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MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
Pharmaceutical Faculty
Department of Pharmacology and Clinical Pharmacy

QUALIFICATION WORK

on the topic: «**ANALYSIS OF THE PRACTICAL IMPLEMENTATION OF MODERN GUIDELINES FOR PHARMACOTHERAPY OF ARTERIAL HYPERTENSION IN A PHARMACY**»

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ANNOTATION

The qualification work analyzed the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy. The main areas that require improvement and the role of the pharmacist in the implementation of these guidelines in the pharmacy were identified. The qualification work presented on 40 pages, includes 2 tables, 17 figures, 36 literature sources and 4 applications.

Key words: arterial hypertension, guidelines for pharmacotherapy, pharmacy, antihypertensive drugs, fixed-dose combination drug.

АННОТАЦІЯ

В кваліфікаційній роботі було проаналізовано практичну реалізацію. сучасних протоколів з фармакотерапії артеріальної гіпертензії в аптечному закладі. Визначені основні напрямки, які потребують удосконалення, та роль фармацевта в реалізації цих протоколів в аптеці. Кваліфікаційна робота викладена на 40 сторінках, включає 2 таблиці, 17 малюнків, 36 джерел літератури та 4 додатки.

Ключові слова: артеріальна гіпертензія, протоколи фармакотерапії, аптека, антигіпертензивні засоби, фіксовані комбінації препаратів.

CONTENTS

ABBREVIATIONS LIST

ACC — American College of Cardiology;

ACE inhibitors — angiotensin-converting enzyme inhibitors;

AH — arterial hypertension;

AHA — American Heart Association;

ARBs — angiotensin II receptor blockers;

BP — blood pressure;

CCBs — calcium channels blockers;

DBP — diastolic blood pressure;

ESC — European Society of Cardiology;

ESH — European Society of Arterial Hypertension;

FDCD — fixed-dose combination drug;

ISH — International Society of Arterial Hypertension;

SBP — systolic blood pressure ;

TDs— thiazide diuretics;

WHO — World Health Organization;

β-blockers —beta-blockers;

$\varphi_{емр.}$ — Fisher's exact test.

INTRODUCTION

Relevance of the topic. Arterial hypertension (AH) is a major public health problem worldwide due to its high prevalence and associated risk of cardiovascular disease. AH is the leading cause of cardiovascular disease and premature death worldwide. According to World Health Organisation (WHO), 1.28 billion adults aged 30-79 years worldwide have AH. Approximately 46% of hypertensive adults are unaware that they have the condition and half of hypertensive adults (42%) are being treated. One of WHO's global targets for none communicable diseases is to reduce the prevalence of AH by 33% between 2010 and 2030. The treatment of hypertensive patients with is a global problem for all countries of the world.

Over the past 5 years, a large number of guidelines have been developed for the AH pharmacotherapy, which are improved almost annually, taking into account new evidence on effective blood pressure (BP) control. Today, AH pharmacotherapy is carried out in accordance with the guideline prepared by the WHO, guideline of the International Society of AH (ISH) Global AH Practice, the European Society of Cardiology (ESC)/European Society of AH (ESH) and the joint guidelines of and American Heart Association (AHA)/ American College of Cardiology (ACC).

The objectives of AH treatment are to prevent the occurrence of cardiovascular disease due to damage to the heart and blood vessels caused by sustained high BP, and consequent functional impairment and death. The following pharmacological classes of antihypertensive drugs are recommended for AH pharmacotherapy: angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin II receptor blockers (ARBs), thiazide diuretics (TDs), calcium channel blockers (CCBs), beta-blockers (β-blockers). Modern guidelines for AH pharmacotherapy favour combination therapy because it lowers BP more than monotherapy and increases the likelihood of achieving target BP. An important aspect of modern AH pharmacotherapy is the use of fixed-dose combination drug (FDCD). According to the WHO recommendations ideally all patients should be

treated with FDCD. AH treatment should be initiated with a “single pill” FDCD rather than using free equivalents (i.e., the same drugs and doses are given as separate tablets). A number of studies have demonstrated greater effectiveness of FDCD in lowering blood pressure by influencing various pathogenetic mechanisms of increased BP. In addition, treatment with FDCD allows for achieving BP control in a shorter time.

Given the data that only 50% of hypertensive patients with BP control, it is important to study the level of practical implementation of modern guidelines for AH pharmacotherapy. Failure to adhere to such evidence-based recommendations may be one aspect of insufficient BP control. And developing ways to increase the practical implementation of these guidelines may be one method of improving the effectiveness of treatment of hypertensive patients.

Purpose of the research. The purpose of the master's thesis was to study the implementation of modern recommendations for AH pharmacotherapy at the pharmacy.

Research objectives:

1. To review current international guidelines on AH pharmacotherapy.

2. To assess the availability of antihypertensive drugs at the pharmacy in accordance with current guidelines on AH pharmacotherapy.

3. To analyze the sales of sing-component antihypertensive drugs at the pharmacy by the separate pharmacological classes.

4. To analyze sales at the pharmacy of antihypertensive drugs in FDCD.

5. To conduct a comparative analysis of the total sales of free equivalents of single-component drugs and FDCD, which consist of the corresponding active substances according to their international non-proprietary name.

6. To assess the practical implementation of guidelines on AH pharmacotherapy at the pharmacy based on an assessment of sales of single-component drugs and FDCD.

Object of research. The object of research is AH.

Subject of research. The subject of research is the practical implementation of modern guidelines on AH pharmacotherapy at the pharmacy.

Research methods. During the execution of the master's thesis, search, analytical, quantitative and statistical research methods were applied. Search and analytical methods were used to conduct a literature review. Analytical and quantitative research methods were used to perform the practical part of the master's thesis - analysis of sales of antihypertensive drugs in a pharmacy. Fisher's exact test was used to establish the significant of the results obtained. Statistical analysis of the results was carried out using Microsoft Excel.

Practical significance of the obtained results lies in the fact that the data obtained in the study allowed us to assess the level of practical implementation of modern guidelines for AH pharmacotherapy. Given that practical implementation was insufficient, the main areas that require improvement were identified. The possible participation of the pharmacist in improving the practical implementation of modern guidelines for the treatment of hypertensive patients was also considered.

Approbation of research results and publication. The results of the study were published in two abstracts:

1. Analysis of the compliance of pharmacy sales of antihypertensive drugs with modern guidelines for arterial hypertension pharmacotherapy / Abdessamed Kinan, scientific supervisor: Associated Professor Zhabotynska N.V. // Актуальні питання створення нових лікарських засобів: матеріали XXXI міжнародної науково-практичної конференції молодих вчених та студентів (23-25 квітня 2025 р., м. Харків). – Харків: НФаУ, 2025. – С. 290. (Application A).

2. Analysis of the provision of antihypertensive drugs to hypertensive patients with according to modern guidelines / Abdessamed Kinan, Nataliia Zhabotynska // 3 Міжнародна науково-практична конференція «Innovative Solutions in Science: Balancing Theory and Practice» (28-30 april 2025, c. San-Fransisco). – San-Fransisco, USA, 2025. – С. 213-215. (Application C).

Structure and volume of master's thesis. The master's thesis consists of an introduction, 3 chapters: literature review, description of research methods, research results and their analysis; conclusions. The master's thesis is presented on 40 pages, includes 2 tables, 17 figures, 36 sources of literature and 4 applications.

CHAPTER 1
LITERATURE REVIEW

1.1. AH incidence

Arterial hypertension (AH) (high blood pressure (BP)) is defined in this report as a systolic blood pressure (SBP) at or above 140mmHg or diastolic blood pressure (DBP) at or above 90mmHg or on medication prescribed for high BP [1, 2]. AH is the leading cause of cardiovascular disease and premature death worldwide. AH is a major public health problem worldwide due to its high prevalence and associated risk of cardiovascular disease. It is one of the most important modifiable risk factors for stroke, coronary heart disease (e.g. angina, heart attacks and heart failure), and kidney disease [1, 2].

According to World Health Organization (WHO), 1.28 billion adults aged 30-79 years worldwide have AH. Approximately 46% of hypertensive adults are unaware that they have the condition and half of hypertensive adults (42%) are being treated. Only about 1 in 5 hypertensive adults (21%) have BP under control. One of WHO's global targets for noncommunicable diseases is to reduce the prevalence of AH by 33% between 2010 and 2030 [1].

The incidence of AH varies depending on the country. For example, AH prevalence in USA in adults age 18 and older was 47.7% and was higher in male (50.8%) than female (44.6%). The prevalence of AH increased with age. The prevalence was 23.4% in adults ages 18-39 and increased to 52.5% for ages 40-59 and 71.6% for 60 and older [3]. Among adults with AH, more than one-half reported taking medication to lower their BP and about one-fifth had their blood pressure under control [4].

In 2019, 22% of people in the Europe aged 15 years and over reported having high BP. Among the Europian countries, the highest shares of high BP were recorded in Croatia (37% of people aged 15 years and over), Latvia and Hungary (both 32%). In contrast, the lowest shares were recorded in Ireland (12%), Luxembourg, Romania and the Netherlands (all 16%) [5].

The incidence of AH in Morocco is high. The overall prevalence of AH in Morocco was 26.6% (26.3% in male and 28.0% in female). Among the hypertensive patients, 85.9% of patients were prescribed antihypertensive medication and/or lifestyle and dietary advice. Nevertheless, only 17.1% had controlled hypertension [6].

Thus, the treatment of hypertensive patients with is a global problem for all countries of the world.

1.2. Pharmacological characteristics of antihypertensive drugs

For the AH pharmacotherapy, first-line drugs (antihypertensive drugs of choice) are selected from the following pharmacological classes [7, 8]:

- angiotensin-converting enzyme inhibitors (ACE inhibitors);
- angiotensin II receptor blockers (ARBs);
- thiazide diuretics (TDs);
- calcium channel blockers (CCBs);
- beta-blockers (β-blockers).

First-line pharmacological clsses include drugs that have proven efficacy in lowering BP. In addition, the selection of the optimal first-line drug for hypertensive patients should take into account the hierarchy of treatment goals: reduction of hypertension-related morbidity and mortality, good tolerability, convenience of dosing, and low cost.

ACE inhibitors lower BP by vasodilating and reducing peripheral vascular resistance. This occurs by binding to the zinc ion of angiotensin-converting enzyme, which leads to a decrease in the rate of conversion to angiotensin II, which is a potent vasoconstrictor. In addition to vasodilation, ACE inhibitors neutralizes the numerous negative effects of angiotensin II on the cardiovascular system and also has, for example, changes in the structure of the heart, blood vessels, and kidneys. Thus, ACE inhibitors have the additional benefit of protecting the cardiovascular system and kidneys from remodeling [9, 10]. The most common side effects of ACE are cumulative: dry cough (10-20%), dizziness

(12-19%), hypotension (7-11%), increased blood urea nitrogen and creatinine (2-11%), syncope (5-7%), hyperkalemia (2-6%) [10]. ACE inhibitors are contraindicated in patients with a history of hypersensitivity to any ACE inhibitor or to any component of the product, angioedema related to previous ACE inhibitor therapy, and in pregnancy, as they are teratogenic to the fetus [10]. The following drugs from the pharmacological class of ACE inhibitors are usually used in the AH treatment: Captopril, Benazepril, Enalapril, Lisinopril, Ramipril, Perindopril, Quinapril, Fosinopril, Trandolapril [9].

Binding of ARBs drugs to angiotensin II receptors results in vasodilation through increased nitric oxide and bradykinin synthesis. In addition, activation of angiotensin II receptors leads to renal sodium excretion. Angiotensin II receptor antagonism has antiproliferative and cardiovascular protective effects [11]. ARBs are generally well tolerated and have a low incidence of side effects. ARBs can cause hypotension and/or renal failure in hypertensive patients whose BP or renal function is highly dependent on the renin-angiotensin-aldosterone system. For this reason, these drugs are contraindicated in patients with bilateral renal artery stenosis or hypertensive patients with heart failure [11]. The following drugs from the pharmacological class of ARB are usually used in the AH treatment: Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan, Azilsartan [12].

The mechanism of action for TDs is inhibiting the apical sodium/chloride transporter in epithelial cells of the distal convoluted tubules to reduce cardiac ejection fraction and cardiac output. In addition to lowering BP, TDs significantly reduce cardiovascular events and death without causing serious side effects. As with any drug, adverse effects are described for TDs [13]. Blood volume depletion, decreased plasma sodium (hyponatremia), decreased plasma potassium (hypokalemia), and increased plasma pH (alkalosis) are the reported prominent side effects for TDs [13, 14]. TDs are contraindicated for use in patients with anuria and Sulfonamide allergies [14].

Thiazide diuretics such as Hydrochlorothiazide, Indapamide and Chlorthalidone are ideal first-line antihypertensive agent as proven through multiple clinical trials [13].

The general mechanism of action of CCBs is that they block the movement of calcium into cells by binding to L-type “long-acting” voltage-gated calcium channels in the heart, vascular smooth muscle, and pancreas. The effects that can be obtained after CCBs use will depend on the type of CCBs. Non-dihydropyridine CCBs have an inhibitory effect on the SA and AV nodes, thereby slowing cardiac conduction and contractility. This property allows the treatment of arterial hypertension, reduces oxygen demand, and helps control the frequency of tachydyarhythmias. Non-dihydropyridine CCBs include Verapamil and Diltiazem [15]. Non-dihydropyridine CCBs may cause constipation, orthostatic hypotension, elevated liver enzymes, dizziness, and fatigue [15, 16].

