

Improving Health status of bronchial asthma patients in Nuclear Materials Authority

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Abstract:

Background: Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. Symptoms include wheezing, coughing, chest tightness and shortness of breath. Asthma can result in variable restriction in the physical, emotional, and social aspects of the patient's life.

Setting: out patient clinic in Nuclear materials Authority

Objectives: This study was done mainly to Improve health status including symptoms and quality of life in bronchial asthma patients in Nuclear Materials Authority

Method: The study was carried out on 51 subjects, they were chosen from those attendants of the out patients clinic in Nuclear Materials Authority in el Katamyia in the period from January to May 2012, by measurement of lung function and bronchial hyperresponsiveness as supplemental tools in evaluating the efficacy of treatment with inhaled corticosteroids (ICS) and other controller medications in asthmatic employees.

Results: the asthmatic patients were 51 patients (36 males and 15 females), their ages ranged from 27-59 (46.2±7.3) years, they were detected from those attendants of the out patient clinic in Nuclear Materials Authority in El Katamyia representing (2.1%) of workers. 15 (29.4%) patients were smoker, and 36 (70.6%) patients never smoked, 21 patients (41.2%) were exposed to radioactive materials in their labs in the form of radioactive substances and 30 patients (58.8%) patients were not exposed. 19 (37.3%) patients had intermittent asthma, 11 (21.6%) patients had mild persistent asthma 9 (17.6%) patients had moderate persistent asthma and 12(23.5%) patients had sever persistent asthma. 11(21.6%) patient used long acting anti-inflammatory medications, 23 (45.1%) patients received other controller medication in the form of short acting steroids as Clenil inhaler and ketotifen as zaditen while the majority of patients received rescue medication 34(66.7%) in the form of short acting bronchodilators and oral steroids.

Conclusion: Patient education, measurement of lung function and review of the treatment plan as supplemental tools in evaluating the efficacy of treatment with inhaled corticosteroids and other controller medications in asthmatic employees improve health status including symptoms and quality of life in bronchial asthma patients in Nuclear Materials Authority.

Introduction:

Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. Symptoms include wheezing, coughing, chest tightness and shortness of breath. Asthma is clinically classified according to the frequency of symptoms, forced expiratory volume in 1 second (FEV1), and peak expiratory flow rate (1), the disease is characterized by a variable degree of bronchial hyper responsiveness and airway remodeling. Recent evidence indicates an important role of inflammation pathways, airways remodeling and epithelium activation in asthma genetics (2).

Improving health status of these patients require close monitoring and follow up by proper history taking, physical examination,

investigation and doing pulmonary function to classify the degree of the disease whether mild, moderate or sever and educating the patients about the triggering factors, type of treatment, proper use of medication as regard timing, how to use and correcting misconceptions (3).

The severity of asthma is classified as intermittent, mild persistent, moderate persistent or severe persistent (1) and (4).

The most effective treatment for asthma is identifying triggers, such as cigarette smoke, pets, or aspirin, and eliminating exposure to them. If trigger avoidance is insufficient, medical treatment is recommended. Treatment plan is scheduled according to the type and degree of asthma. Clinical classification of severity of asthma is done according to symptom frequency, night time symptoms,

%FEV₁ of predicted, FEV₁ variability and frequent use of short-acting beta₂ agonist for symptom control as in **table (1)**. We hypothesized that measurement of lung function and bronchial hyperresponsiveness could serve as supplemental tools in evaluating the efficacy of treatment with inhaled corticosteroids (ICS) and other controller medications in asthmatics.

Asthma Control Questionnaire (ACQ) was developed to meet International guidelines for the treatment of asthma, it measures both the adequacy of asthma control and change in asthma control, which occurs either spontaneously or as a result of treatment. Initially, all questions that might be important for the assessment of asthma control were identified. They included day and night-time symptoms, activity limitations, airway caliber and rescue bronchodilator use. The top 5 symptoms were: woken at night by symptoms, wake in the mornings with symptoms, limitation of daily activities, shortness of breath and wheeze. The optimum measure of airway caliber was FEV₁% predicted pre-bronchodilator and the daily rescue bronchodilator use should be included **(5)**. Spirometry with post bronchodilator response should be obtained as the primary test to establish the asthma diagnosis; physical findings vary with the severity of the asthma and with the absence or presence of an acute episode and its severity. We ask the patient this questionnaire and according to patient's answer, pulmonary functions and clinical examination we can classify asthma severity and make the treatment plan.

