%. The frequency of diuretics was 21,6%, beta-blockers 16,0%, calcium antagonists – 14,9%, combined, clonidine

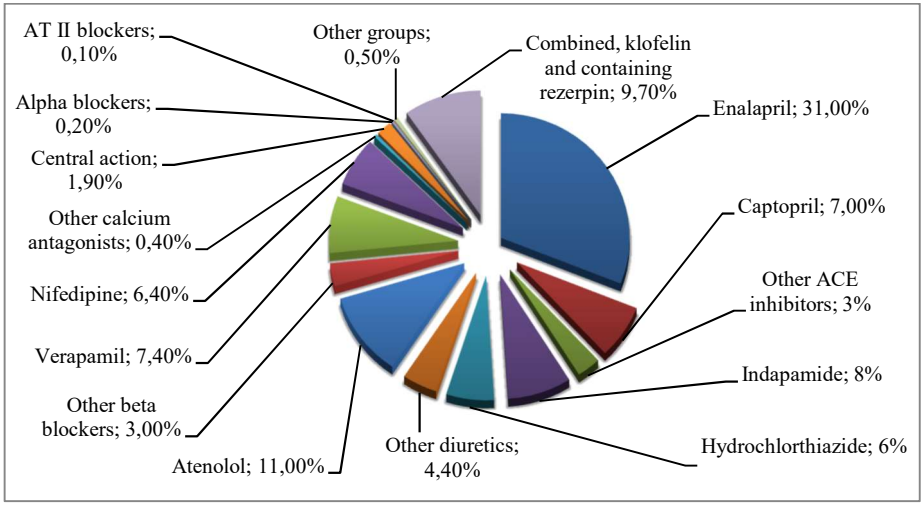
and reserpine-containing drugs – 9,7%, central action drugs – 1,8%, alpha–adrenoblockers 0,2%.

Figure 1. Structure of concomitant diseases in patients with hypertension according to primary medical records.



Source: own research.

Figure 2. General structure of prescriptions of antihypertensive drugs.



Source: own research.

The study of the frequency of prescriptions of antihypertensive drugs with different INN revealed the following order of distribution: enalapril (31%), atenolol (11%), indapamide (8,0%), verapamil (7,4%), hydrochlorthiazide (6%), captopril (7%) and nifedipine (6,4%). Combined medicines were used in 9,7% of cases (Figure 2).

In more detail, data on the drugs administered to patients in the entire study sample, their manufacturers, prevalence, and average prescribed doses are presented in Table 1.

Monotherapy for the treatment of hypertension

In patients who were prescribed one drug as antihypertensive therapy, the pattern of use of different groups of antihypertensive agents differed slightly from that in the general sample, but had similar trends (Figure 3).

Thus, 52,0% of patients were prescribed as ACE monotherapy, 13,0% were betablockers, 9,0% were calcium antagonists, 7,0% were diuretics, and 2,0% were central drugs. The most commonly prescribed for monotherapy are drugs with INN: enalapril – 35%, captopril – 14%, atenolol – 9,5%, verapamil and indapamide – 5,0%, nifedipine – 4,0%, propranolol – 3,5%. Combined drugs are prescribed in 16,5% of cases (60% of them are reserpine-containing). In monotherapy, the most commonly prescribed medications with the commercial names are enap (18,5%), kapoten (15%), atenolol (13%), enam (12%), verapamil (6%), ednit, enalapril, arifon (4,5%), hypothiazide (3%), anaprilin and obsidan (2,5% each).

