

**MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
faculty for foreign citizens' education
department of pharmacology and clinical pharmacy**

QUALIFICATION WORK

on the topic: «**FACTORS CONTRIBUTING TO MEDICATION ADHERENCE
IN MOROCCAN ADULT ASTHMA PATIENTS:
CLINICAL AND PHARMACEUTICAL RESEARCH**»

Prepared by: higher education graduate of group

(ΦМ20*(4,10Д) АНГЛ-01)

specialty 226 Pharmacy, industrial pharmacy

educational program Pharmacy

Houssame MESBAHI

Supervisor: associate professor of higher education institution

of department of pharmacology and clinical pharmacy, PhD,

associate professor Inna OTRISHKO

Reviewer: head of the department of clinical pharmacology

of the Institute for Advanced Training of Pharmacy Specialists

of the National University of Pharmacy, DSc,

professor Yaroslava BUTKO

ANNOTATION

Houssame MESBAHI. Factors contributing to medication adherence in Moroccan adult asthma patients: clinical and pharmaceutical research. – The manuscript. – National University of Pharmacy of Ministry of Healthcare of Ukraine, Kharkiv, 2024.

The qualification work is devoted to the study of the influence of factors contributing to treatment adherence in Moroccan adult asthma patients.

Qualification work is presented on 40 pages of typewritten text, consists of summary, introduction, 3 chapters, conclusions, references. The work is illustrated with 3 tables, 9 figures. The list of references contains 32 resources.

Key words: asthma, efficacy and safety of therapy, pharmacist, Moroccan patients, rational use of medicines

АНОТАЦІЯ

Хуссам МЕСБАХІ. Фактори, що сприяють прихильності до лікування у дорослих пацієнтів з бронхіальною астмою в Марокко: клініко-фармацевтичне дослідження. – На правах рукопису. – Національний фармацевтичний університет МОЗ України, Харків, 2024.

Кваліфікаційна робота присвячена вивченню впливу факторів, що сприяють прихильності до лікування у дорослих пацієнтів з бронхіальною астмою в Марокко.

Кваліфікаційна робота викладена на 40 сторінках машинописного тексту, складається з резюме, вступу, 3 розділів, висновків, списку літератури. Робота проілюстрована 3 таблицями, 9 рисунками. Список літератури містить 32 найменування.

Ключові слова: бронхіальна астма, ефективність та безпека терапії, фармацевт, пацієнти із Марокко, раціональне використання лікарських засобів

TABLE OF CONTENTS

INTRODUCTION	4
CHAPTER 1 MODERN PRESENTATION ABOUT ASTHMA MANAGEMENT (LITERATURE REVIEW).....	7
1.1. Asthma information and facts.....	7
1.2. Modern medication asthma control.....	13
Conclusions for chapter 1	17
CHAPTER 2 MATERIALS AND METHODS.....	18
Conclusions for chapter 2.....	20
CHAPTER 3 Factors contributing to medication adherence in Moroccan adult asthma patients (EXPERIMENTAL PART).....	21
3.1. Survey of adult pharmacy visitors concerning asthma management adherence.....	21
3.2. Discussion of the obtained results	31
3.3. Practical recommendations regarding self-monitoring of the treatment process.....	36
Conclusions for chapter 3.....	39
CONCLUSIONS	40
REFERENCES	41

INTRODUCTION

Relevance of the topic. Asthma affects up to 300 million people worldwide. The incidence of bronchial asthma reaches 18%. In children, this figure ranges from 5-10%. It has been established that in terms of age, the highest prevalence of bronchial asthma is recorded in school age. The high incidence of bronchial asthma in children is characteristic of industrial regions with unfavorable ecology [13].

Bronchial asthma is a heterogeneous disease characterized by chronic inflammation of the bronchial mucosa involving a number of cells (eosinophils, mast cells, Th2 lymphocytes and antigen-presenting cells) and variability in bronchial obstruction. Asthma is one of the most common chronic diseases of the respiratory tract (according to WHO, about 300 million registered cases as of 2020) and by 2025 its number is projected to increase by another 100 million [2, 17, 31].

It is well known and proven in the GINA guidelines that inhalation is the best route of administration in asthma, but in real life this route is technically more difficult for the patient, and asthma control depends on the correct use of the inhaler. That is, there is a certain cohort of patients who often use the inhaler incorrectly.

The inhalation route is time-tested; the first metered-dose pocket aerosol was successfully tested in 1995, and in 1996, the serial production and free sale of the aerosol began.

The success of treatment with an inhaled drug depends on three components, such as: a patient who understands the explanation; a convenient delivery device; a doctor who explains clearly.

That is, patient adherence to therapy is an important element of successful treatment along with the use of inhaler therapy inhalers. Physicians should, firstly, teach patients how to use the inhaler correctly, and secondly, check the correct use of the inhaler during each patient visit [6, 13, 23].

It is worth noting that the correct interpretation of the staged (step-by-step) strategy of BA treatment is very important. Today, there are 5 steps in the treatment of asthma, and doctors must clearly understand when to take a step up, that is, to

expand therapy, and when to go down - to reduce its volume:

- in the absence of complete control of the disease, it is necessary to review the scope of drug therapy in the direction of its strengthening - a step up (step up);
- before taking such a step, it is necessary to check compliance with the treatment plan, the correctness of the inhalation technique and assess the possible influence of new provocative factors and concomitant pathology;
- in children who need treatment with high doses of ICS (800, 1,000 µg/day) and do not have an adequate level of disease control, the diagnosis must be reviewed;
- provided that control of BA is achieved for at least 3 months, the amount of therapy is reduced – a step down.

The aim of the study. The aim of the work is to study the role of factors contributing to medication adherence in Moroccan adult asthma patients.

The objectives of the study. Objectives of the work are the following:

1. To study the basic information about asthma.
2. To study the impact of adherence on quality of Moroccan asthma patients life.
3. To study approaches to modern therapy of asthma.
4. To analyze the opinions and beliefs of pharmacy visitors with asthma concerning efficacy and safety of medication management.
5. To develop practical recommendations for physicians, pharmacists and patients about alternative ways to improve treatment adherences in Moroccan asthma patients.

Object of research: medication adherence in Moroccan adult asthma patients.

Subject of research: role of the factors contributing to medication adherence in Moroccan adult asthma patients.

Research methods. The methodological basis of the study is the principles of objectivity and consistency. The work uses a complex of general scientific and special methods: theoretical, generalization, data systematization, comparison, methods of studying literary sources, analysis, questionnaire method, statistical

methods, etc.

Structure and scope of qualification work. Qualification work is presented on the 40 pages of typewritten text, consists of summary, introduction, 3 chapters, conclusions, references. The work is illustrated with 3 tables, 9 figures. The list of literature contains 32 references.

CHAPTER 1

MODERN PRESENTATION ABOUT ASTHMA MANAGEMENT (LITERATURE REVIEW)

1.1. Asthma information and facts

According to statistics, bronchial asthma (BA) affects approximately 300 million people worldwide. It is a serious global health problem that affects all age groups. The prevalence of asthma is increasing in many developing countries. The costs of treatment are also increasing, which in general represents a significant burden for patients and communities, and this burden is growing. Thus, despite significant progress in the treatment of asthma, it continues to pose a significant challenge to the healthcare system and society, in terms of disability and family burden, especially in pediatric asthma. In addition, asthma remains the cause of a large number of deaths, including among young people. Almost 96% of asthma deaths occur in low- and middle-income countries. [6].

Bronchial asthma develops as a result of increased sensitivity (or sensitization) of the body to various allergens. Allergens can enter the body from the external environment (exo- and heteroallergens) and occur in the body (endo- or autoallergens). The first group of allergens includes infectious and non-infectious. Infectious allergens: bacteria, viruses, fungi (mold), helminths, protozoa. Non-infectious: of plant origin (pollen) – most often entering through the respiratory tract; of industrial origin (pesticides, polymers, cotton and wool dust, etc.); animal origin (dog and cat hair, bird fluff); some insects (ticks, butterflies, beetles, bedbugs, cockroaches, flies, etc.); household (room dust); food (fish, crayfish, eggs, milk, chocolate, onions, etc.); drugs (antibiotics, sulfonamides, novocaine, etc.). Non-infectious allergens can enter the body in different ways: inhalation (dust, chemical products, insect particles, etc.), enteric (blood serum, vaccines, drugs). Disorders of the central nervous system and the endocrine system (in particular, the

adrenal glands) also play a significant role in the development of asthma. Nervous overstrain, severe anxiety, fright often serve as a kind of impetus for an attack of bronchial asthma [12].

There are the following types of asthma by severity:

- mild asthma, which is almost never accompanied by attacks;
- moderate asthma, which may have periodic and prolonged attacks;
- severe asthma, which can lead to serious complications.

Asthmatic status is a condition when asthma worsens to the point that conventional control methods do not help relieve symptoms.

Asthma status is determined by the degree of symptom control and lung function in a patient with asthma. It can be periodic or permanent, and can be defined as mild, moderate or severe.

Another form of asthmatic status is persistent asthma, when symptoms are present on a regular basis, without significant relief between attacks. Treatment of this form of asthma includes regular use of medications to control symptoms and prevent exacerbations, as well as timely use of medications during attacks.

Phenotypes and endotypes of asthma:

1. Th2-high type bronchial asthma (type 2 inflammation): elevated eosinophil count associated with allergic inflammation; biomarkers: increased levels of IgE, IL-4, IL-5, IL-13.
2. Th2-low type bronchial asthma (non-Type 2 inflammation): neutrophilic or paucic granulocytic inflammation; biomarkers: may include IL-17, IL-6.

The most common causes of bronchial asthma are (Fig 1.1):

Allergens. Patients who suffer from allergic rhinitis or atopic dermatitis have a 3-5 times higher risk of developing bronchial asthma. And vice versa: bronchial asthma can be triggered by allergies to certain irritants.

Hereditary predisposition. If one of your relatives had asthma, you are automatically at risk.

Harmful working conditions: exposure to chemical irritants, especially in the workplace.

Low birth weight and/or maternal smoking during pregnancy.

Frequent respiratory illnesses.

Certain medications. Aspirin, a group of anti-inflammatory and painkillers, blood pressure medications (beta-blockers) can also cause bronchial asthma.

Obesity.

Low physical activity.

Factors that contribute to the development of bronchial asthma include household allergens (dust and dust mites, mold), pets (wool, feathers, saliva, etc.), cockroaches, and household chemicals.