Dihydropyridine CCBs are mainly peripheral vasodilators at therapeutic doses. This property makes them useful in the treatment of conditions such as hypertension, vasospasm after intracranial hemorrhage, and migraine [15]. Dihydropyridine CCBs may lead to lightheadedness, flushing, headaches, and peripheral edema. The peripheral edema is likely related to the redistribution of fluid from the intravascular space to the interstitium. More severe adverse events include acute myocardial infarction, exacerbated angina, acute hypotension, syncope, erythema multiforme, and hepatitis, which can vary slightly depending on the chosen agent [15]. Dihydropyridine CCBs include Amlodipine, Felodipine, Isradipine, Nicardipine, Nifedipine (only the extended release form is used), Nimodipine (only used for subarachnoid hemorrhage), Nitrendipine [12].

To date, 3 generations of drugs have been released: nonselective β-blockers, cardioselective β-blockers (selective β1-antagonists), and a third generation of these drugs able to block β1 together with extra vasodilation activity (also called vasodilating β-blockers) either by blocking α1- or by activating β3-AR [17]. Non-selective agents bind to both β-1 and β-2 receptors and induce antagonizing effects via both receptors. Examples include Propranolol, Carvedilol, Sotalol, and

Labetalol. Beta-1 receptor-selective blockers like Atenolol, Bisoprolol, Metoprolol, and Esmolol only bind to the β-1 receptors; therefore, they are cardio-selective [18]. β-blockers are drugs that bind to β-adrenoceptors and block the binding of norepinephrine and epinephrine to these receptors. This inhibits normal sympathetic effects that act through these receptors. Therefore, β-blockers are sympatholytic drugs. Some β-blockers, when they bind to the β-adrenoceptor, partially activate the receptor while preventing norepinephrine from binding to the receptor. These partial agonists therefore provide some "background" of sympathetic activity while preventing normal and enhanced sympathetic activity. Partial agonist β-blockers possess intrinsic sympathomimetic activity [12]. β-blockers decrease BP via several mechanisms, including decreased renin and reduced cardiac output. The negative chronotropic and inotropic effects lead to a decreased oxygen demand; that is how angina improves after β-blocker usage [18]. β-receptors are found all over the body and induce a broad range of physiologic effects. The blockade of these receptors with β-blocker medications can lead to many adverse effects. Bradycardia and hypotension are two adverse effects that may commonly occur. Fatigue, dizziness, nausea, and constipation are also widely reported. Some patients report sexual dysfunction and erectile dysfunction [18]. Less commonly, bronchospasm presents in patients on β-blockers. Asthmatic patients are at a higher risk [19]. Patients with Raynaud's syndrome are also at risk of exacerbation. β-blockers can induce hyperglycemia. All β-blockers, especially in patients with cardiac risk factors, carry a risk of heart block [18].

1.3. Modern approaches to AH pharmacotherapy

Over the past 5 years, a large number of guidelines have been developed for the AH pharmacotherapy, which are improved almost annually, taking into account new evidence on effective BP control.

Today, AH pharmacotherapy is carried out in accordance with the guideline prepared by the WHO [20], guideline of the International Society of AH (ISH) Global AH Practice [21], the European Society of Cardiology (ESC)/European

Society of AH (ESH) [22] and the joint guidelines of and American Heart Association (AHA)/ American College of Cardiology (ACC) [23].

The objectives of AH treatment are to prevent the occurrence of cardiovascular disease due to damage to the heart and blood vessels caused by sustained high BP, and consequent functional impairment and death. Lowering BP does reduce cardiovascular risks; maintaining systolic BP of less than 130 mm Hg demonstrably prevents complications in patients with heart failure, diabetes, coronary artery disease, stroke, and other cardiovascular diseases [24].

In 2019, a step-by-step approach to the AH treatment was proposed with an emphasis on combination therapy (Fig. 1.1).

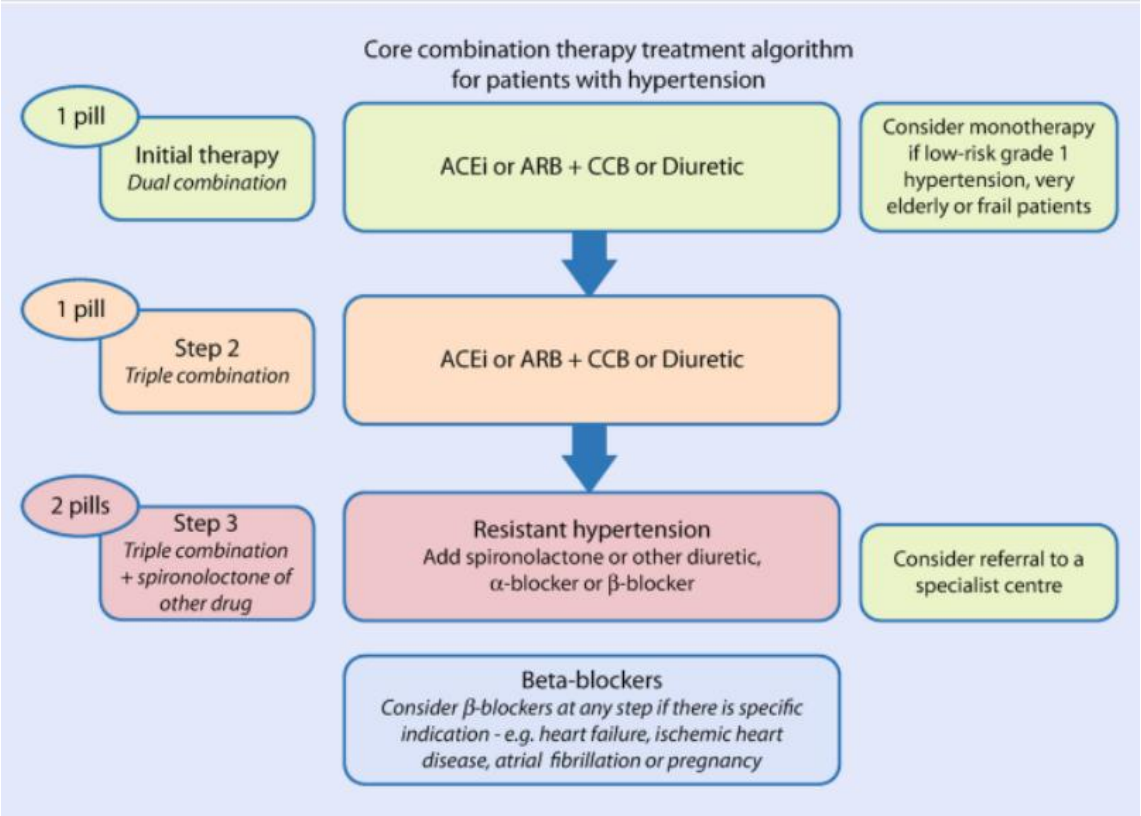

Fig. 1.1. Stepwise strategy for AH pharmacotherapy [25]

All hypertensive patients should be prescribed nonpharmacologic therapy (ie, lifestyle modification) and monitoring every 3 to 6 months.

Patients with stage 1 AH have BP levels of 130-139/80-89 mm Hg and cannot achieve a target BP below 130/80 mm Hg after 6 months of lifestyle changes and are prescribed drug therapy [26].

In patients with stage 1 AH (SBP 130 to 139 mmHg and/or DBP 80 to 89 mmHg), antihypertensive therapy can be initiated with a single drug. For monotherapy, it is recommended to choose ACE inhibitors, ARBs, CCBs, TDs or Thiazide-like diuretic [27].

Initial combination antihypertensive therapy is recommended for patients with stage 2 AH (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg). Treatment should be initiated with low or moderate doses of two antihypertensive drugs with complementary mechanisms of action [27, 28]. When two antihypertensive drugs are used, they should be from different antihypertensive pharmacological classes. In most patients, the drugs should be selected from among the three preferred classes: ACE inhibitors or ARBs, CCBs, and TDs (ideally a thiazide-like rather than a TDs) [23, 27].

In patients whose BP is not controlled despite combination therapy with two drugs, a third drug should be added. For example, in a patient who has not reached target BP despite taking an ACE inhibitor and a CCBs, a thiazide-like diuretic should be added [23, 27]. The addition of β-blockers as a third drug should be considered at any stage of antihypertensive therapy if the patient has an indication for their use. For example, the presences of heart failure, ischemic heart disease, atrial fibrillation, or pregnancy are indications for the use of β-blockers [25, 27].

Patients receiving antihypertensive drug therapy should be reassessed every two to four weeks until their BP is at target. This reassessment interval after initiating or increasing therapy allows long-acting antihypertensive drugs sufficient time to exert their full blood pressure-lowering effect. Reassessment after two weeks (or even earlier) is appropriate for patients with severely elevated BP [23, 27].

Current guidelines for AH pharmacotherapy favour combination therapy because it lowers BP more than monotherapy and increases the likelihood of achieving target BP within a reasonable time frame. In addition, the use of two drugs may lead to achieving target BP with lower doses of each drug, reducing the risk of dose-related side effects [27]. This strategy has a clear pathophysiological

rationale because AH almost always due to a variety of pathogenetic factors and BP is a multiregulated variable, with neural, humoral, and local mechanisms working in concert or against each other to change or defend a given BP value. This makes the multiple BP-lowering mechanisms made available by the combination of different drugs much more effective than one or few. Full support comes from the evidence that compared with increasing the dose of the initial drug, adding a second drug can increase by about 5× the chance of achieving BP control regardless which drug is used initially and which is added [29].

An important aspect of modern AH pharmacotherapy is the use of fixed-dose combination drug (FDCD). According to the WHO recommendations ideally all patients should be treated with FDCD [20]. FDCD are combinations of two or more active drugs in a single dosage form. The Food and Drug Administration, USA defines a combination product as ‘a product composed of any combination of a drug and a device or a biological product and a device or a drug and a biological product or a drug, device, and a biological product’s [30]. FDCD are acceptable when the dosage of each ingredient meets the requirements for the treatment of a specific disease and when the combination has a proven advantage over the individual compounds administered separately in terms of therapeutic effect, safety, or compliance [31]. When choosing FDCD it is necessary to take into account that the drugs in the combination should have different mechanisms of action; their pharmacokinetics must not be widely different; FDCD should not contain excess toxic additional substances [31].

AH treatment should be initiated with a “single pill” FDCD (i.e., both drugs are contained in a single tablet) rather than using free equivalents (i.e., the same drugs and doses are given as separate tablets). Some experts recommend initiating AH pharmacotherapy with a “single pill” FDCD containing low doses of each drug, while others recommend starting with free equivalents and then, after titrating the dose of each drug, switching to a “single pill” FDCD. A “single pill” FDCD has been shown to result in greater BP reduction, better achievement of target BP, and better adherence to treatment compared with free equivalents [27,

32, 33]. However, there are some situations where it is acceptable to use free equivalents for the AH treatment rather than a “single pill” FDCD. For example, in patients with a history of allergies or intolerance to several drugs. In such cases, free equivalents can eventually be replaced by a “single pill” FDCD when BP is under control and the patient tolerates the therapy well [27]. A “single pill” FDCD are often more expensive and may not be covered by drug insurance. In such situations, if free equivalents are available, their use should be preferred.

Conclusion to Chapter 1

AH is the leading cause of cardiovascular disease and premature death worldwide. According to WHO, 1.28 billion adults aged 30-79 years worldwide have AH. Effective AH treatment will prevent the development of complications with damage to target-organs (heart, brain, kidneys, retina) and reduce the risk of fatal cardiovascular events. The following pharmacological classes of antihypertensive drugs are used to AH treatment: ACE inhibitors, ARBs, TDs, CCBs, β-blockers. Each of these pharmacological classes has proven effectiveness in lowering BP, certain mechanisms of action, indications for use, and side effects.

Today, the modern strategy for AH treating is a stepwise approach, which consists of three steps. The vast majority of patients begin treatment with combination therapy, which contains 2 drugs (ACE inhibitors or ARBs with CCBs). If ineffective, they switch to a triple combination with the addition of TDs. The emphasis is on the use of a “single pill” FDCD.

However, according to literature data, only 50% of hypertensive patients achieve target BP levels. Therefore, there is a need to assess the practical implementation of current guidelines for AH pharmacotherapy.

CHAPTER 2
RESEARCH METHODS

The master's thesis was carried out in several stages.

Stage 1 is choosing a topic for the master's thesis. In my opinion, the problem of effective AH treatment is very relevant, since mortality from cardiovascular diseases ranks first in the world, and hypertension is one of the causes of fatal cardiovascular events.

Stage 2 is conducting a literature review. A literature review allows you to obtain the largest amount of information on the issue under study, as well as establish lists of issues that need to be resolved. We conducted a review of 36 literary sources, which consisted of publications in scientific journals and guidelines that regulate the pharmacotherapy of hypertension. The literature review allowed us to update knowledge about modern approaches to the treatment of hypertension and formulate

Stage 3 is formulating of research purpose and objectives. After conducting a literature review, unresolved issues regarding the practical implementation of recommendations for pharmacotherapy of hypertension were identified. Then, the goals of the master's thesis and the tasks that need to be solved to achieve the set goals were formulated.

Stage 4 is creating a research design. After formulating the objectives and research questions, methods for achieving the set objectives were developed. Since the topic of the master's thesis was specifically related to the practical implementation of recommendations for AH pharmacotherapy, it was decided to conduct the study in a pharmacy — an institution that is one of the key links in the process of clarifying BP control.

Scientific research typically uses both quantitative and qualitative research methods.

Quantitative research is the collection and analysis of numerical data to answer research questions. Using this method allows you to quantify the size of the

effect, determine the strength of associations, rank priorities, and weigh the strength of evidence for effectiveness. Quantitative research is used to summarize, average, find patterns, predict and test cause-and-effect relationships, and generalize research results [34].

