Deanship of Graduate Studies

AL-Quds University

Pharmaceutical Care Services for Asthma Patients:A Randomized Control Trial

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Pharmaceutical Care Services for Asthma Patients: A Randomized Control Trial

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Pharmaceutical Care Services for Asthma Patients: A Randomized Control Trial

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Dedication

This thesis is dedicated to my parents who sacrificed a lot for me to be what I am now. And to my husband, who stood by me all through my life and helped me to excel.

Sabrin Elayan

Declaration

I certify that the thesis submitted for the degree of master is the result of my own research, except where otherwise acknowledged, and that this thesis (or any part of the same) has not be submitted for a higher degree to any other university or institution.

Signed: 

Sabrin Othman Hajes Elayan

Date: 8 April 2017

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I owe my loving thanks, appreciation and respect especially to my parents, who encouraged and inspired me all through my educational journey. To my husband, who stood by me all through my life and helped me to excel.

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Abstract

Objectives

The main aim of the study was to investigate the clinical and humanistic impact of pharmaceutical care intervention led by clinical pharmacist in adult patients with asthma.

Methods

This is a prospective randomized control study that was conducted in outpatient clinic at Al Makassed hospital. At baseline the number of patients who participated in the study were 106 and 137 patients in the control and intervention groups, respectively. At 6 months, 101 and 122 patients were in the control and intervention groups, respectively. Finally, at 12 month 90 and 102 patients were in the control and intervention groups, respectively. This study was a 12 month trial during the period from September 2014 to September 2015; the Patients were randomized using computer generated random numbers.

Patients were divided into the intervention group who received pharmaceutical care through asthma education, medication counselling, instructions, asthma care diary, etc., and the control group who were not provided any pharmaceutical care.

Intervention patients received comprehensive medication counselling and asthma education every 3 months, while the control group received the routine medical consultation and dispensing services. The outcome measures were recorded using structured forms at baseline and monitored during a follow-up at 6 and 12 months in both groups. Data were analyzed using SPSS version 22, level of significance was $p<0.05$.

Results

At the end of the study period, the intervention group showed a significant greater improvement in the score for assessing the inhalation technique and the proportion of patients who demonstrated appropriate inhaler technique (score = 7-10) was 31 (30.6%) in control group and

113 (92.6%) in intervention group with a significant p- value = 0.0001 but at 12 month the proportion of patients who demonstrated appropriate inhaler technique was slightly decreased about 88(86.2%) in intervention group and 32(35.5%) in control group, with p-value = 0.021.The knowledge scores improved in the intervention group, whereas there was evidence of deterioration in the control patient group.

In the Asthma Control Test (ACT), the intervention had significantly increased the ACT after 6 months compared with usual care, the proportion of the complete asthma control was 19(15.5%) and 5(4.9%) in intervention and control groups, respectively with p-value = 0.002 but the proportion of the controlled asthma was decreased at the 12 months about 9(8.8%) in intervention group and 7(7.7%) in control group, with non-significant p value = 0.077.

In adherence to medications during the course of the study, patients were classified as adherent, non-adherent or moderate adherence. At baseline the results showed that the patients in the intervention group had the same adherence to medication compared to control group 5(3.64%), 6(5.6%) respectively, with no significant improvement p value = 0.736.

At 6 month, the percentage of adherence to non-adherence medication in intervention group were18(14.7%) and 25(20.4%), compared to control group, about 4(3.9%) were adherent and 46(45.5%) were non-adherent to medications with a p value = 0.0003.

At 12 month the adherence to medication was about 10(9.8%), and non-adherent was about 30(29.4%) in intervention group compared to control group with 3(3.3%) were adherent and 42(46.6%) were non-adherent to medications in control group and the p value was 0.021.

There was no significant difference in continued asthma severity values between both groups about 15(14.1%) in control group and 22(16%) in intervention group, with (p value=0.227). But at 12 month there were a highly significant improvements in continued asthma severity values about 3(2.94%) in intervention group and 10(11.11%) in control groups with p-value=0.001.

At the 12-month follow-up, patients in the intervention group had a significant reduction in both hospital admissions (15 vs. 36) visits with P- value =0.03 and ED visits (29 vs 58) visits with P-value =0.01 and 0.03 respectively. There was no significant difference in GP visits between

control and intervention group (P =0.11). The overall length of hospital stay was significantly lower in the intervention group (49 days) while in control group around (124 days).

Conclusion

The present findings suggest that pharmacist's intervention can have positive impact on asthma-related outcomes in patients, in inhalation technique the intervention group showed a significant greater improvement in the score for assessing the inhalation technique relative to control group.

In the Asthma Control Test (ACT), the intervention had significantly increased the ACT after 6, 12 months compared with usual care in control group, in addition the adherence to medications during the course of the study showed that the patients in the intervention group had more significant adherence to medication compare to control group.

Also in asthma severity values in intervention group are more significant than control group, and the patients in the intervention group had a significant reduction in both hospital admissions days compared to control group.

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Abbreviations

ACT	Asthma Control Test
ACE	Angiotensin-converting-enzyme
AAKQ	Arabic asthma knowledge questionnaire
AAP	Asthma Action Plan
BMI	Body mass index
CFC	Chlorofluorocarbons
DPIs	Dry powder inhalers
DALYs	Disability-adjusted life years
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
FDA	Food and Drug Administration
GINA	Global Initiative for Asthma guidelines
GP	General practitioner
HFAs	Hydrofluoroalkanes
ICSs	Inhaled corticosteroids
LABAs	Long-acting β_2-agonists
MDIs	Pressurized metered-dose inhalers
MOA's	Mechanism of action
MID	. The minimal important difference
PEF	Peak expiratory flow
PFM	Peak Flow Meter
SPSSPC	Social Sciences Personal Computer

Introduction

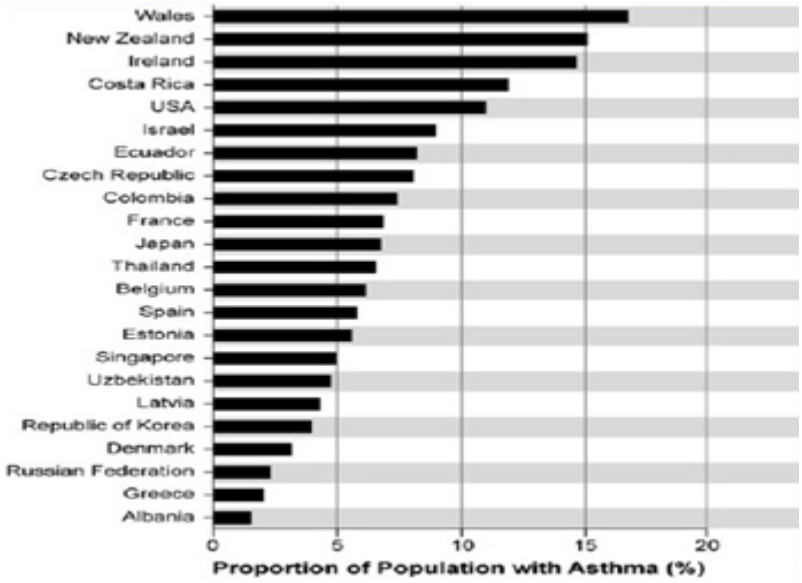
Chapter one

1. Introduction

1.1 Background

Asthma is a common disease that leads to significant degrees of morbidity and mortality. Nowadays, it is estimated that as many as 300 million people of all ages, and all ethnic backgrounds suffer from asthma and the burden of this disease to government, healthcare systems, families, and patients is increasing worldwide. It is estimated that there may be an additional 100 million persons with asthma by 2025 [1]. Nonetheless, based on the application of standardized methods to measure the prevalence of asthma and wheezing illness in children [2] and adults [3], it shows that the global prevalence of asthma ranges from 1% to 18% of the population in different countries. **Figure (1)**.

Figure (1): Prevalence of asthma in different countries



In the Middle East, asthma prevalence is reported to be lower than developed countries (ranges 5–23%) [4-7]. Also in rural Palestinian, the lowest 12 month wheezing prevalence rate was

seen(5.5%) [7]. In neighboring countries like Jordan the prevalence rate for asthma was (4.1%) while wheezing was (8.9%) [5] and the highest prevalence rate was seen in desert population of Saudi Arabia (23%) [8] and in Baghdad (25%) [9].

In other nearby countries such as Turkey the prevalence rate for asthma was seen to be (14.1%) [10],United Arab Emirates (UAE) was (13%) [11], and in Lebanon (12%) [12] .

However, in Israel, whose people share the same (outdoor) environment as Palestine, the 12-months prevalence of wheezing was 17.8%. and Shohat *et al.*[6] indicated that this observed difference in the prevalence of asthma and asthma symptoms between Arabs and Jews might give a clue to the pathogenesis of asthma.

Based on the reported, asthma is the most common chronic disease, this represent a major worldwide public health issue and the basis risk in asthma is acute exacerbations (asthma attacks), this is because a deterioration in symptoms control and objective measures of airflow obstruction [14].

1.2 Definition of asthma:

Asthma is a disorder defined by its clinical, physiological, and pathological characteristics of episodic shortness of breath due to airway obstruction that make expiratory airflow limitation, particularly at night, often accompanied by cough is the most predominant feature of the clinical and physiological history of asthma and the most common physical finding is wheezing auscultation of the chest.

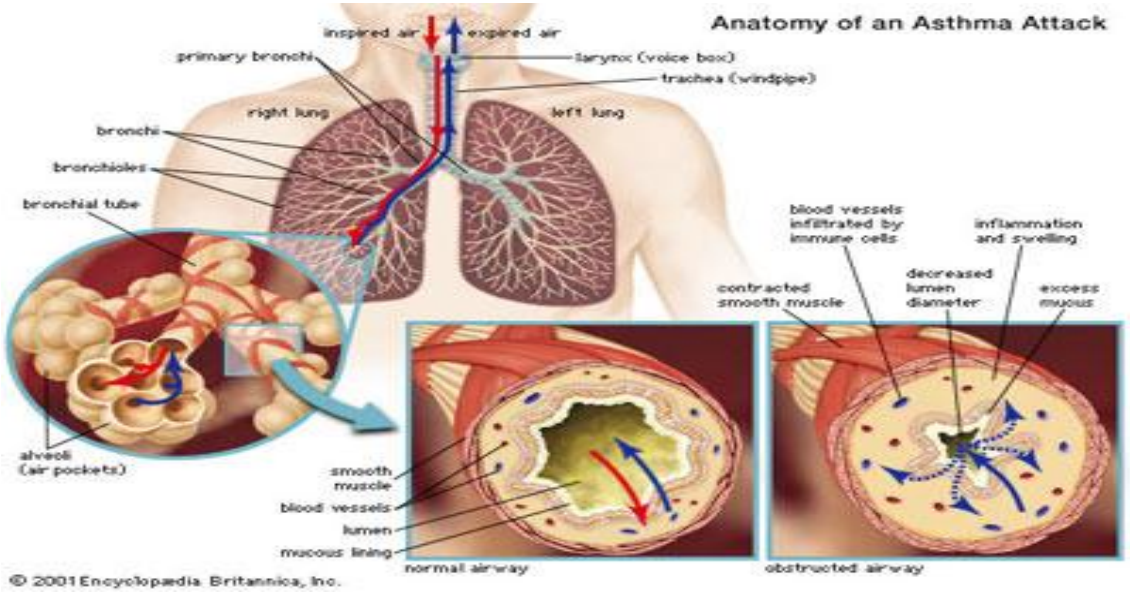
The main dominant pathological feature seen in asthma is airway inflammation, sometimes associated with airway structural changes. People with asthma characterized by inflamed airways. This leads to airways swollen and very sensitive, especially when react strongly to certain substances that are breathed in as shown in **figure (2)**.

This means that when the airways react, the muscles around them tighten, and this leads to the airways to narrow, thus less air flows to the lungs. The swelling may worsen making the airways narrower. Also the cells located in the airways may secret mucus more than normal. This mucus

characterized by sticky, thick liquid that can narrow the airways, so this lead to asthma symptoms and these symptoms can happen each time the airways are irritated [15].

Commitment use the appropriate treatment of asthma surely leads to control the clinical manifestations of asthma symptoms, sleep disturbances, limitations of daily activity, impairment of lung function and this control leads to rare occasional recurrence of symptoms and severe exacerbations [13].

Figure (2): Characteristics of lung in asthma.



1.3 Causes of asthma:

The exact and main cause of asthma is not known, so asthma can't be cured but it can be prevented and controlled. So with a good asthma management, the symptoms become free and the patient will enjoyed in all life and well become active.

There are different factors that influence the risk of asthma and can be divided into those that cause the development of asthma that include host factors (which are primarily genetic) and

those that trigger asthma symptoms that are usually environmental factors; and some do both [16]. However, the mechanisms of how they influence the development and expression of asthma are complex and interactive. For example, to determine asthma susceptibility genes likely interact both with other genes and with environmental factors [17]. In addition, there are other important factors that modify the risk of asthma in genetically susceptible patients such as developmental aspects like the maturation of the immune response and the timing of infectious exposures during the first years of life.

Because the lack of a clear definition for asthma presents there are a significant problem in studying the role of different risk factors in the development of this complex disease, so there are different factors that influence the causes of asthma divided to:

1.3.1 Host factors.

1.3.1.1 Allergen:

Although there are indoor and outdoor allergens and they cause asthma exacerbations, their allergens specific role in the development of asthma is still not fully resolved.

Different studies have shown sensitization to house dust mite allergens, cat dander, dog dander and *Aspergillus* mold are independent risk factors for asthma [26]. However, the relationship between allergen exposure and sensitization in patient is not straightforward. It may depend on the allergen, the dose, the time of exposure, the patient's age or may be related to genetic factors. In addition, the prevalence of sensitization appears with direct exposure to allergens such those derived from house dust mites and cockroaches [2]. However, although some studies suggest that exposure to house dust mite allergens may be a causal factor in the development of asthma [27]; others have questioned this interpretation.

1.3.1.2 Genetics:

Asthma is not a simple disease, it has a heritable component. Based on different studies. More than one gene can lead to asthma [18]. these genes can develop asthma by production specific IgE antibodies, hyper-responsiveness of the airway, release of inflammatory mediators like

cytokines, and determination the ratio between Th1 and Th2 immune responses (as relevant to the hygiene of asthma) [19].

Family studies show that there are a chromosomal regions associated with asthma susceptibility. For example, a tendency to produce an elevated level of total serum IgE is co-inherited with airway hyper-responsiveness, and a gene (or genes) governing airway hyper-responsiveness is located near a major locus that regulates serum IgE levels on chromosome 5q [20]. However, the search for a specific gene (or genes) involved in susceptibility to IgE antibodies or asthma continues [18].

1.3.1.3 Gender:

The differences that we related to sex are not clear. However, the lung size at birth is smaller in males than females but at adulthood it is larger [25].

In addition, males have a risk factor for asthma in children. Prior to the age of 14, the prevalence of asthma is nearly twice as great in boys as in girls [24]. Also the difference in asthma between the sexes narrows when children get older, the prevalence of asthma is greater in women than in men by adulthood.

1.3.1.4 Obesity and Diet:

Obesity plays an important role as a risk factor for asthma. Leptins as a mediators may affect airway function and increase the likelihood of asthma development [23]; diet and breast feeding play an important role in developing asthma as shown in different studies, so the data reveals that infants fed formulas of intact cow's milk or soy protein have a higher incidence of wheezing illnesses in early childhood compared with those fed breast milk [27].

Nevertheless, some data suggesting that certain characteristics of Western diets, such as increased use of processed foods and decreased antioxidant (in the form of fruits and vegetables), increased n-6 polyunsaturated fatty acid (found in margarine and vegetable oil) and decreased n-

3 polyunsaturated fatty acid (found in oily fish) intakes have contributed to the recent increases in asthma [22].

1.3.1.5 Occupational allergens:

Asthma is the most common occupational respiratory disorder in industrialized countries [2]. Farming and agricultural work, painting (including spray painting), cleaning work, and plastic manufacturing are the most common occupations associated with high risk for asthma [27].
The exposure to an agent encountered in the work environment has been associated with over 300 substances that causes asthma [17]. These substances include highly reactive small molecules such as isocyanates, irritants that may alter airway responsiveness, known immunogens such as platinum salts, and complex plant and animal biological products which lead to stimulation in IgE production(**Table 1**). Occupational asthma arises predominantly in adults [18] and about 1 in 10 cases of asthma among adults of working age are estimated to be caused by occupational sensitizers [19].

However, the factors that sensitize some people but not others to develop occupational asthma in response to the same exposures are not well identified. “Irritant induced asthma” (formerly called the reactive airways dysfunctional syndrome) may be due to very high exposure to inhaled irritants even in non-atopic persons. Tobacco smoking may increase the risk of occupational sensitization, but screening individuals for atopy is of limited value in preventing occupational asthma [28]. Elimination or reduction of exposure to occupational sensitizers seems to be the most important method of preventing occupational asthma.