Unfavorable weather conditions (cold air), strong emotional (fear or anger) and physical stress can cause symptoms to worsen or complications to develop.

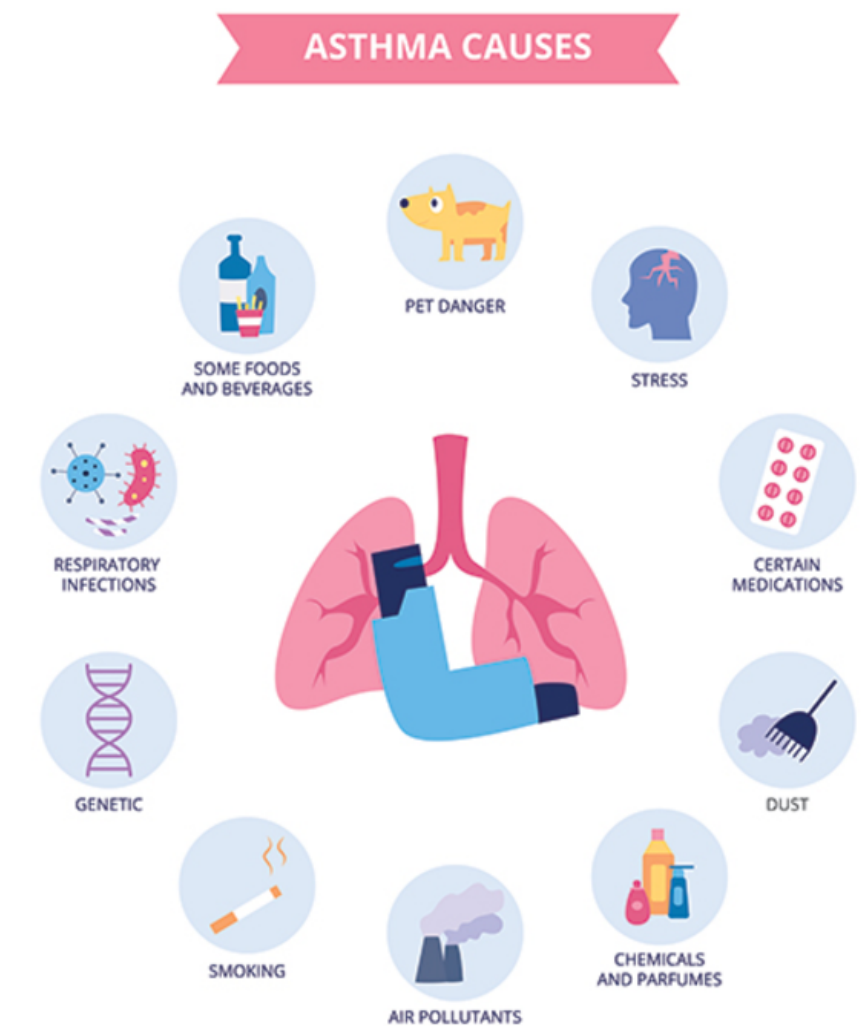


Fig.1.1 Asthma causes

The main symptoms of the disease are attacks of shortness of breath, which occur more often at night. A typical attack begins with a feeling of nasal congestion, coughing, and shortness of breath. Inhalation and especially exhalation are always difficult. There is a tension of the abdominal muscles, ladder muscles, pectoral muscles, sternocleidomastoid muscles. The patient is in a forced position - sitting, leaning on his hands, fixing the shoulder girdle. Cyanosis of the lips, cheeks, and nasal tip is often noted. During lung percussion, a short, often tympanic percussion sound is heard, and during auscultation - dry, whistling rales. The pulse is rapid, the body temperature is normal, sometimes it can rise to 38-39 °C. The duration of the attack varies: it can end with a rapid expectoration of viscous gray sputum, but in some patients there is a slower decrease in dyspnea. Sometimes an asthmatic condition develops in which the attack does not go away for many hours, days, rarely weeks, or after a short break, a new attack begins. Asthma can be fatal.

According to the severity of the course, there are 4 degrees:

Grade 1 - intermittent asthma. It is manifested by short-term episodes of cough, paroxysmal dyspnea and wheezing. Indicators of external respiratory function outside the exacerbation are within the physiological norm.

Grade 2 - mild persistent asthma. Symptoms do not occur every day; physical activity and sleep quality decrease; development of a cough variant of asthma.

Grade 3 - moderate persistent asthma. Symptoms occur daily, once a week. Nighttime attacks of suffocation occur.

Grade 4 - severe persistent asthma. Daily clinical manifestations of the disease, frequent severe exacerbations; nighttime attacks of suffocation; physical activity of patients is reduced, despite the therapy.

Immunological mechanisms of bronchial asthma

In a significant proportion of patients with bronchial asthma, altered bronchial reactivity occurs as a result of disorders of the immunocompetent system, which occur according to types I, III, IV hypersensitivity. These immune reactions occur in the mucous membrane of the respiratory tract, regardless of the type of allergic reaction. The pathogenesis of bronchial asthma involves the following pathological

processes:

I. The immunological phase is characterized by sensitization of the body, which can occur in immediate or delayed allergic reactions. In the first type, signs of asphyxiation appear in 10-15 minutes or instantly from the onset of contact with the allergen, in the second type - in 4-5 hours or more. The immediate type is characteristic of non-infectious allergic bronchial asthma, and the delayed type is more typical for the infectious allergic form. In the immediate type reaction, the leading role is played by a group of proteins - immunoglobulins: IgA, IgM, IgG, IgE.

Substances that react with antigen are called reactants. These primarily include IgE, which is detected in 60% of cases of atopic bronchial asthma. IgE forms a complex with antigen on the surface of mast cell membranes. The immunological stage of the delayed type characterizes cellular and tissue immunity due to the presence of a "transfer factor" in peripheral blood lymphocytes and lymphoid elements. As a result of exposure to the antigen, the genetic apparatus of lymphocytes is restructured, which acquire immune properties. Lymphocytes are sensitized [10, 23, 32].

II. The pathochemical phase is characterized by the release of allergic inflammatory mediators associated with both hereditary adenylyl cyclase deficiency (in the case of atopic asthma) and a decrease in its activity due to the sensitizing effect of bacterial toxins (in the infectious allergic form of asthma). Adenylyl cyclase stimulates the conversion of ATP to cyclic 3,5-adenosine monophosphate (cAMP). The latter regulates the secretion of allergic inflammatory mediators. Mediators of type I allergic reactions include histamine, serotonin, acetylcholine, and a slow-reacting substance. The main mediators of type IV allergic reactions are lymphokines (acting on macrophages, epithelial cells) and lysosomal enzymes.

III. Pathophysiological phase, which occurs under the influence of biologically active substances (histamine, serotonin) and is characterized by a pronounced and rather complex symptom complex of asthma (spasm and narrowing of small bronchi, secretion of large amounts of viscous mucus, edema of the bronchial mucosa, increased permeability of the microcirculatory bed, shortness of breath, dyspnea).

Type III reactions (immunocomplex type or Arthus phenomenon) occur in the area of antigen excess with the participation of precipitating antibodies. The reaction develops under the influence of exoallergens (microorganisms, enzymes, dust, antibiotics) and endoallergens. In this type of reaction, antibodies are formed, which belong mainly to immunoglobulins of class G and M. The damaging effect of the formed antigen-antibody complex is realized mainly through the activation of complement, the release of lysosomal enzymes.

There is damage to the basal membrane, spasm of bronchial smooth muscles, vasodilation, increased permeability of the microcirculatory bed. In the formation of altered bronchial reactivity, an important role is assigned to the local “breakdown” of immune defense: there is a decrease in secretory IgA, the phagocytosis system is disrupted, which in the respiratory system is represented mainly by alveolar macrophages.

On May 5, 2023, the World Health Organization announced the end of the COVID-19 pandemic and the and the related emergency situation. But the end of the of the pandemic does not mean that the global health threat from the coronavirus has disappeared.

In the early stages of the pandemic, bronchial asthma (BA) was considered a risk factor for increased susceptibility to COVID-19, and SARS-CoV-2, like other pneumotropic viruses, was expected to worsen both the course of asthma in general, and be a risk factor for disease exacerbation.

Later it was found that COVID19 infection in children with asthma was usually not severe, regardless of the severity of asthma and disease control during the previous year [4]. According to many studies, the presence of allergic rhinitis, asthma with or without allergic rhinitis, atopic dermatitis and passive tobacco exposure were not associated with hospitalization due to COVID-19 [29].

Immune response in patients with COVID-19 and bronchial asthma is presented in Fig. 1.2.