Qualitative research is a type of research that examines the experiences and/or behaviours of participants. This type of research answers the questions of how and why rather than how much or how many. Qualitative research, by its very nature, asks open-ended questions such as “how” and “why.” The answers to which are not easily translated into numbers, but they help to explain the processes and patterns of human behaviour that are being studied [35].

To assess the practical implementation of modern recommendations for the AH treatment, we used the quantitative method of follow-up. The study was conducted in a city Oualidia in Pharmacie Ben Aziz. The materials of the study were pharmacy sales reports of antihypertensive drugs for 3 months (from October to December 2024).

Stage 5 is analyzing the data. An important step in any research study is to analyze the data you have collected. In the master's thesis, percentages and Fisher's exact test (φ_{emp}.) were used.

Fisher's exact test (φ_{emp}.) or “Fisher's angular transformation” is used to compare two samples by the frequency of occurrence of the effect of interest. The criterion assesses the reliability of differences between the percentages of two samples and has no restrictions on the number of samples. The principle of the method is to convert percentages (fractions) into a value φ, the distribution of which is close to normal [36]. To calculate Fisher's exact test, an on-line calculator was used, available at https://www.omnicalculator.com/statistics/fishers-exact-test.

Microsoft Excel programs from the Microsoft Office suite were used to analyze the obtained data. The results of statistical data processing were presented in the form of diagrams and tables for greater clarity.

Stage 6 is formulating conclusions. One of the most important stages of the study is writing conclusions based on the results of data analysis. Formulating

conclusions allows you to assess whether the goals and objectives set in the study have been achieved, as well as formulate practical recommendations based on the results of the study.

Stage 7 is writing and approving the master's thesis. The final stage of the study was the approval of the master's thesis in accordance with the requirements of the National University of Pharmacy.

After approval, the manuscript was sent for plagiarism checking and received a positive conclusion.

Conclusion to Chapter 2

The master's thesis was completed in 7 stages: choosing a topic, conducting a literature review, formulation of research goals and objectives, creating a research design, analyze the data, conclusions writing and approving the master's thesis. During the study, search, analytical, quantitative and statistical research methods were applied. The master's thesis was prepared in accordance with the requirements and was checked for plagiarism.

CHAPTER 3
THE RESULTS OF THE RESEARCH. THE DISCUSSION OF THE RESULTS

3.1. Analysis of pharmacy stock of antihypertensive drugs

A studying of the practical implementation of modern guidelines for AH pharmacotherapy was conducted in a pharmacy "PHARMACIE BEN AZIZ" in city Oualidia during July to September 2024. The antihypertensive drugs are represented by all recommended pharmacological classes: ACE inhibitors, ARBs, TDs, CCBs, β-blockers. Each pharmacological class is represented by drugs with different active ingredients (Table 3.1).

Table 3.1.

Pharmacological classes of antihypertensive drugs presented at the pharmacy

Pharmacological classes	Drugs
ACE inhibitors	Enalapril Lisinopril Ramipril
ARBs	Losartan Valsartan
TDs	Hydrochlorothiazide Indapamide Chlorthalidone
CCBs	Non-dihydropyridine — Diltiazem Dihydropyridine: Amlodipine Lercanidipine
β-blockers	Bisoprolol Metoprolol Nebivolol

Only the pharmacological class of TDs in the pharmacy was provided with all three recommended drugs. The ACE inhibitors class was represented by only three drugs, although the recommendations include 9 drugs. The ARBs class was represented by only two drugs, although the recommendations include 8 drugs. Non-dihydropyridine CCBs were represented by only one of the two recommended drugs, while dihydropyridine CCBs were represented by two of the seven recommended drugs. The β-blockers class was represented by only three selective drugs, although the recommendations include 8 drugs, including selective and non-selective drugs.

Analysis of the pharmacy's stock of antihypertensive drugs showed that all recommended pharmacological classes are available. However, most classes are represented by a significantly smaller number of drugs than recommended by the guidelines.

All pharmacological classes of antihypertensive drugs are represented by drugs that consist of one active ingredient — single-component drugs or combined drugs in the form of FDCD (Table 3.2).

Table 3.2.

Pharmacological classes of antihypertensive drugs in the FDCD presented at the pharmacy

Pharmacological classes	Combinations of active ingredients (international non-proprietary names)	Trade names
Dual FDCD		
ACE inhibitors + TDs	Enalapril+ Hydrochlorothiazide	Enap H Enap HL Enalozide
	Perindopril + Indapamide	Ko-Perinesa Noliprel Arginine Noliprel Forte

Pharmacological classes	Combinations of active ingredients (international non-proprietary names)	Trade names
ACE inhibitors + β-blockers	Perindopril + Bisoprolol	Prestilol
ARBs + CCBs	Amlodipine + Valsartan	Valodip
Triple FDCD		
ACE inhibitors + TDs + CCBs	Perindopril + Indapamide + Amlodipine	Tripliksam
ARBs + TDs + CCBs	Valsartan + Indapamide + Amlodipine	Ko-Valodip

FDCD at the pharmacy are represented by three dual combinations and two triple combinations. Dual combinations consisted of ACE inhibitors or ARBs with TDs or CCBs or β-blockers. Triple combinations consisted of fourth pharmacological classes of antihypertensive drugs — ACE inhibitors or ARBs + TDs + CCBs, excluding β-blockers. Each combination is represented by preparations with three trade names. Among all FDCD, the most widely represented are dual FDCD, which consist of ACE inhibitors (Enalapril or Perindopril) and TD (Hydrochlorothiazide or Indapamide).

It is noteworthy that almost all FDCD are presented at the pharmacy in different dosages, which allows for an individual approach to choosing the dose of an antihypertensive drug for each patient. For example, Ko-Perinesa, Prestilol and Valodip are presented in two dosages and Tripliksam in three dosages.

Dual FDCD presented at the pharmacy allow for the implementation of modern guidelines for the AH treatment in the first step, when most patients are recommended to start treatment with dual FDCD. Moreover, it is recommended to choose combinations that are ACE inhibitors or ARBs with CCBs or TD available at the pharmacy. Triple combinations of SDS FDCD available in the pharmacy allow implementing recommendations regarding the 2 steps of AH treatment,

when patients are recommended triple combinations consisting of ACE inhibitors or ARBs with TDs and CCBs. The availability of a wide selection of single-component drugs from all pharmacological classes at the pharmacy allows providing hypertensive patients with appropriate treatment when it is necessary to use single-component drugs, or at step 3, when a fourth antihypertensive drug (β-blocker or Spironolactone) is added to the triple FDCD.

Based on the described data, it can be concluded that the pharmacy is provided with all pharmacological classes of drugs for the AH treatment in the form of single-component drugs and FDCD in various dosages. However, it is desirable to expand the number of trade names of drugs to provide patients with a freer choice of antihypertensive drugs.

3.2. General analysis of sales of antihypertensive drugs in a pharmacy

For the period from July to September 2024, 587 packages of drugs for the AH treatment were sold, which amounted to 12.76% of the total volume of drug sales in the pharmacy. Next, a more detailed analysis of sales of antihypertensive drugs was conducted depending on pharmacological groups, single-component drugs and single-component drugs

The distribution of sold antihypertensive drugs by pharmacological groups is presented in Fig. 3.1. In terms of absolute number of packages, ACE inhibitors sales took the first position. At the same time, sales of ACE inhibitors significantly ($\varphi_{emp.}$ = 6.607; p = ≤0.01) exceeded sales of angiotensin II receptor blockers by 1.84 times. Sales volumes of calcium channel blockers (CCBs) and β-blockers were the same. And sales of CCBs and β-blockers were 1,49 times significantly ($\varphi_{emp.}$ = 2.62; p = 0.0044) higher than those of thermal preparations (TDs). The lowest sales volumes were in TDs: 3.65 times lower than ACE inhibitors; 1.98 times lower than ARBs and 1.49 times lower than CCBs and β-blockers. This result shows that most often for AH pharmacotherapy are used ACE inhibitors, ARBs, CCBs and β-blockers, which corresponds to modern approaches to AH pharmacotherapy.

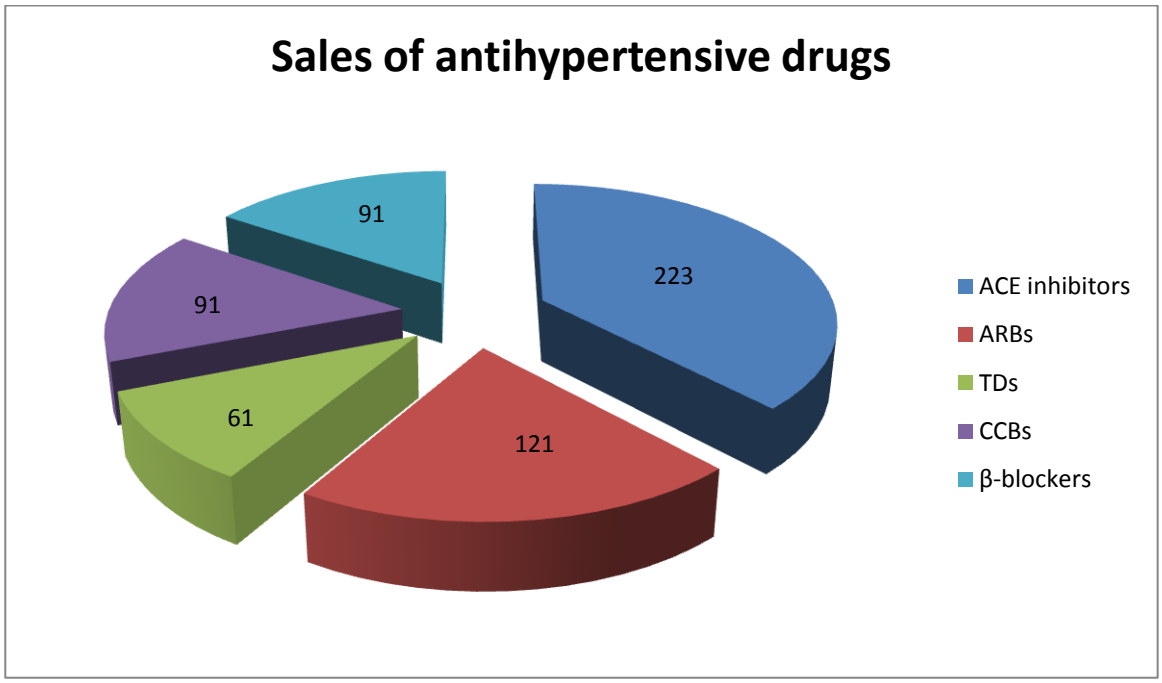

Fig. 3.1. Distribution of pharmacy's sold antihypertensive drugs by pharmacological classes

Since antihypertensive drugs are presented at the pharmacy in the form of single-component drugs and single-component drugs, a comparative analysis of their sales was conducted (Fig. 3.2.).

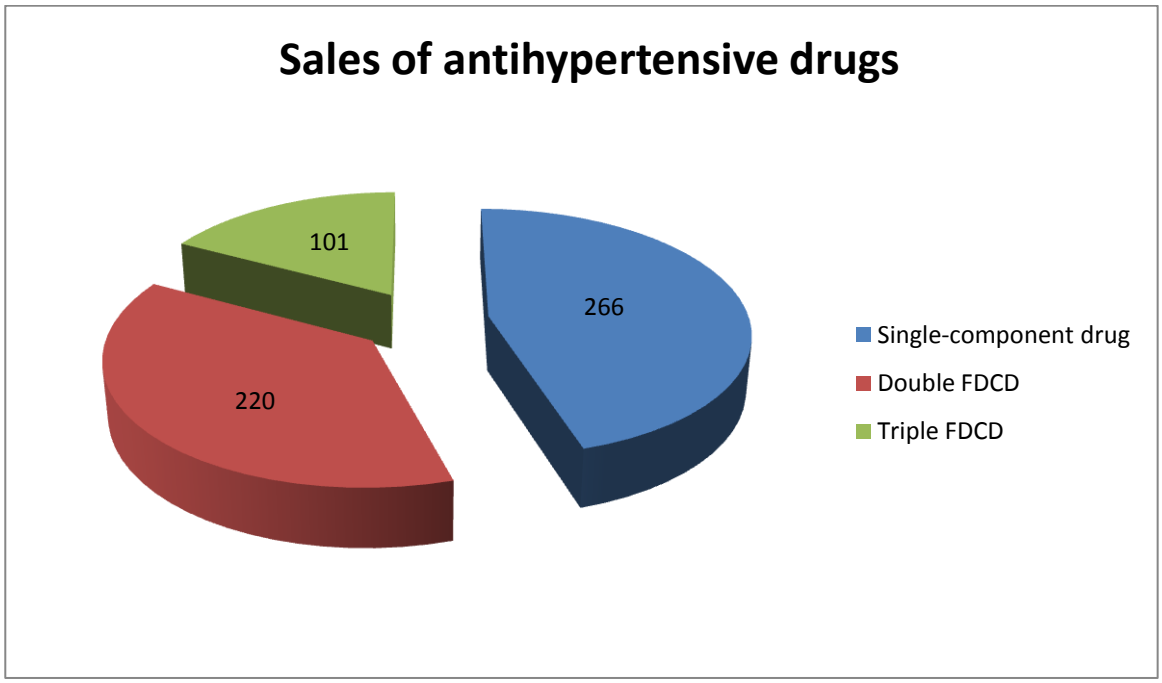

Fig. 3.2. Comparative analysis of sales of single-component drugs and FDCD

A comparative analysis of sales showed a significantly ($\varphi_{emp.}$ = 3.215; p = 0.0007) predominance of FDCD over single-component ones. However, sales of single-component preparations were significantly ($\varphi_{emp.}$ = 2.729;p = 0.0032) more than sales of dual FDCD. And sales of triple FDCD were significantly ($\varphi_{emp.}$ = 7.919; p = ≤0,01)**.** Despite significantly (p = ≤0,01) higher total FDCD sales, sales of single-component antihypertensive drugs exceeded sales of both dual and triple FDCD separately.