Medications for asthma are broadly classified into fast-acting and long-acting categories **(6)** this means that medications used to treat asthma are divided into two general classes: quick-relief medications used to treat acute symptoms and long-term control medications used to prevent further exacerbation **(7)**. Bronchodilators are recommended for short-term relief of symptoms. In those with occasional attacks, no other medication is needed. If mild persistent disease is present (more than two attacks a week), low-dose inhaled glucocorticoids or alternatively, an oral leukotriene antagonist or a mast cell stabilizer is recommended. For those who suffer daily attacks, a higher dose of inhaled glucocorticoid

is used. In a severe asthma exacerbation, oral glucocorticoids are added to these treatments. Avoidance of triggers is a key component of improving control and preventing attacks. The most common triggers include: allergens, smoke (tobacco and other), air pollution, non selective beta-blockers, and sulfite-containing foods **(8)**.

For allergic asthmatics, who in spite of the effective use of combined controllers and relievers are still problematic to treat, there is a special type of treatment available as anti IgE immunoglobulins and thermoplasty.

Anti-IgE antibodies (Omalizumab) are an antibody which forms complexes with free (unbound) IgE but not with IgG or IgA. It blocks the binding of IgE to cell-membrane receptors, thereby inhibiting the release of mediators, but it does not bind to cell-bound IgE. Anti-IgE treatment reduces exacerbations and symptoms **(9)**.

The Alair Bronchial Thermoplasty System: Bronchial thermoplasty is a non-drug procedure for severe persistent asthma that delivers thermal energy to the airway wall in a precisely controlled manner to reduce excessive airway smooth muscle. Reducing airway smooth muscle decreases the ability of the airways to constrict, thereby reducing the frequency of asthma attacks. Initial clinical studies including the Asthma Intervention Research (AIR) 1 trial found that bronchial thermoplasty reduces exacerbations and improves morning peak expiratory flow and symptoms in patients with severe asthma **(10)**.

Aim of work:

Improving health status including symptoms and quality of life in bronchial asthma patients in Nuclear Materials Authority by measurement of lung function and bronchial hyperresponsiveness as supplemental tools in evaluating the efficacy of treatment with inhaled corticosteroids and other controller medications in asthmatic employees.

Subjects and methods:

This study was carried out on 51 subjects, they were chosen from those attendants of the out patients clinic in Nuclear Materials Authority in el Katamya in the period from January 2012 to May 2012.

Bronchial asthma was diagnosed according to **National Heart Lung and Blood Institute**

(11) and The Egyptian society of chest diseases and tuberculosis (12).

Measurements: Data were obtained from medical examinations, patient questionnaires, and daily diaries. The clinical effectiveness outcomes were days per month without asthma symptoms, limitation of activity, use of beta-agonists, sleep disturbance, and episodes of asthma. The economic effectiveness outcomes were frequency and type of unscheduled health care contacts, use of beta-agonist inhalers, consumption of non asthma medications, and days of absence from work or school.

Goals to be achieved in Asthma control include the following points:

- Achieve and maintain control of symptoms
- Prevent asthma episodes or attacks
- Minimal use of reliever medication
- No emergency visits to doctors or hospitals
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal as possible
- Minimal (or no) adverse effects from medicine.

All patients were subjected to the following:

1-Full detailed clinical history:

-To recognize controlled patients from uncontrolled we asked the patients about the presence of any of the asthma symptoms as wheezing, shortness of breath, chest tightness and coughing, and if the symptoms are worsened at night, in the early morning, in response to exercise or cold air, any fumes or dust in work place or any other triggers.

-History of exposure to radioactive materials at work place were reviewed in details as some asthmatic patients were exposed at their labs to detect any relation with the occurrence of the asthmatic attacks and whether the attack occur at work place or not, also we asked patients about the presence of proper ventilation and protective measures as masks and gloves and if they wore these protectors or not.

-History of drug therapy for asthma, if oral or inhaler and we asked about the use of controller medications and drug therapy of coexisting disease (Information on drug use from patient diaries was checked).

-Written informed consent was obtained from each subject.