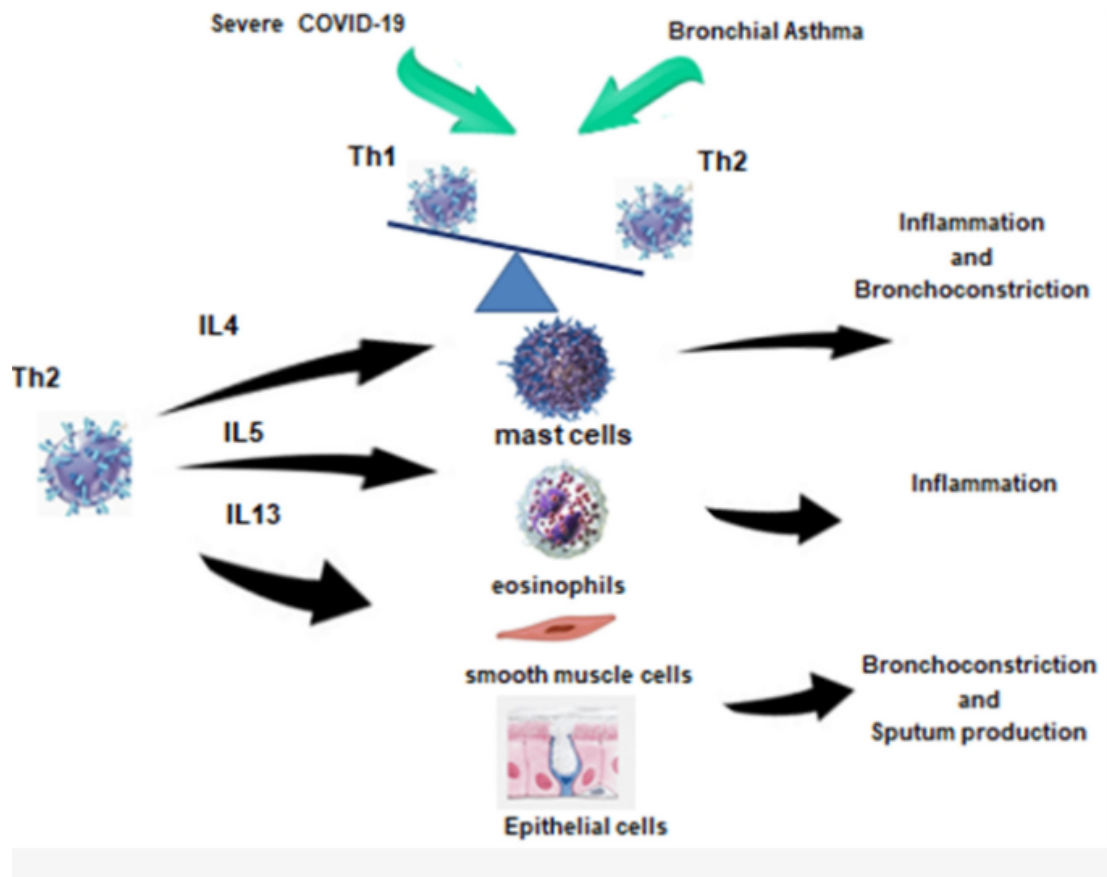


Fig. 1.2 Immune response in patients with COVID-19 and bronchial asthma

The SARS-CoV-2 coronavirus enters host cells through host cells through the structural glycoprotein angiotensin-converting enzyme 2 (ACE2/ACE2). The SARS-CoV-2 adhesion protein is primed by the transmembrane transmembrane serine protease 2 (TMPRSS2), which promotes fusion of viral and cell membranes in host cells. ACE2 is expressed in epithelial cells of the nose and alveolar cells of the nose and type II alveolocytes and is significantly increases in the presence of environmental stimuli and environmental stimuli and respiratory tract inflammation. Thus, increased ACE2 expression in the lungs increases susceptibility to SARS-CoV-2 and the severity of this infection.

1.2. Modern medication asthma controls

The GINA republished the main approaches to asthma therapy in 2023 (Fig. 1.3) [4, 5, 11, 14, 16, 18, 19].

GINA 2023 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

**TRACK 1: PREFERRED
CONTROLLER and RELIEVER**
Using ICS-formoterol as the
reliever* reduces the risk of
exacerbations compared with
using a SABA reliever, and is a
simpler regimen

STEPS 1 – 2

As-needed-only low dose ICS-formoterol

STEP 3

Low dose
maintenance
ICS-formoterol

STEP 4

Medium dose
maintenance
ICS-formoterol

STEP 5

Add-on LAMA
Refer for assessment
of phenotype. Consider
high dose maintenance
ICS-formoterol,
± anti-IgE, anti-IL5/5R,
anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

**TRACK 2: Alternative
CONTROLLER and RELIEVER**
Before considering a regimen
with SABA reliever, check if the
patient is likely to adhere to daily
controller treatment

STEP 1

Take ICS whenever
SABA taken*

STEP 2

Low dose
maintenance ICS

STEP 3

Low dose
maintenance
ICS-LABA

STEP 4

Medium/high
dose maintenance
ICS-LABA

STEP 5

Add-on LAMA
Refer for assessment
of phenotype. Consider
high dose maintenance
ICS-LABA, ± anti-IgE,
anti-IL5/5R, anti-IL4Rα,
anti-TSLP

RELIEVER: as-needed ICS-SABA*, or as-needed SABA

Other controller options (limited
indications, or less evidence for
efficacy or safety – see text)

Low dose ICS whenever
SABA taken*, or daily LTRA,
or add HDM SLIT

Medium dose ICS, or
add LTRA, or add
HDM SLIT

Add LAMA or LTRA or
HDM SLIT, or switch to
high dose ICS

Add azithromycin (adults) or
LTRA. As last resort consider
adding low dose OCS but
consider side-effects

*Anti-inflammatory reliever (AIR)

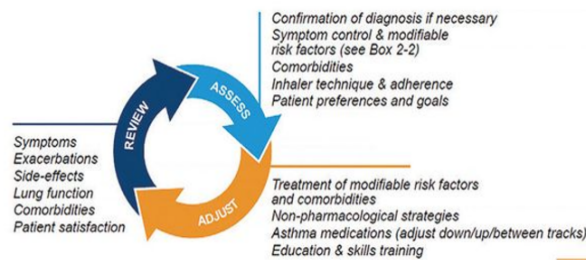


Fig.1.3 GINA treatment figure for adults and adolescents ≥ 12 years.

GINA in 2023 offers 5 categories of asthma medications:

1) Maintenance therapy (describes a set frequency of use rather than a specific class of medication for asthma) - taken daily, on a regular basis, even when there are no symptoms. Includes ICS - ICS, ICS/LABA, ICS/LABA/LAMA; leukotriene receptor antagonists; biological therapy.

2) Drugs for control (controller): aimed at both components of control (control of symptoms and control of symptoms and future risks). These include ICS-containing drugs. Previously, they were used mainly on a regular basis, so maintenance therapy and controlling therapy were synonymous. The introduction of the combination of ICS/formoterol combination for use on an as-needed basis introduced disharmony and some uncertainty in the terminology.

3) Medications for symptom reduction (medications for “first aid”, reliever). They are used when needed, to quickly reduce asthma symptoms, are taken as needed. These include SABA, low-dose ICS/formoterol combinations,

ICS/salbutamol combinations, ICS/other short-acting beta₂-agonists.

4) Anti-inflammatory drug to reduce symptoms (anti-inflammatory reliever). These drugs contain low doses of ICS and a fast-acting bronchodilator: these are fixed combinations of budesonide/formoterol, beclomethasone/formoterol and currently a fixed combination of ICS/salbutamol. They are used as needed to reduce symptoms, before physical activity and allergen exposure to prevent symptoms of asthma and bronchospasm. Some anti-inflammatory relievers can be used as the only treatment in steps 1-2 if needed asthma (only anti-inflammatory reliever treatment) (almost all of the evidence base for this for this is based on the combination of ICS/formoterol).

ICS/formoterol combinations can be used in steps 3-5 in the MART regimen. It should be emphasized that combinations containing other long-acting beta₂-agonists, not formoterol, should not be used for symptom relief, as SSRIs and in the MART regimen.

5) Maintenance (basic) therapy and symptomatic therapy with a single inhaler therapy with one inhaler (Maintenance and Reliever Therapy - MART). This is a treatment regimen where the patient uses a fixed combination of ICS/formoterol in one inhaler daily (maintenance dose) and the same combination to reduce symptoms, if necessary). MART - only combination ICS/formoterol – budesonide/formoterol and beclomethasone/formoterol!!! Other combinations of ICS with a nonformoterol LABA or combinations ICS/SABA are not used for this regimen. The abbreviation SMART (Single inhaler Maintenance and Reliever Therapy). SMART = MART (Maintenance and Reliever Therapy).

The GINA 2023 updates emphasize the most important role of ICS therapy in achieving asthma control and preventing exacerbations.

However, patient adherence to therapy remains quite low, so an approach that allows to manage both symptoms and exacerbations simultaneously is simpler, and remains the preferred way to treat of asthma.

Global approaches to asthma treatment - limitations, where possible, the use of SABA and the preference for delivery devices and treatment regimens that have a

lower environmental impact.

Management of patients according to their personalized action plan and establishing localized protocols can limit the use of SABA, improve asthma outcomes for the patient and improve the environmental impact.

Treatment for asthma usually involves the use of anti-inflammatory medications, such as corticosteroid inhalers, as well as bronchodilators to relieve bronchial spasm and make breathing easier.

To control asthma, doctors may recommend keeping a special diary of symptoms, avoiding triggers that can cause an attack, and regularly checking lung function. It is also important to pay attention to a healthy lifestyle, a balanced diet, and vigorous regular physical activity.

Asthma treatment should be individualized and carried out under the supervision of a qualified specialist.

Conclusions for chapter 1

1. Asthma, an airway inflammation disease, is one of the most debilitating chronic diseases impacting people worldwide and is a common disorder with a variety of etiologies, including environmental and genetic variables. In 2019, the World Health Organization estimates that asthma affected 262 million people and caused 461.000 deaths globally.

2. The GINA 2023 update recommendations for treatment and prevention of asthma. The data included in this guideline are based on the principles of evidence-based efficacy and safety in medicine and pharmacy.

3. Increased medication adherence leads to better asthma control and health outcomes, decreases the risk of future asthma exacerbations and healthcare costs.

CHAPTER 2

MATERIALS AND METHODS

The experimental part of the master thesis was conducted in collaboration with Al Ikhwa Fez pharmacy, Morocco.

The study was conducted in the period from September 04, 2023 to August 30, 2024. Our study included pharmacy visitors who were diagnosed with asthma.

For the purposes of the master thesis a questionnaire was developed for surveying of patients / pharmacy visitors with asthma (table. 2.1.)

The questionnaire included questions of a general nature regarding the age, gender, genetic predisposition, as well as special questions related asthma control, medication adherence and quality of life. Particular attention was also paid to the assessment of criteria of efficacy and safety in asthma patients.

The study analyzed the drugs used by respondents and compared them with current recommendations *in* GINA 2023.

Materials were presented in hard copy, and there was also (optionally) an opportunity to take a Google Form survey.

Also, based on the results of the survey, practical recommendations for physicians, pharmacists and patients about alternative ways to improve treatment adherences in Moroccan asthma patients.

Based on the results of the study, the information material was grouped and organized in the form of memos for patients. This information material was offered to pharmacy visitors in order to raise their awareness of the effectiveness and safety of asthma therapy.

The methodological basis of the study is the principles of objectivity and consistency. The work uses a complex of general scientific and special methods: theoretical, generalization, data systematization, comparison, methods of studying literary sources, analysis, questionnaire method, statistical methods, etc.

The data obtained from the experimental study were analyzed and stylistically processed and presented in the form of tables and diagrams to illustrate the results.