3.3. Sales analysis of single-component antihypertensive drugs

During research, an analysis of sales of single-component drugs was conducted depending on the pharmacological classes (Fig. 3.3.).

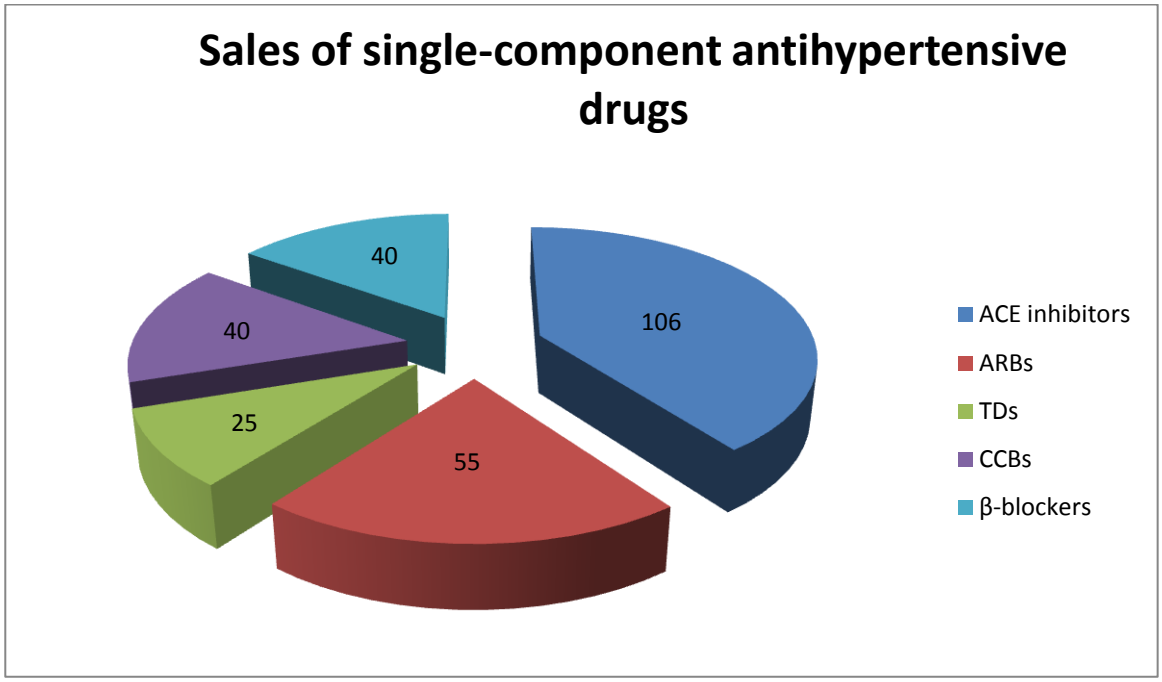

Fig.3.3. Sales analysis of single-component antihypertensive drugs of different pharmacological classes

Sales of single-component drugs accounted for 45.3% of the total sales of antihypertensive drugs at the pharmacy over 3 months. In terms of absolute number of packages, ACE inhibitors sales took the first position. At the same time, ACE inhibitors sales significantly ($\varphi_{emp.}$ = 4.8; p = ≤0,01) exceeded ARBs sales,

and CCBs and β-blockers sales were significantly ($\varphi_{emp.}$ = 1.998; p = 0.0228) higher than TDs. Sales of CCBs and β-blockers were the same.

ACE inhibitors monopreparations were presented by Enalapril, Lisinopril, Ramipril. Sales of Enalapril significantly ($\varphi_{emp.}$ = 6.697; p = ≤0,01) exceeded sales of the other two drugs — Lisinopril, Ramipril (Fig. 3.4.).

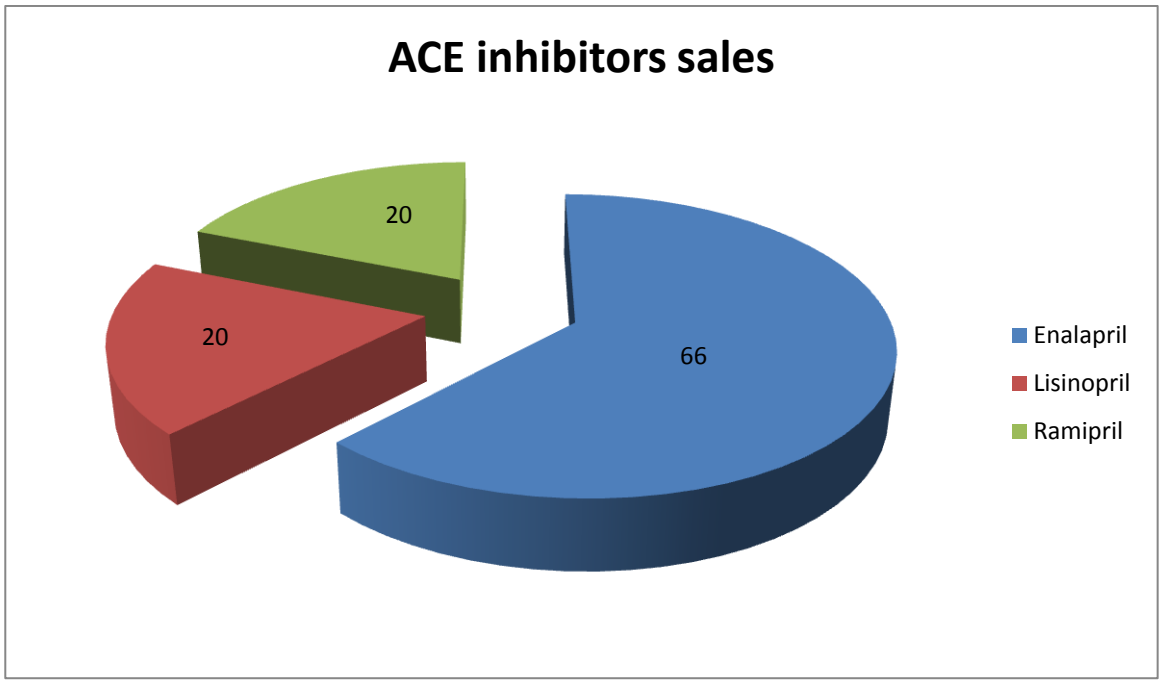

Fig.3.4. Sales analysis of ACE inhibitors single-component drugs

Enalapril in the form of enalapril maleate is the best known and most widely used ACE inhibitor. It is recommended for the treatment hypertensive patients with chronic heart failure and chronic kidney disease. Therefore, it sells better than other ACE inhibitors.

ARBs monopreparations were presented at the pharmacy by Losartan, Valsartan. Sales of Valsartan 2,66 times significantly ($\varphi_{emp.}$ = 4.569; p = ≤0,01) higher than Losartan (Fig.3.5). If we analyze the total sales of drugs that lower blood pressure by affecting the renin-angiotensin system, we can determine that the total sales of ACE inhibitors and ARBs amounted to 60,53% of the total sales of single-component drugs and significantly ($\varphi_{emp.}$ = 4.892; p = ≤0,01) exceeded the sales of drugs of other pharmacological classes. Such sales are fully consistent

with current recommendations for AH pharmacotherapy, since ACE inhibitors and ARBs are recommended as the drugs of choice for initial therapy at all stages of hypertensive patients.

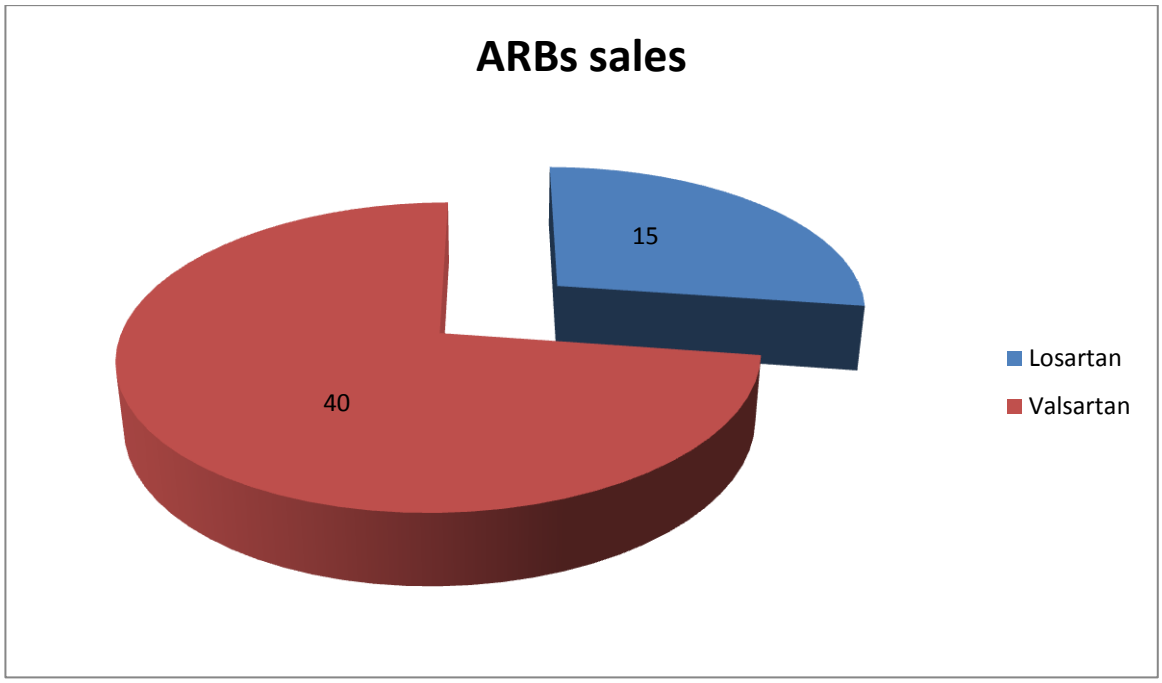

Fig.3.5. Sales analysis of ARBs single-component drugs

The CCBs pharmacological class was presented at the pharmacy by three drugs: Diltiazem, Amlodipine, Lercanidipine. Sales of Amlodipine amounted to 60% and significantly ($\varphi_{emp.}$ = 1.801; p = 0.0359) exceeded sales of the other two drugs — Diltiazem and Lercanidipine (Fig. 3.6.).

Amlodipine is a dihydropyridine CCBs. This drug has the largest evidence base for its effectiveness in cardiovascular diseases. In modern guidelines for AH pharmacotherapy, it is listed as the recommended drug. Amlodipine is recommended for the treatment of hypertensive patients combined with ischemic heart disease, the manifestation of which is stable and vasospastic (like Prinzmetal's angina) angina. Therefore, the largest sales among SVRs are justified.

The β-blockers pharmacological class was presented at the pharmacy by three drugs: Bisoprolol, Metoprolol, Nebivolol. Sales of Nebivolol amounted to

55%, but not significantly exceeded sales of the other two drugs — Bisoprolol, Metoprolol (Fig. 3.7.).