Table (1): Causes of occupational asthma

Agent	Occupations	Agent	Occupations
Animal products: ➢ **Dander.** ➢ **Excereta.** ➢ **Serum.** ➢ **Secretions.**	➢ Animal handlers. ➢ Laboratory workers. ➢ Veterinarians.	Metals: ➢ Platinum. ➢ Nickel. ➢ Cobalt. ➢ Vanadium.	➢ Platinum and Nickel refining workers. ➢ Hard metal worker.
Plants: ➢ **Grain.** ➢ **Flour.** ➢ **Tobacoo.** ➢ **Hops.** ➢ **Dust.**	➢ Grain handlers. ➢ Tea workers. ➢ Bakers. ➢ Natural oil manufacturing workers. ➢ Healthcare workers.	➢ Soldering fluxes	➢ Solderers.
Anhydrides: ➢ **Phthalic anhydrates.** ➢ **Trimelliticanhydrates.**	➢ Epoxy resin and plastics workers.	Wood dust: ➢ Oak. ➢ Mahogany. ➢ California.	➢ Carpenters. ➢ Sawmill workers. ➢ Furniture workers.
Vegetables: ➢ **Gum acacia.** ➢ **Gum tragacanth.**	➢ Printers. ➢ Gum ➢ Manufacturing workers.	Others: ➢ Crab. ➢ Prawn.	➢ Crab and Prawn processors.

1.3.1.6Environmental factors:

There are a relationship between environmental factors that influence the risk of developing asthma and factors that cause asthma symptoms for example, occupational sensitizers that belong to this both categories. In addition, air pollution and some allergens there are some important causes of asthma symptoms such as air pollution and some allergens which have not been clearly linked to the development of asthma.

1.3.1.7 Infections:

There are a numerous number of viruses associated with the inception of the asthmatic phenotype during infancy such viruses are: Respiratory syncytial virus (RSV) and para-influenza virus that produce a different symptoms including bronchiolitis in childhood asthma. Several studies show that about 40% of children who was admitted to the hospital as a result of RSV will continue to wheeze or may have asthma into later childhood [28]. On the other hand, a certain respiratory infections early in life, such as measles and sometimes even RSV, may be protect against the development of asthma [23].

The "hygiene hypothesis" of asthma suggests that when the patients exposure to infections early in life this lead to the development of a child's immune system along a "non-allergic" pathway, leading to a reduced the risk of asthma and other allergic diseases. Although the hygiene hypothesis continues to be investigated, this mechanism may explain observed associations between family size, birth order, day care attendance, and the risk of asthma.

1.3.1.8 Smoking:

Tobacco smoking is associated with accelerated decline of lung function in people with asthma, increases asthma severity, and may decrease the control of likelihoodfor asthma and render patients less responsive to inhaled and systemic glucocorticosteriods[20].
The exposure to tobacco smoke both in prenatally and after birth lead to the harmful effect including a greater risk of developing asthma like symptoms in early childhood [16].

Although distinguishing the independent contributions of prenatal and postnatal maternal smoking is problematic. According to that , there are different studies related to a lung function immediately after birth have shown that maternal smoking during pregnancy has an influence on lung development and found that infants of smoking mothers are 4 times more likely to develop wheezing illnesses in the first year of life [17].

1.4 Diagnosis of asthma:

Asthma is a very common condition all over the world with a high level of awareness and it is the most common cause of chronic respiratory symptoms in young adult.
The key diagnostic indicators are a history of cough, wheeze, shortness of breath and airway obstruction; either spontaneously over time or in response to treatment.
Asthma symptoms may be intermittent and their significance may be overlooked by patients and physicians, or because they are non-specific, they may result in misdiagnosis.

1.4.1 Symptoms of asthma:

A clinical diagnosis of asthma is often prompted by symptoms such as episodic breathlessness, wheezing, cough, and chest tightness. There are different diagnostic guides that play an important role in diagnosis of asthma such as episodic symptoms after an incidental allergen exposure, seasonal variability of symptoms and a positive family history of asthma and atopic disease. Asthma associated with rhinitis may occur intermittently, with the patient being entirely asymptomatic between seasons or it may involve seasonal worsening of asthma symptoms or a background of persistent asthma. Because of these different symptoms the asthma diagnosis are variability; and appropriate asthma therapy is needed [28].

1.4.2Exercise induced asthma:

Physical activity play an important is an important cause of asthma symptoms in most asthma patients, and for some it is the only cause.
Exercise induced bronchoconstriction typically develops for example when running as main potent triggers within 5-10 minutes after completing exercise. The asthma symptoms and troublesome cough will resolve spontaneously within 30-45 minutes [17]. The more common condition that led to the Exercise induced bronchoconstriction when the patient is breathing dry, cold air and less common in hot, humid climates [18].

1.4.3 Cough variant asthma:

Patients with cough variant asthma have chronic cough. It is common in children, and it worsen at night; but during the day becomesnormal. So these patients have a variability in lung function or of airway hyper-responsiveness, and possibly a search for sputum eosinophils, are particularly important [23]. So patients with Cough variant asthma must be distinguished from called eosinophilic bronchitis in which patients have cough and sputum eosinophils but normal indices of lung function when assessed by spirometry and airway hyper-responsiveness [13].
There are different things considered as cough induced such angiotensin converting enzyme (ACE) inhibitors, gastroesophageal reflux, postnasal drip, chronic sinusitis and vocal cord dysfunction [16].

1.5 Tests for diagnosis and monitoring of asthma:

1.5.1 Measures of lung function:

The diagnosis of asthma is mainly depends on the presence of characteristic symptoms. However, measurements of lung function, and particularly the demonstration of reversibility of lung function abnormalities, greatly enhance diagnostic confidence. This is because patients with asthma frequently have poor recognition of their symptoms and poor perception of symptom severity, especially if their asthma is long-standing [2]. Assessment of symptoms such as dyspnea and wheezing by physicians may also be inaccurate [27].

There are various methods that are available to assess airflow limitation. For example; spirometry, particularly the measurement of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), and peak expiratory flow (PEF) measurement.
These Predicted values of FEV1, FVC, and PEF based on age, sex, and height have been obtained from population studies and being continually revised.

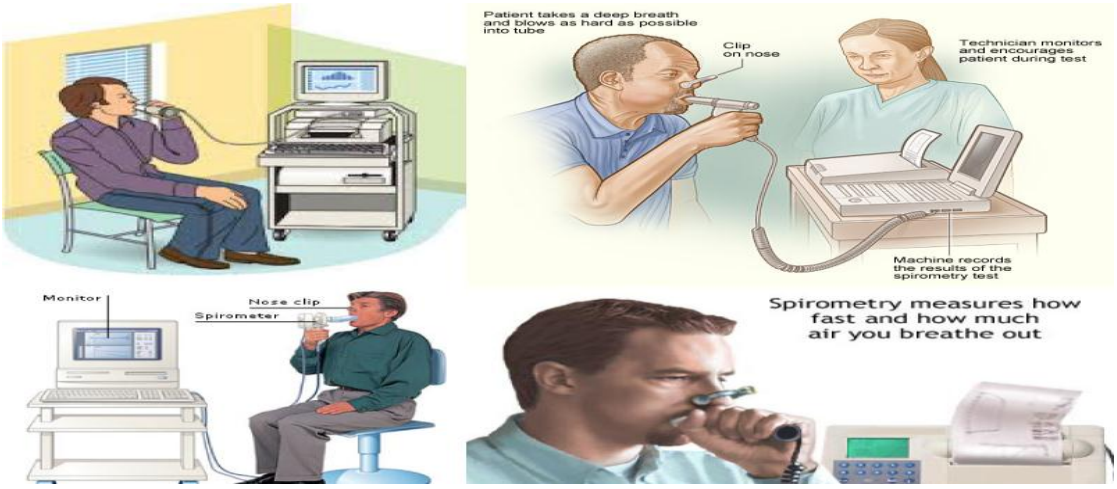
1.5.2Spirometer:

It is the usual recommended method of measuring airflow limitation and reversibility to establish a diagnosis of asthma. Measurements of FEV1 and FVC are undertaken during a forced expiratory using a spirometer as shown in **figure (3)**.

Recommendations for the standardization of spirometry have been published [22]. The degree of reversibility in FEV1 which indicates a diagnosis of asthma is generally accepted as ≥12% (or ≥200 ml) from the pre-bronchodilator value 13. However most asthma patients will not exhibit reversibility at each assessment, particularly those on treatment, and the test therefore lacks sensitivity.

Spirometry is reproducible, and effort dependent, thus proper instructions on how to perform the forced expiratory maneuver must be given to patients, and the highest value of three recordings taken. Repeated testing at different visits is advised and because the differences in spirometric values have been demonstrated, appropriate predictive equations for FEV1 and FVC should be established for each patient. The normal range of values is wider and predicted values are less reliable in young people (< age 20) and in the elderly (> age 70). Because many lung diseases may result in reduced FEV1, a useful assessment of airflow limitation is the ratio of FEV1 to FVC. The FEV1/FVC ratio is normally greater than 0.75 to 0.80, and possibly greater than 0.90 in children. Any values less than these suggest airflow limitation.

Figure (3): Spirometry measurement



1.5.3 Peak expiratory flow (PEF):

Peak flow meter measurements aid in diagnosis and monitoring of asthma. A modern PEF meters can be used at home settings for day-to-day objective measurement of airflow limitation. Therefore they are relatively inexpensive, portable, plastic and ideal. However, measurements of PEF are not interchangeable with other measurements of lung function such as FEV1 in either adults or children [28].

PEF can underestimate the degree of airflow limitation, particularly as airflow limitation and gas trapping worsen. Because values for PEF obtained with different peak flow meters vary and the range of predicted values is too wide, PEF measurements should preferably be compared to the patient's own previous best measurements using his/her own peak flow meter [23]. The previous best measurement is usually obtained when the patient is asymptomatic or on full treatment and serves as a reference value for monitoring the effects of changes in treatment, the previous best measurement is usually obtained.

Careful instruction is required to reliably measure PEF because PEF measurements are effort-dependent. Most commonly, PEF is measured first thing in the morning before treatment is taken, when values are often close to their lowest,and last thing at night when values are usually

higher. One method of describing diurnal PEF variability is as the amplitude (the difference between the maximum and the minimum value for the day), expressed as a percentage of the mean daily PEF value, and averaged over 1-2 weeks. Another method of describing PEF variability is the minimum morning pre-bronchodilator PEF over 1 week, expressed as a percent of the recent best (Min%) [15]. This latter method has been suggested to be the best PEF index of airway labiality for clinical practice because it requires only a once-daily reading, correlates better than any other index with airway hyper-responsiveness, and involves a simple calculation.

1.6 Classification of asthma:

Many attempts have been made to classify asthma according to etiology, particularly with regards to environmental sensitizing agents. And despite, such a classification is limited by the existence of patients in whom no environmental cause can be identified. Still an effort to identify an environmental cause for asthma (for example, occupational asthma) should be part of the initial assessment to enable us to adapt avoidance strategies in asthma management. Describing patients as having allergic asthma is usually of little benefit, since single specific causative agents are seldom identified.

1.6.1 Asthma severity:

A four categories of asthma were subdivided by the previous GINA documents by severity based on the level of symptoms, airflow limitation, and lung function variability: Intermittent, Mild persistent, moderate persistent, or severe persistent [29] (**Table 2**). Classification of asthma by severity is useful when decisions are being made about management at the initial assessment of a patient. It is important to recognize, however, that asthma severity involves both the severity of the underlying disease and its responsiveness to treatment [16]. Thus, asthma can present with severe symptoms and airflow obstruction and be classified as Severe Persistent on initial presentation, but respond fully to treatment and then be classified as Moderate Persistent asthma. In addition, asthma may change over months or years as its severity is not an unvarying feature of an individual.

Table (2): GINA classification of asthma severity

	Symptoms/day	Symptoms/night	PEF or FEV1	PEF variability
Step 1 Intermittent	▪ <1 time a week. ▪ Asymptomatic and normal PEF between attack.	<or = 2 times a month.	> or =80%	< 20%
Step 2 Mild persistent	▪ >1 time a week but <1 time a day. ▪ Attack may affect activity.	> 2 times a month.	> or =80%	20-30%
Step 3 Moderate persistent	▪ Daily. ▪ Attack affectsactivity.	> 1 time a week.	60-80%	> 30%
Step 4 Severe persistent	▪ Continuous. ▪ Limited physical activity.	Frequent.	< or = 60%	> 30%

PEF: Peak expiratory flow, FEV1: Forced expiratory volume in the first second.

1.6.2Asthma Control:

There is evidence that reducing inflammation with controller therapy achieves clinical control, but because of the cost and/or general unavailability of tests such as endobronchial biopsy and measurement of sputum eosinophils and exhaled nitric oxide [17], it is recommended that treatment be aimed at controlling the clinical features of disease, including lung function abnormalities. (**Table 3)** provides the characteristics of controlled, partly controlled and uncontrolled asthma. Complete control of asthma is commonly achieved with treatment, the aim of which should be to achieve and maintain control for prolonged periods with due regard to the safety of treatment, potential for adverse effects, and the cost of treatment required to achieve this goal [18].

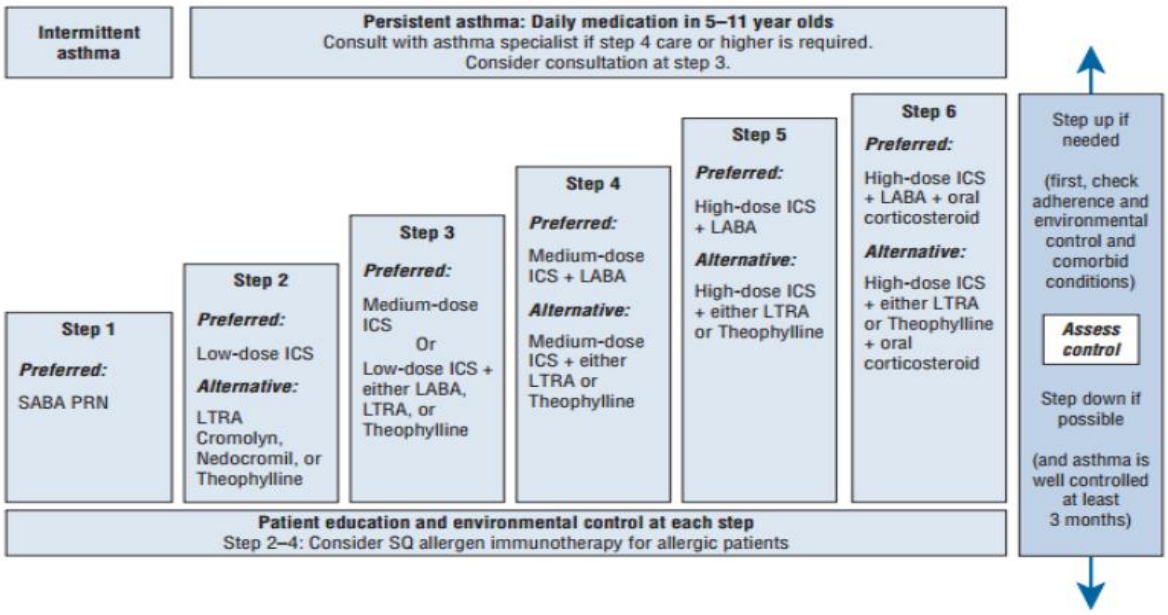
Table (3): Characteristics of controlled, partly controlled and uncontrolled asthma.

Characteristic	Controlled	Partly controlled	Uncontrolled
Daytime symptoms	None (twice /less a week)	More than twice a week	3 or more features of partly controlled asthma
Limitation of activities	None	Any	
Nocturnal symptom	None	Any	
Need for relieve/rescue treatment	None (twice /less a week)	More than twice a week	
Lung function(FEV or PEF)	Normal	<80%predicted or personal best(if known)	

1.7 Asthma medications(controllers and relievers):

The effectiveness of drug therapy in asthma has been established for many years, it remains the mainstay of asthma management, and almost all adults of asthma will benefit from some form of drug therapy. So the goal of asthma treatment is to achieve and maintain clinical control in order to improve quality of life for the patients. Medications as seen in **figure (4)** to treat asthma can be classified as controllers or relievers.

Figure (4): Asthma step up treatment chart (GINA)



Controllers are medications taken daily on a long-term basis so they are the opposite of as needed of PRN medication to keep asthma under clinical control mainly through their anti-inflammatory effects. They include inhaled and systemic (including oral and intravenously medication) glucocorticosteroids, leukotriene modifiers, long acting inhaled β_2-agonists in combination with inhaled glucocorticosteroids, sustained release theophylline, cromones, anti-IgE, and other systemic steroid sparing therapies. Inhaled glucocorticosteroids are the most effective controller medications currently available for treatment of persistent asthma.

Relievers are medications used on an as needed basis that act quickly to reverse bronchospasm during acute exacerbation and relieve its acute symptoms. They include short acting inhaled β_2-agonists (SABA), inhaled anticholinergics, short acting theophylline, and short acting oral β_2-agonists.