Table 2.1

Questionnaire for patients / pharmacy visitors with asthma

1.	Sex and age	
2.	Smoking status: ex-smoker, non-smoker, passive smoker, active smoker?	
3.	How long have you had asthma?	
4.	Do any of your immediate family members suffer from asthma? Yes / No	
5.	What comorbid, chronic diseases do you have?	
6.	What are the main manifestations of this disease?	
7.	Which medicines do you use to control asthma?	
8.	Effect of therapeutic patient education on asthma control: well-controlled, particularly controlled, uncontrolled?	
9.	Effect of therapeutic patient education on medication adherence: high adherence, medium adherence, low adherence?	
10.	Effect of therapeutic patient education on quality of life: good, average, low?	
11.	What criteria of treatment effectiveness are most important to you?	
12.	What side effects did you experience most often during the asthma therapy? By which groups of medications?	
13.	Do you follow the rules for rational prescribing of medicines?	
14.	How often do you see your doctor and monitor your condition?	
15.	Does this disease affect your quality of life?	

Conclusions for chapter 2

1. The experimental part of the master thesis was conducted in collaboration with Al Ikhwa Fez pharmacy, Morocco. For the purposes of the survey were pooled 40 pharmacy visitors with asthma.

2. For the purposes of the master thesis a questionnaire was developed. The questionnaire included questions of a general nature regarding the age, gender, genetic predisposition, as well as special questions related directly to asthma control, medication adherence and quality of life. Particular attention was also paid to the assessment of criteria of efficacy and safety of asthma patients.

CHAPTER 3

FACTORS CONTRIBUTING TO MEDICATION ADHERENCE IN MOROCCAN ADULT ASTHMA PATIENTS (EXPERIMENTAL PART)

3.1. Survey of adult pharmacy visitors concerning asthma management adherence

The total number of surveyed pharmacy visitors was 40. The inclusion criteria were: diagnosis with asthma, use of inhaled therapy; volunteering to take part in the survey.

The main characteristics of the surveyed pharmacy visitors are presented in the table 3.1.

Table 3.1

Characteristics of surveyed pharmacy visitors with asthma

#	Patients characteristics	Indicator	% from total amount
1.	Sex		
	Female	30	75.00
	Male	10	25.00
2.	Minimal age, years	28	
3.	Maximal age, years	69	
4.	Smoking patients	2	5.00
5.	Experience of inhaled therapy	40	100

From all surveyed pharmacy visitors, 30 were females (75.0%) and 10 were male (25,0%). The average age was 46.5, the youngest respondent was 28 years old and the oldest – 69 years old. 5 % of pharmacy visitors were smoking persons with

asthma. From the surveyed pharmacy visitors, 100 % experienced inhaled therapy.

Characteristics of asthma patients according to medications are presented in Table 3.2.

Table 3.2

Patients with asthma according to medications

Frequency of administration of inhaler		
Once	2	5%
Twice	30	75%
On need	8	20%
Onset of action of inhaler		
5 min	12	30%
20 min	1	2,5%
5-20 min	14	35%
30 min	13	32,5%
Type of device		
Aerolizer	14	35%
Metered-dose inhaler (MDI)	5	12,5%
Turbohaler	13	32,5%
Handihaler	2	5%
Diskus	4	10%
Breezhaler	1	2,5%
Evohaler	1	2,5%
Type of drug		
Budesonide	8	20%
Formoterol	5	12,5%
Salbutamol	7	17,5%
Budesonide/formoterol	14	35%
Fluticasone/salmeterol	3	7,5%
Glycopyrinum bromide	1	2.5%
Tiotropium	1	2.5%
Ipratropium	1	2.5%

This study found that patients with bronchial asthma were more likely to use inhalation twice a day, which was the most convenient mode of administration for them, confirmed by the best indicators of efficacy and safety of therapy.

As the most preferred, they indicated a time of effect development of 5-20 min.

The drugs that gave the best results in asthma control were based on the budesonide/formoterol combination.

Different variant's of adherence of asthma patients are shown in Fig. 3.1: 38.20% of respondents had good adherence, 19.40% – intermediate adherence, 31.30% – poor adherence.

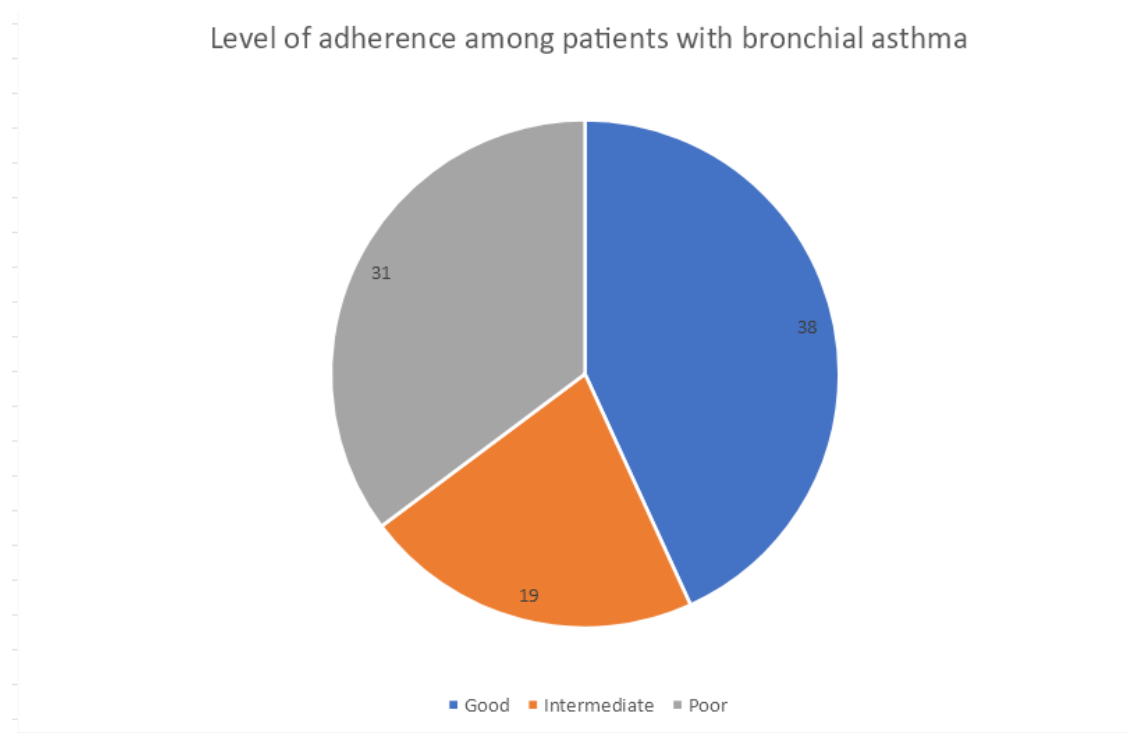


Fig.3.1. Adherence level in asthma patients

Successful inhalation therapy depends not only on the right choice of drug, but also on an adequate method of drug delivery to the respiratory tract. The ideal delivery device should ensure the deposition of a finely dispersed fraction of the drug in the area of pathological changes, be easy enough to use, reliable, and available for use at any age and in severe forms of the disease.

This study shows that 75% of the respondents preferred to prescribe the drug twice a day, 5% preferred to prescribe the drug once a day and the remaining 20%

used the drug as and when required (Fig. 3.2).

We also assessed the level of treatment adherence according to this parameter. At twice-daily therapy 14 respondents rated adherence as good, 11 – as intermediate.

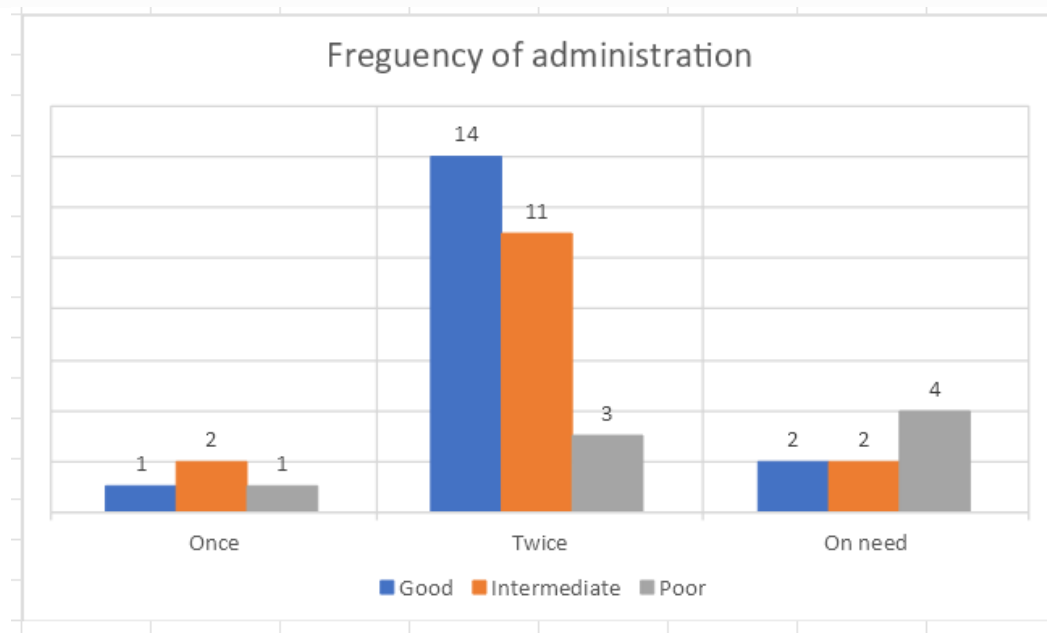


Fig.3.2. Frequency of administration of anti-asthmatic drugs and therapy adherence

The highest adherence rates were seen in patients who took medications that developed an effect in 5-20 min, which did not require frequent use of medications throughout the day as was the case with short-acting medications (Fig. 3.3).

When analyzing the parameter of time onset of action (Fig.3.3), the majority of respondents (35%) noted 5-20 minutes. Adherence to treatment was also highest when the effect occurred within 5-20 minutes, and the lowest level of adherence was observed with a rapid onset of action within 5 minutes.

This can be explained by the fact that the use of short-acting medications forced patients to take them daily, which consequently reduced their adherence to treatment.