-The Asthma Control Questionnaire (ACQ) was developed to meet these criteria.

The Questionnaire:

The ACQ has 5 questions (the top scoring 5 symptoms: woken at night by symptoms, wake in the mornings with symptoms, limitation of daily activities, shortness of breath and wheeze), and FEV₁% predicted and daily rescue bronchodilator use. Patients were asked to recall how their asthma has been during the previous week and to respond to the symptom and bronchodilator use questions. Clinically, the FEV₁% predicted on a 7-point scale was done. The questions are equally weighted and the ACQ score is the mean of the 7 questions and therefore between 0: totally controlled and 6: severely uncontrolled (as the FEV₁ predicted is not a question but a test) (5).

2-Full clinical examination to detect common signs of asthma including wheezing, shortness of breath, chest tightness and coughing. Symptoms were often worse at night or in the early morning, or in response to exercise or cold air. Some people with asthma only rarely experience symptoms, usually in response to triggers, whereas other may have marked persistent airflow obstruction (13). Some asthmatic patients complain of gastro-esophageal reflux disease and sleep disorders (14).

3-Spirometric lung function test: Spirometry is needed to establish a diagnosis of asthma. The British Thoracic Society determines a diagnosis of asthma using a 'response to therapy' approach, if the patient responds to treatment, then this is considered to be a confirmation of the diagnosis of asthma. The response measured is the reversibility of airway obstruction after treatment. Airflow in the airways was measured with a peak flow meter or spirometer, and the following diagnostic criteria were used according to the British Thoracic Society.

-≥20% difference on at least three days in a week for at least two weeks;

-≥20% improvement of peak flow following treatment, for example:

-10 minutes of inhaled beta-agonist (e.g., salbutamol);

-six weeks of inhaled corticosteroid (e.g., beclometasone);

-14 days of 30 mg prednisolone.
- $\geq 20\%$ decrease in peak flow following exposure to a trigger (e.g., exercise) (15).

-Lung function testing was used also for clinical classification of bronchial asthma.

The following tests were done: FVC, FEV₁, The ratio (FEV₁/FVC)% and (FEF₂₅₋₇₅)%. The FEV₁ (forced expiratory volume 1) is the volume of air forcefully exhaled in 1 second, whereas the FVC (forced vital capacity) is the volume of air that can be maximally forcefully exhaled and therefore contains the FEV₁ within it. FEF₂₅₋₇₅% is the average expired flow over the middle half of the FVC maneuver

4-We made a review for the treatment plan for each patient, those who refused to use inhalers we educated them by explanation, convention and use of booklets and switched the uncontrolled and persistent cases to inhaled drugs to get better response and minimal side effects with stress on inhaled steroids and Leukotriene antagonists and those who complained of expensive drugs we offered them long acting inhalers monthly at the clinic.

5-Patient Education: the following points were discussed with the patient:

-Explaining the nature of the disease to the patient is important to keep him adherent to treatment for life as it is a chronic disease similar to hypertension and diabetes, so it is controlled by medication and avoidance of triggering factors but never cure.

-We explained the triggering factors and advised patients to avoid them as possible to prevent the asthmatic attacks.

- We explained the differences between rescue (relievers or fast acting) medications which are used in asthma attack to treat acute symptoms and the controllers (long acting) medications which are used to reduce the occurrence of the attacks and reduce inflammation of the air ways and prevent further exacerbation.

-Fast acting drugs include short acting beta₂-adrenoceptor agonists (SABA), such as salbutamol, the first line treatment for asthma symptoms. Anticholinergic medications, such as ipratropium bromide, provide additional benefit when used in combination with SABA

in those with moderate or severe symptoms. Anticholinergic bronchodilators can also be used if a person cannot tolerate a SABA (16).

-Glucocorticoids are the most effective treatment available for long term control. Inhaled forms are usually used except in the case of severe persistent disease, in which oral steroids may be needed. Inhaled formulations may be used once or twice daily, depending on the severity of symptoms, Long term control: as Fluticasone propionate metered dose inhaler commonly used for long term control (17).

