Role of leukotriene receptor antagonist in the treatment of asthma in adults

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Abstract

Leukotrienes are a group of many substances which may be responsible for the effects of an inflammatory response. A randomized, double-blind, placebo-controlled, clinical trial, prospective study compared the clinical effect of oral leukotriene receptor antagonist groups (Montelukast, and Zafirlukast) and placebo group in the management of mild and moderate bronchial asthma. A total of 150 patients (84 females, and 66 males) with mild to moderate asthma were included in this study, their age range between 15 to 70 years. The study was conducted in Al-Sherqat general hospital during the period from January to the August/ 2008. After history taken, all patients under-gone complete general examination, and chest examination. Measurement of height and peak expiratory flow rates (PEFR) and compared to the predicted average normal PEFR (liter/minute) to make sure that the patient had mild-moderate asthma according to classification of asthma severity (13). Two and half milliters of venous blood sample were obtained from basalic vein in the anticubital fossa of each patient included in the study by using disposable syringe after sterilization by 70% alcohol, this sample of blood was collected in a tube containing an anticoagulant (EDTA tube) for measurement of white blood cell count, ESR, & eosinophil count. Those patients were followed up after 1 month and after 3 months from the first visit. In each visit, measurement of PEFR, asthma symptoms score, eosinophils level, ESR, and WBC were done. One hundred fifty patients entered first period (1), 50 patients received montelukast, 50 patients received zafirlukast, and 50 patients received placebo. 76% of patients who received placebo complete period (1,2), 78% of patients who received montelukast complete first & second period (1,2), and 84% of patients who received zafirlukast complete the first & second period (1,2) fig. (1). The discontinuation rate was higher in the placebo 24% than the zafirlukast 16%, and montelukast 22%. The result of the group treated with montelukast regarding gender distribution show that about 44% were males and 56% were females. While group treated with placebo show that 54% were male and 46% were female, and group treated with zafirlukast show that about 36% were males and 64% were females. Asthmatic patients were treated with Montelukast significantly reduced eosinophil count from 0.38 before treatment to 0.33 after 1 month from starting treatment and 0.26 after 3 months. While there is a non significant difference in decrease of eosinophil counts after 1 month between zafirlukast and placebo.

Introduction

Leukotrienes are naturally produced eicosanoid lipid mediators, which may be responsible for the effects of an inflammatory response. Leukotrienes use both autocrine signalling and paracrine signaling to regulate the body's response. Leukotrienes are produced in the body from arachidonic acid by the enzyme 5-lipoxygenase.

Their production by the body is part of a complex response that usually includes the production of histamine (1).

Leukotrienes are synthesized in response to many triggers, including receptor activation, antigen-antibody interaction, physical stimuli such as cold, and any stimulation that increases intercellular calcium (2).

These potent inflammatory mediators promote neutrophil-endothelial interactions, inducing bronchoconstriction and enhancing airway hyperresponsiveness.

They also stimulate smooth muscle hypertrophy, mucus hypersecretion, and the influx of eosinophils into airway tissues. Therefore, inhibition of Leukotrienes potentially plays an important role in the treatment of asthma and other allergic conditions such as allergic rhinitis, atopic dermatitis, and chronic urticaria (3).

Leukotrienes are a group of many substances like leukotriene A_4 (LTA_4), leukotriene B_4 (LTB_4), leukotriene C4 (LTC4), leukotriene D4 (LTD4), leukotriene E_4 (LTE_4), and leukotriene F_4 (LTF_4) (1).

LTC4, LTD4 and LTE4 are often called cysteinyl leukotrienes due to the presence of the amino acid in their structure. Collectively, the cysteinyl leukotrienes make up the slow reacting substance of anaphylaxis (SRS-A). There are actually 2 types of leukotrienes. The first type called chemotactic leukotriene which act mainly in conditions such as cystic fibrosis, inflammatory bowel disease, and psoriasis. The second type of leukotrienes, called cysteinyl-leukotrienes, is connected more with eosinophil and mast cell induced-bronchoconstriction in asthma (1).