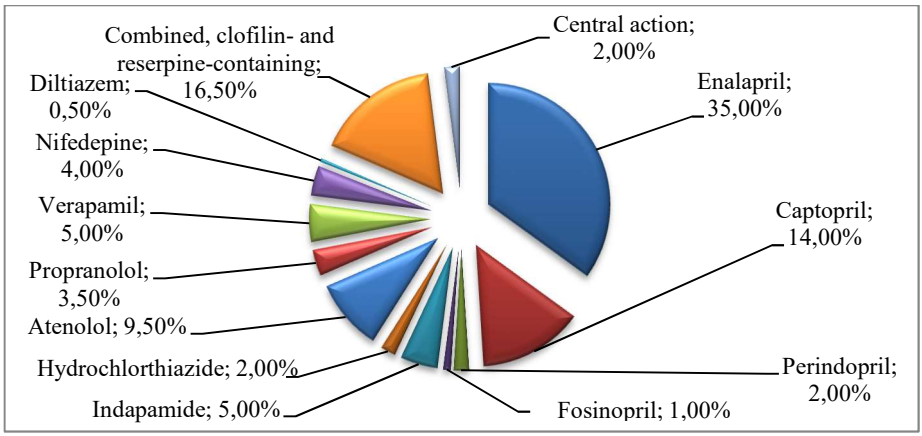
To determine the age-specific features of antihypertensive monotherapy, the structure of prescriptions in patients 60 years and older was considered. Arterial hypertension is one of the most important cardiovascular risk factors. Also patients with isolated systolic hypertension benefit from treatment. Specific methods of blood pressure reduction are finding their way into guidelines and we incorporate them into our daily practice, taking into account the patient's clinical status. One current trend in treating the elderly, as well as other hypertensive patients, is the use of fixed single-pill combinations. There were no significant differences in the purpose of the main groups of antihypertensive drugs, however a significant difference ($p<0,05$) was noted in the structure of commercial names. Thus, in patients older than 60 years, by frequency of prescriptions, adelfan (14,5%) took first place, followed by enap (11%), verapamil (9,5%), enap-N (7,5%), enam and enalapril (6% each). Clofeline was administered at 3,5%.

Table 1 The name of the antihypertensive drugs, their manufacturers and the frequency of appointments within the respective clinical and pharmacological groups

	The commercial name of the drugs	Companies - manufacturers	The proportion of appointments within the group, %	Average daily doses, mg
ACE inhibitors	Enap	Krka	31,5	9,9
	Kapoten	BMS	25,8	51,2
	Enam	Dr. Reddy`s Lab	19,6	8,4
	Enalapril	Hemofarm	6,8	9,6
	Ednit	Gedeon Richter	6,5	7,9
	Tensiomin	Egis	2,9	31,2
	Renitek	Merck Sharp & Dohme	2,6	7,5
	Captopril	Krka	2,7	34,3
	Prestarium	Servier	0,8	4
	Monopril	BMS	0,8	20
Beta blockers	Atenolol	IpcaLab.; Norton healthcare; Pliva	71,4	53,1
	Obsidan	Schwarz Pharma	12,9	51,4
	Anaprilin	BMS	13,6	60
	Atenobene	Merckle	2,1	100
Diuretics	Arifon	Servier	53,4	2,5
	Hypothiazide	Chinoin	29,6	37,4
	Indapamide	Hemofarm	13,3	2,3
	Furosemide	Polpharm	3,7	40
Calcium antagonists	Verapamil	Different manufacturers	40,8	92,9
	Phenigidine	Different manufacturers	11,8	27,5
	Isoptin	Knoll	9,8	90
	Nifedipine	Pliva	9,1	20
	Kordafen	Polfa	8,5	23,3
	Corinfar	AWD	5,7	35
	Kordaflex	Egis	5,4	15
	Diltiazem	Different manufacturers	5,3	140
	Cordypin	Krka	2,5	20
	Adalat-osmo	Baer	1,1	20
Centrally acting drugs	Clofeline	Different manufacturers	52	0,025
	Dopegit	Egis	31,7	0,075
	Reserpine	Different manufacturers	16,3	0,01
Combination drugs	Adelfan	Novartis	59,2	2,1 tab.
	Capozid	Akrikhin	14,1	34,3
	Viscaldix	Egis	8,5	0,8 tab.
	Enap-N	Krka	8,7	10
	Cristepin	Lechiva	8	2 tab.
	Trirezid K	Pliva	1,5	2 tab.