Asthma treatment for adults can be administered in different ways inhaled, orally or parenterally (by subcutaneous, intramuscular, or intravenous injection), usually inhaled therapy is the most common way for asthma treatment. The major advantage of inhaled therapy is that drugs are

delivered directly into the airways, producing higher local concentrations into the lungs with significantly less risk of systemic side effects especially for glucocorticoids treatment.
Inhaled medications for asthma are found for different types as pressurized metered-dose inhalers (MDIs), breath actuated MDIs, dry powder inhalers (DPIs), soft mist inhalers, and nebulized or Wet aerosols. Inhaler devices differ in their efficiency of drug delivery to the lower respiratory tract, many factors interfere in their efficacy including; form of the device, formulation of medication, particle size, velocity of the aerosol cloud or plume (where applicable), and ease with which the device can be used by the majority of patients. Individual patient preference, convenience, and ease of use may influence not only the efficiency of drug delivery but also important for patient adherence and compliance to treatment and long-term control.

Pressurized MDIs (pMDIs) require training and skill to coordinate activation of the inhaler and inhalation, take cap off, breath out, hold 1-2 inch away from your mouth or on your mouth between your lips, start breathing, then press bottom, breath slowly and deeply, hold your breath for 10 seconds then breath out slowly.

Medications in these devices can be dispensed as a suspension in chlorofluorocarbons (CFCs) or as a solution in hydrofluoroalkanes (HFAs). For a pMDI containing CFCs, the use of a spacer (holding chamber) improves drug delivery, increases lung deposition, and may reduce local and systemic side effects, spacer reduce deposition of particles in oropharynx this reduce absorption from gastrointestinal tract which thing reduce system bioavailability thus reduce systemic side effect [30]. However, CFC inhaler devices are being phased out due to the impact of CFCs upon the atmospheric ozone layer, and are being replaced by HFA devices. For pMDIs containing bronchodilators, the switch from CFC to HFA inhalers does not result in a change in efficacy at the same nominal dose [31].

However, for some glucocorticosteroids, the HFA formulations provide an aerosol of smaller particle size that results in less oral deposition (with associated reduction in oral side effects), and correspondingly greater lung deposition which is an advantage over CFC.

This may result in greater systemic efficacy at equivalent ex-actuator doses, but also greater systemic exposure and risk of side effects [32, 33].
Pressurized MDIs may be used by patients with asthma of any severity, including during exacerbations. Breath actuated aerosols may be helpful for patients who have difficulty using the "press and breathe" pressurized MDI [2].

Soft mist inhalers appear to require less coordination. Dry powder inhalers are generally easier to use, but they require a minimal inspiratory flow rate and may prove difficult for some patients. DPIs differ with respect to the fraction of ex-actuator dose delivered to the lung. For some drugs, the dose may need to be adjusted when switching from an MDI to a DPI they are not exchangeable [27]. Nebulized aerosols are rarely indicated for the treatment of chronic asthma in adults [34].

1.7.1 Controller medications:

1.7.1.1 Long acting inhaled β_2-agonists (LABA):

Long-acting inhaled β_2-agonists, including formoterol and salmeterol, should not be used as monotherapy in asthma as these medications do not appear to influence the airway inflammation in asthma usually there are combined with glucocorticosteroids.

They are most effective when combined with inhaled glucocorticosteroids[49], and this combination therapy is the preferred treatment when a medium dose of inhaled glucocorticosteroid alone fails to achieve control of asthma in moderate severe asthma. Addition of long-acting inhaled β_2-agonists to a daily regimen of inhaled glucocorticosteroids improves symptom scores, decreases nocturnal asthma, improves lung function, decreases the use of rapid-acting inhaled β_2-agonists [50], reduces the number of exacerbations [50], and achieves clinical control of asthma in more patients, more rapidly, and at a lower dose of inhaled glucocorticosteroids than inhaled glucocorticosteroids given alone, thus reduce risk of asthma exacerbation [51].

This greater efficacy of combination treatment has led to the development of fixed combination inhalers that deliver both glucocorticosteroid and long acting β_2-agonist simultaneously (fluticasone propionate plus salmeterol, budesonide plus formoterol). Controlled studies have shown that delivering this therapy in a combination inhaler is as effective as giving each drug separately [27]. Fixed combination inhalers are more convenient for patients, may increase compliance [52], and ensure that the long acting β_2-agonist is always accompanied by a glucocorticosteroid. In addition, combination inhalers containing formoterol and budesonide may be used for both rescue and maintenance because formoterol has a rapid onset of action almost similar to albetrol, because it is full agonist as albetrol.

Both components of budesonide formoterol given as needed contribute to enhanced protection from severe exacerbations in patients receiving combination therapy for maintenance and provide improvements in asthma control at relatively low doses of treatment because formoterol rapid effect [53].

Long acting β_2-agonists as formoterol may also be used to prevent exercise induced bronchospasm, and for this purpose may provide longer protection than rapid acting inhaled β_2-agonists [54]. Salmeterol and formoterol provide a similar duration of bronchodilation (about 12h the duration of action of asthma) and protection against bronchoconstrictors, but there are pharmacological differences between them. Formoterol has a more rapid onset its onset of action within 3 minutes, however salmeterol its onset of action 30-48 minutes [55], which may make formoterol suitable for symptom relief as well as symptom prevention[56].

The possible side effects when taking long acting inhaled β_2-agonists is fewer systemic adverse effects, because they have local effect, however the systemic effect that may occur. Such as cardiovascular stimulation that may increase the risk of arrhythmia and electrocardiogram changes. Skeletal muscle tremor, and hypokalemia, this effect is usually transient than oral therapy. The regular use of rapid acting β_2-agonists in both short and long acting forms may lead to relative refractoriness to β_2-agonists [57]. Data indicating a possible increased risk of asthma related death associated with the use of salmeterol in a small group of individuals [58] led to advisories from the US Food and Drug Administration (FDA) and Health Canada that long

acting β2 agonists are not a substitute for inhaled or oral glucocorticosteroids, and should only be used in combination with an appropriate dose of inhaled glucocorticosteroid as determined by a physician. A study has identified that the asthma of subjects with an unusual genotype for the beta-adrenergic receptor (with substitution of arginine for glycine at position B16) may deteriorate with regular use of salmeterol whether or not administered with inhaled glucocorticosteroids, also formoterol alone many increase risk of asthma exacerbation and these increase mortality [21].

1.7.1.2Theophylline:

Theophylline is a bronchodilator and, when given in a lower dose, has modest anti-inflammatory properties [59]. It is available in sustained release formulations that are suitable for once or twice daily dosing. Data on the relative efficacy of theophylline as a long term controller is lacking. However, available evidence suggests that sustained release theophylline has little effect as a first line controller [60]. It may provide benefit as add on therapy in patients who do not achieve control on inhaled glucocorticosteroids alone [19].

Additionally in such patients the withdrawal of sustained release theophylline has been associated with deterioration of control [61]. As add on therapy, theophylline is less effective than long acting inhaled β_2-agonists, theophylline usually preferred in patients with respiratory center depression, or in respiratory muscle weakness, sleep apnea, hyper-apnea[62].

The most common side effects of theophylline are gastrointestinal symptoms, loose stools, cardiac arrhythmias, seizures, and even death. Nausea and vomiting are the most common early events.

1.7.1.3 Inhaled glucocorticosteroids (ICS):

Inhaled glucocorticosteroids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma, glucocorticosteroids considered as corn stone for controlling asthma. Studies have demonstrated their efficacy in reducing asthma symptoms, improving quality of life, reducing morbidity and improving lung function [35], decreasing airway hyper-responsiveness, controlling airway inflammation, reducing frequency and severity of

exacerbations, and reducing asthma mortality [36]. However, they do not cure asthma they control it, and when they are discontinued deterioration of clinical control follows within weeks to months in a proportion of patients thus considered as long term treatments [37].

Inhaled glucocorticosteroids differ in potency and bioavailability, but because of relatively flat dose-response relationships or estimated equipoint daily doses. In asthma relatively few studies have been able to confirm the clinical relevance of these differences.

The efficacy of some products varies when administered via different inhaler devices [38]. Most of the benefit from inhaled glucocorticosteroids is achieved in adults at relatively low doses, in order to achieve best treatment equivalent to 400 mg of budesonide per day, anti-inflammatory effect including reduce number of mast cells and eosinophils, increase number of receptors which increase effectiveness, improve receptor response, reduce mucus secretion and the hypersensitivity, reduces airway edema[27].

Increasing to higher doses provides little further benefit in terms of asthma control but increases the risk of side effects [39]. However, there is marked individual variability of responsiveness to inhaled glucocorticosteroids and because of this and the recognized poor adherence to treatment with inhaled glucocorticosteroids, many patients will require higher doses to achieve full therapeutic benefit result in more adverse effect. As tobacco smoking reduces the responsiveness to inhaled glucocorticosteroids, higher doses may be required in patients who smoke, smoking usually will exacerbate asthma.

The possible local side effects when takinginhaled glucocorticosteroids include oropharyngeal candidiasis which may occur in many patients, dysphonia, and occasionally coughing from upper airway irritation. For pressurized MDIs the prevalence of these effects may be reduced by using certain spacer devices [30].

Mouth washing (rinsing with water, gargling, and spitting out) after inhalation, is the best method which may reduce oral candidiasis. The use of prodrugs that are activated in the lungs but not in the pharynx (e.g. ciclesonide and beclometasone)[40], and new formulations and

devices that reduce oropharyngeal deposition, may minimize such effects without the need for a spacer that retain the large particles or mouth washing.

1.7.1.4 Leukotriene modifiers:

Leukotriene modifiers include cysteinylleukotriene 1 (CysLT1) receptor antagonists (montelukast, pranlukast, and zafirlukast) and a 5-lipoxygenase inhibitor (zileuton). Clinical studies have demonstrated that leukotriene modifiers have a small and variable bronchodilator effect, so they are not the first choice in asthma treatment reduce symptoms including cough [40], improve lung function, and reduce airway inflammation and asthma exacerbations [22].

They may be used as an alternative treatment for adult patients with mild persistent asthma [28], and some patients with aspirin sensitive asthma respond well to leukotriene modifiers also in smokers sometimes are much effective [41]. However, when used alone as controller, the effect of leukotriene modifiers are generally less than that of low doses of inhaled glucocorticosteroids, and, in patients already on inhaled glucocorticosteroids, leukotriene modifiers cannot substitute for this treatment without risking the loss of asthma control [42].

Leukotriene modifiers used as add on therapy may reduce the dose of inhaled glucocorticosteroids required by patients with moderate to severe asthma this is advanced stages they can't be used alone or controller drugs [43], and may improve asthma control in patients whose asthma is not controlled with low or high doses of inhaled glucocorticosteroids[44]. With the exception of one study that demonstrated equivalence in preventing exacerbations [45], several studies have demonstrated that leukotriene modifiers are less effective than long-acting inhaled β2 agonists as add on therapy or as a combination with glucocorticoids [46, 47].

Leukotriene modifiers are well tolerated, and few if any class related effects have so far been recognized. Zileuton has been associated with liver toxicity as a side effect, so monitoring of liver function tests is recommended during treatment with this medication specially monitor serum ALT (prior to initiation, once monthly for the first three month, then every 2-3 months for the first year). The apparent association of leukotriene modifiers with Churg Strauss syndrome (Eosinophilic granulomatosis with polyangititis) is probably largely the result of reductions in

the doses of systemic and or inhaled glucocorticosteroids unmasking the underlying disease, but a causal association in some patients cannot be entirely excluded [48].

1.7.1.5 Cromones: sodium cromoglycate and nedocromil sodium:

The role of sodium cromoglycate and nedocromil sodium in long term treatment of asthma in adults is limited. Efficacy has been reported in patients with mild persistent asthma and exercise induced bronchospasm. Their anti-inflammatory effect is weak and they are less effective than a low dose of inhaled glucocorticosteroid[18].

The side effects are uncommon and include coughing upon inhalation and sore throat. Some patients find the taste of nedocromil sodium unpleasant.

1.7.1.6 Long acting oral β_2-agonists:

Long acting oral β_2-agonists include slow release formulations of salbutamol, terbutaline, and bambuterol, a prodrug that is converted to terbutaline in the body. They are used only on rare occasions when additional bronchodilation is needed.

The possible side effects when taking long acting oral β_2-agonists is higher than that of inhaled β_2-agonists, and includes cardiovascular stimulation (tachycardia), anxiety, and skeletal muscle tremor hypokalemia through intracellular shunting. Regular use of long-acting oralβ_2-agonists as monotherapy is likely to be harmful and these medications must always be given in combination with inhaled glucocorticosteroids.

1.7.1.7 Anti IgE (Omalizumab):

AntiIgE (omalizumab) that prevents binding of IgE to mast cell is a treatment option limited to patients with elevated serum levels of IgE, given as subcutaneous every 2-4 weeks for 6 months. The dose and frequency based on body weight and pre-treatment of total IgE serum level, the dose should not be adjusted based on IgE level taking during treatment or less than one year following interruption of therapy.

Its current indication is for patients with severe allergic asthma who are uncontrolled on inhaled glucocorticosteroids, although the dose of concurrent treatment has varied in different studies. Improved asthma control is reflected by fewer symptoms, less need for reliever medications, and fewer exacerbations [63].

Further investigations will likely provide additional clarification of the role of anti IgE in other clinical settings. The main side effect is anaphylaxis that usually occurs within the first or second dose and with onset of ≤60 minutes up to four days, if anaphylaxis reaction does occur then the treatment needs to be discontinued.

1.7.2Reliever medications:

Reliever medications act quickly to relieve bronchoconstriction and its accompanying acute symptoms.

1.7.2.1 Short acting inhaled β2 agonists(SABA):

Short acting inhaledβ_2-agonists are the medications of choice for relief of bronchospasm during acute exacerbations of asthma and as prophylaxis for the pre-treatment of exercise-induced bronchoconstriction. They include salbutamol, terbutaline, fenoterol, reproterol, and pirbuterol.
Formoterol, a long acting β_2-agonist, is approved for symptom relief because of its rapid onset of action, but it should only be used for this purpose in patients on regular controller therapy with inhaled glucocorticosteroids, because alone will increase risk of asthma exacerbation.

Short acting inhaled β_2-agonists should be used only on an as-needed basis at the lowest dose and frequency required. Increased use, as a reliever especially daily use, is a warning of deterioration of asthma control and indicates the need to reassess treatment either by increasing doses or adding another combination, Similarly, failure to achieve a quick and sustained response to β_2-agonist treatment during an exacerbation mandates medical attention, and may indicate the need for short term treatment with oral glucocorticosteroids .
Uses of oral β_2-agonists given in standard doses are associated with more adverse systemic effects such as tremor and tachycardia than occur with inhaled preparations that have less side effects.

1.7.2.2 Anti -cholinergics:

Anticholinergic bronchodilators used in asthma include ipratropium bromide and oxitropiumbromide, they are on M2, M3 receptors with long duration of action six to eight hours. Inhaled ipratropium bromide is a less effective reliever medication in asthma than rapid acting inhaled β_{2}- agonists. The benefits of ipratropium bromide in the long term management of asthma have not been established, although it is recognized as an alternative bronchodilator for patients who experience such adverse effects as tachycardia, arrhythmia, and tremor from short acting B2 agonists usually anticholinergics are preferred in patients with COPD.
Inhalation of ipratropium or oxitropium can cause a dryness of the mouth and a bitter taste. There is no evidence for any adverse effects on mucus secretion [65].

1.7.2.3Systemic glucocorticosteroids:

Systemic glucocorticosteroidscan be administered including oral or IV. However oral glucocorticosteroids are usually as effective as those administrated intravenously and are preferred because this route of delivery is less invasive and less expensive unless vomiting occur re-administrated intravenously. Although systemic glucocorticosteroids are not usually thought of as reliever medications, they are important in the treatment of severe acute exacerbations because they prevent progression of the asthma exacerbation, reduce the need for referral to emergency departments and hospitalization, prevent early relapse after emergency treatment, and reduce the morbidity of the illness. The main effects of systemic glucocorticosteroids in acute asthma are only evident after four to six hours. Oral therapy is preferred and is as effective as intravenous hydrocortisone[16].

A typical short course of oral glucocorticosterods for an exacerbation is 40-50 mg[64]prednisolone given daily for five to ten days depending on the severity of the exacerbation. When symptoms have subsided and lung function has approached the patient's personal best value, the oral glucocorticosteroids can be stopped or tapered, provided that treatment with inhaled glucocorticosteroids continues thus when patients discharge, after asthma exacerbation should take systemic (oral) glucocorticoids in order to reduce risk of relapse.

Intramuscular injection of glucocorticosteroids has no advantage over a short course of oral glucocorticosteroids in preventing relapse[16].
Adverse effects of shortterm highdose systemic therapy are uncommon but include reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, rounding of the face, mood alteration, hypertension, peptic ulcer.

1.7.2.4 Theophylline:

Short acting theophylline may be considered for relief of asthma symptoms, they are not prepared in sustained release formula in order to give fast onset of action [13]. The role of theophylline in treating exacerbations remains controversial. Short acting theophylline may provide no additive bronchodilator effect over adequate doses of rapid acting β_2-agonists.

1.7.2.5 Short acting oral β_2-agonists*:*

Short acting oral β_2-agonists are appropriate for use in a few patients who are unable to use inhaled medications. This is due to a higher prevalence of adverse effects.

Despite the availability of highly effective medication it remains a poorly controlled disease. Reasons for this poor control include non-implementation and inherent limitations of the asthma management guidelines, poor compliance with asthma therapy, incorrect use of inhaler devices and insufficient treatment of peripheral airway inflammation[66].