There has also been postulated the existence of leukotriene G4 (LTG4), a metabolite of LTE4 in which the cysteinyl moiety has been oxidized to an alpha-keto-acid (i.e., the cysteine has been replaced by a pyruvate). Very little is known about this putative leukotriene (1).

Leukotrienes assist in the pathophysiology of asthma, causing or potentiating the following symptoms: airflow obstruction, increased secretion of mucus, mucosal accumulation, bronchoconstriction, infiltration of inflammatory cells in the airway wall, increase vascular permeability & bronchial edema (4).

Cysteinyl leukotriene receptors CysLT1 and CysLT2 are present on mast cells, eosinophil and endothelial cells. During cysteinyl leukotriene interaction, they can stimulate pro-inflammatory activities such as endothelial cell adherence and chemokine production by mast cells. As well as mediating inflammation, they induce asthma and other inflammatory disorders, thereby reducing the airflow to the alveoli (5).

Pharmacological characterizations identified at least two subtypes of cysteinyl leukotriene (CysLT) receptor based on agonist and antagonist potency for biological responses. The rank potency of agonist activation for the CysLT1 receptor is LTD4>LTC4>LTE4 and for the CysLT2 receptor is LTC4=LTD4>LTE4. CysLT1 selective receptor antagonists are efficacious in the treatment of asthma (6,7).

The CysLT1 receptor is most highly expressed in spleen, peripheral blood leukocytes including eosinophils, and lung smooth muscle cells and interstitial lung macrophages. The CysLT2 receptor is most highly expressed in the heart, adrenal medulla, placenta and peripheral blood leukocytes (8, 9).

Montelukast is a selective, reversible leukotriene receptor antagonist (10). Montelukast is administered orally once daily and is approved for treatment of asthma in patients two years or older. The bioavailability is similar regardless of patient age, and absorption is not affected by food. No drug interactions have been documented. Bronchodilator effects may begin within two hours, but the preventive anti-inflammatory effects will not begin for up to one week (9, 11).

Montelukast appears to be well tolerated. In clinical trials, the most common adverse effect reported was headache, occurring in approximately 18% of patients. Rash, dyspepsia, dizziness, and abdominal pain were all reported in less than 2% of patients. Elevated liver transaminases have been reported with montelukast use, but not at a greater incidence than with placebo. A small percentage of patients have experienced diarrhea, sinusitis, and otitis media during montelukast clinical trials, bleeding tendency, suicidal attempts, & eosinophilia (12).

The aim of the study is to evaluate the therapeutic effects of leukotriene receptor antagonist in management of bronchial asthma.

While the Objectives are: 1-To determine the therapeutic effects of leukotriene receptor antagonists (Montelukast & zafirlukast) on the symptomatic improvement of bronchial asthma. 2-Also, to evaluate the improvement

in peak expiratory flow rate PEFR by use Montelukast & zafirlukast in asthmatic patient. 3-And, to study the effect of these drugs on some hematological parameter such as ESR and eosinophils count. 4-Moreover, to compare the therapeutic effects of both montelukast and zafirlukast on the above mentioned parameters. 5-Finally, to detect the possible side effects of montelukast and zafirlukast and to compare safety between these drugs.

Patients and Methods

A randomized, double-blind, placebo-controlled, clinical trial, prospective study compared the clinical effect of oral leukotriene receptor antagonist groups (Montelukast, and Zafirlukast) and placebo group in the management of mild and moderate bronchial asthma. A total of 150 patients (84 females, and 66 males) with mild to moderate asthma were included in this study, their age range between 15 to 70 years. The study was conducted in Al-Sherqat general hospital during the period from January to the August/ 2008.

The diagnosis of asthma is made on the basis of a complete clinical history combined with ≥ 20% improvement in PEFR 15 minutes after inhalation of short acting bronchodilator. Full history was taken include gender, age, address, occupation, detail history of asthma, including asthma symptoms, number of day symptoms attacks, number of nocturnal symptoms attacks/w, number of times of uses of β2-agonist/w, and effect of asthma on physical activity and then clinical assessment according to (ASTHMA CONTROL SCORING SYSTEM), (13).