Source: own research.

Figure 3. The structure of prescriptions of antihypertensive drugs for monotherapy of hypertension.

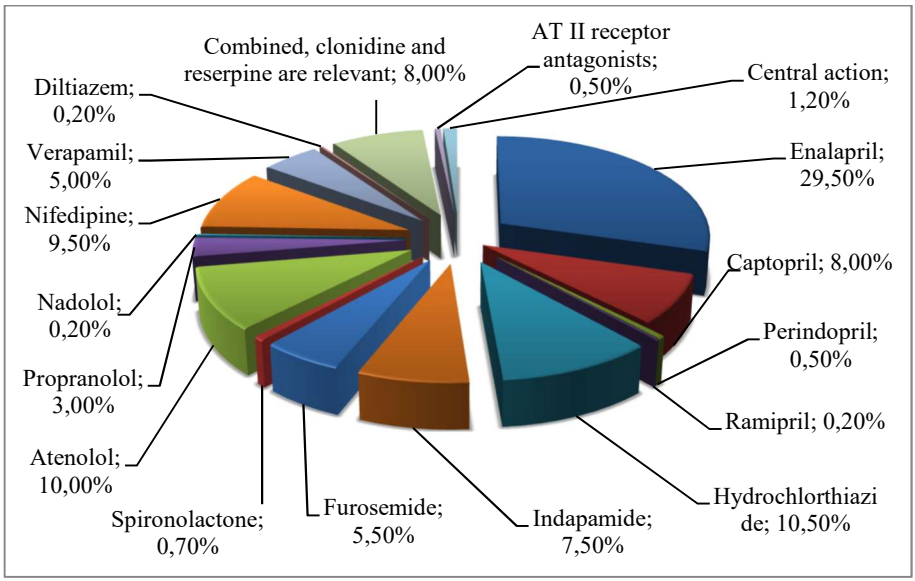


Source: own research.

When administered to patients with two antihypertensive drugs, the most common (38%) was a combination of ACE and diuretics. The use of ACE in combination with betablockers was noted in 16,5%, and with calcium antagonists - in 14%. The combination of diuretics with betablockers was used in 5%, and even less frequently with calcium antagonists (3,5%). Other combinations accounted for 0,2 to 2,5%. In 5% were combinations of irrational nature, for example, combinations of different drugs from the same clinical and pharmacological group. In the structure of appointments with combined antihypertensive therapy using two drugs, as in other groups, the place was taken by ACE. They accounted for 38,0%. The share of diuretics was 24,2%. Calcium antagonists were administered in this group of patients in 14,7%, and betablockers in 13,0%. In 8% were prescribed combined and reserpine-containing drugs. Central action drugs accounted for 1,2% and AT II receptor antagonists 0,5%. Assignment analysis based on INN, showed that ACE in 78% represented enalapril, captopril was prescribed in 20,5%, and perindopril and ramipril in 2% and 0,5%, respectively. In the group of calcium antagonists, the most common drugs were nifedipine (62%), with only 4,5% of them prescribed in the form of long-acting. The drug verapamil in this pharmacological group was 38%, of which 1,0% - retard. Among the diuretics, hydrochlorthiazide (46%)

and indapamide (30%) were the most prescribed. The furosemide and spironolactone were 23 and 3%, respectively. Betablockers were represented by atenolol (73%), propranolol (27%) and nadolol (1,5%). The structure of appointments for two-component therapy is presented in Figure 4.

Figure 4. The structure of prescriptions of antihypertensive drugs in two-component treatment of hypertension.