In conclusion; medications for treatment of asthma are used to treat, prevent and control asthma symptoms, to reduce the number and severity of asthma episodes and to improve airflow. Asthma treatment includes the use of bronchodilators, mainly β_2-adrenergic agonists, muscarinic receptor antagonists and corticosteroids or leukotriene antagonists as anti-inflammatory agents. These active drugs are administered either separately or given as a fixed dose combination medication into a single inhaler[67].

Inhaled therapy, still the cornerstone of asthma management, this is because its therapeutic agents are delivered directly to the lungs, the inhaled route offers a more rapid onset of action, allows smaller doses to be used and has a better efficacy to safety ratio compared to systemic

therapy. Long-acting β_2-agonists (LABAs) and inhaled corticosteroids (ICS) have become the pharmacological mainstay of management programs, treating the symptoms of disease and the underlying inflammatory processes, respectively[68].Inhaled corticosteroids are delivered through a variety of devices including metered dose inhalers (MDIs), dry powder inhalers (DPIs), or nebulizer[69].Some of the commonly available devices are summarized in **Table (4).**

Table(4): Common inhaled devices

Type	Device	Advantages	Disadvantages
Aerosols	• Metered dose inhaler with or without integral spacer.	Inexpensive	• Difficult for patients to coordinate actuation and inspiration. • Inefficient drug delivery as a result of poor technique. • Some still contain CFCS.* • Local side effects because of drug deposition in the mouth.
	• Breath actuated metered dose inhaler. • Small volume spacer available for some devices.	• No requirement for coordination. • Portable. • Simple to use with minimal effort.	• Click on actuation may be off-putting. • Some devices may be expensive.

Dry powder	• Turbohaler. • Clickhaler. • Accuhaler.	• Simple to use with minimal inspiratory effort. • Indicator of number of doses remaining. • Portable. • Robust devices.	• Devices may be expensive. • Not refillable.
	• Diskhaler. • Spinhaler. • Rotahaler. • Aerochamber.		• Difficult for some patients to load or prime. • Requirement to protect the capsules against extremes of temperatures and humidity.
Nebuliser	• Compressor	• Simple to use. • Deliver high doses.	• Over reliance may be a problem. • Inefficient drug delivery. • Steroids require a mouthpiece rather than a mask. • Expensive.

1.8 Pharmaceutical care

Pharmaceutical care was originated from a term, defined in 1975 by Mikeal *et al*[31] as a subset of medical care. After that, the concept developed, according to the environment of the changing community and its demands on the pharmacy. Pharmaceutical care includes the drug needs for a given patient, which involves providing the services needed for safe and effective therapy and the required drugs [2,27]. The role of the pharmacist which was traditionally restricted to the

preparation, dispensing and selling of medicines expanded by this form of practice to enjoin the pharmacist, in addition to dispensing of medicines, and achieving specific therapeutic outcomes, also he assume the responsible of improving the quality of patients outcomes [19].

Since then, pharmacists have worked to develop pharmaceutical care practices. There are several published literature that show many examples of these practices, suggesting that the participation of a pharmacist in the evaluation of patients drug therapy regimen improves outcomes [70, 71] Although, pharmaceutical care which involves the detection, prevention, and solution of drug-related problems has proved beneficial in diseases such as asthma and cancer [72, 73], also it can provide beneficial with all kinds of diseases on any type of drug therapy, thereby; meeting the drug related needs of individuals and communities [19]. This is because most patients are prescribed multiple drug regimens, there are some studies shows multiple drug regimens such as study done by Perkin *et al*. that show the complex of drug regimens are usually associated with noncompliance especially after discharge from hospital [74]. Also the study that done Strand *et al*. revealed that pharmacists may resolve this problem by encouraging patients compliance and consequently improving treatment outcomes by engaging the patient in pharmaceutical care activities such as monitoring, counseling, resolving drug related problems [75].

The main objectives of pharmaceutical care is to solve medication problems and it also helps to achieve positive clinical outcomes and optimize the health related quality of life of the patient within realistic expenditure [76]. Medication errors increase the cost of health care; account for higher utilization of hospitals, nursing homes, and physician visits; and health risks for patients [77, 78]. So using the pharmaceutical care and working closely with patients and other healthcare professionals in designing, implementing, and monitoring a therapeutic plan to produce specific outcomes [79, 80].

The pharmacist knowledge and skills are very important to teach patients to self-manage asthma. These abilities include how to identify if a patient's asthma is controlled or uncontrolled, identify drug or non-drug-related issues that may be hindering a patient's asthma control, identify patients without an emergency action plan, and facilitate a plan with the patient and the physician to help improve the patient's asthma control. If pharmacists shift their focus from delivering information about drug therapy to integrating drug and device information into a program

focusing on achieving asthma control then pharmacists and patients would be approaching asthma management from similar perspectives [81].

A study by Knoell et al [82], suggested that when pharmacists became involved in asthma care, improvements in symptom control and patient satisfaction were noted. In the study, patients had a consultation that lasted up to 60 minutes with a pharmacist had an individualized self-management plan introduced and had at least one follow up visit. Other studies have also shown that patients report an increased level of satisfaction with a service which includes a pharmacist and that increased patient education, coupled with a comprehensive asthma health management program, that improves both the process of care and the treatment outcomes [83-86].

The role of pharmacist in patient's educating is to provide information about asthma medications and demonstrate how to use inhaled medications and peak flow meters. They can help patients understand their asthma management plan. In addition, Pharmacists have become more and more active in patient care over the past years and can demonstrate a positive impact on the outcomes of drug therapy in asthma patients [87,88].

The aim of pharmaceutical care is to optimize drug therapy, minimize drug related problems, and improve self-management and quality of life of patients. The pharmacist is part of the health care team, and extensive communication between pharmacist, physician, and patient is necessary to achieve defined health outcomes.[89,90]. Since then, pharmacists have worked to develop pharmaceutical care practices. The participation of a pharmacist in the evaluation of patients drug therapy regimen improves outcomes, and many examples of these practices show such thing in published literature [70, 71, 91].

In conclusion, to achieve the clinical, economic, and humane outcomes, pharmacists need to apply the philosophy of pharmaceutical care by working closely with patients and other healthcare professionals in designing, implementing, and monitoring a therapeutic plan to produce specific outcomes [79, 92]. The differences between traditional dispensing and pharmaceutical care are list in **table (5).**

Table (5): The Differences between traditional dispensing and pharmaceutical care

Traditional drug dispensing	***Pharmaceutical care***
Focus on dispensing the medicine	Focus on patient's management and outcomes with the drug treatment.
Patient's education and counseling	In addition with technical advice, the concentrate on technical advice pharmacist is training the patient to practice in everyday life.
No monitoring of the outcomes of the drug treatment	The pharmacist is finding methods to drug treatment monitor the outcomes of the drug treatment.
Drug related problems will emerge if the patient tells about them.	The pharmacist is actively and systematically identifying possible problems in drug treatment.
No responsibility for the drug treatment	The pharmacist takes responsibility that the desired outcomes of the drug treatment will be achieved.

1.9 Problem statements

1.9.1 Poor Asthma Control

Most asthma patients in the general population are not properly controlled and this appears to be a worldwide problem. So Asthma management guidelines provide recommendations for the optimal control of asthma and asthma therapies of proven efficacy [93]. The International

guidelines Global initiatives for asthma (GINA guidelines) that define control of asthma as minimal chronic symptoms, minimal (infrequent) exacerbations, no emergency visits, minimal use of as needed rapid acting β_2-agonists, no limitations on activities, daily peak expiratory flow (PEF) variation of less than 20%, near normal PEF and minimal adverse effects from medications [29].

International guidelines Global initiatives for asthma (GINA) clearly establish the importance of anti-inflammatory drugs and bronchodilators for optimal control of the disease. However, and despite the fact that the currently available therapeutic arsenal against persistent asthma is excellent, but many patients have poor control of the disease [29]. This is because of the poor adherence to prescribed medication, particularly inhaled steroids, and partly because of the abuse of inhaled short-acting bronchodilators to relieve symptoms [94,95]. Furthermore, the improvement of the quality of care in asthma requires a comprehensive knowledge of patients and the management of their asthma. Therefore, some studies have reported better asthma control when the patients themselves felt adequately informed on asthma and when they were involved in the management of their disease.

So when asthma was controlled this leads to a significant reduction in costs, that due to uncontrolled disease and result from admission to hospital, use of emergency services, and absenteeism from school and work. Therefore, controlling the condition benefits patients in particular and society in general.

1.9.2 Patient Non-Compliance:

Patient's compliance with inhaled therapy leads to successful treatment outcome, this compliance even when they are feeling well and suffering no overt symptoms of their disease. The importance of regular inhaled corticosteroids should be emphasised. Also Patient education should distinguish between reliever, preventer and controller medication and the patient should be aware of inhaler technique, such as rinsing their mouth or brushing their teeth after using their corticosteroid inhaler in order to minimize local side-effects.

Pharmacists in both community and hospital practice are well placed to provide continued information and reinforcement of key messages to improve compliance with medication and the outcomes of asthma management plans.

So asthma management guidelines recommend the appropriate drug treatment for patients based upon the severity of their disease. The choice of delivery device is equally important like the choice of therapeutic agent, because the amount of drug delivered to the lungs differs from device to device. Furthermore, the device choice should be easy to use and consistency of drug release which all have implications for patient compliance. However, patients are frequently non-compliant with their therapy due in part to non-implementation of and non-adherence to asthma management guidelines by the doctors and also due to misuse of inhaler devices.

The major cause of poor asthma control is related to patient non-compliance with therapy [96]. The reasons for patient non-compliance with asthma therapy are complex and involve both drug-related and non-drug-related factors. Drug related factors include a difficulty using the inhaler device; complicated treatment regimens; side effects of treatment; cost; the fact that people do not like taking drugs or that the treatment is not readily available. Other important nondrug related factors for patient's non-compliance include; not understanding the instructions; worrying about side effects; not trusting the doctor; not being supervised when taking medication so compliance is never checked; and anger about being ill. Finally, cultural factors such as; patients do not like being labeled with the disease, they may forget to take the treatment.

1.9.3 Difficulty Using Inhalers

The administration of inhaled medications is a fundamental component of the clinical treatment of patients with pulmonary disease. The use of inhalers makes it possible to selectively reach the lungs, this lead to increasing the concentration of the drug so reducing systemic adverse effects. The effectiveness of the inhaled medication depends on the formulation and the type of device used and also on the ability of the patient to perform the inhalation technique correctly [97].

The major reason for patient's noncompliance therapy is the inability to use the inhaler device correctly and this may impact negatively on asthma control. Therefore, theuse

of inhalers requires accurate completion of multiple steps to ensure effective medication delivery. The effectiveness of inhaler therapy depends not only on compliance, but also on the inhaler technique [98].

There are many different types of inhaler devices available to patients and they can differ in the way in which the inhaler dispenses the medication; whether it is passively or actively generated (i.e. the aerosol-generating properties which can be propellant, mechanical, or compressed air), Dose preparation for DPIs (dry powder inhalers), the type of formulation (e.g. solution, dry powder etc.).The inhalers may contain medication in a single or multi dose, disposable or refillable, or contain a reservoir [99].

The most prescribed inhaler device worldwide is pMDI (pressurized metered dose inhalers) although most patients cannot use it correctly. This is because pMDIs require good coordination of patient inspiration and inhaler activation to ensure correct inhalation and deposition of drug in the lung. Patients frequently fail to continuously inhale slowly after activation of the inhaler and exhale fully before the inhalation [68].

There are different problems when using the pMDI included: patients had difficulty to co-ordinate aerosol release with inspiration (54% patients); they stop inhalation upon release of the aerosol (24% patients) and breathe through the nose whilst actuating the inhaler in the mouth (12% patients) [100]. For example in 1982, 633 patients (54%) attending hospital during a 3 month period were found to be unable to use a pMDI efficiently after reading the patient information leaflet for the inhaler or having the correct use of a pMDI demonstrated to them [100]. And By 2000, only 21% of patients were able to use a pMDI correctly after reading the package insert, and just over half of patients (52%) used a pMDI correctly after receiving instruction [101]. By contrast, 89% of patients were able to use a dry powder inhaler (DPI) or breath activated device correctly following instruction [101].

According to these observations the majority of asthmatic patients probably derive incomplete benefit from the use of pMDIs. Although training apparently results in a more efficient use of the canisters, training sessions must be repeated, and the results checked at regular intervals by a member of the medical staff.In patients who repeatedly fail to achieve a correct inhalation technique, the drug should be given using an alternative inhalation device.

The improper use of pMDIs is not confined to patients. Both nurses and physicians have also been shown to use pMDIs incorrectly despite their increased awareness of the importance of a correct inhalation technique in the use of the pMDI[102].

There are the Dry powder inhalers (DPIs) that have several advantages over pMDIs; they are breath activated (avoiding coordination difficulties between actuation and inhalation), easy and convenient to use, and environmentally friendly [103].

1.10 Thesis Objectives

1.10.1 Aim of the study

The main aim of the study was to investigate the clinical and humanistic impact of pharmaceutical care intervention led by clinical pharmacist in adult patients with asthma.

1.10.2 Objectives of the study

1- To assess the impact of pharmacist intervention on disease control among asthmatic patients as measured by Asthma Control Test (ACT).

2- To assess the impact of pharmaceutical care intervention on patient knowledge about their disease and its management.

3- To assess the impact of the pharmaceutical care on patient's adherence to asthma therapy measured by Morisky adherence questionnaire.

4- To assess the Inhalation Techniques and determine the risk factor for poor techniques.

1.11Research Questions

1. Does patient with asthma have good compliance with his inhaled therapy?

2. Does patient with asthma improve his inhalation technique?

3. Can pharmaceutical care be successful in improving asthma control, medication adherence and patient's knowledge?

Literature review

Chapter two

Literature review

As asthma is associated with an enormous social, psychological, and economic burden, various patient education programs have been developed to improve outcomes, including quality of life. A number of randomized controlled trials showed the effectiveness of community pharmacy-based interventions on lung function, health related quality of life, and self-management in asthma patients. In this section, I am going to discuss a number of these trials which showed the significant positive impact of pharmaceutical care services for asthma patients.

2.1 Pharmaceutical Care Services for Asthma Patients: A Controlled Intervention Study.

In the ***Hamburg*** city, a 26 of intervention pharmacy and 22 of control pharmacy were agreed to participate in the study. The mission of intervention pharmacies were asked to deliver a pharmaceutical care in one to one meeting in counseling room.

In this study, the authors evaluated the effectiveness of community pharmacy-based interventions on lung function, health-related quality of life, and self-management in asthma patients in a 12 month controlled intervention study in 26 intervention and 22 control pharmacies. According to this, patients (ages 18-65) with mild to severe asthma attending the pharmacies were allocated to the intervention (n = 161) or control group (n = 81), respectively. Intervention patients were educated on their disease, pharmacotherapy, and self-management; inhalation technique was assessed and, if necessary, corrected. As a result of pharmaceutical care a significant improvement in inhalation technique, peak flow, self-efficacy, and knowledge were observed [104].

2.2 Assessment of a community pharmacy-based program for patients with asthma.

In Malta,a 11 patients of intervention group were received verbal counseling, an information leaflet, an educational video, but a 11 patients of control group received a routine dispensing services.

The intervention patients have a greater improvement in inhaler technique, medication knowledge, and quality of life at 12 months [105]. Post intervention follow up a Maltese study reported that a community pharmacy based asthma education and monitoring program had a positive impact on quality of life, inhaler technique, peak expiratory flow, compliance with therapy and number of hospitalizations at 4, 8, and 12 months [106].Health-related quality of life of the intervention patients improved at 12 months ($p=0.044$). In the same time period, PEF significantly decreased in control patients compared with intervention patients ($p=0.009$) whereas inhaler technique improved in the intervention group ($p=0.021$). There were significantly fewer self-reported hospitalizations in intervention patients.

2.3 Pharmacy Asthma Care Program (PACP) improves outcomes for patients in the community.

In Australia, a randomized controlled study was conducted to assess the impact of a community pharmacy asthma care program on asthma control, clinical and humanistic outcomes. In the study about 191 and 205 patients were recruited in the intervention and control groups respectively.

The outcomes measures were recorded at baseline and 6 months later. The findings of the study reported a significant improvements in the intervention group compared to the control group in relation to asthma control, adherence to preventer medication, quality of life, asthma knowledge and inhaler technique [109].

2.4 Developing and marketing a community pharmacy-based asthma management program.

This study the program was developed by an independent community pharmacy. In the study, patients who completed one year in the program had a 77% decrease in hospitalization and 78%

decrease in emergency department visits compared with year prior to enrollment in the program. Accordingly, that program proved to be an effective, practical, and profitable addition to the portfolio of services offered by the pharmacy[108].

2.5 Community pharmacy-based pharmaceutical care for asthma patients.

This study evaluate the effectiveness of pharmaceutical care with regard to clinical, humanistic, and economic outcomes in adults with asthma, this include an intervention study that conducted over 12 months, and the study included 39 community pharmacies, 84 primary care physicians, and 183 patients aged from 18-65 years and diagnosed with asthma; and al the results compared with those of control group.