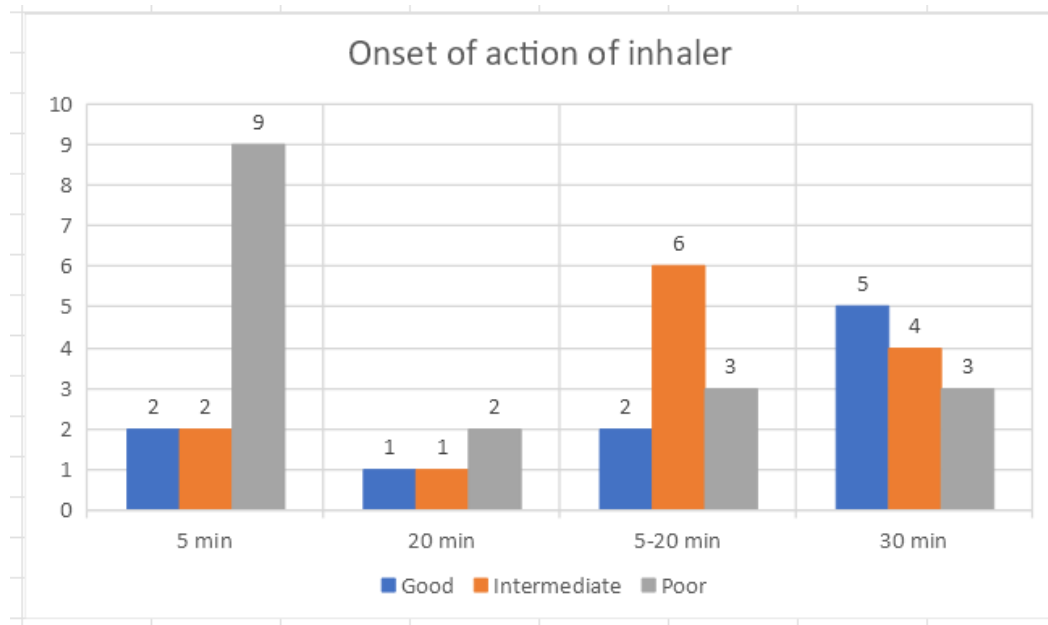


Fig.3.3. Onset of action of anti-asthmatic drugs and therapy adherence

At the next stage of the study, were determined that the highest level of adherence was in case of use of turbohaler and aerolizer in asthmatic patients in comparison with the use of MDI (Fig. 3.4).

It was this device that our respondents preferred the most, as confirmed by the research data.

The results about the types of medicines used by our respondents are presented in Fig.3.5.

The most sought-after in our study was the combination of Budesonide/formoterol. Specifically, 35% of respondents preferred its use, followed by budesonide-based medications (20% of respondents). Salbutamol was used by 17.5% of respondents in our study, which is less than the previously mentioned medications.

Therefore, long-acting anti-asthmatic medications held the leading positions, surpassing short-acting medications.

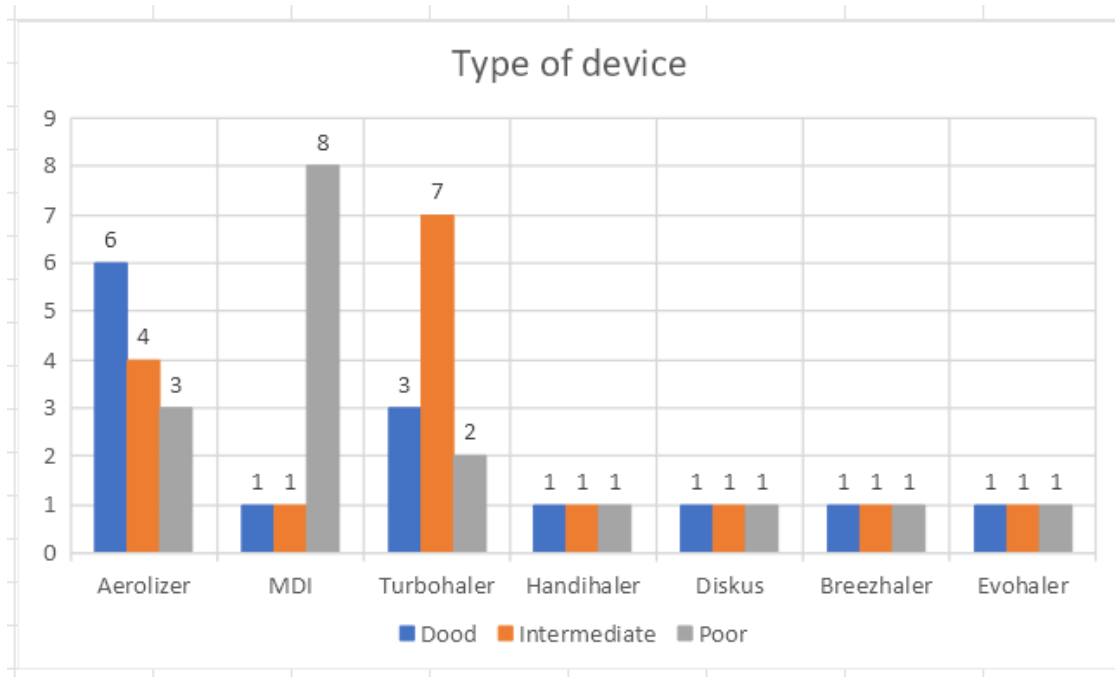


Fig.3.4. Type of device of anti-asthmatic drugs and therapy adherence

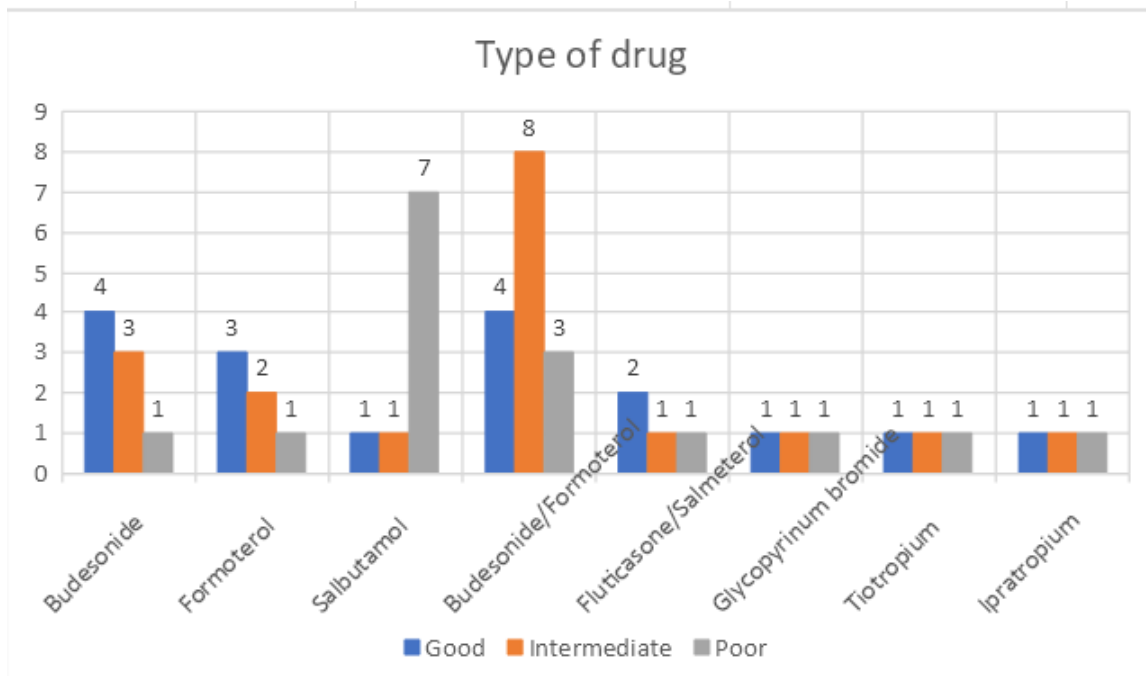


Fig.3.5. Type of anti-asthmatic drugs and therapy adherence

Adherence to treatment is a concept that characterizes how accurately and consistently a patient follows the recommendations given by the doctor. In other words, adherence is the degree to which a patient's behavior matches the recommendations provided by the doctor, with particular attention given to the issue of the patient's active participation in the treatment process.

Non-adherence to treatment is an unconscious decision made by the patient as a result of their own analysis of costs/benefits, assessing the ratio of (cost + risk)/benefit of the intervention based on their own perceptions and available information. The greatest difficulty arises in the case of comprehensive treatment of patients with comorbid conditions. Most often, these are elderly patients with combined pulmonary and cardiovascular pathology. Poor adherence to treatment is demonstrated by patients when multiple doses of medication are required. Thus, in the case of a 4-times daily medication regimen, patients receive less than 70% of the prescribed dose, and with a 5-times daily regimen, less than 60%. Insufficient use of medications is observed much more frequently than excessive use. Therefore, one of the tasks in addressing the issue of improving treatment adherence is the creation of various forms of combined medications with simple dosing regimens.

Negative impacts on treatment adherence in patients with asthma are the following:

1) *medication*:

- difficulties in using the inhaler (inhalers should be prescribed only after patients have been trained in the use of the device and have demonstrated satisfactory technique);
- inconvenient regimen of pharmacotherapy (4 times a day, many drugs);
- side effects;
- cost of medications;
- interruptions in the supply of necessary medicines to the pharmaceutical market;

2) *non-pharmacological*:

- unclear or insufficient instruction;

- fear of side effects;
- lack of contact and dissatisfaction with medical staff;
- vague fear or anxiety;
- unreasonable expectations on the part of both the patient and the doctor;
- insufficient observation of the patient, lack of quality monitoring;
- irritation (depression) about their condition or the quality of treatment;
- underestimation of the severity of the condition, forgetfulness, unjustified calmness;
- cultural traditions;
- a special position regarding their health (antisocial people).

Patients with asthma should be offered self-management education that focuses on individual needs and supported by a written individualized treatment plan. This plan, developed by highly trained clinicians, should be provided to patients receive before being discharged from the hospital.

Patient education is a long process, the main link of which is self-control. For its competent implementation, the following elements are mandatory:

- patient awareness (the system of influence of medical professionals; the most effective is the joint work of a group consisting of a doctor, a nurse and a pharmacist);
- reliable measurement of exhalation rates (objectification of the patient's condition by means of puff flowmetry);
- instructions that are clear to the patient and absolutely specific, regarding algorithm of actions at the beginning of an attack;
- flexible and long-term contacts between doctor, nurse and patient (prescribed monitoring system - appointment schedules, patient diaries).