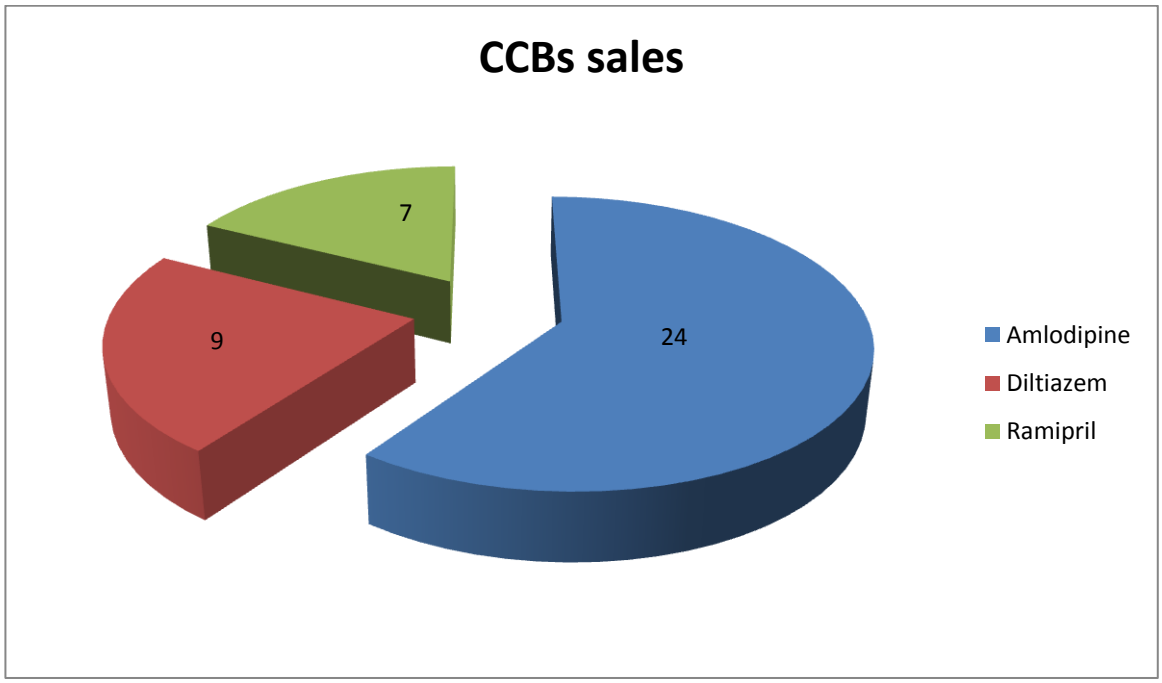

Fig.3.6. Sales analysis of CCBs single-component drugs

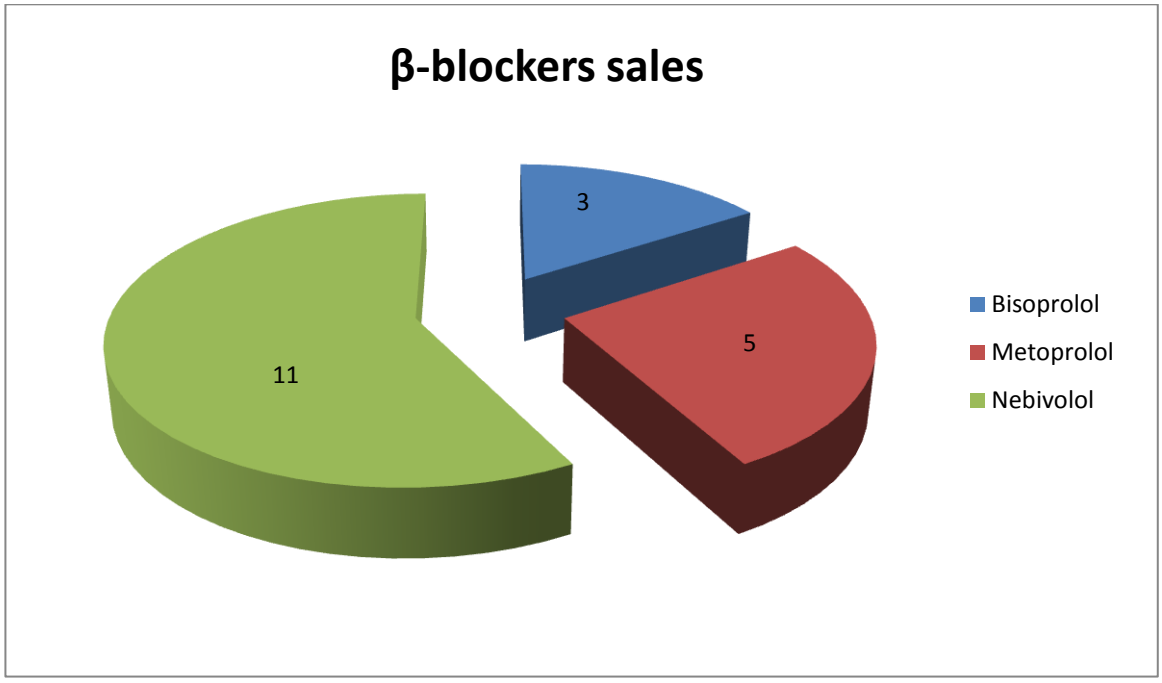

Fig.3.7. Sales analysis of β-blockers single-component drugs

Nebivolol is a third-generation cardioselective beta-blocker with additional (vasodilatory) properties due to modulation of nitric oxide release. Nebivolol is recommended for the treatment of hypertensive patients combined with ischemic heart disease (stable angina) and sinus tachycardia. Also, unlike other β -blockers, it can be used in hypertensive patients with metabolic syndrome and type 2 diabetes, chronic obstructive pulmonary disease. Perhaps it is this expanded list of indications for use that explains the greater sales of Nebivolol among all β-blockers.

The TDs pharmacological class was presented at the pharmacy by three drugs: Hydrochlorothiazide, Indapamide, Chlorthalidone. Sales of Hydrochlorothiazide amounted to 44%, but not significantly exceeded sales of the other two drugs — Chlorthalidone and Indapamide, the sales of which were the same (Fig. 3.8.).

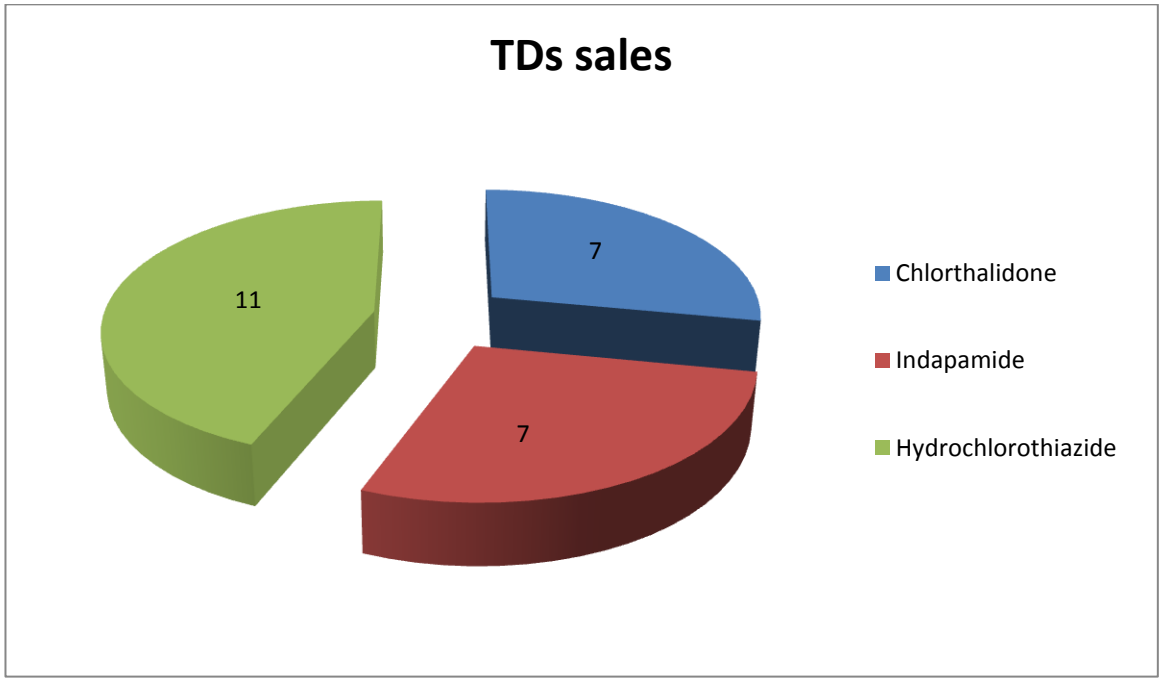

Fig.3.8. Sales analysis of TDs single-component drugs

Additionally, an analysis of sales of individual preparations was conducted according to their international non-proprietary name (Fig.3.9.).

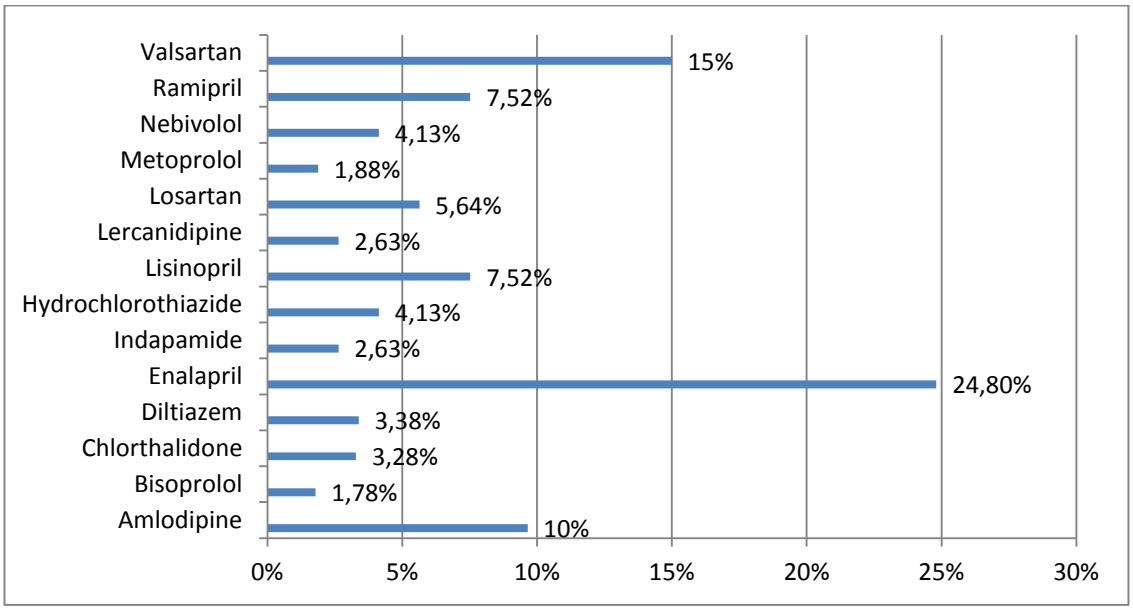

Fig.3.9. Sales analysis of single-component drugs according to their international non-proprietary name

The highest sales among single-component antihypertensive drugs were in Enalapril, Valsartan, Amlodipine. These drugs also occupied probably the best positions in their pharmacological classes.

Summarizing the results of the analysis of sales of single-component antihypertensive drugs of different pharmacological classes, it can be said that sales of ACE inhibitors and ARBs probably prevailed. In the corresponding pharmacological class, significantly ($p = \leq 0{,}05$) higher sales were observed in Enalapril, Valsartan, Amlodipine.

3.4. Sales analysis of antihypertensive FDCD

Antihypertensive FDCD were presented at the pharmacy in dual and triple combinations. Dual combinations were presented in ACE inhibitors + TDs; ACE inhibitors + β-blockers; ARBs + CCBs. Triple combinations were presented in ACE inhibitors + TDs + CCBs and ARBs + TDs + CCBs.

Among dual SDS, sales of ACE inhibitors + TD significantly ($\varphi_{emp.} = 11.051$; $p = \leq 0.01$) prevailed over other dual SDS variants and accounted for 70.45% (Fig. 3.10.).

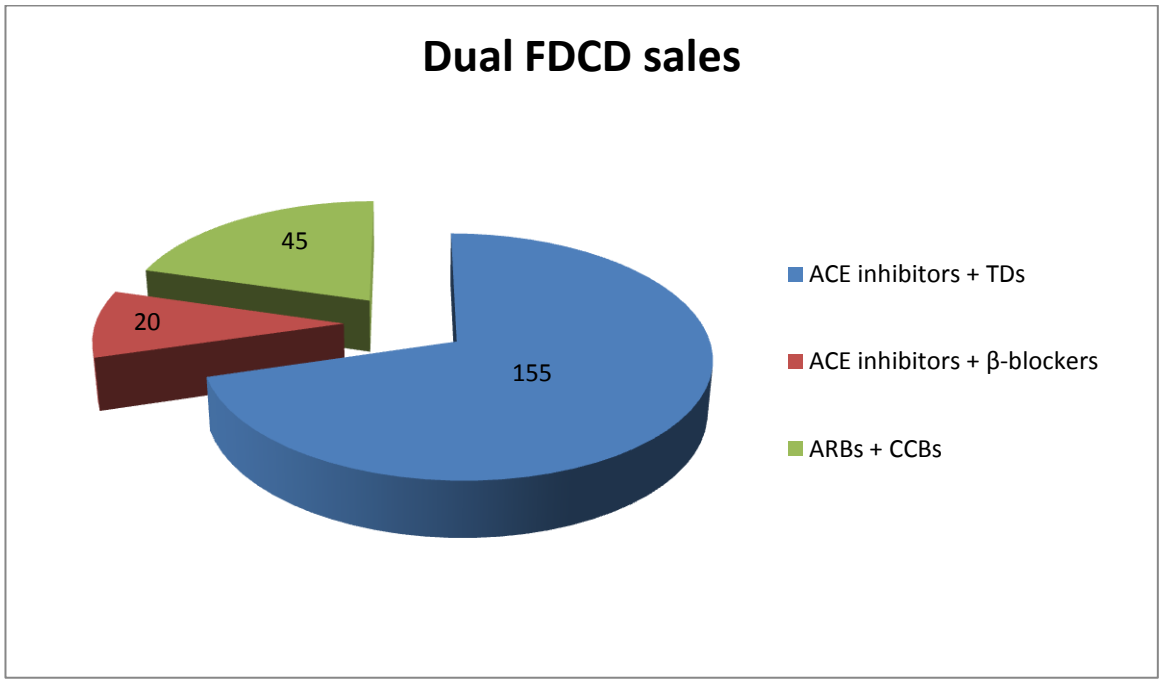

Fig.3.10. Sales analysis of dual FDCD

ACE inhibitors + TDs is one of the best for initial AH therapy. Therefore, their largest sales correspond to modern AH pharmacotherapy guidelines. The combination ARBs + CCBs is recommended in case of ineffectiveness or contraindications for the use TDs or CCBs. Adding β-blockers to combination therapy requires the patient to have clear indications, such as chronic heart failure, ischemic heart failure, atrial fibrillation or pregnancy.

Analysis of dual FDCD sales, consisted from ACE inhibitors + TDs, showed that sales Perindopril + Indapamide amounted to 85,16% and significantly ($\varphi_{emp..}$ = 13.732; p = ≤0,01) outweighed sales Enalapril + Hydrochlorothiazide (Fig.3.11.).

Comparativ analysis of dual FDCD sales, consisted from ACE inhibitors + β-blockers and ACE inhibitors + TDs, showed that sales Perindopril + Indapamide amounted to 86,84% and significantly ($\varphi_{emp.}$ = 13.732; p = ≤0,01) outweighed sales Perindopril + Bisoprolol (Fig.3.12.).