-Steroids had to be taken in the early morning to coincide with the natural release of cortisone by the adrenal glands to decrease withdrawal symptoms (18). Long acting beta-adrenoceptor agonists (LABA) have at least a 12-hour effect. They are not to be used without a steroid due to an increased risk of severe symptoms. Leukotriene antagonists (such as zafirlukast) are an alternative to inhaled glucocorticoids, but are not preferred. They may also be used in addition to inhaled glucocorticoids but in this role is second line to LABA.

-Mast cell stabilizers (such as cromolyn sodium) are another non-preferred alternative to glucocorticoids (8).

-Changing the beliefs of asthmatic patients is the most important challenge in managing asthmatic patients, most patients refuse to use the inhalers because they are afraid to get use of them, other patients prefer the oral or Parenteral drugs so we explained to the patients that the use of inhalers will reduce the side effects of the drugs as they are used for life, explaining that the inhalers reach directly to the lung and they are delivered in micrograms with minimal side effects on other organs, in contrast to the oral drugs which have many side effects and they are delivered in milligrams.

-Most patients were afraid of using corticosteroids because of their side effects, we have to tell the patient about their important anti inflammatory effect to the lung and using them by inhalation had minimal side effects. They must learn to use very short courses of oral steroids in sever cases and discontinue the oral route after improvement and shift to inhale route.

-We educated the patients how to use inhaler medications which are typically provided as metered-dose inhalers (MDIs) in combination

with an asthma spacer or as a dry powder inhaler, proper technique reduce oropharyngeal deposition and maximize the delivered powder into the lung for better response (19).

-We explained the suspected side effects of long-term use of inhaled glucocorticoids at large doses as thrush which can be prevented by thoroughly rinsing the mouth and/or brushing the teeth after using an inhaled steroid. Some people experience a hoarse voice after using inhaled steroids; this can be prevented by using metered dose inhaled forms along with a spacer. Osteoporosis (Thinning of the Bones) with large doses of Inhaled steroids, prevention of this effect occurs with supplemental calcium in the diet (3 servings of dairy foods a day or 1,500mg of calcium daily), weight bearing exercises (such as walking), and minimizing the dose of inhaled steroids needed, also large doses may cause cataracts and Glaucoma in the elderly, so routine annual eye exams by a qualified ophthalmologist for people with chronically use inhaled steroids, particularly at high doses should be done (20). Most common side effects of leukotriene receptor antagonists are headache and gastrointestinal upsets (8).

-We made an internal booklet in NMA explaining pulmonary diseases including bronchial asthma with stress on self education about triggering factors, protective measures, encouraging asthmatics to use inhaler drugs and the proper methods of using them.

6- Follow up of the patients by re-evaluation of symptoms to detect if asthmatic patients benefit from this study.

Results:

In Nuclear Materials Authority the asthmatic patients were 51 patients (36 males and 15 females), their ages ranged from 27-59 (46.2 ± 7.3) years, they were detected from those attendants of the out patient clinic in Nuclear Materials Authority in El Katamya in the period from January to May 2012, they represent (2.1%) of workers. The real number may be more because of the fact that not all asthmatics seek medical advice and attend our clinic.

15 (29.4%) patients were smoker, and 36 (70.6%) patients never smoked those whom were exsmoker were considered non smokers also.

Some patients were exposed to radioactive materials in their labs (21 patients) in the form of radioactive substances, they represent (41.2%) of patients. The majority of patients were not exposed to radioactive materials in work place (30 patients) representing (58.8%), **table (2)** and **figure (1)** shows personal data of the patients.

Clinical classification of asthma was done according to history taking, physical examination, and pulmonary function tests and according to the clinical classification of severity (1). The majority of patients had intermittent asthma: 19 patients representing (37.3%), 11 patients had mild persistent asthma representing (21.6%), 9 patients had moderate persistent asthma representing (17.6%) and 12 patients had sever persistent asthma representing (23.5%) **table (3)** and **figure (2)** show clinical classification of severity of asthma.

As regard medication only 11 patient used long acting anti-inflammatory medications in the form of inhaled steroids and long acting bronchodilator in the form of Seretide, Symbicort, Foradil, Meflonid and Pulmicort inhalers, representing (21.6%) of patients and 23 (45.1%) patients received other controller medication in the form of short acting steroids as Clenil inhaler and ketotifen as zaditen while the majority of patients received rescue medication 34(66.7%) in the form of short acting bronchodilators and oral steroids **figure (3)** shows Medication of patients.