Adherence to asthma treatment is inextricably linked to skills in the effective use of inhaler devices. In the GINA 2023 outcome document states that the majority of patients (up to 80%) cannot or do not know how to use their inhaler correctly. To overcome this problem, the physician is encouraged to follow the 4C rule:

- Choose: Choose the most comfortable device for the patient. Ideally, all

inhaled medications should be delivered through one device.

- Check: Check the inhalation technique at every opportunity.
at every opportunity. Ask the patient to show you how they use the inhaler.
the inhaler.
- Correct: During the hands-on demonstration, point out any incorrect steps.
Check the technique again, up to 2-3 times if necessary.
- Confirm: Ensure that the patient has the instructions for each of the inhalers
prescribed and can demonstrate the correct technique in each case.

Provisions that play a key role in patient education:

1. Good psychological contact between doctor, nurse and patient.
2. Providing the patient and his/her family with qualified information about the
(conversation, information sheets, popular developments written in clear language,
posting information on the website). written in a clear language, posting information
on the institution's website, possible interactive).
3. Coverage of educational activities (asthma school, talks, videos, etc, work of
special associations, etc.)
4. Availability of an individual written treatment plan for the patient and its
monitoring (dosage of basic medications with appropriate peak flow meter,
indications for the use of bronchodilators, rules for keeping a self-monitoring diary,
etc.)

Analysis of the use of various strategies to improve the adherence of patients to
asthma treatment suggests that the most effective are the following:

- joint decision-making;
- simplification of the treatment regimen (taking the drug once a day instead of
2 times a day);
- comprehensive patient education during home visits by a nurse;
- use of a reminder device built into the inhaler;
- monitoring the patient's diary.

To facilitate self-monitoring of treatment, you can use a special system for
assessing the patient's objective condition with the help of pulse oximeter.

Three colors (green, yellow, and red) on the pulse oximeter scale indicate the corresponding state of the patient. Each color corresponds to a so-called “zone” with the corresponding symptoms of the disease.

The “green zone” means that asthma is under control. Sleep, physical activity are not disturbed, symptoms of the disease are minimal or absent. The peak expiratory flow rate is 80-100% of the normal, and daily fluctuations do not exceed 20%. The patient receives effective planned therapy prescribed by a doctor. If the patient's condition corresponds to the “green zone” for at least three months, the doctor should consider the possibility of a cautious reduction in the medication load – “step down”.

“Yellow zone” means “Attention”. It is characterized by the appearance of coughing, wheezing, or shortness of breath during normal physical activity, indicators of peak expiratory flow rate in the range of 60-80% of proper, and the daily fluctuations of the indicators do not exceed 30%. It is necessary to consult a doctor, because the transition to the “yellow zone” means not entirely successful control of asthma against the background of ongoing therapy (call your doctor).

“Red zone” is an alarm signal. Asthma symptoms are present both with minimal physical activity and at rest. The value of the peak expiratory volume expiratory flow rate is 60% – lower than the normal or best individual values. Short-acting β_2 -agonists should be used and, if, after their use, the peak expiratory flow rate remain less than 60%, urgently seek medical attention (examination by a specialist or emergency medical care).

Patients are advised to keep a self-monitoring diary with registration of morning and evening pulse flowmetry values. According to the zone, the attending the doctor develops a treatment plan, taking into account the individual characteristics of the patient and the course of the disease.

Thus, in the practice of a physician in cooperation with a patient the following issues need to be addressed:

- deciding on treatment and dose selection;
- whether the inhaler has a device to remind you of missed doses (dose

counter);

- reducing the complexity of the treatment regimen (once or twice a day);
- comprehensive asthma education with home visits by specially trained nurses (small children, elderly people);
- feedback on the implementation of doctor's prescriptions (questionnaires, self-assessment), monitoring.

Attention is drawn to the fact that at each stage before making a decision to increase the volume of therapy, it is mandatory to checking inhalation technique and adherence to treatment. Patient awareness and self-management skills help patients understand the nature of the disease and the need for long-term treatment.

Thus, proper control of bronchial asthma by the joint efforts of the patient and medical staff will significantly improve the effectiveness and safety of drug therapy for bronchial asthma.

3.2. Discussion of the obtained results

Bronchial asthma is a common disease characterized by chronic inflammation of the airways, bronchial hyperreactivity, and reversible airway obstruction. According to estimates by the World Health Organization (WHO), in 2019, the number of people with bronchial asthma was 262 million. Every year on the first Tuesday of May, which in 2023 falls on May 2, the global community observes World Asthma Day to raise awareness about this disease. This year, the Global Initiative for Asthma (GINA) has chosen the theme "Asthma Treatment for All," as the majority of the burden of morbidity and mortality from the disease falls on low- and middle-income countries [31].

Bronchial asthma can affect people of any age and often begins in childhood, although it can also first develop in adults. In children, the disease sometimes disappears or its severity decreases during adolescence, but it can return later in life. The pathology causes swelling (inflammation) of the airways that carry air to and from the lungs. This makes the airways very sensitive, so they can temporarily

narrow, causing symptoms such as coughing, wheezing, shortness of breath, and a feeling of tightness in the chest. This is called an exacerbation, episode, or attack of bronchial asthma. An exacerbation can occur randomly or after exposure to a provoking factor (trigger). Triggers can include viral infections, allergies (dust, pet hair), smoke, polluted and cold air. Symptoms often worsen at night, during physical exertion, or when experiencing strong emotions.

Currently, it is impossible to cure patients with bronchial asthma, but there are therapeutic methods that can help keep the symptoms under control. However, if they are ignored, especially when the severity of symptoms increases, and the treatment plan is not followed, it can cause certain problems such as constant fatigue, stress, depression, lung infections (pneumonia), and so on. There is also a risk of severe disease attacks, which can be life-threatening.

The most common factors contributing to the development of bronchial asthma include having the disease in parents, experiencing a severe respiratory infection in childhood, allergies, exposure to certain chemical irritants or industrial dust in the workplace, smoking, polluted air, and obesity [6].

The experimental part of the master thesis was conducted in collaboration with Al Ikhwa Fez pharmacy, Morocco. For the purposes of the survey were pooled 40 pharmacy visitors with asthma.

For the purposes of the master thesis a questionnaire was developed. The questionnaire included questions of a general nature regarding the age, gender, genetic predisposition, as well as special questions related directly to asthma control, medication adherence and quality of life. Particular attention was also paid to the assessment of criteria of efficacy and safety of asthma patients.

From all surveyed pharmacy visitors, 30 were females (75.0%) and 10 were male (25.0%). The average age was 46.5, the youngest respondent was 28 years old and the oldest – 69 years old. 5 % of pharmacy visitors were smoking persons with asthma. From the surveyed pharmacy visitors, 100 % experienced inhaled therapy.

This study found that patients with bronchial asthma were more likely to use inhalation twice a day, which was the most convenient mode of administration for

them, confirmed by the best indicators of efficacy and safety of therapy.

As the most preferred, they indicated a time of effect development of 5-20 min.

The drugs that gave the best results in asthma control were based on the budesonide/formoterol combination.

Different variant's of adherence of asthma patients were determined in this study: 38.20% of respondents had good adherence, 19.40% – intermediate adherence, 31.30% – poor adherence.

Inhalers with 5-20 min of action onset were more often used by asthma patients. It were determined that the highest level of adherence was in case of use of turbohaler and aerolizer with budesonide/formoterol.

The most sought-after in our study was the combination of Budesonide/formoterol. Specifically, 35% of respondents preferred its use, followed by budesonide-based medications (20% of respondents). Salbutamol was used by 17.5% of respondents in our study, which is less than the previously mentioned medications.

To improve adherence to treatment, the following steps can be taken:

Determining poor adherence:

- markers of poor adherence: missed appointments, insufficient response to prescribed treatment;
- ask the patient about obstacles to consistent medication intake without creating confrontation with the patient.

Emphasize the importance of adhering to the medication regimen and the positive impact of good treatment adherence.

Ask the patient about their feelings regarding their ability to follow the doctor's prescriptions, and if necessary, provide the patient with the required support.

Provide the patient with simple, clear instructions and simplify the treatment regimen as much as possible.

Offer a specific system for taking medications.

Listen to the patient and adjust the regimen according to the patient's needs and preferences.

Involve family support if necessary.

Reinforce the desired behavior and outcomes when appropriate. Suggest more "convenient" medications (the effectiveness of the drugs is less dependent on delays in taking them) when the likelihood of good adherence to treatment is high:

- drugs with a prolonged half-life;
- depot forms of medications;
- transdermal medications.

Successful inhalation therapy depends not only on the correct choice of medication but also on the adequate method of delivering the drugs to the respiratory tract. The ideal delivery device should ensure the deposition of the fine fraction of the drug in the area of pathological changes, be easy to use, reliable, and suitable for application at any age and in severe forms of the disease.

Advantages of aerosol therapy:

- direct action on the target organ;
- reduction in the time to achieve the therapeutic effect;
- high concentration of drugs in the respiratory tract with a low therapeutic dose of the drug (15–20 times less compared to the dose administered orally);
- enhancement of the therapeutic effect;
- reduction in the frequency of adverse side effects on the body as a whole;
- absence of systemic action of the drugs;
- reduction in the risk of hospitalizations, repeated outpatient visits to the doctor, shortening the treatment period;
- facilitation of emergency care for the patient.

Disadvantages of aerosol therapy:

- Dependence of the effect on the form of the medication and delivery devices to the respiratory tract;
- the necessity of performing special breathing maneuvers, which reduces the age limits for application;

- low deposition of drugs in the medium and small bronchi;
- negative impact on the oral mucosa;
- the need to train the patient and the possibility of errors when performing breathing maneuvers;
- the impossibility of precise dosing of medications;
- the use of auxiliary devices increases the cost of therapy.

Ways to overcome the disadvantages of aerosol therapy:

- the use of non-CFC (hydrofluoroalkane) aerosols;
- the use of forms with ultra-fine drug particles in the aerosol;
- the use of inhalers activated by inhalation;
- the use of "soft" – soft-mist aerosols (aqueous solutions of drugs);
- the use of spacers;
- the use of nebulizers.