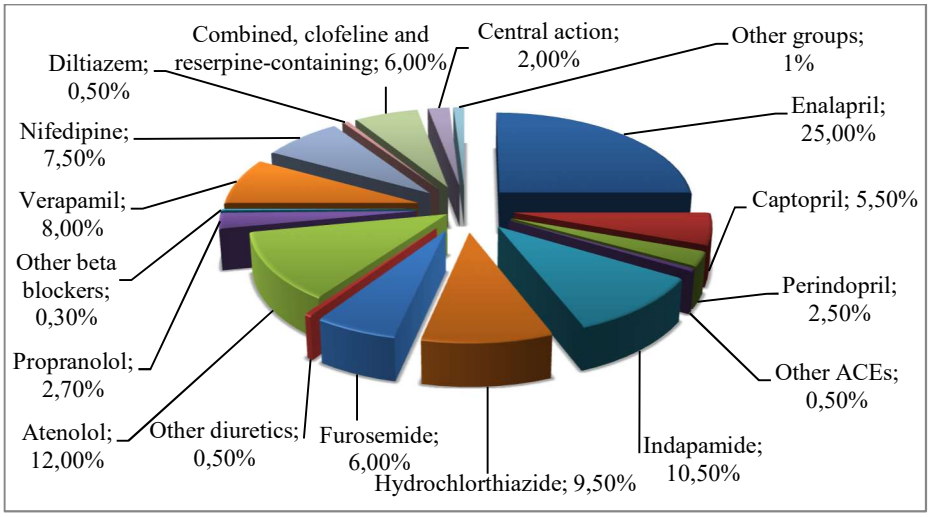
Source: own research.

The most commonly prescribed drugs with commercial names are hypothiazide (10,5%), enam (11%), enap and atenolol (9,5%), kapoten (6,0%), furosemide (5,5%), ednit (5,0%), arifon (5,0%), verapamil (4,5%) and enalapril (4,0%). A total of 46 drugs were administered in different combinations.

For antihypertensive therapy with the use of three or more drugs, the combination of ACE, diuretics and betablockers (19%) was most often prescribed. The combination of ACE inhibitors, diuretics and calcium antagonists was reported in 12,5%. A combination of ACE, betablockerand calcium antagonist was used in 2%. The same amount was attributed to the proportion of combinations of diuretics, betablockers and calcium antagonists.

In 42%, when using a combination of three or more drugs, the appointment of two drugs from the same pharmacological groups was noted. According to the frequency of appointments of pharmacological groups in the order of decrease, they were arranged as follows: ACE (33,5%), diuretics (26%), calcium antagonists (16%), betablockers (15%), drugs of central action (2,0%). Other groups accounted for less than 1% (Figure 5).

Figure 5. The structure of appointments in combination antihypertensive therapy of hypertension with the use of three or more drugs.



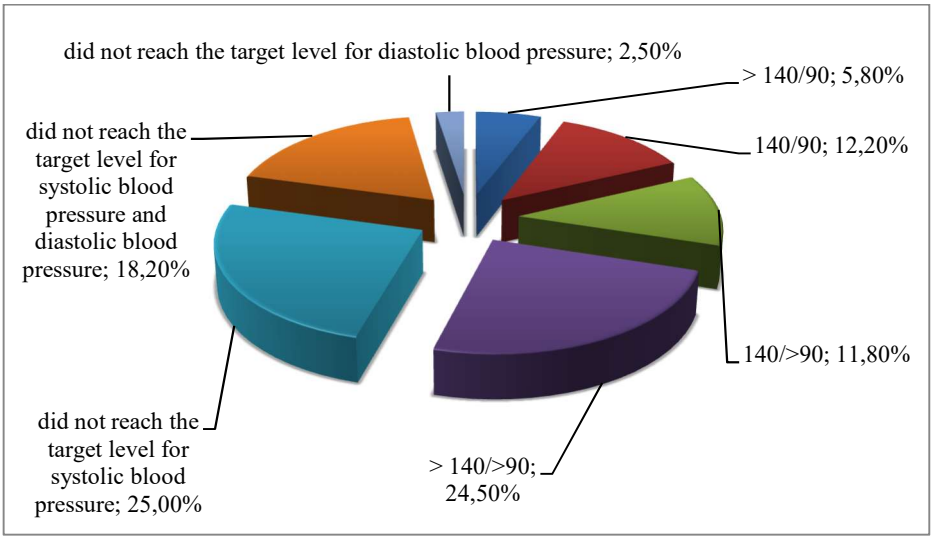
Source: own research.