Table (4) and **figure (4)** shows pulmonary functions of asthmatic patients while the tables (5) and (6) shows ACQ questionnaire at the start and at the end of the study respectively, the results of ACQ score in patients ranged between 0 (totally controlled) and 6 (severely uncontrolled).

Table (7) and **figure (7)** shows FEV1% predicted at the start and the end of the study.

Discussion:

Asthma is one of the most common diseases confronted not only by the physicians and pediatricians, but also by primary care physicians and general medical practitioners. It also accounts for high disease related morbidity measured on indices such as the school or work absenteeism, emergency-room visits and hospitalization. It is, therefore, a matter of

concern to know that the management of asthma in the community is inadequate and the quality of life is poor (21). For the purpose of improving health status and quality of life in bronchial asthma patients in Nuclear Materials Authority Asthma Control Questionnaire (ACQ) was done after a period of re-evaluation of symptoms and treatment. Information on drug use from patient diaries was checked.

In this study there was improvement in all ACQ parameters after treatment interventions by controlled medications in the form of ICS, Leukotriene and other controllers medication together with a plan for patient education and follow up by pulmonary function tests.

Our results were in consistent with the results of **Dijkstra et al (22)** who studied lung function decline in asthma and found that treatment with ICS in adult patients with moderate to severe asthma was associated with a reduction in the decline in FEV₁ over a 23 year follow up period in men who had smoked <5 pack years, and those of **kim et al (23)** who deduced that inhaled Budesonide at a total dose of 800 µ g daily significantly improved symptom scores, asthma exacerbation rates, lung function, and bronchial hyperresponsivness as assessed by Cold air challenge in asthmatic children aged 2 to 5 yr

The same results were obtained by **Patel et al (24)** who made a randomized, open labeled, comparative study to assess the efficacy and safety of controller medications as add on to inhaled corticosteroid and long-acting beta₂ agonist in the treatment of moderate-to-severe persistent asthma and deduced that controller medications helped, with a significant improvement of lung functions and asthma symptoms.

Our results were explained by **Peter and Barnes (25)** who suggested that corticosteroids switch off inflammatory genes by recruiting the nuclear enzyme histone deacetylase-2 to the activated inflammatory gene initiation site so that activators of this enzyme might also have anti-inflammatory effects or might enhance the anti-inflammatory effects of corticosteroids.

As regard quality of life our results were similar to those of **Thomas et al (26)** who searched for health-related quality of life assessment using St. George's respiratory questionnaire in asthmatics on inhaled corticosteroids and concluded that the early

response in quality of life improvement with fluticasone was observed in patients with moderate and severe persistent asthma, and the results of **Rutherford et al (27)** on his study concluding that there was improvement in health-related quality of life with fluticasone propionate, budesonide and beclomethasone dipropionate in adults with severe asthma. Similar results were done by **Ohshima et al (28)** on his work on addition of leukotriene receptor antagonists to inhaled corticosteroids to improve quality of life in patients with bronchial asthma surveyed in suburban area and suggested that the frequency of visits to an emergency room was decreased by complementing the anti-inflammatory effect of ICS with further treatment of inflammation, particularly with Leukotriene antagonist.

In contrast to our results, **Tantisira et al (29)** studied genetics of glucocorticoids in asthma and found no change in annual asthma exacerbation rates despite improvement in controller use, also the results of **Holimon et al (30)** were different from our study, he found no effect of ICS on nocturnal asthma symptoms in asthmatic patients in his study and suggested addition of theophylline or long-acting beta₂ agonists to control symptoms.

Conclusion:

Patient education, measurement of lung function and review of the treatment plan as supplemental tools in evaluating the efficacy of treatment with inhaled corticosteroids and other controller medications in asthmatic employees improve health status including symptoms and quality of life in bronchial asthma patients in Nuclear Materials Authority.

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Table 1): Clinical classification of severity (1).