The goals of treatment for bronchial asthma are to achieve proper symptom control, maintain a normal level of activity, and minimize the risk of future exacerbations and side effects of medications. Therapy may include a whole range of different methods and combine medication with lifestyle adjustments. Inhaled corticosteroids are the cornerstone of therapy and the standard for long-term treatment of patients with bronchial asthma. There are two types of inhalers: reliever inhalers (used as needed for quick reduction of symptom severity for a short period) and preventive inhalers (used daily to prevent the onset of disease symptoms).

Control of bronchial asthma can be effectively achieved only through adherence to the treatment regimen, compliance with therapy, proper use of the inhaler, understanding of provoking factors, and their avoidance.

Pharmacists, as participants in the healthcare system, also play an important role in the lives of patients with bronchial asthma (Fig. 3.6). They are on the front line of advisory contact with citizens regarding medical issues. Thus, pharmaceutical workers can identify individuals who may be developing bronchial asthma and recommend consulting a specialist doctor for diagnosis and treatment.



Fig. 3.6. Role of pharmacists in asthma management

3.3. Practical recommendations regarding self-monitoring of the treatment process in asthma patients

The patient should have a good understanding of self-monitoring the treatment process.

- Components of successful self-management of the treatment process:
 - Acceptance and understanding of bronchial asthma and its treatment
 - Effective and compliant use of medications
 - Having a peak flow meter at home and monitoring peak expiratory flow rate (PEFR) values
 - Written instructions for various issues.
- As part of self-management of the treatment process, the patient may be provided with written recommendations regarding individual peak expiratory flow rate (PEFR) thresholds and treatment instructions.
 - If the symptoms have increased in frequency and the need for short-acting bronchodilators has risen, the dose of inhaled glucocorticoids should be doubled for two weeks.
 - If the morning PFFR is repeatedly less than 80-70% of the optimal, the patient

should be prescribed a course of oral prednisolone at a dose of (20-)30-40 mg per day for 1-2 weeks. If the PEF value in the morning is repeatedly less than 80-70% of the optimal, the patient is prescribed a course of oral prednisolone at a dose of (20-)30-40 mg per day for 1-2 weeks.

- The patient should seek emergency medical assistance or contact a healthcare facility to initiate an oral course of prednisolone if the PEF value is less than 50% of the optimal.

- During a respiratory infection, it is recommended to increase the dose of the inhaled glucocorticoid for 2 weeks even in the absence of a decrease in PEF values; the patient should also take short-acting bronchodilators 3-4 times a day.

Peak flowmetry is an important method of functional diagnostics used to measure the peak expiratory flow rate (PEFR). This indicator is critically important in the detection and monitoring of bronchial obstruction, which is characteristic of conditions such as bronchial asthma and chronic obstructive pulmonary disease (COPD). Peak flowmetry reflects the volume of air a person can quickly exhale in the first second and is an important indicator of lung function.

Objectives and tasks of peak flowmetry

For patients with bronchial asthma:

Monitoring condition: Peak flowmetry allows asthma patients to regularly measure and record their readings, which is critically important for disease control and timely detection of exacerbations.

Adaptation of the treatment plan: The results of peak flowmetry can help the doctor determine the effectiveness of the treatment and, if necessary, adjust the therapeutic plan.

Prevention of exacerbations: Regular use of a peak flow meter helps patients timely recognize a decline in lung function and take necessary measures to prevent a full-blown asthma attack.

Recommendations about correct use of pulse flow meter:

The test should always be performed in an upright position (standing).

Take a deep breath.

Wrap your lips tightly around the mouthpiece.

Exhale as hard as you can.

Follow the steps above three times, and then record the highest reading of the three, or the device will do it for you.

To get accurate readings, make sure you know how to use the puffometer correctly. Ask your healthcare provider to instruct you on how to perform pulse oximetry.

Thus, all of the above methods of physical, laboratory and instrumental control of asthma will help patients to control the disease more effectively.

Conclusions for chapter 3

1. The experimental part of the master thesis was conducted in collaboration with Al Ikhwa Fez pharmacy, Morocco. From all surveyed pharmacy visitors, 30 were females (75.0%) and 10 were male (25.0%). The average age was 46.5, the youngest respondent was 28 years old and the oldest – 69 years old. 5 % of pharmacy visitors were smoking persons with asthma. From the surveyed pharmacy visitors, 100 % experienced inhaled therapy.

2. It was determined that 38.20% of respondents had good adherence, 19.40% – intermediate adherence, 31.30% – poor adherence. Inhalers with 5-20 min of action onset were more often used by asthma patients. It was determined that the highest level of adherence was in case of use of turbobhaler and aerolizer with budesonide/formoterol.

3. Despite the availability of therapies, asthma control remains suboptimal due to low adherence, poor inhaler technique, and several patient-related factors. Asthma management depends on several factors, including trigger avoidance, smoking cessation, medication adherence, proper inhalation technique, asthma knowledge, and recognition of worsening of asthma symptoms.

4. Medical and pharmaceutical specialists should be involved in the pharmacotherapy process for patients with bronchial asthma, which will positively impact the effectiveness and safety indicators of the therapy for this disease.

CONCLUSIONS

1. Asthma is a serious world global health problem affecting all age groups. This disease significantly affects the quality of life indicators for patients. Therefore, improving the effectiveness and safety of therapy will contribute to increasing patient adherence to treatment.

2. The experimental part of the master thesis was conducted in collaboration with Al Ikhwa Fez pharmacy, Morocco. From all surveyed pharmacy visitors, 30 were females (75.0%) and 10 were male (25.0%), the average age was 46.5 years. From the surveyed pharmacy visitors, 100 % experienced inhaled therapy.

3. A total of 42.2% of asthma patients had good adherence, 22.9% intermediate adherence, and 34.9% poor adherence. Inhalers with 5-20 min of action onset were more often used by asthma patients.

4. Despite the availability of therapies, asthma control remains suboptimal due to low adherence, poor inhaler technique, and several patient-related factors. Asthma management depends on several factors, including trigger avoidance, smoking cessation, medication adherence, proper inhalation technique, asthma knowledge, and recognition of worsening of asthma symptoms.

5. Medical and pharmaceutical specialists should be involved in the pharmacotherapy process for patients with bronchial asthma, which will positively impact the effectiveness and safety indicators of the therapy for this disease.

REFERENCES

1. A review of the unique drug development strategy of indacaterol acetate/glycopyrronium bromide/ mometasone furoate: a first-in-class, once-daily, single-inhaler, fixed-dose combination treatment for asthma / D. Brittain et al. *Adv. Ther.* 2022. Vol. 39 (6). P. 2365–2378.
2. Ahmad S., Kew K. M., Normansell R. Stopping long-acting beta2-agonists (LABA) for adults with asthma well controlled by LABA and inhaled corticosteroids. *Cochrane Database Syst. Rev.* 2015. Vol. 6. P. CD011306.
3. As-needed budesonide-formoterol versus maintenance budesonide in mild asthma / E. D Bateman et al. *N. Engl. J. Med.* 2018. Vol. 378 (20). P. 1877–1887.
4. Association of inhaled corticosteroids and long-acting β -Agonists as controller and quick relief therapy with exacerbations and symptom control in persistent asthma a systematic review and meta-analysis / D. M. Sobieraj et al. *JAMA.* 2018. Vol. 319 (14). P. 1485–1496.
5. Asthma pharmacotherapy: an update on leukotriene treatments / H. K. T. Trinh et al. *Expert Rev. Respir Med.* 2019. Vol. 13 (12). P. 1169–1178.
6. Asthma prevalence and its risk factors among a multi-ethnic adult population / A. Jeyagurunathan et al. *Yale J. Biol. Med.* 2021. Vol. 94 (3). P. 417–427.
7. Budesonide-formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial / J. Hardy et al. *Lancet.* 2019. Vol. 394 (10202). P. 919–928.
8. Consequences of long-term oral corticosteroid therapy and its side-effects in severe asthma in adults: a focused review of the impact data in the literature / T. Volmer et al. *Eur. Respir. J.* 2018. Vol. 52 (4). P. 1800703.
9. Controlled trial of budesonide-formoterol as needed for mild asthma / R. Beasley et al. *N. Engl. J. Med.* 2019. Vol. 380 (21). P. 202.

- 10.Desai D., Brightling C. Cough due to asthma, cough-variant asthma and non-asthmatic eosinophilic bronchitis. *Otolaryngol Clin. North. Am.* 2010. Vol. 43 (1). P. 123–130.
- 11.Dupilumab Efficacy in Steroid-Dependent Severe Asthma by Baseline Oral Corticosteroid Dose / C. Domingo et al. *J. Allergy Clin. Immunol Pract.* 2022. Vol. 10 (7). P. 1835–1843.
- 12.EAACI Guidelines on allergen immunotherapy: house dust mite-driven asthma / I. Agache et al. *Allergy.* 2019. Vol. 74 (5). P. 855–873.
- 13.Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group / M. M. Cloutier et al. *J. Allergy Clin. Immunol.* 2020. Vol. 146 (6). P. 1217–1270.
- 14.GINA 2019: a fundamental change in asthma management: treatment of asthma with short acting bronchodilators alone is no longer recommended for adults and adolescents / H. K. Reddel et al. *Eur. Respir. J.* 2019. Vol. 53 (6). P. 1901046.
- 15.Global strategy for asthma management and prevention. 2022. URL: <https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf> (Date of access: 30.04.2024).
- 16.Kew K. M., Dahri K. Long-acting muscarinic antagonists (LAMA) added to combination long-acting beta2-agonists and inhaled corticosteroids (LABA/ICS) versus LABA/ICS for adults with asthma. *Cochrane Database Syst Rev.* 2016. Vol. 1. P. CD011721.
- 17.Koskela H. O., Purokivi M. K., Kokkarinen J. Stepping down from combination asthma therapy: the predictors of outcome. *Respir Med.* 2016. Vol. 117. P. 109–115.
- 18.Long-term role of zileuton in the treatment of chronic rhinosinusitis in aspirin exacerbated respiratory disease / C. A. Makary et al. *Am. J. Otolaryngol.* 2022. Vol. 43 (1). P. 103–227.
- 19.Macrolides versus placebo for chronic asthma / K. Undela et al. *Cochrane Database Syst. Rev.* 2021. Vol. 11 (11). P. CD002997.