Analysis of sales of double FDCD consisting of ACE inhibitors + β-blockers or TDs showed a significantly (p = ≤0,01) steady predominance of sales of

combination ACE inhibitors + TDs containing Perindopril + Indapamide. This combination is recommended for initial AH therapy at 1 step of treatment.

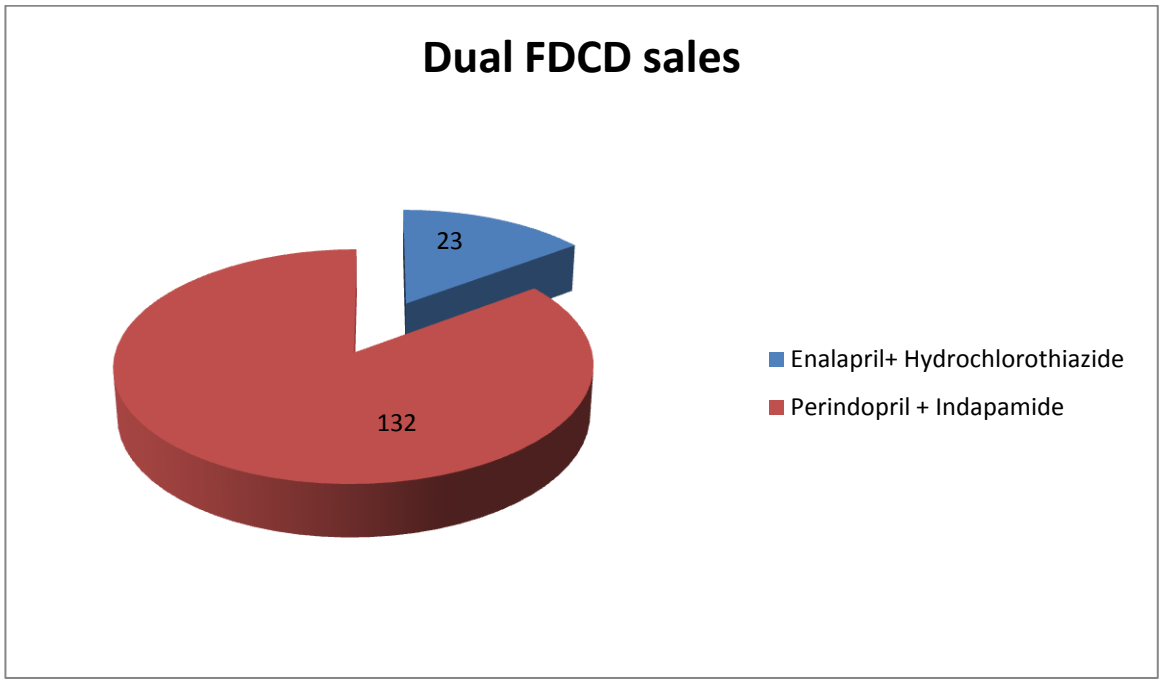

Fig.3.11. Sales analysis of FDCD, consisted from ACE inhibitors + TDs

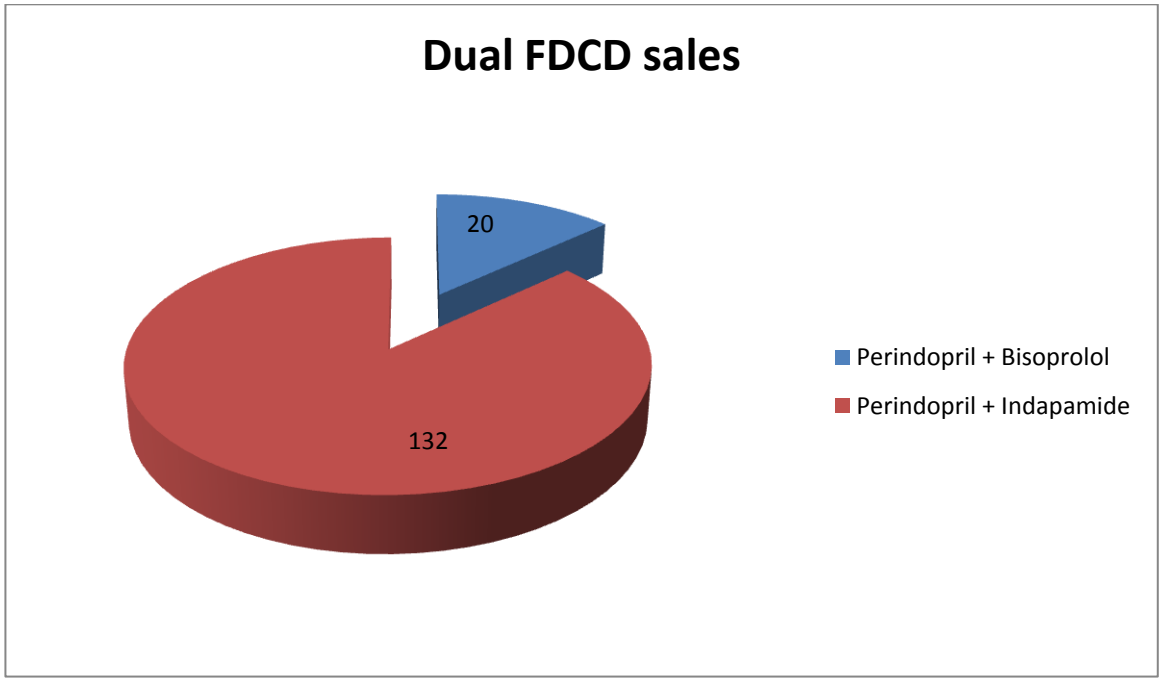

Fig.3.12. Comparativ analysis of dual FDCD sales, consisted from ACE inhibitors + β-blockers and ACE inhibitors + TDs

Comparative analysis of triple FDCD sales showed that sales ACE inhibitors + TDs + CCBs amounted to 96,04% and significantly ($\varphi_{emp.}$ = 16.63; p = ≤0,01) outweighed sales ARBs + TDs + CCB (Fig.3.13.).

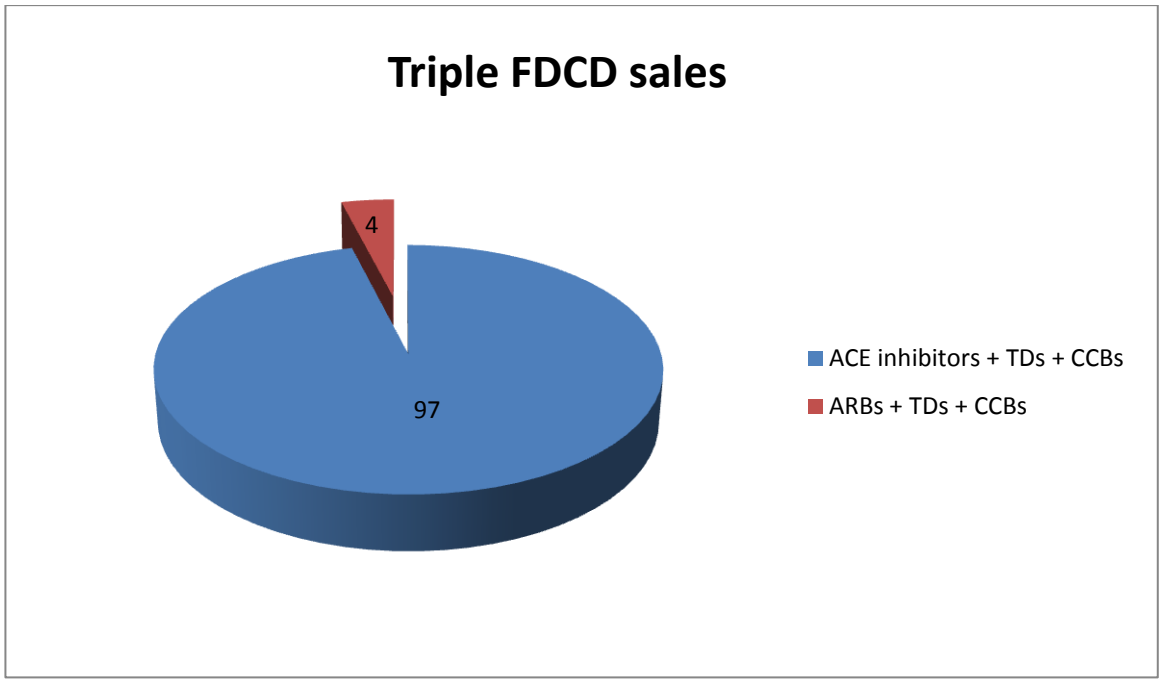

Fig.3.13. Comparative sales analysis of triple FDCD

Combination ACE inhibitors + TDs + CCBs was presented in Perindopril + Indapamide + Amlodipine (trade name Tripliksam). Combination ARBs + TDs + CCB was presented in Valsartan + Indapamide + Amlodipine (trade name Ko-Valodip). During the sales analysis, we noticed that among both single-component ACE inhibitors and FDCD containing ACE inhibitors, Perindopril from a certain manufacturer has the highest sales. Therefore, the highest sales of drugs from this manufacturer may be due to their marketing policy in the pharmacy.

The analysis showed significantly higher sales of FDCD. Analysis of sales of double FDCD showed a significantly (p = ≤0,01) steady predominance of sales combination ACE inhibitors + TDs. Analysis of sales of triple FDCD showed a significantly (p = ≤0,01) predominance of sales combination ACE inhibitors + TDs + CCBs. The influence of a particular drug manufacturer on sales of both single-component drugs and FDCD was also revealed.

3.5. Comparative analysis of sales of FDCD and total sales of the free equivalents

In modern guidelines for the AH treatment, special attention is paid to the use of not just combination therapy, but specifically FDCD. Therefore, further research was aimed at a comparative analysis of total sales of the free equivalents and FDCD with the same composition.

Comparative sales analysis of free equivalents and dual FDCD ACE inhibitors + TDs was carried out only on the combination Enalapril + Hydrochlorothiazide, since the single-component drug of Perindopril wasn't available at the pharmacy. Analysis results demonstrated a significantly ($\varphi_{emp.}$ = 8.067; p = ≤0,01) predominance of total sales of free equivalents Enalapril and Hydrochlorothiazide compared to dual FDCD (Fig.3.14.). This result indicates non-compliance with modern guidelines for AH pharmacotherapy.

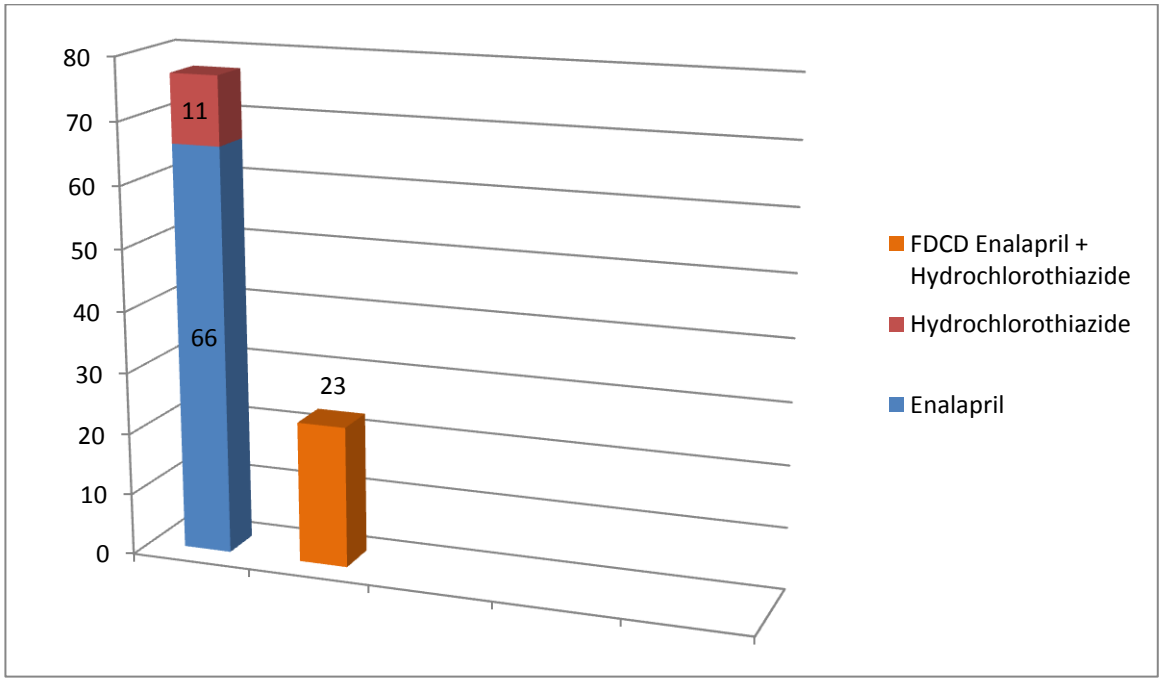

Fig.3.14. Comparative sales analysis of free equivalents and dual FDCD ACE inhibitors + TDs

Comparative sales analysis of free equivalents and dual FDCD ARBs + CCBs was carried out on the combination Amlodipine + Valsartan. Analysis

results demonstrated a significantly ($\varphi_{emp.}$ = 2.587; p = 0.0048) predominance of total sales of free equivalents Amlodipine and Valsartan (Fig.3.15.). This result indicates non-compliance with modern guidelines for AH pharmacotherapy.