Severity in patients \geq 12 years of age	Symptom frequency	Night time symptoms	%FEV ₁ of predicted	FEV ₁ Variability	Use of short-acting beta ₂ agonist for symptom control
Intermittent	≤ 2 per week	≤ 2 per month	$\geq 80\%$	$< 20\%$	≤ 2 days per week
Mild persistent	> 2 per week but not daily	3–4 per month	$\geq 80\%$	20–30%	> 2 days/week but not daily
Moderate persistent	Daily	> 1 per week but not nightly	60–80%	$> 30\%$	Daily
Severe persistent	Throughout the day	Frequent (often 7 \times /week)	$< 60\%$	$> 30\%$	Several times per day

Table 2: Shows personal data of the patients.

Number of patients	Age in years (mean \pm SD)	Sex (male/female)	Smoker	Non smoker	Exposure to radioactive materials	Not exposed to RA
51	46.2 \pm 7.3	36/15	15	36	21	30

Figure 1: Shows personal data of the patients.

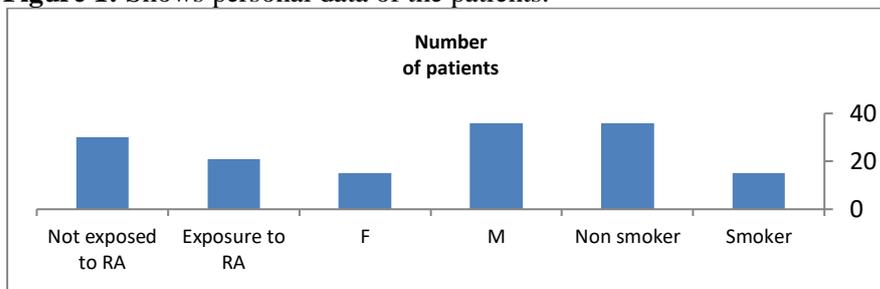


Table 3: Clinical classification of severity of asthma

Type of asthma				Medication		
Intermittent	Mild persistent	Moderate persistent	Sever persistent	Use of rescue medication	Use of short acting controller medication	Use of long acting controller medication (ICS)
19	11	9	12	34	23	11

There is difference in number of patients as some patients receive rescue medication, short acting controller medication and long acting controller medication.

Figure 2: Clinical classification of severity of asthma

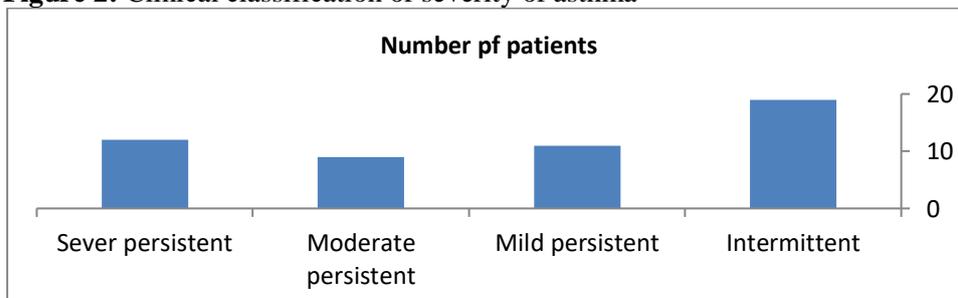


Figure 3: Medication of patients

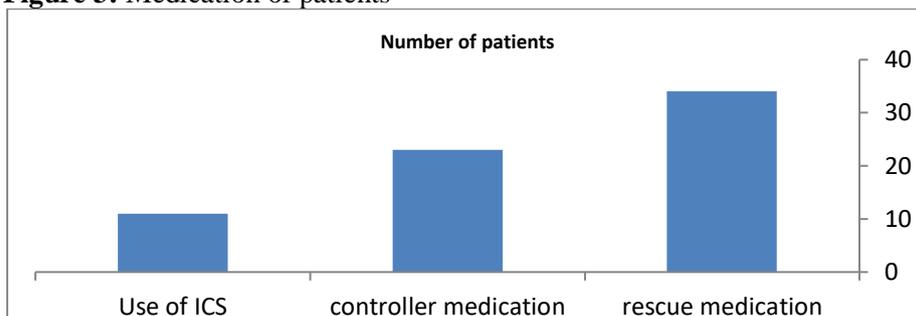


Table 4: Pulmonary Functions of asthmatic patients

Ventilatory functions	At the start of the study	
	Mean	SD
(FVC) %	93.7%	7.53
(FEV ₁) %	75.2%	13.8
(FEV ₁ /FVC)%	78.6%	12.7
(FEF ₂₅₋₇₅)%	72.1%	21.8