The results of the study showed that a significant improvement for all humanistic outcomes such as; asthma specific quality of life, self-efficacy, knowledge, medication adherence.

In addition, asthma severity, self-reported symptoms, peak expiratory flow, and patient's inhalation technique were improved. Also, the study shows that pharmaceutical care for people with asthma has a positive impact on humanistic outcomes [107].

2.6Significanceof the study

Pharmaceutical care practice is intended to meet a need in the health care system that has arisen due to the increase in complexity of drug therapy and the significant of drug related mortality and morbidity associated with drug use. Therefore, the introduction of pharmaceutical care is required to aid in the resolution of medication related problems. So in this study we implemented and assessed hospital based pharmaceutical care services for patients with asthma in Al-Makassed hospital – Jerusalem.

Methodology

Chapter three

Methodology

3.1 Demography of the study area:

Al-Makassed Islamic Charitable Society was officially established in 1956. It is a Palestinian non-profit, nongovernmental organization that provides diversified humanitarian services in the In 1964, the society began construction of the hospital on the Mount of Olives in Jerusalem. The hospital was officially inaugurated in 1968 as a small community hospital with several departments and a limited number of beds.

Al-Makassed Hospital today is the leading medical center in Palestine, providing secondary and tertiary health services for all citizens of Palestine. Now, Al-Makassed Hospital has 250 beds and is staffed by 750 employees.

3.2Study Design

This is a prospective randomized control study that was conducted in outpatient clinic at Al-Makassed hospital after an approval and permission of Al-Makassed hospital with supervisor Dr. Amro Alastal. This study was a 12 month randomized controlled trial during the period from September 2014 to September 2015; the patients were randomized using computer generated random numbers.

Targeted patients who are 18 years of age or over. With persistent asthma and who were followed up by their physicians and receiving treatment with an inhaled corticosteroid (alone or in combination with a long acting bronchodilator) as maintenance treatment for the control of asthma. Patients gave their informed consent to participate in the study.

3.3. Sample size

The sample size was estimated using the Raosoft sample size calculator [110]. Minimum sample sizes for different potential analyses were calculated using the methods described by Cohen [111].

Simple randomization was used to allocate the patients either to controlled or intervention group based mainly on gender, asthma severity and asthma duration.

A sample of 243 patients agreed to participant in this study, at baseline the number of patients who participated in the study were 106 and 137 patients in the control and intervention groups, respectively. At 6 months, 101 and 122 patients were in the control and intervention groups, respectively. Finally, at 12 month 90 and 102 patients were in the control and intervention groups respectively as shown in **Figure(5).**

3.4 Data Collection

During clinic visits, the well trained clinical pharmacist administered the standard questionnaires. Patients were evaluated according to FEV1,symptoms, clinical data and disease characteristics by the physician. Age, sex, weight, height, body mass index (BMI), education, smoking status, social insurance coverage, duration of asthma, concomitant diseases, asthma-associated diseases (rhinitis, sinusitis, gastroesophageal reflux), and status of the disease in the last year were recorded. Patients were asked questions pertaining to anti-asthma medications they had received for asthma in the last 12 months prior to inclusion in the study. The patients were asked if they have been prescribed or given Peak Flow Meter (PFM) and Asthma Action Plan (AAP) tools, whether they found them useful, and what problems they perceived with their use.

Pharmacists evaluated patient's inhaler technique, using specific check lists for each study inhaler device type, both before and after providing training in inhaler use. For each patient, they recorded the number of attempts of using the inhaler and the length of education time required before obtaining adequate inhaler technique. At the end of the training session, the pharmacist gave complete written instructions for the patient, personalized according to observed inhaler technique and the errors that had been identified **Appendix (1)**.

3.5Inclusion criteria:

The inclusion criteria includes: (1)Patients had to be 18 years of age or over with a 6 month history of diagnosed persistent asthma and receiving treatment for at least the last 6 months with

inhaled (alone or in combination with a long-acting bronchodilator) as maintenance treatment for the control of asthma.(2) Patients in a stable condition during the previous month who had not required changes in maintenance treatment for asthma during this period.(3)Patients had to have given their informed consent to participate in the study.

3.6 Exclusion criteria

The exclusion criteria as follows: (1) Terminal stage illness with less than 6 months life expectancy. (2) Presence of psychological or psychiatric disorders would prevent a correct evaluation of the evaluation of the degree of asthma control. (3) Intravenous or oral corticosteroids during the previous month (4) Admission to a hospital or institution at enrollment as a result of asthma. (5) Non-fulfillment of all the inclusion criteria.

3.7 Questionnaires Data

The questionnaires required for study completion included:

1) Demographic and clinical data about the participants (Appendix2).

2) Asthma Control Test (ACT) (Appendix 3).

3) Medication Adherence Test (Appendix 4).

4) Asthma Knowledge Questionnaire (Appendix5).

5) Manual (Appendix 6).

6) Asthma Action Plan(AAP)(Appendix7).

3.8 Measurements

3.8.1 Demographic and clinical data about the participants

Demographic data (age, sex, and race), socioeconomic data (level of education), data on daily activities were recorded. Thropometric parameters; weight and height were recorded. In addition, clinical variables included a history of smoking, medication use, GP(general practitioner) visits

and number of admissions due to asthma during the last year were also obtained in a customized questionnaire. **Appendix (2)**.

3.8. 2 Asthma Control Test (ACT)

Asthma control test is a self-administered 5 item questionnaire developed for assessing asthma control level [112]. It evaluates the most recent 4 week time period; each item is scored between 1 and 5, with the total score ranging from 5 to 25. An ACT score of 25 indicates that asthma is "controlled," whereas a score between 20 and 24 shows partially controlled asthma and a score of <20 indicates "uncontrolled" asthma. Thus, asthmatic patients were classified as follows: patients with a score of 25 were considered as totally controlled; those with a score of 20-24 were considered as partially controlled and those with a score of ≤ 19 as uncontrolled asthmatics. Then, the totally controlled and partially controlled patients were regrouped as controlled patients (ACT>19) and others were included in the uncontrolled group.

In the original validation of the ACT, the internal consistency of the questionnaire was good (Cronbach's a coefficient = 0.84) [113], and satisfactory internal consistency (Cronbach's a > 0.80) has been reported in other published validation studies from other countries [111, 114, 115] including for an Arabic version of the ACT evaluated in Lebanon and Saudi Arabia (Cronbach's a = 0.92) [116], that is considered as clinically important for (Asthma Control Questionnaire) ACQ is 0.5 on the 7-point scale.
A pilot study was done on 10 patients from Al-Makassed hospital. The Cronbach's Alpha is 0.79 that indicates a good internal consistency and reliability and suitability for our study, **Appendix (3)**.

3.8. 3Medication Adherence Test

The Morisky medication adherence scale is a commonly used adherence screening tool. It is composed of four yes or no questions about past medication use patterns and is thus quick and simple to use during drug history interviews [17].

In 1986, *Dr.Morisky* and his colleagues published the instrument Morisky Medication Adherence Scale (MMAS) that was first validated in antihypertensive drugs in outpatient settings [117], where higher scores indicate higher levels of reported adherence.

A pilot study was done on 10 patients from Al-Makassed hospital, The Cronbach's Alpha for all 0.81 a good internal consistency and reliability. **Appendix (4)**.

3.8. 4Asthma Knowledge Questionnaire:

The Original asthma knowledge questionnaire in English language was translated into Arabic language and termed as Arabic asthma knowledge questionnaire (AAKQ). A thorough validation and reliability testing was performed on AAKQ. Results revealed that the AAKQ came out with good reliability and consistency to evaluate the level of asthma awareness[118].

It is a 7 item questionnaire Designed to measure asthma knowledge of health care consumers. Participants answer a series of true or false questions. A higher score indicates better asthma knowledge. **Appendix**(5).

3. 8. 5Manual:

A well-organized manual book of simple written language was given to the patients in the intervention group prepared to assist in the education session and the patients were given a copy to take home with them.

This manual contained useful information about asthma, its causes, its triggers and the best evidence of its management and about inhaler techniques.

Moreover, the patients were taught about the use of written action plan to monitor their condition and reduce flare up, **Appendix(6)**.

3. 8. 6Asthma action plan (AAP)

An asthma action plan is a set of written instructions that can help a person manage breathing problems. That way, the person doesn't have to go to the doctor or hospital all the time. A doctor works with a person to design a plan that works best for him or her. It can include a list of what

triggers the person's symptoms and how to avoid these triggers, a list of symptoms to watch for and what to do if they happen, and the names and doses of medications the person needs and when to use them. It may also include information on what to do in an emergency. **Appendix(7)**.

3.9.1 Control patients

Control patients received usual hospital outpatient care from medical and nursing staff, but did not receive the structured intervention by the clinical pharmacist as intervened patients.

During clinical visits, the patient completed several questionnaires that served as baseline measures of self-reported asthma related quality of life, perceived control of asthma, and asthma knowledge. The pharmacist was recorded the patient's demographic details, asthma history, asthma severity, medication profile, medication adherence, and their use of health care services over the preceding12 months.

During the study period, the control patients received usual care (no pharmaceutical care intervention).

3.9.2Intervention patients

Intervention patients were educated individually by the clinical pharmacist on asthma, their prescribed medication, the importance of adherence, inhaler technique (written information were provided) and the management of asthma symptoms. The clinical pharmacist ensured that the patient know the indications, side effects and when to use the rescue and maintenance medication.

The pharmacist demonstrated inhaler techniques and then asked the patients to carry out the techniques to ensure that they fully understand how to perform them.

At each outpatient clinic visit (every 6 months arranged by the hospital consultant), intervention group patients received education on asthma and its treatment from the clinical pharmacist. In addition, follow up telephone calls each 3 months by the clinical pharmacist to reinforce the education and motivate the patients to achieve their goals were made at 6 and 12 months, i.e.

between outpatient clinic appointments. At each visit all intervention patients were provided with written action plan, written medication lists and their uses, and asthma manual book.

4. Data Analysis

Data was collected and analyzed by the computer software Statistical Package for Social Sciences Personal Computer (SPSSPC) version 22, Chi-square statistic was used to test for independency of the distribution of both controlled and uncontrolled asthma among the various categories of study variables. The level of significance set at *P*-value 0.05 or less. Results were presented and discussed in tables, bar graphs and computed in percentages.

Chapter four

4. Results

4.1 Sociodemographic data:

The number of patients at baseline was 106 and 137 patients in the control and intervention groups, respectively. At 6 months, 101 and 122 patients were in the control and intervention groups, respectively. Finally, at 12 month 90 and 102 patients were in the control and intervention groups, respectively. During the study period 35 patients of the intervention group and 16 of the control dropped out. In the intervention group, 3 patients died and 9 patients refused to continue, 10 could not complete the study, and others transferred to another clinic for follow-up. In the control group, 3 patients died,8 could not complete the study and others transfered to another clinic. As shown in figure (5).

In the control group, the study population enrolled was 41(38.6%)males and 65(61.3%)females, while those in the intervention group were 60 (43.7%) males and 77 (56.2%) females and the distribution of patients according to their age in the control group was 39 (36.7%) patients (18-40 years), 44 (41.5%) patients (41-60 years), 23 (21.6%) patients were (>60 years), and that of the intervention group was 58 (42.3%), 44 (32.1%),35 (25.5%) patients respectively.

The data was also evaluated smoking habits. Results have shown that the intervention group had highest percentage69 (50.3%) than control group 61(57.5%). Also, using drugs or combinations of drugs are used to control asthma or improve compliance in asthmatic patients. In our study, nearly 33 (24%) of asthmatic patients in intervention were using Ventolin and 29(27.3%) in control group. Whereas 28(20.4%) and 22(20.7%) were using Symbicortin intervention and control group consequently. And the least uses was the combination of Ventolin+ Spiriva around 2(1.4%)in intervention and 2(1.8%)control group.

The health status of control and intervention groups ranged from good to very good, 41 (29.9%), 65(47.4%)in intervention group and 36(33.9%), 56 (52.8%) patients in control group. As shown in **table (6)**. In general, at baseline none of the parameters evaluated showed a significant

difference between the two groups meaning that the control and intervention groups were similar at study initiation.

Table (6): Sociodemographic data

Characteristics	Control group n(%) (n=106)	Intervention group n(%) (n=137)	P-value*
Age			0.319
18-40	39(36.7%)	58(42.3%)	
41-60	44(41.5%)	44(32.1%)	
>60	23(21.6%)	35(25.5%)	
Sex			0.422
Male	41(38.6%)	60(43.7%)	
Female	65(61.3%)	77(56.2%)	
Social status			0.078
Married	9(8.4%)	21(15.3%)	
Unmarried	92(86.7%)	103(75.1%)	
Otherwise	5(4.7%)	13(9.4%)	
Educational status			0.820
Primary	2(1.8%)	5(3.6%)	
Preparatory	16(15%)	23(16.7%)	
Secondary	45(42.4%)	51(37.2%)	
College	21(19.8%)	25(18.2%)	
University	22(20.7%)	33(24%)	
Employment status			0.793
Government employee	30(28.3%)	34(24.8%)	
House wife	51(48.1%)	61(44.5%)	
Retired	12(11.3%)	18(13.1%)	
Self-employed	7(6.6%)	13(9.4%)	
Student	6(5.6%)	11(8%)	
Health insurance			0.860
Government	70(66%)	95(69.3%)	
Special	23(21.6%)	27(19.7%)	
No insurance	13(12.2%)	15(10.9%)	
Average income			0.634
<2000-2500	17(16%)	17(12.4%)	

2500-4000	63(59.4%)	81(59.1%)	
>4000	26(24.5%)	39(28.4%)	
Smoking status			0.896
Smoker	61(57.5%)	69(50.3%)	
Non-smoker	33(31.3%)	45(32.8%)	
Ex-smoker	12(11.2%)	23(16.7%)	
Drug uses			0.806
Ventolin	29(27.3%)	33(24%)	
Symbicort	22(20.7%)	28(20.4%)	
Seretide	13(12.2%)	18(13.1%)	
Aerovent	5(4.7%)	2(1.4%)	
Ventolin+Symbicort	17(16%)	22(16%)	
Ventolin+Seretide	15(14.1%)	26(18.9%)	
Ventolin+Aerovent	3(2.8%)	6(4.3%)	
Ventolin+Spiriva	2(1.8%)	2(1.4%)	
Health status			0.255
Excellent(90-100%)	8(7.5%)	12(8.7%)	
Very good (80-90%)	56(52.8%)	65(47.4%)	
Good(60-70%)	36(33.9%)	41(29.9%)	
Little(<50)	4(3.7%)	16(11.6%)	
Acceptable(50%)	2(1.8%)	3(2.1%)	
Mean (SD) of FEV1%VC	71.5(15.1)	70.1(13.2)	

**cross tab,Chi-Square Test*

4.2 Knowledge about medications and disease management:

The patients had fair knowledge about their medications and disease management at baseline, as measured by the asthma knowledge questionnaire. Patient knowledge in the intervention group were higher at 6 and 12 months as shown in **curve (1),** and the percentage of intervention patients who answered correct answers were increased from baseline to 12 month, about 88% of intervention patients answered question one in 12 month compared with baseline about (50%), and about (40%) in both baseline and 12 month in control group. And at 12 month about (90%, 50%, 50%, 77%, 70%, 80%) of patients in intervention group answered question (2, 3, 4, 5, 6, 7)respectively, compared to baseline, but in the control group, the percentage of patients who

answered correct answer sat 12 month were (40%, 70%, 30%, 30%, 60%, 45%, 77%) of questions (2, 3, 4, 5, 6, 7)respectively, compared to baseline as shown in **table (7).**

Curve (1): Asthma knowledge test in control and intervention group.