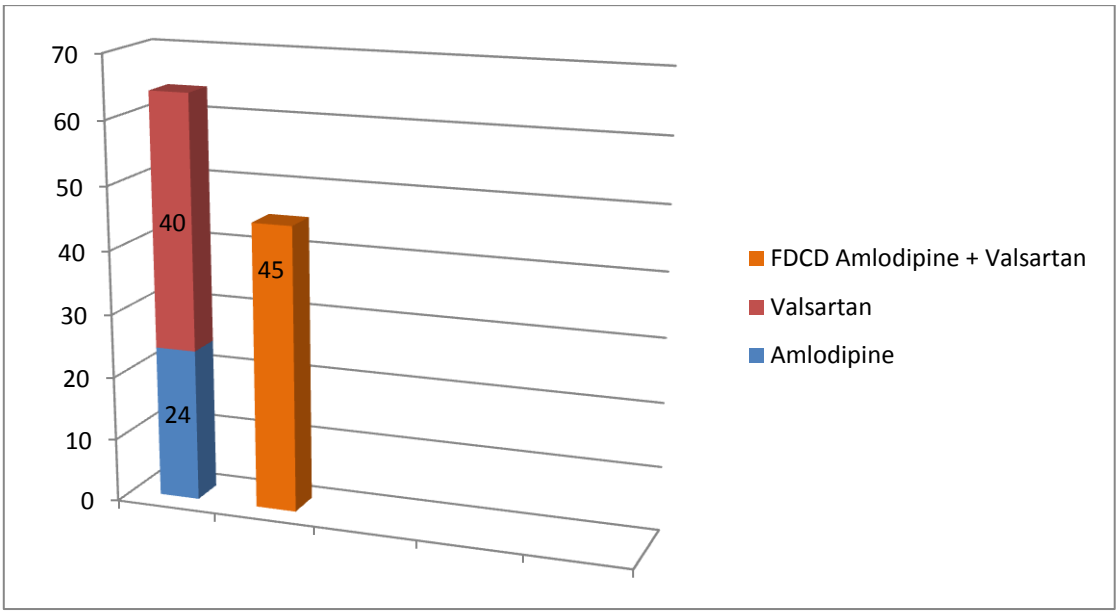

Fig.3.15. Comparative sales analysis of free equivalents and dual FDCD ARBs + CCBs

A comparative analysis of total sales free equivalents and triple FDCD ARBs + TDs + CCBs was also conducted. Analysis results demonstrated a significantly ($\varphi_{emp.}$ = 13.53; p = ≤0,01) predominance of total sales of free equivalents Valsartan and Indapamide and Amlodipine compared to triple FDCD (Fig.3.16.). This result indicates non-compliance with modern guidelines for AH pharmacotherapy also.

A comparative analysis of total sales of free equivalents and FDCD showed that total sales of free equivalents significantly (p = ≤0,01) outweigh sales of both dual and triple FDCD. Unfortunately, this situation does not correspond to modern guidelines for AH pharmacotherapy. The use of FDCD allows influencing several mechanisms of increasing BP at once, and also increases the adherence of hypertensive patients with to treatment. In our opinion, this situation can be influenced by the pharmacist. He can offer the patient FDCD instead of two

separate free equivalents. At the same time, the pharmacist can explain to the patient the advantages and higher effectiveness of treatment with FDCD. In this way, the implementation of practical recommendations on AH pharmacotherapy will increase.

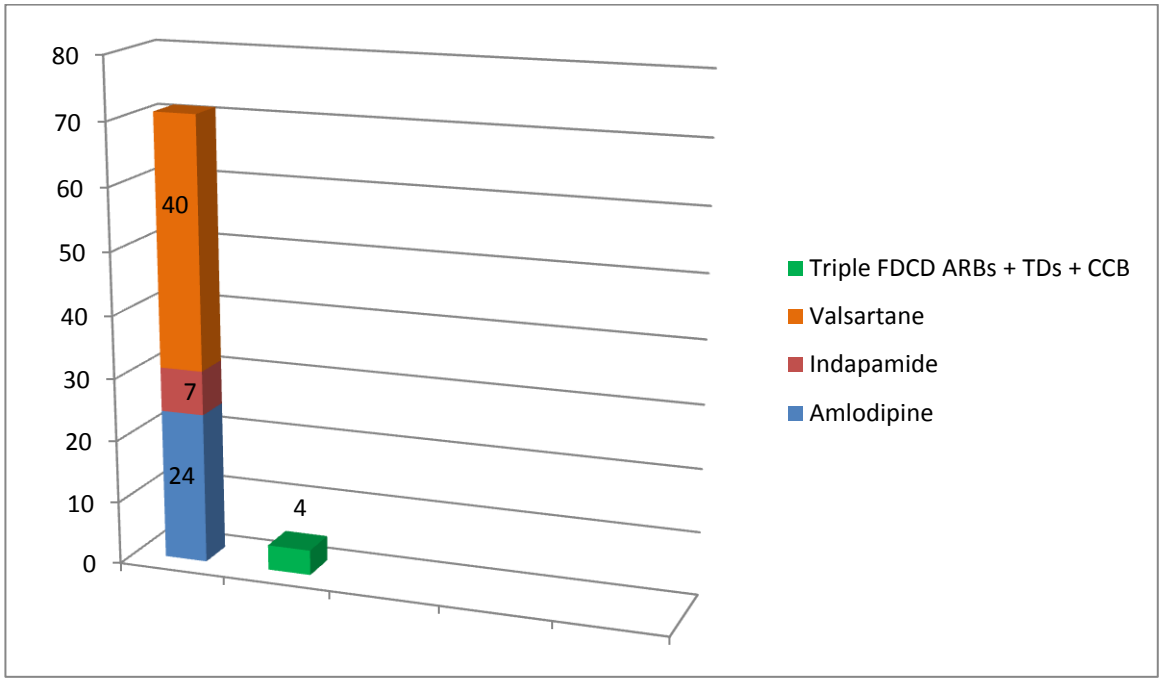

Fig.3.16. Comparative sales analysis of free equivalents and triple FDCD ARBs + TDs + CCB

3.6. Assessment of the practical implementation of modern guidelines on AH pharmacotherapy

The results of the research showed that the pharmacy is provided with all five first-line pharmacological classes of antihypertensive drugs the AH pharmacotherapy. But the insufficient availability of drugs with different international non-proprietary names in the pharmacy is noteworthy. Therefore, the ACE inhibitors were represented by three of the 9 recommended; the ARBs was represented by only two drugs of the 8 recommended drugs. The presence of FDCD in the pharmacy allows us to implement recommendations for initial AH pharmacotherapy at both steps 1 and 2 of AH treatment.

The study also found that sales of both dual and triple FDCD significantly ($p = \leq 0,01$) exceeded sales of single-component drugs. However, a separate comparison of sales of single-component drugs with different FDCD demonstrated that sales of single-component drugs were higher than sales of separate dual FDCD and separate triple FDCD.

The leaders in sales were such pharmacological classes of drugs as ACE inhibitors and ARBs and FDCD based on them (for example, ACE inhibitors + TDs or ARBs + CCBs). The dual FDCD based on ACE inhibitors or ARBs in combination with TDs or CCBs that are recommended at the 1st step of AH treatment. That is, the pharmacy has the ability to provide hypertensive patients with FDCD for initial therapy of hypertension.

A comparative analysis of total sales of free equivalents and FDCD showed significantly ($p = \leq 0,01$) higher sales of free equivalents, regardless of the pharmacological class of antihypertensive drugs. Unfortunately, this situation does not correspond to modern recommendations for AH pharmacotherapy.

The results of the analysis of implementation at the pharmacy demonstrated insufficient compliance with modern guidelines for AH pharmacotherapy using FDCD. The main discrepancy is the predominance of total sales of single-component drugs compared to FDCD. In our opinion, pharmacists can play a leading role in increasing the use of FDCD.

Conclusions to Chapter 3

This chapter of the master's thesis presents the results of a study of the provision of antihypertensive drugs at the pharmacy according to recommended guidelines. The results of the analysis of total sales of equivalents and FDCD are also presented, based on which conclusions are drawn regarding compliance with modern guidelines for AH pharmacotherapy.

CONCLUSIONS

1. To study and summarize information on current recommendations for AH pharmacotherapy, 36 literature sources were reviewed, which included scientific articles with an evidence base for the use of antihypertensive drugs and international guidelines for the AH treatment.

2. Analysis of the pharmacy's stock of antihypertensive drugs showed that all recommended pharmacological classes (ACE inhibitors, ARBs, TDs, CCBs, β-blockers) are available. The pharmacy has both single-component drugs and FDCD. Almost all FDCD are presented at the pharmacy in different dosages, which allows for an individual approach to choosing the dose of an antihypertensive drug for each patient. However, most classes are represented by a significantly smaller number of drugs than recommended by the guidelines.

3. Total sales of double and triple FDCD exceeded sales of single-component drugs. But sales of single-component antihypertensive drugs exceeded sales of both dual and triple FDCD separately. The total sales volume of single-component drugs of the pharmacological classes of ACE inhibitors and ARBs amounted to 60.53% of the total sales volume of single-component drugs and significantly ($p = \leq 0.01$) exceeded the sales volume of drugs of other pharmacological classes. In the corresponding pharmacological class, significantly ($p = \leq 0,05$) higher sales were observed in Enalapril, Valsartan, Amlodipine.

4. Analysis of sales of double FDCD showed a significantly ($p = \leq 0,01$) steady predominance of sales combination ACE inhibitors + TDs. Analysis of sales of triple FDCD showed a significantly ($p = \leq 0,01$) predominance of sales combination ACE inhibitors + TDs + CCBs. The influence of a particular drug manufacturer on sales of both single-component drugs and FDCD was also revealed.

5. A comparative analysis of total sales of free equivalents and FDCD showed that total sales of free equivalents significantly ($p = \leq 0,01$) outweigh sales

of both dual (ACE inhibitors + TDs; ARBs + CCBs) and triple FDCD (ARBs + TDs + CCBs).

5. The results of the analysis of implementation at the pharmacy demonstrated insufficient compliance with modern guidelines for AH pharmacotherapy using FDCD. The main discrepancy is the predominance of total sales of single-component drugs compared to FDCD. In our opinion, pharmacists can play a leading role in increasing the use of FDCD, by offering them to the hypertensive patients with as an alternative to taking two separate single-component drugs of different pharmacological classes.

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APPLICATIONS

APPLICATION A

In cases where the HbA1c level remains above 9%, basal insulin (Degludec, Glargine U-100) is recommended to improve control of the type 2 DM.

Conclusions. Summarizing the modern guidelines, it becomes clear that pharmacotherapy of type 2 DM should be comprehensive: diet, lifestyle modification, first-line drug — Metformin. Patients with CKD, CVD at high risk are recommended to use inhibitors of iSGLT-2 (Empagliflozin, Canagliflozin, Dapagliflozin) or GLP-1 agonists (Liraglutide, Semaglutide, Dulaglutide). In patients unable to achieve the target HbA1c level with first-line drugs, treatment intensification can be used by prescribing iDPP-4 or TZDs. If the target HbA1c level is not achieved, basal insulin is recommended.

ANALYSIS OF THE COMPLIANCE OF PHARMACY SALES OF ANTIHYPERTENSIVE DRUGS WITH MODERN GUIDELINES FOR ARTERIAL HYPERTENSION PHARMACOTHERAPY

Abdessamad Kinan
Scientific supervisor: Zhabotynska N.V.
National University of Pharmacy, Kharkiv, Ukraine
kinanabdessamad@gmail.com

Introduction. Current data less than 50% of adults with arterial hypertension (AH) receive effective antihypertensive therapy. Initial antihypertensive monotherapy is often ineffective or slow to achieve target effective blood pressure (BP) levels. According to modern guidelines for arterial hypertension (AH) treatment, combined pharmacotherapy using fixed-dose combination drug (FDCD) in "single pill" comes first, which allows influencing several pathogenetic mechanisms of AH development at once and achieving more effective BP control.

Aim. The aim is assessing the compliance of pharmacy sales of drugs for the AH treatment with modern guidelines.

Materials and methods. During the research, an analysis of pharmacy sales reports of antihypertensive drugs containing a single active ingredient and fixed combinations of two or three active ingredients in a "single pill" was conducted. The data were processed using statistical methods, in particular, using the Fisher's exact test.

Results and discussion. According to pharmacy sales reports for 3 months, the sales volume of combined antihypertensive drugs amounted to 566 drugs. Sales of combined antihypertensive drugs significantly ($\varphi_{emp.} = 4.531; p \leq 0.01$) exceeded sales volumes of drugs containing one active substance. At the same time, sales of double combinations in a "single pill" significantly ($\varphi_{emp.} = 9.623; p \leq 0.01$) exceeded sales of triple combinations. But the frequency of total sales of two drugs of different pharmacological classes, as separate drugs, is higher than sales of drugs of two or three pharmacological classes, as combinations in a "single pill". At the same time, by individual active substances among angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, sales of combinations in a "single pill" prevailed.

Conclusions. Data on the pharmacy sale of FDCD of two or three active substances in a "single pill" demonstrated the compliance of antihypertensive drug sales with modern guidelines for AH pharmacotherapy, which provide for the appointment of combination therapy to the vast majority of patients with AH. Probably, lower sales of triple FDCD are associated with a statistically lower number of patients with severe stage III AH who do not achieve blood pressure control with dual combination pharmacotherapy.

APPLICATION B

APPLICATION C

Proceedings of the 3rd International Scientific and Practical Conference
"Innovative Solutions in Science: Balancing Theory and Practice"
April 28-30, 2025
San Francisco, USA
EUROPEAN OPEN SCIENCE SPACE

Section: Pharmaceutics

ANALYSIS OF THE PROVISION OF AHD TO HYPERTENSIVE PATIENTS WITH ACCORDING TO MODERN GUIDELINES

Kinan Abdessamad
Master's student
Zhabotynska Natalia
PhD, associate professor
Department pharmacology and clinical pharmacy
National University of Pharmacy, Kharkiv, Ukraine

Summary. The article presents data on the study of the pharmacy's ability to provide patients with antihypertensive drugs and analyzes their compliance with modern guibdelines for arterial hypertension pharmacotherapy.