FEV₁=Forced Expiratory Volume1, **FVC**= Forced Vital Capacity, **(FEF₂₅₋₇₅)%**=**Forced Expiratory Flow rate**

Figure 4: Pulmonary Functions of asthmatic patients

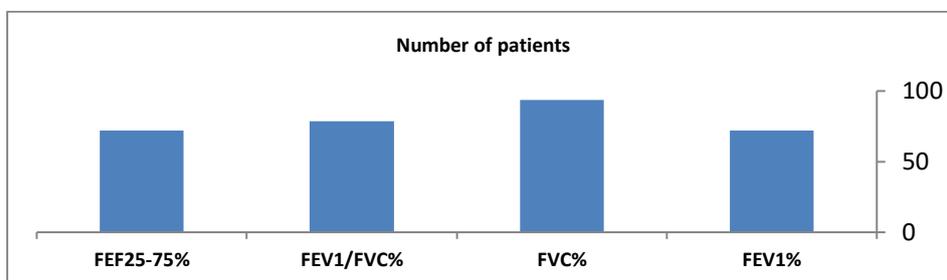


Table 5: ACQ questionnaire at the start of the study

	wake in the mornings with symptoms	night time symptoms	limitation of daily activities	shortness of breath	Wheeze	daily rescue bronchodilator use
No. of patients	32	45	30	10	48	34

Figure 5: Shows ACQ questionnaire at the start of the study.

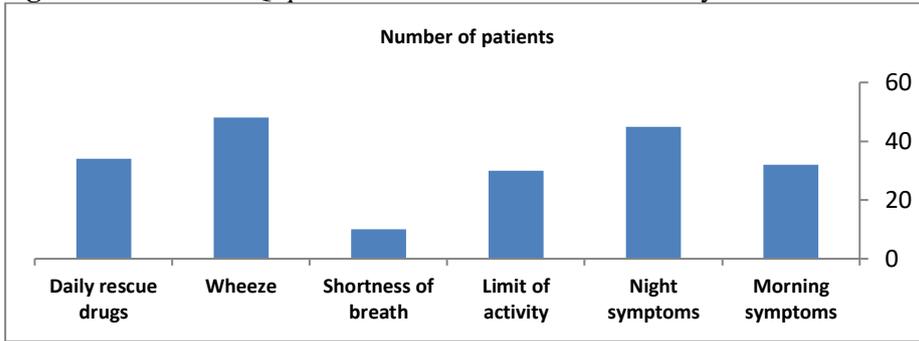


Table 6: ACQ questionnaire at the end of the study.

	wake in the mornings with symptoms	night time symptoms	limitation of daily activities	shortness of breath	Wheeze	daily rescue bronchodilator use
No. of patients	20	16	10	8	15	22

Figure 6: Shows ACQ questionnaire at the end of the study.

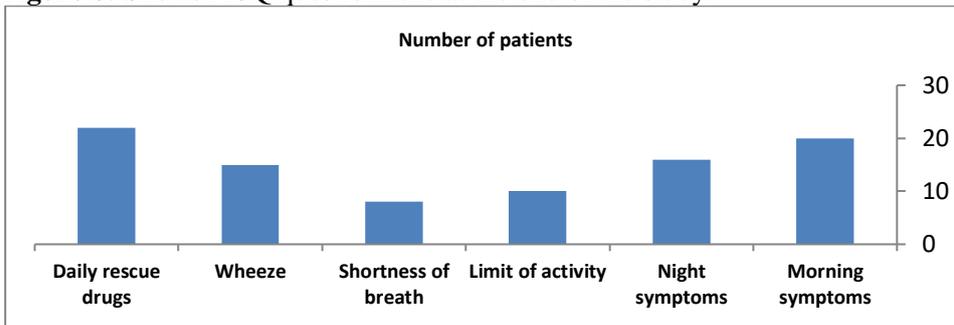


Table 7: FEV1% predicted at the start and the end of the study

Number of patients	FEV ₁ % predicted at the start of the study Mean ± SD	FEV ₁ % predicted at the end of the study Mean ± SD
51	75.2% ± 13.8	85.2% ± 19.8

Figure 7: Shows FEV1% predicted at the start and the end of the study.