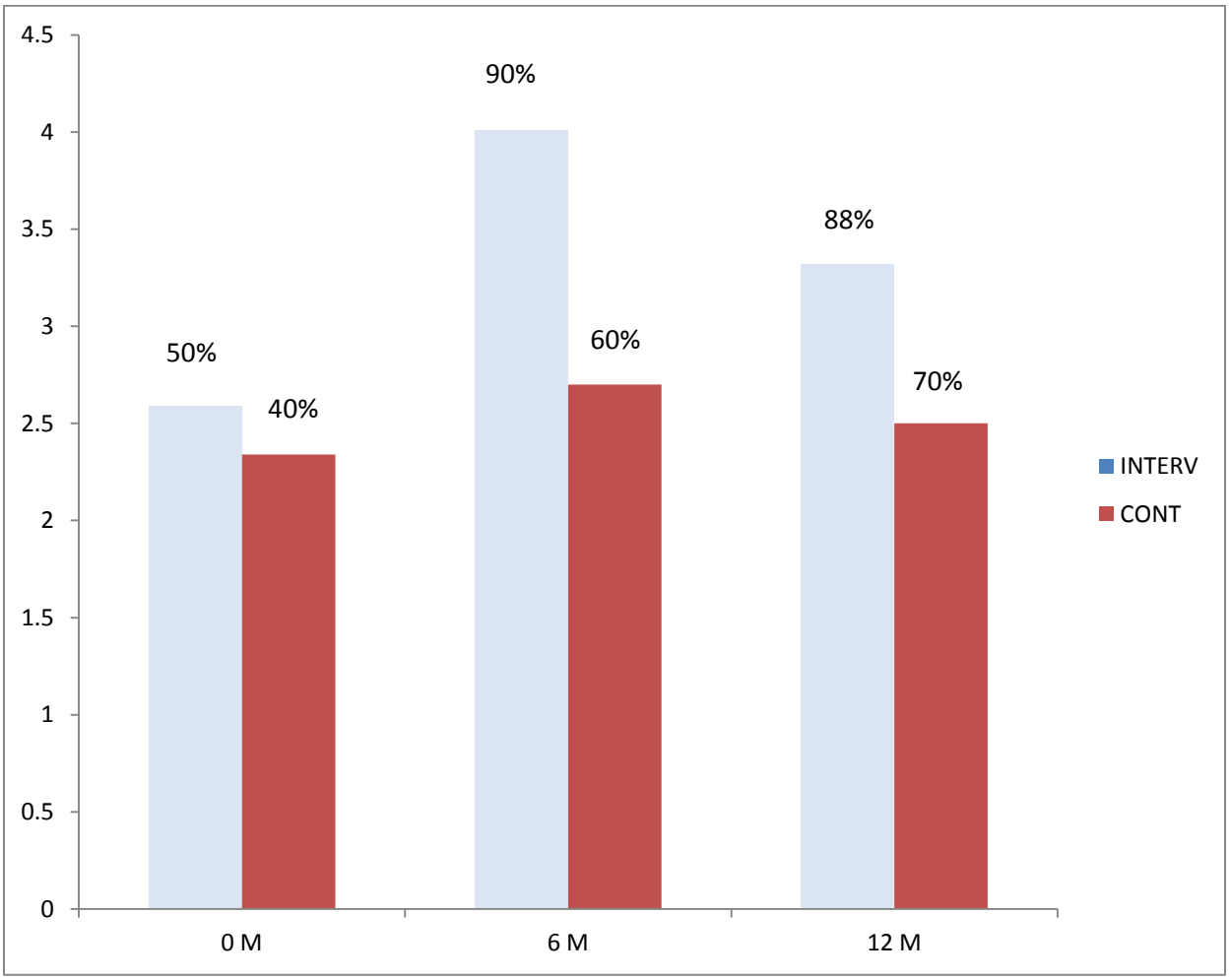


Table (7): The percentages of patients who answered correctly in the intervention and control groups at 0, 6, 12 month.

Question	Group	0 month (%) true	6 month (%) true	12 month (%) true
People who suffer from asthma, they should avoid exercise because breathing becomes more difficult during any kind of physical exertion	Intervention	50%	90%	88%
	Control	40%	60%	40%
Asthma attack does not require immediate attention	Intervention	50%	89%	90%
	Control	30%	73%	70%
It can be fatal asthma.	Intervention	32%	39%	50%
	Control	12%	32%	30%
Asthma attack occur suddenly, without warning	Intervention	48%	52%	50%
	Control	24%	22%	30%
There are many medications to control asthma, depending on the severity of the disease.	Intervention	58%	70%	77%
	Control	40%	55%	60%
The presence of different irritants cause asthma incidence	Intervention	46%	50%	70%
	Control	32%	49%	45%
There is no cure for asthma.	Intervention	20%	63%	80%
	Control	15%	50%	77%

4.3 Adherence to prescribed medications:

An improvement in adherence can be directly beneficial to a patient's clinical condition, and medication counseling contributes to improved medication adherence to prescribed regimens. Adherence to medications during the course of the study, at baseline the results show that the patients in the intervention group have a same adherence to medication compared to control group5(3.64%), 6(5.6%)respectively, with no significant improvement p value= 0.736.

At 6 month, the percentage of adherence to non-adherence medication in intervention group were18(14.7%) and 25(20.4%), compared to control group, about 4(3.9%) were adherent and 46(45.5%) were non-adherent to medications with a p value = 0.0003.

At 12 month the adherence to medication about 10(9.8%), and non-adherence about 30(29.4%) in intervention group compared to control group with 3(3.3%) were adherent and 42(46.6%) were non-adherent to medication in intervention group and the p value was 0.021.As shown in **table (8)**.

Table (8): Medication adherence test

	Medication adherence test	Control group (n,%)	Intervention group (n,%)	P – value*
Baseline(0M) (Control=106) (Intervention=137)	High adherence (0) Moderate adherence (1-2) Non-adherence(3-4)	6(5.6%) 53(50%) 47(44.3%)	5(3.64%) 72(52.55%) 60(43.79%)	0.736
6 month (Control=101) (Intervention=122)	High adherence (0) Moderate adherence (1-2) Non-adherence(3-4)	4(3.9%) 51(50.4%) 46(45.5%)	18(14.7%) 79(64.7%) 25(20.4%)	0.0003

12 month (Control=90) (Intervention=102)	High adherence (0) Moderate adherence (1-2) Non-adherence(3-4)	3(3.3%) 45(50%) 42(46.6%)	10(9.8%) 62(60.7%) 30(29.4%)	0.021

**Chi-Square Test*

4.4 Asthma control test:

In this study, the intervention had significantly increased the ACT after 6 months compared with usual care, the proportion of the complete asthma control is 19(15.5%) and 5(4.9%) in intervention and control groups, respectively with p-value =0.002 but the proportion of the controlled asthma was decreased at the 12 months about 9(8.8%) in intervention group and 7(7.7%) in control group, with non-significant p value = 0.077. As shown in **table (9)**.

Table (9): Asthma control test

	Asthma control test	Control group (n, %)	Intervention group (n, %)	P – value*
Baseline(0M) (Control=106) (Intervention=137)	Complete control(20-25) Partial control(15-19) Bad control(<15)	7(6.6%) 37(34.9%) 62(58.4%)	8(5.8%) 46(33.5%) 83(60.5%)	0.936
6 month (Control=101) (Intervention=122)	Complete control(20-25) Partial control(15-19) Bad control(<15)	5(4.9%) 36(35.6%) 59(58.4%)	19(15.5%) 57(46.7%) 46(37.7%)	0.002
12 month (Control=90) (Intervention=102)	Complete control(20-25) Partial control(15-19) Bad control(<15)	7(7.7%) 35(38.8%) 48(53.3%)	9(8.8%) 55(53.9%) 38(37.2%)	0.077

**Chi-Square Test*

4.5 Asthma inhaler technique:

At the baseline enrollment, there was no significant difference and the proportion of patients who demonstrated appropriate inhaler technique (score=7-10) was 37(34.9%)in control group and 49(35.7%) in intervention group, with (p value =0.736) between both groups. At 6 month the proportion of patients who demonstrated appropriate inhaler technique (score=7-10) was 31(30.6%)in control group and 113(92.6%) in intervention group with a significant p-value=0.0001 but at 12 month the proportion of patients who demonstrated appropriate inhaler technique was slightly decreased about 88(86.2%) in intervention group and 32(35.5%) in control group, with p-value =0.021.As shown in **table (10)**.

Table (10): Asthma inhaler technique

	Asthma inhaler technique	Control group (n,%)	Intervention group (n,%)	*P –value
Baseline(0M) (Control=106) (Intervention=137)	Appropriate(7-10) Inappropriate(1-6)	37(34.9%) 69(65%)	49(35.7%) 88(64.2%)	0.736
6 month (Control=101) (Intervention=122)	Appropriate(7-10) Inappropriate(1-6)	31(30.6%) 70(69.3%)	113(92.6%) 9(7.3%)	0.0001
12 month (Control=90) (Intervention=102)	Appropriate(7-10) Inappropriate(1-6)	32(35.5%) 58(64.4%)	88(86.2%) 14(13.7%)	0.021

**Chi-Square Test*

4.6 Asthma severity:

In this study at the baseline enrollment, there was no significant difference in continued asthma severity values between both groups about 15(14.1%) in control group and 22(16%) in intervention group, with (p value=0.227). But at 12 month, there was a highly significant improvement in continued asthma severity values about 3(2.94%) in intervention group and 10(11.11%)in control groups with p-value=0.001.As shown in **table (11)**.

Table (11): Asthma severity test

	Asthma severity	Control group (n,%)	Intervention group (n,%)	P –value*
Baseline(0M) (Control=106) (Intervention=137)	Intermittent light continue moderate continue severe continue	19(17.9%) 37(34.9%) 35(33%) 15(14.1%)	14(10.2%) 43(31.3%) 58(42.3%) 22(16%)	0.227
6 month (Control=101) (Intervention=122)	Intermittent light continue Moderate continue Severe continue	17(16.8%) 36(35.6%) 40(39.6%) 8(7.9%)	16(13.1%) 61(50%) 39(31.9%) 6(4.9%)	0.137
12 month (Control=90) (Intervention=102)	Intermittent light continue Moderate continue Severe continue	12(13.33%) 31(34.44%) 37(41.11%) 10(11.11%)	20(19.6%) 56(54.9%) 23(22.54%) 3(2.94%)	0.001

**Chi-Square Test*

4.7 Hospital visit:

At the 12-month follow-up, patients in the intervention group had a significant reduction in both hospital admissions (15 vs 36) visits with P- value =0.03 and ED visits (29 vs 58) visits with P-value =0.01 and 0.03 respectively. There was no significant differences in GP visits between control and intervention group (P =0.11). The overall length of hospital stay was significantly

lower in the intervention group (49 days) while in control group around (124 days) as shown in **table (12)**.

Table (12): Hospital admission, emergency department (ED) visits and general practitioner (GP) visits during the 12-month follow-up period.

Variable	Control (90)	Intervention (102)	P-Value
Gp Visit	166	159	0.11†
ED Visit	58	29	0.01†
Hospital admission	36	15	0.03†
Hospital Days	124	49	0.001*

*†: χ^2 test. * Mann–Whitney test, ED: Emergency Department*

Chapter five

5.1 Discussion

This randomized controlled clinical trial was conducted in outpatient clinic at Al-Makassed hospital after an approval and permission of Al-Makassed hospital with supervisor Dr. Amro Alastal. This study was a 12 month randomized controlled trial during the period from *September* 2014 to *September*2015 and the targeted patients who are 18 years of age or over with persistent asthma and who were followed up by their physicians and receiving treatment with an inhaled corticosteroid (alone or in combination with a long acting bronchodilator) as maintenance treatment for the control of asthma. Patients were divided into the intervention group who received pharmaceutical care through asthma education, medication counseling and the control group who were not provided any pharmaceutical care.

This thesis reports is the first randomized controlled trial assessing the impact of a community pharmacist intervention promoting optimal asthma medication use on asthma control in Palestine especially in Al -Makassed hospital.

Intervention improved both the inhalation technique and medication adherence, which are both a key stone for successful asthma management.

The intervention also improved asthma control of insufficiently controlled patients and, for the entire study group, reduced the use of reliever medication and the frequency of using it.

Although a correct use of inhaler device is the essential way for a medicine to arrive at its target organ. There is evidence that poor inhaler technique is associated with poor asthma control [119].

In the baseline of this study, many patients in control and intervention groups (score less than 7) about 69 (65%)and 88 (64.2%) respectively did not use their inhaler devices correctly, and there was no significant difference (p value 0.736) between two groups so the pharmaceutical care by pharmacists could play an important role in this area, by teaching the patients how to use their inhaler devices properly and regularly checking the technique during the course of treatment (especially when therapeutic goals are not met), this improvement was showed in 6 month the

proportion of patients who demonstrated appropriate inhaler technique (score= 7-10), it was 31 (30.6%)in control group and 113 (92.6%) in intervention group with a significant p-value=0.0001 but at 12 month the proportion of patients who demonstrated appropriate inhaler technique was slightly decreased with p-value =0.021. The reason for this, when patients become better than before the compliance decrease.

Thus, proper technique skills must be demonstrated to the patients, and should be checked in every visit to reinforce good technique. Many studies have shown that education could have a large impact on the percentage of patients who use their inhaler correctly [120-122].

Besides inhalation techniques, asthma management also depends on the patient's adherence to their medications. Several studies have shown that adherence to asthma therapy is low mainly with inhaled corticosteroids[123, 124].

The importance of patient education about his inhaled medications is a way to improve adherence, it should be emphasized that the medication profile such as type and daily dose of asthma medication, should be taken in a good and correct manner to improve patient’s adherence to their medication.

In the present study, at baseline the results showed that the patients in the intervention group and control group were the same and has no significant difference p value=0.736,then improvements in symptom control seen in the intervention group rather than control group. This proves the importance of education on adherence.

The patients had fair knowledge about their medication and disease management at baseline, as measured by the asthma knowledge questionnaire. There was no significant difference between the intervention and control groups (P = 0.413). Overall, the percentages of patients who answered a true answer at 6 and 12 month increased compared to baseline.

As such, the intervention group showed a significant improvement during the follow up with regard to knowledge about asthma. This study points out the effective role that a pharmacist can

play in providing patients with deeper insights into their disease and drug therapy through patient counseling.

The improved knowledge is a good base for safe and rational drug use and will help patients to gain confidence in appropriate self-management of asthma, different studies have shown that patients who have increased knowledge about their disease and drug therapy have better control asthma, and our results were in line with other previous studies [125, 126].

The use of ACT or in clinical pharmacy could be an efficient tool to improve asthma control, whereby the pharmacist's advice could depends on the patients ACT score.
An ACT score of 20-25 indicates good or complete asthma control, so these patients need a little specific advice. For patients who have an ACT score of 15-19, indicating partial controlled asthma, the pharmacist could improve the patient's inhalation technique and point the patient at the importance of adherence to the maintenance treatment. In case of an ACT score below 15, this mean that the patient has bad control to asthma and needs more counseling and care because there is a high risk for severe asthma attacks.

Asthma control test in our study showed that the intervention had significantly increased the ACT after 6 months compared with usual care with p-value =0.002 but the proportion of the controlled asthma was decreased at the 12 months with non-significant p value = 0.077.It seems likely that these clinical improvements result from the more appropriate use of the asthma controller medication.

Likewise the pharmaceutical care and asthma management in this study decreasedat the 12-month follow-up, patients in the intervention group had a significant reduction in both hospital admissions (15 vs 36) visits with P- value =0.03 and ED visits (29 vs 58) visits with P- value =0.01 and 0.03 respectively. There was no significant differences in GP visits between control and intervention group (P =0.11). The overall length of hospital stay was significantly lower in the intervention group (49 days) while in control group around (124 days).
Different studies have reported a reduction in emergency visits and hospital admissions as a result of educational and self-management interventions. And our results were in line with other previous studies [127. 128], as in inhaler technique the proportion of patients who demonstrated

appropriate at 12 months was slightly decreased with p-value =0.021. The reason for this, when patients become better than before the compliance decrease.

Conclusions and Future directions

Chapter six

Conclusions and Future directions

6.1Conclusions

The aim of the asthma management is to gain and maintain control of asthma. Clinical pharmacists can develop clinical management plans and asthma action plans for asthma patients, reviewing and educating on inhaler technique as patients who know more about their disease and their drug therapy reach better control of their asthma are better prepared to cope with asthma [129].

Patient counselingalso by a clinical pharmacists can lead to get better patient understanding of their disease and the role of medications in its treatment, improvement in asthma control, asthma knowledge and medication adherence to asthma as shown in different studies[130,131], at the end the asthma patients achieve the desired health outcomes. Moreover, a good professional rapport will be built between the pharmacist and patients.

In addition, asthma control can be optimized if patients regularly monitor their asthma. To achieve this, the patient needs self-management by detection of changes in their condition, making timely adjustments to his asthma medications and knowing when to seek medicinal care.

Finally, pharmacists and other health care professionals would appreciate the role of pharmacist in counseling and educating patients.