Key words: arterial hypertension, antihypertensive pharmacotherapy, modern guidelines, pharmacy.

Introduction. Arterial hypertension (AH) is a major public health problem worldwide due to its high prevalence and associated risk of cardiovascular disease. According to WHO, 1.28 billion adults aged 30-79 years worldwide have AH. Only about 1 in 5 hypertensive adults (21%) have blood pressure (BP) under control [1]. The following first-line pharmacological classes of AHD are recommended for AH pharmacotherapy: angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin II receptor blockers (ARBs), thiazide diuretics (TDs), calcium channel blockers (CCBs), beta-blockers (β-blockers) [2]. An important aspect of modern AH pharmacotherapy is the use of fixed-dose combination drug (FDCD) [3,4]. Current guidelines for AH pharmacotherapy favour combination therapy because it lowers BP more than monotherapy and increases the likelihood of achieving target BP within a reasonable time frame [5]. Studying the capabilities of pharmacy to provide hypertensive patients with recommended drugs is quite relevant.

The purpose of the research was to study the pharmacy's ability to provide patients with antihypertensive drug (AHD) in accordance with modern guidelines for AH pharmacotherapy. The task of the study was to analyze the range of AHD at the pharmacy and assess their compliance with current guidelines for AH pharmacotherapy of hypertension.

The result of research. The AHD are represented at the pharmacy by all recommended first-line pharmacological classes: ACE inhibitors, ARBs, TDs, CCBs, β-blockers. Only the pharmacological class of TD in the pharmacy was provided with all three recommended drugs. The ACE inhibitors class was represented by only three drugs, although the recommendations include 9 drugs. The ARBs class was represented

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by only two drugs, although the recommendations include 8 drugs. Non-dihydropyridine CCBs were represented by only one of the two recommended drugs, while dihydropyridine CCBs were represented by two of the seven recommended drugs. The β-blockers class was represented by only three selective drugs, although the recommendations include 8 drugs, including selective and non-selective drugs. FDCD at the pharmacy are represented by three dual combinations and two triple combinations. Dual combinations consisted of ACE inhibitors or ARBs with TDs or CCBs or β-blockers. Triple combinations consisted of fourth pharmacological classes of AHD — ACE inhibitors or ARBs + TDs + CCBs, excluding β-blockers. Each combination is represented by preparations with three trade names. Among all FDCD, the most widely represented are dual FDCD, which consist of ACE inhibitors and TDs. It is noteworthy that almost all FDCD are presented at the pharmacy in different dosages, which allows for an individual approach to choosing the dose of an antihypertensive drug for each patient.

Dual FDCD presented at the pharmacy allow for the implementation of modern guidelines for the AH treatment in the first step, when most patients are recommended to start treatment with dual FDCD. Moreover, it is recommended to choose combinations that are ACE inhibitors or ARBs with CCBs or TD available at the pharmacy. Triple FDCD available in the pharmacy allow implementing the 2 steps of AH treatment, when patients are recommended triple combinations consisting of ACE inhibitors or ARBs with TDs and CCBs. The availability of a wide selection of single-component drugs from all pharmacological classes at the pharmacy allows providing hypertensive patients with appropriate treatment when it is necessary to use single-component drugs, or at step 3, when a fourth AGD is added to the triple FDCD.

Conclusion. Based on the described data, it can be concluded that the pharmacy is provided with all pharmacological classes of AHD in the form of sing-component drugs and FDCD in various dosages. However, it is desirable to expand the number of trade names of drugs to provide patients with a freer choice of AHD.

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Proceedings of the 3rd International Scientific and Practical Conference
"Innovative Solutions in Science: Balancing Theory and Practice"
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EUROPEAN OPEN SCIENCE SPACE

Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines / P. K. Whelton et al. J. Am. Coll. Cardiol. 2018. № 71(19). P. 127–248.

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APPLICATION D

Ф А 2.2.1-32-366

National University of Pharmacy

Faculty Pharmaceutical
Department of Pharmacology and Clinical Pharmacy

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

APPROVED
The Head of Department
Pharmacology and
Clinical Pharmacy

Sergii SHTRYGOL
«02» September 2024

ASSIGNMENT

FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Abdessamed KINAN

1. Topic of qualification work: «**A**nalysis of the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy», supervisor of qualification work: Nataliia ZHABOTYNSKA, PhD, assoc. prof.
approved by order of NUPh from "27" of September 2024 № 237
2. Deadline for submission of qualification work by the applicant for higher education: May 2025.
3. Outgoing data for qualification work: publications on problems in the pharmacotherapy of arterial hypertension.
4. Contents of the settlement and explanatory note (list of questions that need to be developed):
Assess the availability of antihypertensive drugs in the pharmacy in accordance with current recommendations for arterial hypertension pharmacotherapy; analyze the sale of single-component antihypertensive drugs in the pharmacy by individual pharmacological classes, the sale of FDCD, and also analyze the sales of free equivalents of single-component drugs and FDCD consisting of the corresponding active substances according to their international non-proprietary name.
5. List of graphic material (with exact indication of the required drawings):
- stepwise strategy for AH pharmacotherapy (1 figure);
- pharmacological classes of antihypertensive drugs presented at the pharmacy as single-component drugs and FDCD (2 tables);
- sales of antihypertensive drugs at the pharmacy (16 figures);

6. Consultants of chapters of qualification work

Signature	**Name, SURNAME, position of consultant**	**Signature, date**	
		assignment was issued	**assignment was received**
1	Nataliia ZHABOTYNSKA, associate professor of higher education institution of Clinical Pharmacology and Clinical Pharmacy department	12.09.2024	12.09.2024
2	Nataliia ZHABOTYNSKA, associate professor of higher education institution of Clinical Pharmacology and Clinical Pharmacy department	06.03.2025	06.03.2025
3	Nataliia ZHABOTYNSKA, associate professor of higher education institution Clinical Pharmacology and Clinical Pharmacy department	03.04.2025	03.04.2025

7. Date of issue of the assignment: “02” September 2024

CALENDAR PLAN

№	**Name of stages of qualification work**	**Deadline for the stages of qualification work**	**Notes**
1.	Writing Chapter 1 "Literature Review"	December 2024	**done**
2.	Development of a questionnaire for conducting a survey of patients	December 2024	**done**
3.	Conducting a patient survey, writing Chapter 2 "Research Methods"	March 2025	**done**
4.	Statistical processing of survey results	March 2025	**done**
5.	Writing Chapter 3 "Research Results"	March 2025	**done**
6.	Finalization of qualification work and preparation of documents	May 2025	**done**

An applicant of higher education _____ Abdessamed KINAN

Supervisor of qualification work _____Nataliia ZHABOTYNSKA

ВИТЯГ З НАКАЗУ № 237

По Національному фармацевтичному університету

від 27 вересня 2024 року

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу Фм20(4,10д) 2024-2025 навчального року, освітньо-професійної програми – Фармація, другого (магістерського) рівня вищої освіти, спеціальності 226 – Фармація, промислова фармація, галузь знань 22 Охорона здоров'я, денна форма здобуття освіти (термін навчання 4 роки 10 місяців), які навчаються за контрактом (мова навчання англійська та українська) згідно з додатком № 1.

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
по кафедрі фармакології та клінічної фармації				
Кінан Абдессамед	Аналіз практичної реалізації сучасних протоколів з фармакотерапії артеріальної гіпертензії в аптечному закладі.	Analysis of the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy.	доцент Жаботинська Н.В.	професор Литвинова О.М.

Ректор

Вірно. Секретар

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«05» травня 2025 р. № 331121084

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Кінан Абдессамед, групи Фм20(4,10)англ-04, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Аналіз практичної реалізації сучасних протоколів з фармакотерапії артеріальної гіпертензії в аптечному закладі / Analysis of the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
проректор ЗВО з НПР,
професор **Інна ВЛАДИМИРОВА**

Ф А 2.2.1-32-353

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Abdessamed KINAN

on the topic: «Analysis of the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy»

Relevance of the topic. Arterial hypertension is a major public health problem worldwide due to its high prevalence and associated risk of cardiovascular disease. Approximately 46% of hypertensive adults are unaware that they have the condition and only 42% are being treated. The goal of arterial hypertension treatment is to prevent cardiovascular complications that lead to functional impairment and death. Current guidelines favor combination therapy using fixed-dose combination drugs. Given that only 50% of patients with hypertension have blood pressure under control, it is important to examine the level of practical implementation of current guidelines for pharmacotherapy of hypertension, especially with the use of fixed-dose combination drugs.

Practical value of conclusions, recommendations, and their validity. The practical value of conclusions of the master's thesis consists in assessing the practical implementation of modern guidelines for the pharmacotherapy of arterial hypertension and identifying the main areas that require improvement, and the participation of the pharmacist in improving the practical implementation of modern recommendations for the treatment of hypertensive patients.

Assessment of work. The qualification work is a completed research, designed in accordance with all requirements. It is recommended to conduct an additional check of spelling errors.

General conclusion and recommendations on admission to defend. The work is performed in full, designed in accordance with the current requirements for the

qualification works at the National University of Pharmacy, and can be recommended for submission to the Examination commission for further defense.

Scientific supervisor _____ Nataliia ZHABOTYNSKA

«12» May 2025

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Abdessamed KINAN

on the topic: «Analysis of the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy»

Relevance of the topic. Treatment strategies for arterial hypertension are changing rapidly. Adherence to current pharmacotherapy recommendations for hypertension is a key factor in its effective treatment. Learning how to implement current approaches to arterial hypertension treatment can improve blood pressure control in hypertensive patients and reduce the risk of cardiovascular complications that can lead to death in these patients.

Theoretical level of work. The qualification work has a high theoretical level, based on the international guidelines for the pharmacotherapy for arterial hypertension.

Author's suggestions on the research topic. The author analyzed the compliance of the assortment of antihypertensive drugs in the pharmacy with modern recommendations on pharmacotherapy of arterial hypertension, and also analyzed the sales of antihypertensive drugs in the pharmacy according to various criteria. Based on the results obtained, problematic aspects in compliance with modern recommendations on pharmacotherapy of arterial hypertension were identified.

Practical value of conclusions, recommendations, and their validity. The results of the work and the conclusions drawn on their basis are of high practical importance for improving the practical implementation of recommendations on pharmacotherapy of arterial hypertension in order to increase the effectiveness of the treatment of this disease with the participation of pharmacists.

Disadvantages of work. There are grammatical and punctuation errors, unsuccessful stylistic turns in the work.

General conclusion and assessment of the work. The work meets the requirements for qualification work in National University of Pharmacy and can be recommended for defense.

Reviewer _____ Olga LYTVYNOVA

«14» May 2025

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
ВИТЯГ З ПРОТОКОЛУ № 19
засідання кафедри фармакології та клінічної фармації

15 травня 2025 р. м. Харків

Голова: завідувач кафедри, доктор мед. наук, професор Штриголь С. Ю.
Секретар: кандидат фарм. наук, доцент Вєтрова К. В.

ПРИСУТНІ: зав. каф., проф. Штриголь С.Ю., проф. Деримедвідь Л.В., доц. Бєлік Г.В., доц. Вєтрова К.В., доц. Жаботинська Н.В., доц. Кононенко А. В., доц. Матвійчук А.В., доц. Отрішко І.А., доц. Очкур О.В., доц. Рябова О.О., доц. Савохіна М.В., доц. Степанова С. І., доц. Таран А.В., ас. Верховодова Ю.В., ас. Підгайна В.В. та здобувачі вищої освіти.

ПОРЯДОК ДЕННИЙ:
1.Розгляд кваліфікаційних робіт здобувачів вищої освіти для подання робіт до Екзаменаційної комісії.

СЛУХАЛИ:
1.Здобувача вищої освіти Кінан Абдессамеда зі звітом про проведену наукову діяльність за темою кваліфікаційної роботи: «Аналіз практичної реалізації сучасних протоколів з фармакотерапії артеріальної гіпертензії в аптечному закладі» («Analysis of the practical implementation of modern guidelines for pharmacotherapy of arterial hypertension in a pharmacy»).

УХВАЛИЛИ:
1. Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Кінан Абдессамед допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Голова
Завідувач кафедри, проф. Штриголь С. Ю.

Секретар, доц. Вєтрова К. В.

Ф А 2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Абдессамед КІНАН до захисту кваліфікаційної роботи за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньо-професійною програмою Фармація
на тему: «Аналіз практичної реалізації сучасних протоколів з фармакотерапії артеріальної гіпертензії в аптечному закладі».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Микола ГОЛІК /

Висновок керівника кваліфікаційної роботи

Кваліфікаційна робота здобувача вищої освіти Абдессамеда КІНАНА є самостійним оригінальним дослідженням, виконана на високому науковому рівні, відповідає всім вимогам, може бути представлена в Екзаменаційну комісію Національного фармацевтичного університету та рекомендована до захисту на здобуття освітньо-кваліфікаційного рівня магістра та заслуговує позитивної оцінки.

Керівник кваліфікаційної роботи

_____ Наталія ЖАБОТИНСЬКА

"12" травня 2025 року

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Абдессамед КІНАН допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри
фармакології та клінічної фармації

_____ Сергій ШТРИГОЛЬ

"15" травня 2025 року

Qualification work was defended

of Examination commission on

« » June 2025

with the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Volodymyr YAKOVENKO /