20. On-demand intermittent beclomethasone is effective for mild asthma in Brazil / P. Camargos et al. *Clin. Transl. Allergy*. 2018. Vol. 8 (7). P. 209–220.
21. Real-world efficacy of treatment with Benralizumab, dupilumab, mepolizumab and reslizumab for severe asthma: a systematic review and meta-analysis / D. Charles et al. *Clin. Exp. Allergy*. 2022. Vol. 52 (5). P. 616–627.
22. Reducing tolerance for SABA and OCS towards the extreme ends of asthma severity / P. Bakakos et al. *J. Pers. Med.* 2022. Vol. 12 (3). P. 504.
23. Risk factors for asthma exacerbation and treatment failure in adults and adolescents with well controlled asthma during continuation and step-down therapy / E. DiMango et al. *Ann. Am. Thorac Soc.* 2018. Vol. 15 (8). P. 955–961.
24. Rodrigo G. J., Castro-Rodríguez J. A. What is the role of tiotropium in asthma? A systematic review with meta-analysis. *Chest*. 2015. Vol. 147 (2). P. 388–396.
25. Short- and long-term real-world effectiveness of omalizumab in severe allergic asthma: systematic review of 42 studies published 2008–2018 / K. M. MacDonald et al. *Expert Rev. Clin. Immunol.* 2019. Vol. 15 (5). P. 553–569.
26. Short-acting β_2 -agonist prescriptions are associated with poor clinical outcomes of asthma: the multi-country, cross-sectional sabina III study / E. D. Bateman et al. *Eur. Respir J.* 2022. Vol. 59 (5). P. 2101402.
27. Should recommendations about starting inhaled corticosteroid treatment for mild asthma be based on symptom frequency: A post-hoc efficacy analysis of the START study / H. K. Reddel et al. *Lancet*. 2017. Vol. 389 (10065). P. 157–166.
28. The efficacy and safety of reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: a systematic review and meta-analysis / J. Li et al. *J. Asthma*. 2017. Vol. 54 (3). P. 300–307.
29. The further paradoxes of asthma management: time for a new approach across the spectrum of asthma severity / R. Beasley et al. *Eur. Respir J.* 2018. Vol. 52 (5). P. 1800694.
30. The role of aspirin desensitization followed by oral aspirin therapy in managing patients with aspirin-exacerbated respiratory disease: a work group report from the rhinitis, rhinosinusitis and ocular allergy committee of the american academy of

- allergy, asthma immunology / W.W. Stevens et al. *J. Allergy Clin. Immunol.* 2021. Vol. 147 (3). P. 827–844.
31. Trends in worldwide asthma prevalence / M. I. Asher et al. *Eur. Respir. J.* 2020. Vol. 56 (6). P. 197–221.
32. Use of biologic therapies in the treatment of asthma – A comparative real world data analysis on healthcare resource utilization and costs before and after therapy / F. Hardtstock et al. *J. Asthma Allergy.* 2022. Vol. 15. P. 407–418.

National University of Pharmacy

Faculty for foreign citizens' education

Department of clinical pharmacology and clinical pharmacy

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy

Educational program Pharmacy

APPROVED
Head of Department
of Pharmacology and
Clinical Pharmacy

Sergii SHTRYGOL`
«02» of September 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Houssame MESBAHI

1. Topic of qualification work: «Factors contributing to medication adherence in Moroccan adult asthma patients: clinical and pharmaceutical research», supervisor of qualification work: Inna OTRISHKO, PhD, assoc. prof.

approved by order of NUPh from «06th» of February 2024 № 34

2. Deadline for submission of qualification work by the applicant for higher education: November 2024.

3. Outgoing data for qualification work: asthma, efficacy and safety of therapy, pharmacist, Moroccan patients, rational use of medicines.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): to study the basic information about asthma; to study the impact of adherence on quality of Moroccan asthma patients life; to study approaches to modern therapy of asthma; to analyze the opinions and beliefs of pharmacy visitors with asthma concerning efficacy and safety of medication management; to develop practical recommendations for physicians, pharmacists and patients about alternative ways to improve treatment adherences in Moroccan asthma patients.

5. List of graphic material (with exact indication of the required drawings):
tables – 3, figures – 9.

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1.	Inna OTRISHKO, associate professor of higher education institution of clinical pharmacology and clinical pharmacy department	09.02.2024	09.02.2024
2.	Inna OTRISHKO, associate professor of higher education institution of clinical pharmacology and clinical pharmacy department	09.02.2024	09.02.2024
3.	Inna OTRISHKO, associate professor of higher education institution of clinical pharmacology and clinical pharmacy department	09.02.2024	09.02.2024

7. Date of issue of the assignment: «09» February 2024

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Conducting a literature review on the issues of the work.	February-March 2024	done
2.	Conducting a survey of pharmacy visitors.	April-June 2024	done
3.	Experimental data processing.	July-August 2024	done
4.	Writing the qualification work.	September-October 2024	done
5.	Registration of the work and accompanying documents and submission to the Examination Committee of the NUPh.	November 2024	done

An applicant of higher education

Houssame MESBAHI


Supervisor of qualification work

Inna OTRISHKO

ВИТЯГ З НАКАЗУ № 34
По Національному фармацевтичному університету
від 06 лютого 2024 року

1. Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу 2 циклу ФМ20*(4,10д) 2024-2025 навчального року, ступінь вищої освіти «магістр», галузь знань 22 Охорона здоров'я, спеціальність 226 – Фармація, промислова фармація, освітньо-професійна програма – Фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців). Мова навчання англійська.

навчання англійською.					
№ з/п	Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• по кафедрі фармакології та клінічної фармації					
22.	Месбахі Хуссам	Фактори, що сприяють прихильності до лікування у дорослих пацієнтів з бронхіальною астмою в Марокко: клініко-фармацевтичне дослідження	Factors contributing to medication adherence in Moroccan adult asthma patients: clinical and pharmaceutical research	доцент Отрішко І.А.	професор Бутко Я.О.





Ректор

Вірно. Секретар

ВИСНОВОК

**експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі**

здобувача вищої освіти

«24» листопада 2024 р. № 329738831

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Месбахі Хуссам, Фм20*(4,10д)-англ-01, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Фактори, що сприяють прихильності до лікування у дорослих пацієнтів з бронхіальною астмою в Марокко: клініко-фармацевтичне дослідження / Factors contributing to medication adherence in Moroccan adult asthma patients: clinical and pharmaceutical research», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (копіляції).

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



Інна ВЛАДИМИРОВА

REVIEW

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

Houssame MESBAHI

**on the topic: «Factors contributing to medication adherence in Moroccan
adult asthma patients: clinical and pharmaceutical research»**

Relevance of the topic. According to statistics, bronchial asthma (BA) affects approximately 300 million people worldwide. It is a serious global health problem that affects all age groups. The prevalence of asthma is increasing in many developing countries. The costs of treatment are also increasing, which in general represents a significant burden for patients and communities, and this burden is growing.

Practical value of conclusions, recommendations and their validity. The research conducted in this work is the basis for further clinical and pharmaceutical studies, development and implementation of principles for optimizing the use of anti-asthmatic medicines. The implementation of these principles and provisions in practical medicine and pharmacy will help to increase the effectiveness and safety of asthma therapy.

Assessment of work. The work is performed at a sufficient scientific and methodological level. In terms of relevance, scientific novelty and practical significance, it fully meets the requirements for qualification works.

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 EC for further defense.

Scientific supervisor

Inna OTRISHKO

«08» November 2024

REVIEW

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

Houssame MESBAHI

**on the topic: «Factors contributing to medication adherence in Moroccan
adult asthma patients: clinical and pharmaceutical research»**

Relevance of the topic. Asthma affects up to 300 million people worldwide. The incidence of bronchial asthma reaches 18%. In children, this figure ranges from 5-10%. It has been established that in terms of age, the highest prevalence of bronchial asthma is recorded in school age.

Theoretical level of work. The literature review conducted on the subject of the study illustrates the state of medication adherence of patients today and outlines the prospects for research in this area.

Author's suggestions on the research topic. The provisions of the author of the work on medication adherence are of practical importance for the modern health care system.

Practical value of conclusions, recommendations and their validity. According to the results of research, approaches to the rational use of anti-asthmatic medicines have been developed. The author discusses the main approaches to increase the medication adherence in case of asthma therapy. Practical recommendations for all healthcare providers are proposed.

Disadvantages of work. Single grammatical and spelling errors do not affect the overall positive assessment of the work.

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

Reviewer _____

prof. Yaroslava BUTKO

«11» November 2024

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ**

**Витяг
з протоколу № 7
«11» листопада 2024 року**

м. Харків

засідання кафедри фармакології та клінічної фармації

ПРИСУТНІ: зав. каф., проф. Штриголь С.Ю., проф. Деримедвідь Л.В., доц. Белік Г.В., доц. Ветрова 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.

ПОРЯДОК ДЕННИЙ:

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

СЛУХАЛИ:

1. Здобувача вищої освіти Хуссам МЕСБАХІ зі звітом про проведену наукову діяльність за темою кваліфікаційної роботи: «Фактори, що сприяють прихильності до лікування у дорослих пацієнтів з бронхіальною астмою в Марокко: клініко-фармацевтичне дослідження».

УХВАЛИЛИ:

1. Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Хуссам МЕСБАХІ допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри фармакології
та клінічної фармації, професор

Сергій ШТРИГОЛЬ

Секретар кафедри фармакології
та клінічної фармації, доцент

Катерина ВЕТРОВА

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

**ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ**

Направляється здобувач вищої освіти Хуссам МЕСБАХІ до захисту кваліфікаційної роботи за галуззю знань 22 Охорона здоров'я спеціальністю 226 Фармація, промислова фармація освітньою програмою Фармація на тему: «Фактори, що сприяють прихильності до лікування у дорослих пацієнтів з бронхіальною астмою в Марокко: клініко-фармацевтичне дослідження» / «Factors contributing to medication adherence in Moroccan adult asthma patients: clinical and pharmaceutical research».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Хуссам МЕСБАХІ виконав весь необхідний обсяг робіт. Кваліфікаційна робота може бути рекомендована до подачі в ЕК НФаУ для подальшого її захисту.

Керівник кваліфікаційної роботи

Інна ОТРИШКО

«08» листопада 2024 року

Висновок кафедри про кваліфікаційну роботу

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

Завідувач кафедри
фармакології та клінічної фармації

Сергій ШТРИГОЛЬ

«11» листопада 2024 року

Qualification work was defended
of Examination commission on
«28» November 2024
with the grade _____

Head of the State Examination commission,
DPharmSc, Professor

_____ / Oleh SHPYCHAK /