A study of the distribution of drugs according to their INN showed that in this group the healing position was occupied by enalapril (25%). It was followed by atenolol (12%), indapamide (10,5%), hydrochlorthiazide (9,5%), verapamil (8,0%), nifedipine (7,5%), furosemide (6,0%), captopril (5,5%). Among the most commonly used brands were atenolol (12%), hypothiazide (9,5%), ednit (8,5%), arifon (8,0%), enam (7,0%), enap (6,0%), furosemide (6,0%), kapoten (5,0%), verapamil (8,0%).

Assessment of the effectiveness of treatment of patients with hypertension, performed by analysis of primary medical records, showed that the level of blood pressure, the initial value of which was on average 175,2 ± 0,9

/ 99 ± 0,5 mm Hg, significantly decreased (p<0,01) under the influence of treatment and amounted to 146,4 ± 0,8 / 88,4 ± 0,4 mm Hg. Significant decrease in blood pressure was observed in patients of all groups receiving different amounts of drugs. However, only 54,3% achieved its target level, which did not exceed 140/90 mm Hg. (Figure 6).

Figure 6. Structure of blood pressure levels achieved against antihypertensive therapy.



Source: own research.

Against the background of antihypertensive therapy, 12,7% of patients had a systolic blood pressureof 141–150 mm Hg, 13,8% 151–160 mm Hg, and 18,2% exceeded 161 mm Hg. The level of diastolic blood pressure in the range of 91-95 mm Hg was observed in 0,3% of patients, 96–100 mm Hg. – at 5,9%, more than 101 mm Hg – in 2,8% (Figure 7).

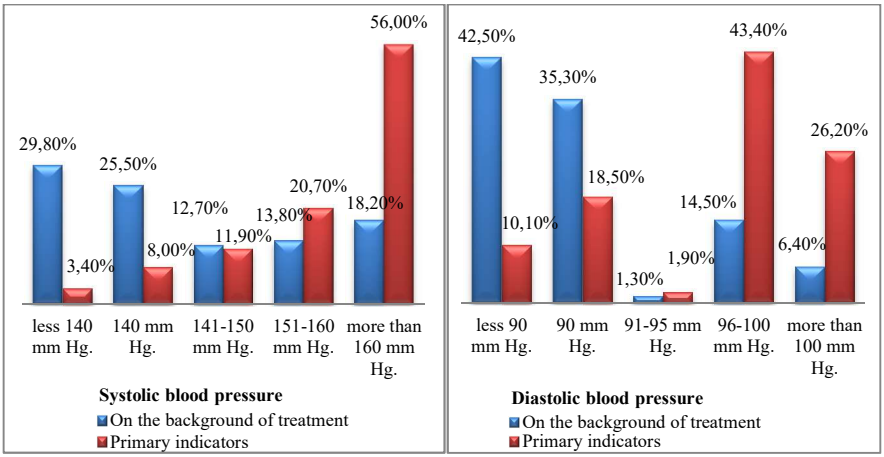
Conclusions

Thus, the lowest level of blood pressure against antihypertensive treatment was observed in patients receiving one drug (142 ± 1,0 / 68 ± 0,5 mm Hg), which was significantly (p <0,01) less than the levels of arterial the pressure

that was on patients who were assigned two, as well as three or more drugs. In patients in these groups, the blood pressure at the background of treatment was 151,5 ± 1,0 / 90,5 ± 0,5 and 155,5 ± 1,0 / 92,0 ± 0,5 mm Hg. in accordance.

For further study, we need a more detailed analysis of the antihypertensive activity of drugs that belong to the main pharmacological groups used in arterial hypertension mototherapy.

Figure 7. Restructuring of source and reached the level of blood pressure during antihypertensive treatment blood pressure level.



Source: own research.

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