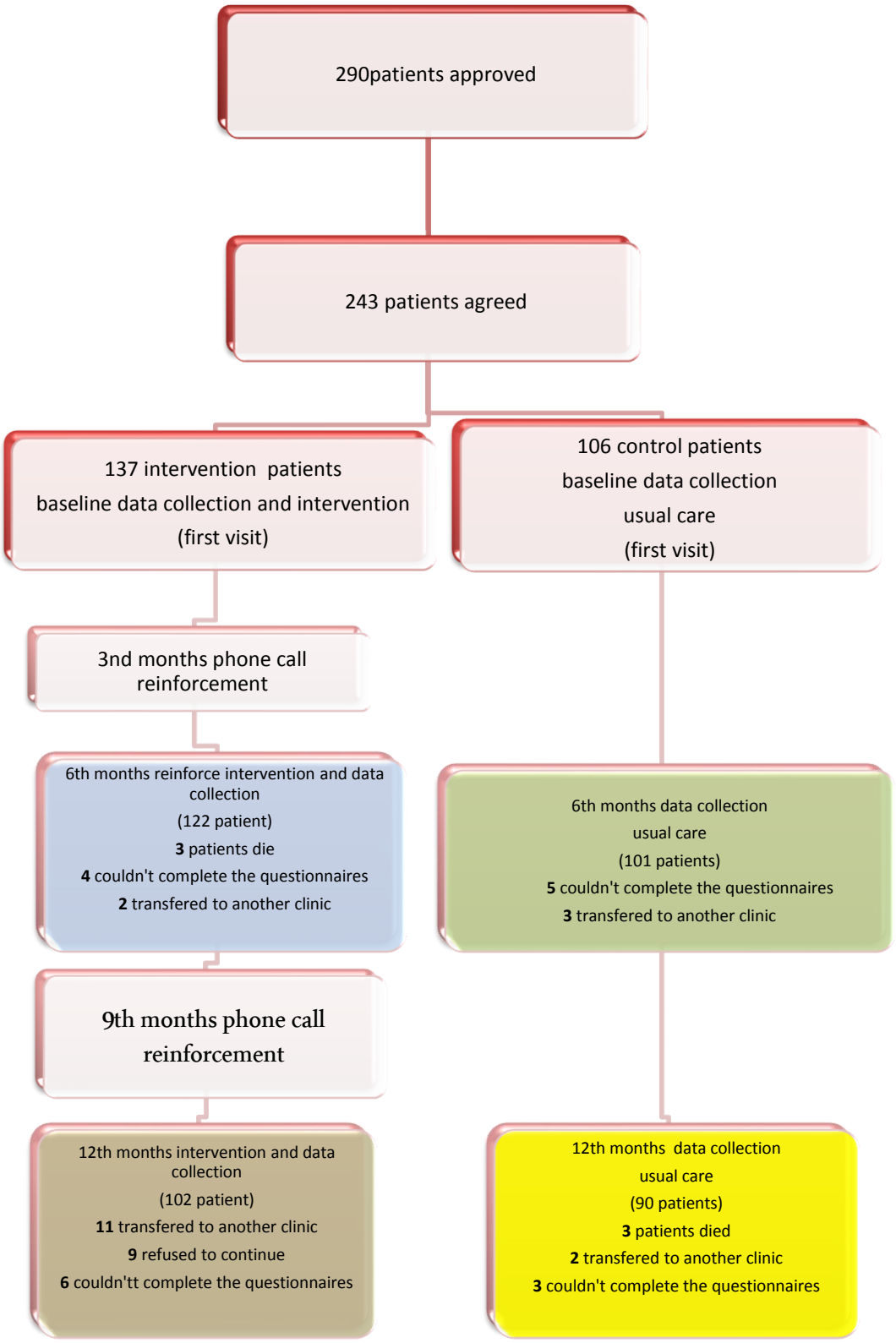
6.2 Future directions

There are different studies performed in different fields related to pharmaceutical care. However, implementation on a large scale still appears to be lacking, despite the positive outcomes of most studies.

Because many pharmacists recognize the importance of pharmaceutical care, so we expect more and more pharmaceutical care services by pharmacies in the future. However, in addition to reforming the attitude, knowledge and skills of pharmacists, there must be some remuneration for their provision of pharmaceutical care. And the pharmacist will be recognize that he is responsible for detecting, protecting and correcting drug related problems.

Finally, pharmaceutical care should be an important part of the pharmacy profession and good pharmacy practice.

Figure (5):Flow chart of our study:



Appendix (1): Asthma inhaler technique

تقنية استخدام أدوية الربو

يطلب من المريض أن يظهر لك كيفية استخدام جهاز الاستنشاق و التأكد من طريقة مرضاك الذين يعانون من الربو يستخدامون أجهزة الاستنشاق بالشكل الصحيح.

Pressurised metered-dose inhaler: Is a pocket size, pressurized multiple-dose inhalation delivery systems, able to deliver small, precisely measured therapeutic doses, greatly minimising the risk of side effects.
The medication in a metered dose inhaler is most commonly a bronchodilator, corticosteroid or a combination of both.

- 1.إزالة الغطاء
- 2. تحقق جرعة المحتوى (إن وجد)
- 3.ارفع جهاز الاستنشاقللأعلى وبشكل مستقيم وهز جيدا
- 4.تنفس خارج بلطف، بعيدا عن جهاز الاستنشاق
- 5.وضع بوق بين الأسنان دون عض و الاغلاق بالشفتين لتشكيل ختم جيد
- 6. البدء في التنفس ببطء من خلال الفم و في نفس الوقت، اضغط لأسفل بشدة على اسطوانة.
- 7. الاستمرار في التنفس ببطء وبعمق
- 8. مسك التنفس لمدة 5 ثوان
- 9.وانت ماسك النفس.أزل جهاز الاستنشاق من الفم
- 10.الزفير بلطف، بعيدا عن جهاز الاستنشاق

Turbunhaler: Is a tube-shaped inhaler which has the medication inside in the form of a dry powder. They have a removable cover and a twisting base. The device is ‘breath-activated’ which means the dry powder medication is ‘sucked’ from the device rather than ‘fired’ like it is from other devices.
Contain Pulmicort (preventer), Symbicort (combination medication), Oxis (symptom controller) and Bricanyl (reliever).

- 1.فك وازالة الغطاء
- 2. تحقق من جرعة المحتوى
- 3. الحفاظ على جهاز الاستنشاق بشكل مستقيم في حين التواء القبضة
- 4.لف القبضة ثم عد للوراء حتى تسمع نقرة
- 5. الزفير بلطف، بعيدا عن جهاز الاستنشاق
- 6.ضع بوقا بين الأسنان دون عض والاغلاق بالشفاه لتشكيل ختم جيد
- 7.تنفس بقوة وبعمق
- 8. مسك النفس لمدة 5 ثوان
- 9.إزالة جهاز الاستنشاق من الفم
- 10. الزفير بلطف بعيدا عن جهازالاستنشاق

Accuhaler: Is a round plastic devices that have medication inside them in the form of a dry powder. The device is 'breath-activated' which means the medication is sucked from the device rather than 'fired' like in some other types of puffers.
Contain Flixotide (preventer medication), Serevent (symptom controller medication) and Seretide (combination medication)

- 1.تحقق من جرعة المحتوى
- 2. افتح غطاء باستخدام الإبهام
- 3. ارفع الجهاز أفقيا، تجهيز الجرعة عن طريق تحريك الذراع حتى تستقر
- 4. تنفس خارج بلطف، بعيدا عن جهاز الاستنشاق
- 5. ضع فتحة اخذ الدواء في الفم وضم الشفتين لتشكيل ختم جيد، والحفاظ على الاستنشاق الأفقي.
- 6.تنفس فيه باطراد وبعمق
- 7.أخذ نفس لمدة 5 دقائق
- 8وانت تأخذ نفس ، ازل جهاز الاستنشاق من الفم
- 9. الزفير بلطف، بعيدا عن جهاز الاستنشاق
- 10. إذا يوصف جرعة إضافية (وليس بشكل عام مستحسن)، كرر الخطوات من 3-9

Ellipta: Inhalation powder contains a combination of fluticasone and vilanterol. Fluticasone is a steroid. It prevents the release of substances in the body that cause inflammation. Vilanterol is a bronchodilator. It works by relaxing muscles in the airways to improve breathing.

- 1 .تحقق من جرعة المحتوى
- 2. أزح الغطاء لأسفل حتى تسمع نقرة (لا يهز جهاز الاستنشاق)
- 3. الزفير بلطف، بعيدا عن جهاز الاستنشاق
- 4. ضع فتحة خروج الدواء في الفم وضم الشفتين لتشكيل ختم جيد. لا تحجب تنفيس الهواء بأصابعك
- 5. التنفس بشكل مطرد وبعمق
- 6. مسك التنفس لمدة 5 ثوان
- 7. وانت ماسك النفس، ازل جهازالاستنشاق من الفم
- 8. الزفير بلطف، بعيدا عن جهاز الاستنشاق
- 9. حرك الغطاء صعودا بقدر ما سوف يذهب لتغطية الفتحة التي يخرج منها الدواء

Autohaler: it is L-shaped plastic outer case, a metal canister inside, and a lever at the top. This is an automatic device, so it automatically 'fires' the medication when it senses you breathing in through the mouthpiece. Contain Airomir (reliever medication) and Qvar (preventer medication).

- **1 .** إزالة الغطاء
- **2.** ارفع جهاز الاستنشاق بشكل مستقيم وهز جيدا
- **3.** ادفع الرافعة للاعلى
- **4.** تنفس خارج بلطف، بعيدا عن جهاز الاستنشاق
- **5. وضع** البوق بين الأسنان دون العض وضم الشفاه لتشكيل ختم جيد
- **6.** تنفس ببطء وبعمق. احتفظ بالنفس الى ما بعد سماع نقرة
- **7.** مسك النفس لمدة 5 ثوان
- **8.** وانت ماسك النفس,ازل جهاز الاستنشاق من الفم
- **9.** الزفير بلطف، بعيدا عن جهاز الاستنشاق
- **10.** دفع الرافعة لأسفل

Appendix (2): Demographic and clinical data

جامعة القدس-أبو ديس

كلية الصيدلة

استبيان عن مرض الربو

الرجاء الإجابة على الأسئلة التالية: Demographic and clinical data

1. العمر : .....
2. الوزن : .....
3. الطول : .....

- الجنس :
  - ذكر
  - انثى

- الحالة الاجتماعية :
  - اعزب
  - متزوج
  - غير ذلك

المستوى التعليمي :
اساسي
اعدادي
ثانوي
كلية
جامعة

المهنة :
موظف حكومي
ربة منزل
متقاعد
عامل لحسابه الخاص
طالب
غير ذلك

وجود تأمين صحي (نعم / لا) :
حكومي
خاص
غير مؤمن

معدل الدخل :
قليل (2000 أو أقل)
متوسط (2500 – 4000)

عالي (أكثر من 4000)

حالة التدخين :
غير مدخن
مدخن
مدخن سابق

الحالة الصحية :
ممتاز (90 – 100%)
جيد جداً (80 – 90%)
جيد (60 – 70%)
ضعيف (أقل من 50%)
مقبول (50%)

شدة الربو :
متقطعة
خفيفة الاستمرار
معتدلة الاستمرار
شديدة الاستمرار

هل تستخدم أدوية لعلاج الربو؟
نعم
لا

اسماء الأدوية المستخدمة:
1. 2.
3. 4.

خلال 12 شهر الماضية:
كم مرة زرت طبيبك بسبب الربو؟

كم مرة ذهبت للطوارئ بسبب الربو؟

Appendix(3): Asthma Control Test (ACT)

تقييم مدى السيطرة علىالربو: **Asthma Control Test (ACT)**

في الأربعة اسابيع الماضية, كم من الوقت منعك مرض الربو من الانجاز في العمل, المدرسة أو البيت؟مجموع النقاط

جميع الأوقات – 1	معظم الأوقات – 2	بعض الأوقات - 3	قليلاً من الأوقات – 4	لم يحدث أبداً – 5

خلال الأربعة أسابيع الأخيرة, كم من مرة أصابك قصور في التنفس؟

أكثر من مرة في اليوم – 1	مرة واحدة في اليوم – 2	3-6 مرات في الأسبوع - 3	مرة أو مرتين في الأسبوع - 4	ولا مرة – 5

خلال الأربعة أسابيع الأخيرة, كم مرة تسببت أعراض الربو (الصفير, السعال, ضيق في التنفس, ضيق الصدرأو الألم) في ايقاظك في الليل أو في وقت سابق من المعتاد في الصباح؟

أربع ليال أو أكثر في الأسبوع – 1	اثنين أو ثلاثة ليال في الأسبوع – 2	مرة واحدة في الأسبوع - 3	مرة أو مرتين في الأسبوع - 4	ولا مرة – 5

خلال الأربعة أسابيع الأخيرة, كم مرة استخدمت أجهزة الاستنشاق؟

ثلاث مرات أو أكثر في اليوم – 1	مرةواحدة أو مرتين في اليوم – 2	مرتين أو ثلاث مرات في الأسبوع - 3	مرة واحدة في الأسبوع او أقل – 4	ولا مرة – 5

كيف تقيّم سيطرتك على مرض الربو خلال الأربعة اسابيع الأخيرة؟

غير مسيطر على الإطلاق – 1	سيئ السيطرة – 2	مسيطر إلى حدٍ ما – 3	مسيطر بشكل جيد - 4	مسيطر تماماً – 5

مجموع النقاط :
(25) سيطرة كاملة
(20-25) سيطرة جيدة
(15-19) سيطرة جزئية
(أقل من 15) سيئ السيطرة

Appendix(4): Medication adherence test.

تقييم مدى الالتزام بأدوية الربو :Medication adherence

هل نسيت من قبل أن تأخذ أدوية الربو؟
نعم
لا

هل اهملت من قبل أخذ أدوية الربو؟
نعم
لا

عندما تشعر بتحسن , هل تتوقف عن أخذ أدوية الربو؟
نعم
لا

أحياناً, اذا شعرت أن حالتك الصحية قد اسوأت بعد أخذ أدوية الربو, هل تتوقف عن أخذها؟
نعم
لا

مجموع النقاط :

(0) التزام عالي
(2-1) التزام متوسط
(4-3) التزام قليل

Appendix (5): Asthma knowledge questionnaire

Asthma knowledge questionnaire

أي البيانات التالية صحيحة وأيها خاطئة:

1. الناس الذين يعانون من الربو يجب عليهمتجنب ممارسة الرياضة لأن التنفس يصبح أكثر صعوبة خلال أي نوع من المجهود البدني.

صحيح خطأ

2. لا يحتاج نوبة الربو اهتماما فوريا.

صحيح خطأ

3. يمكن أن يكون الربو قاتلة.

صحيح خطأ

4. نوبة الربو تحدث فجأةبدون سابق انذار.

صحيح خطأ

5. هناك العديد من الأدوية للسيطرة على الربوبالاعتماد على شدة المرض.

صحيح خطأ

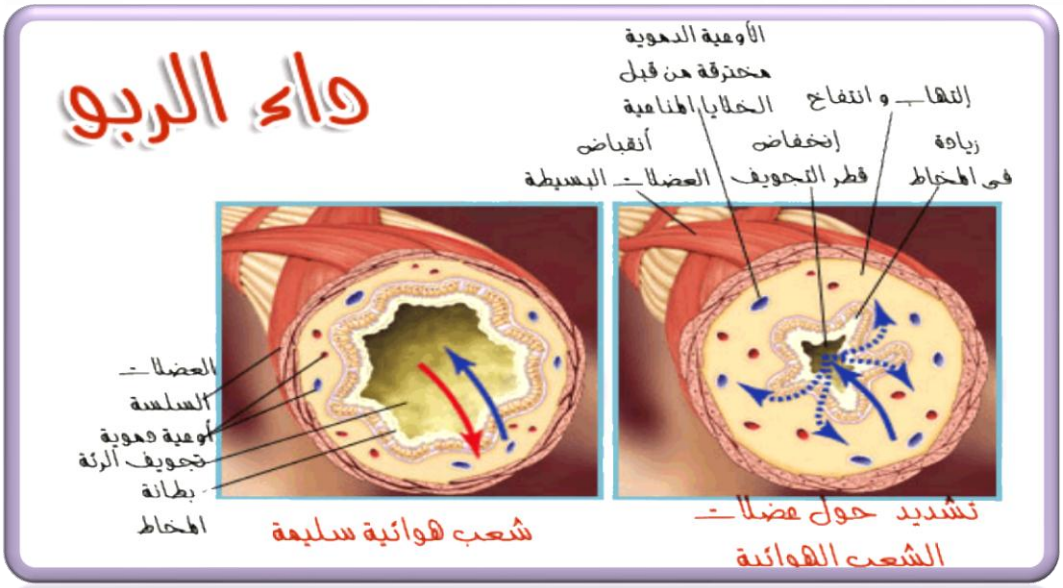
6. وجود المهيجات المختلفة تسبب حدوث الربو

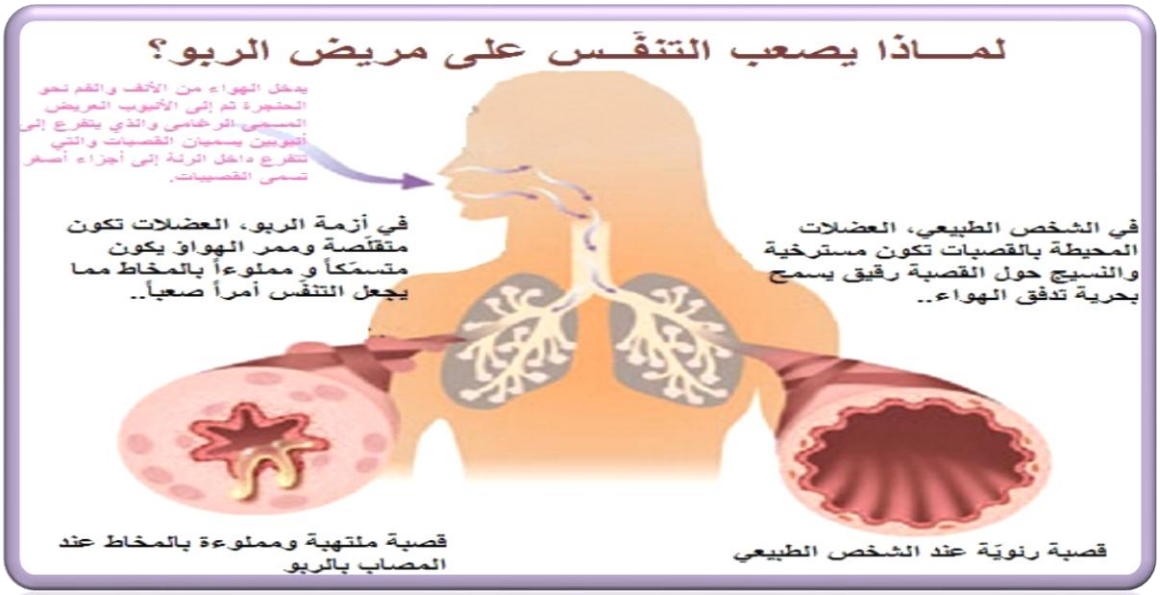
صحيح خطأ

7. لا يوجد علاج للربو.

صحيح خطأ

Appendix (6): Manual




لمـــاذا يصعب التنفّــس على مريض الربو؟
يدخل الهواء من الأنف والفم نحو الحنجرة ثم إلى الأنبوب الهريض المسمى الرغامى والذي يتفرع إلى أنبوبين يسميان القصبات والتي تتفرع داخل الرئة إلى أجزاء أصغر تسمى القصيبات.
في الشخص الطبيعي، العضلات المحيطة بالقصبات تكون مسترخية والنسيج حول القصبة رقيق يسمح بحرية تدفق الهواء..
في أزمة الربو، العضلات تكون متقلّصة وممر الهواء يكون متسمّكاً و مملوءاً بالمخاط مما يجعل التنفّس أمراً صعباً..
قصبة رئويّة عند الشخص الطبيعي
قصبة ملتهبة ومملوءة بالمخاط عند المصاب بالربو


أعراض مرض الربو
السعال .
صوت تصفير أثناء الزفير
صعوبة في التنفس .
انقباض في الصدر
زيادة إفراز المخاط.
أربع قواعد للسيطرة على الربو
التعرُّف على منبهاته ومهيجاته وتفاديها
تناول الدواء طبقاً للإرشادات
التنبُّه لوقوع النوبة مبكراً
معرفة ما يلزم عمله في حالة ازدياد نوبة الربو
طرق علاج الربو
عن طريق استخدام البخاخات وهي أفضل وسيلة للعلاج
أنواع البخاخات
سريعة المفعول وتستخدم وقت حدوث النوبة
طويلة المفعول وتستخدم كعلاج إضافي للبخاخات الواقية


Symbicort
SINGULAIR
SINGULAIR PAEDIATRIC
4mg Chewable Tablets
SINGULAIR PAEDIATRIC
4mg GRANULES
MAX
Ventolin
Ventolin
Ventolin
ادويه الربو


١ انزع الغطاء، امسك البخاخة كما هو موضح هنا.
٢ خض البخاخة.
٣ تنفس إلى الخارج ببطء.
٤ ضع البخاخة في الفم. أطبق الشفتين بإحكام حول المبسم.
٥ تنفس إلى الداخل ببطء وأضغط على العبوة بإحكام.
٦ اترك الهواء داخل الرئة لمدة ثوان ثم تنفس الى الخارج بصورة طبيعية.
٧ تأكد من طريقة إستخدامك للبخاخة أمام المرآة. إذا رأيت بخارا باهتا تأكد من الخطوات 4 و 5
٨ للحصول على أكبر فائدة استخدم البخاخة بإستمرار حسب إرشادات الطبيب.

علاجات الربو

(موسعات الشعب ذات المدى الطويل)

(موسعات الشعب سريعة المفعول)

(العلاجات المركبة وهي عبارة
عن كورتيزون مستنشق
وموسع شعب طويل المدى)

(الكورتيزون المستنشق)

Appendix (7): Asthma action plan.

خطة عمل الربو

الاسم:.....رقم الهاتف:.....

اسم الطبيب:.....توقيع الطبيب:.....

التاريخ:.....

المنطقة الخضراء: أنت بخير وبأمان

1.التنفس جيد 2.لا سعال أو أزيز 3.يمكن اللعب والعمل 4.ينام جيدا في الليل 5. peak flow meterيجب ان يكون 80% فما فوق. 	يجب أخذ الادوية الطويلة المدى long –term control (medications) كل يوم بالاضافة الى(anti-inflamatory drugs): اسم الدواء عدد مرات أخذه متى يجب عليك اخذ الدواء .... قبل التمرين:.....2أو 4 بخات قبل التمرين ب5 دقائق.

المنطقةالصفراء:يزداد سوءا

1.بعض مشاكل التنفس 2.سعال, أزيز أو ضيق الصدر 3.مشاكل عند اللعب والعمل 4.استيقاظ بالليل بسبب الربو 5.لا يستطيع عمل كل الاعمال المطلوب عملها 6. peak flow meter تكون بين 50% - 79%. 	أولا: استعمل أدوية سريعة المفعول (quick relief medicines) مع الاستمرارية بأخذ الأدوية في المنطقة الخضراء ..... (short acting B2 agonist) 2 أو 4 بخات كل 20 دقيقة ثانيا: اذا رجعت حالتك الى طبيعتها ,ارجع للمنطقة الخضراء أو إذا لم تتحسن حالتك أو ازداد سوءا لا ترجع للأدوية الموجودة في المنطقة الخضراء. بل: 1.خذ ..... (short-acting B2 agonist) 2 أو 4 بخاخات. 2.اضف.....(oral steroids) ملغم/اليوم لمدة .....(3-10) أيام. 3.اتصل بالطبيب قبل /خلال .....ساعة بعد أخذ oral steroids.

المنطقةالحمراء:تنبيه

1. الكثير من المشاكل في التنفس. 2. لا يستطيع اللعب والعمل . 3. أدوية quick reliefلا تساعد. 4. Peak flow meter أقل من 50%. 	في هذه الحالة: 1.خذ.....(short-acting B2 agonist) 4أو6 بخات. 2.....(oral steroids) ملغم. ثم اتصل بطبيبك الان واعرف انك ما زلت بالمنطقة الحمراء بعد 15 دقيقة.

العلامات الخطرة

1.عدم المقدرةعلى المشي والحديث بسبب ضيق في التنفس.
2.الشفاهأوالأظافرزرقاءاللون.
فيهذهالحالة:
خذ 4أو 6 بخات من quick relief medicationsواذهب الى المستشفى أواتصل بالاسعاف.

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خدمات الرعاية الصيدلانية لمرضى الربو: تجربة عشوائية ومراقبة

إعداد: صابرين عثمان هاجس عليان

إشراف: الدكتور ماهر الخضور

ملخص

الأهداف:

إن الهدف الرئيسي من هذه الدراسة هو معرفة مدى تأثير الرعاية الصيدلانية من قبل الصيدلي السريري في المرضى البالغين الذين يعانون من الربو.

الطريقة:

هذه الدراسة دراسة عشوائية, أجريت الدراسة في العيادات الخارجية في مستشفى المقاصد. وشملت الدراسة 137 و106 مريضا في مجموعات التدخل(Intervention group) والسيطرة (Control group) على التوالي في الزيارة الاولى, وحوالي 122 و101مريضا في مجموعات التدخل(Intervention group) والسيطرة (Control group) على التوالي في 6 شهور, أما فى 12 شهر فقد كان عدد المرضى حوالي 102 و90 مريضا في مجموعات التدخل(Intervention group) والسيطرة (Control group) على التوالي. وكانت مدة هذه الدراسة العشوائية 12 شهرا (سنة) خلال الفترة من سبتمبر 2014 إلى سبتمبر 2015، حيث تم اختيار المرضى بصورة عشوائية عن طريق أرقام عشوائية باستخدام الكمبيوتر.

تم تقسيم المرضى إلى مجموعة التدخل(Intervention group)التي حصلت على الرعاية الصيدلانية عن طريق الصيدلاني بخصوص مرض الربو ، وتقديم المشورة للمريض عن طريق معرفة الأدوية التي يأخذها,وكيفية استعمالها,واعطائهم مذكرات الرعاية وغيرها، أما مجموعة السيطرة (Control group)فلم تقدم لهم أي رعاية صيدلانية.
وتلقى مرضى مجموعة التدخل (Intervention group) الذين حصلو على الرعاية الصيدلانية كل 3 أشهر، في حين ان مجموعة السيطرة (Control group)تم جمع المعلومات منها بشكل روتيني كل 3 أشهر من دون أن يحصلو على أية

مشورة. وتم تسجيل النتائج من بداية الزيارة وخلال متابعة المرضى في 6 و 12 شهرا في كل من المجموعتين. وقد تم تحليل البيانات باستخدام SPSS النسخة 22، وكان مستوى الدلالة (p<0.05).

النتائج:

في نهاية فترة الدراسة، أظهرت مجموعة التدخل (Intervention group)أن هناك تحسين كبير في كيفية الاستعمال الصحيح لأجهزة الربو حيث أنفي 6 اشهر فان نسبة المرضى الذين حصلوا على مجموع علامات ما بين 7-10 كان عددهم حوالي 31(30%) في مجموعة السيطرة (Control group) وحوالي (92%)113 في مجموعةالتدخل (Intervention group) مع قيمة (p=0.0001).لكن في 12 شهر فان نسبة المرضى الذين يظهرون تقنية الاستنشاق المناسبة انخفضت قليلا اي حوالي (86.2%) 88 في مجموعة التدخل (Intervention group) و(35.5%) 32 في مجموعة السيطرة (Control group), مع القيمة الاحتمالية (p=0.021).

وقد زاد Asthma Control Test في مجموعة التدخل (Intervention group) في الأساس أيضا بكميات كبيرة في زيارة 6 أشهر مقارنة مع الرعاية المعتادة, فان نسبة السيطرة على الربو بصورة كاملة كانت حوالي (15.5%) 19 و (4.5%) 9 في مجموعة التدخل(Intervention group) ومجموعة السيطرة (Control group) على التوالي, مع القيمة الاحتمالية (0.002>P).

ولكن في 12 شهر فان نسبة السيطرة على الربو قد انخفضت بحوالي (8.8%) 9 في مجموعة التدخل (Intervention group) وحوالي (7.7%) 7 في ومجموعة السيطرة (Control group) مع قيمة احتمالية كبيرة (P =0.077).

وفي مدى الالتزام بأخذ الأدوية فأظهرت النتائج خلال فترة الدراسة أن المرضى في مجموعة التدخل (Intervention group) والسيطرة (Control group) هي نفسها وليس لها أي تحسن وهي حوالي (3.64%) 5 في مجموعة التدخل (Intervention group) و (5.6%) 6 في مجموعة السيطرة (Control group) حيث ان قيمة p قيمة كبيرة = 0.736، ولكن في 6 أشهر هناك تحسن كبير في الالتزام أدوية الربو في مجموعة التدخل (Intervention group) حيث ان الالتزام هو 14.7%, مع قيمة احتمالية تساوي 0.0003.

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وكما تشير الدراسة ايضا ان هناك تحسن كبير جدا في اختبار شدة الربو في مجموعات التدخل (Intervention group) مع القيمة الاحتمالية = 0.001. وفي 6 و 12 شهر هناك تحسن كبير للغاية في قلة التردد لزيارة المستشفى في مجموعة التدخل (Intervention group),حيث أن القيمة الاحتمالية = 0.0001 مقارنة مع خط الأساس.

وايضا لم يكن هناك اختلاف كبير في استمرارية شدة الربو بين المجموعتين, حوالي (14.1%) 15 في مجموعة السيطرة (Control group) و (16%) 22 في مجموعة التدخل (Intervention group) مع قيمة احتمالية تساوي 0.227.

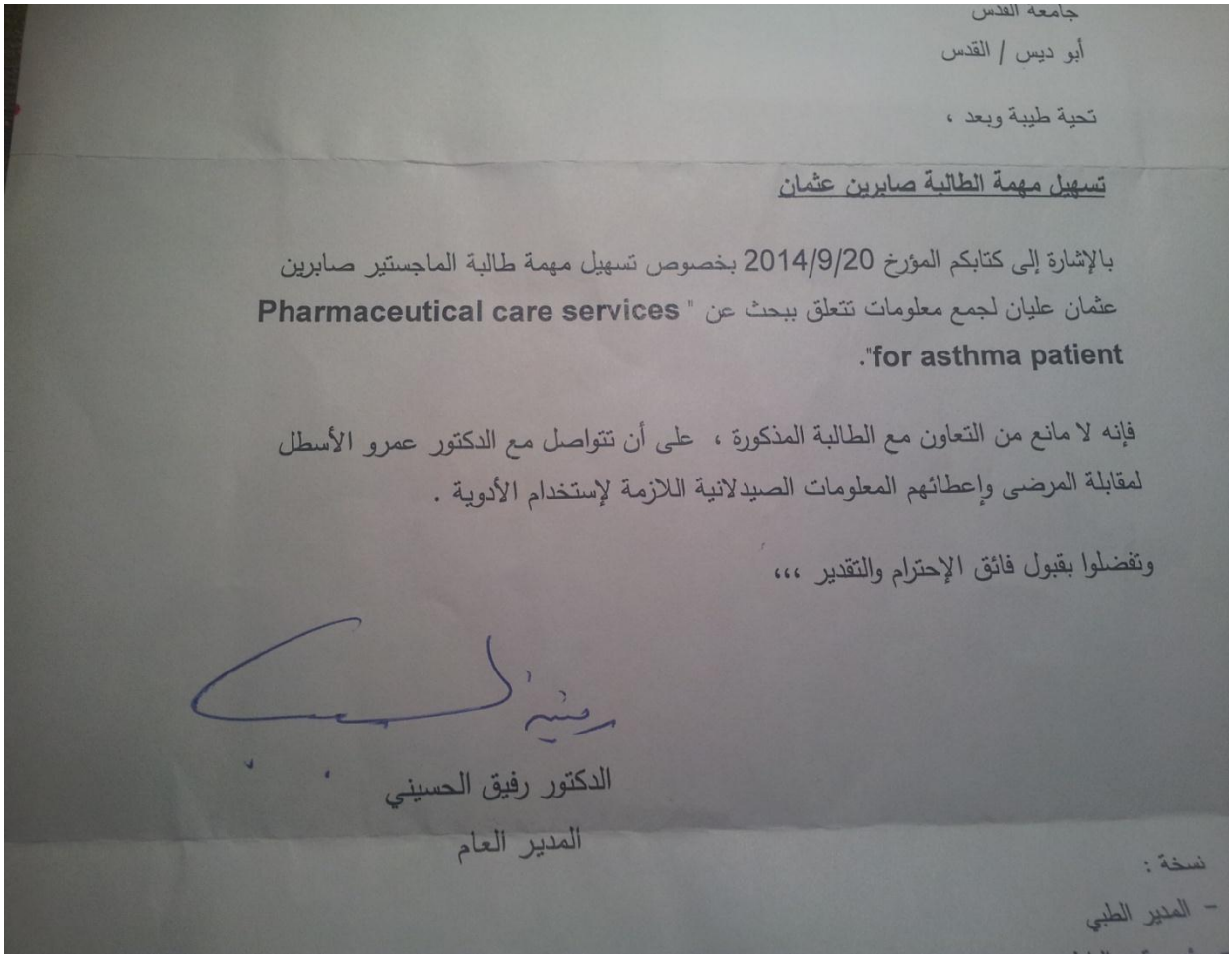
ولكنفي 12 شهرهناك تحسن كبير جدا في مجموعة التدخل (Intervention group) اي حوالي (2.94%) 3 , اما في مجموعة السيطرة (Control group) فكانت حوالي (11.11%) 10 مع القيمة الاحتمالية =0.001.

وايضا في مجموعةالتدخل(Intervention group)هناك انخفاض كبير في عدد ايام دخول المستشفيات اي حوالي (15) يوما مقابل (36) يوموبقيمة (P-value = 0.03) وفي عدد مرات دخول الطوارئ (ED) حوالي (29) يوما مقابل (58) يوموبقيمة (P-value = 0.01) مقارنة مع مجموعة التحكم (Control group).ولم يكن هناك فرق بين عدد الزيارات بين مجموعةالتدخل (Intervention group)ومجموعة التحكم (Control group) حيث ان (P-value = 0.11).وكان ايضا مدة الإقامة في المستشفى أقل بكثير في مجموعة التدخل اي حوالي (49 يوما)، بينما في مجموعة في التحكم (Control group)حوالي (124 يوما).

الاستنتاج:

وتشير النتائج الحالية أن التدخل الصيدلي يمكن أن يكون لها تأثير إيجابي على النتائج المتعلقة بالربو في المرضى.

The hospital approval:



جامعة القدس
أبو ديس / القدس

تحية طيبة وبعد ،

تسهيل مهمة الطالبة صابرين عثمان

بالإشارة إلى كتابكم المؤرخ 2014/9/20 بخصوص تسهيل مهمة طالبة الماجستير صابرين عثمان عليان لجمع معلومات تتعلق ببحث عن " **Pharmaceutical care services for asthma patient**".

فإنه لا مانع من التعاون مع الطالبة المذكورة ، على أن تتواصل مع الدكتور عمرو الأسطل لمقابلة المرضى وإعطائهم المعلومات الصيدلانية اللازمة لإستخدام الأدوية .

وتفضلوا بقبول فائق الإحترام والتقدير ،،،

الدكتور رفيق الحسيني
المدير العام

نسخة :
- المدير الطبي