After history taken, all patients under-gone complete general examination, and chest examination. Measurement of height and peak expiratory flow rates (PEFR) and compared to the predicted average normal PEFR (liter/minute) to make sure that the patient had mild-moderate asthma according to classification of asthma severity (13).

All patients with the following criteria were excluded :- Acute severe asthma, patient with chronic obstructive pulmonary diseases, pregnant women, patients with liver disease, heart failure and cor-pulmonale, active upper respiratory tract infection & diabetes mellitus.

The proper measurement of PEFR was taken by asking the patient to take breath normally in relaxed pattern and ask to take inspiration deeply and then take off expiration as force as possible to read PEFR (lit/min) using Peak Flow Meter (Haloscale Wright Peak flow meter, England).

Two and half milliters of venous blood sample were obtained from basalic vein in the anticubital fossa of each patient included in the study by using disposable syringe after sterilization by 70% alcohol, this sample of blood was collected in a tube containing an anticoagulant (EDTA tube) for measurement of white blood cell count, ESR, & eosinophil count

Then the patients divided into 3 groups:

1. Group (1): 50 patients (29 female, 21 male) received Montelukast 10 mg (put in white capsule) once daily at bed time for 3 months.
2. Group (2):50 patients (23 female, 27 male) received placebo (white capsule containing lactose) (25 patients once at bed time, and 25 patients twice daily) for 3 months.
3. Group (3): 50 patients (32 female, 18 male) received Zafirlukast 20 mg (put in white capsule) twice daily for 3 months.

Those patients were followed up after 1 month and after 3 months from the first visit. In each visit, measurement of PEFR, asthma symptoms score, eosinophils level, ESR, and WBC were done.

Statistical Analysis were done by using SPSS program (version 14) was used. Paired t-test was used to compare between the mean of measured parameters at beginning, after 1 month , and after 3 month in each study group. Chi square was used to explain the distribution according to gender, residence, and family history for non parametric parameters. All the statistical results were considered significant at P value equal or less than 0.05. All data were presented as a mean & standard deviation (SD).

Results

One hundred fifty patients entered first period (1), 50 patients received montelukast, 50 patients received zafirlukast, and 50 patients received placebo. 76% of patients who received placebo complete period (1,2), 78% of patients who received montelukast complete first & second period (1,2), and 84% of patients who received zafirlukast complete the first & second period (1,2) fig. (1). The discontinuation rate was higher in the placebo 24% than the zafirlukast 16%, and montelukast 22%.

Regarding gender distribution of study population, the results show that 44.66% of them were male and 55.33% were females. The mean age of patients treated with montelukast was 33.98 year, while the mean age of patients treated with zafirlukast was 31.21 year, and those treated witg placebo was 31.08, (Table (1). The results indicate, that 59.33% of them were from rural area and 40.66% were from urban. Regarding residence distribution of group treated with montelukast, the data shows that about 64% were from rural area, and 36% were from urban area. While about 58% of patients treated with placebo were from rural area, and 42% were from urban area. In group treated with zafirlukast 56% were from rural area and 44% were from urban area.

The result of the group treated with montelukast regarding gender distribution show that about 44% were males and 56% were females. While group treated with placebo show that 54% were male and 46% were female, and group treated with zafirlukast show that about 36% were males and 64% were females.

The distribution of population regarding family history of allergic disease show that 75.33% had postive family history, and 24.66% had negtive family history.

The family history of the group treated with montelukast was +ve in 80%, and the group treated with placebo show that 72%% had + ve family history, and the group treated with zafirlukast show that 74% had + ve family history.

1- Comparsion between Montelukast and placebo:-

Asthmatic patients were treated with Montelukast significantly reduced eosinophil count from 0.38 before treatment to 0.33 after 1 month from starting treatment and 0.26 after 3 months, (Table (2). There is a significant increase in PEFR from 311.41 liter/minute before treatment to 337.50 liter/minute after 1 month and to 349 liter/minute after 3 months, (Table (2). Also, there is significant increase in clinical assessment score from 65.57% before treatment to 70.46% after 1 month and to 71.28% after 3 months. Table (2).

While, there is a non significant decrease in ESR from 15.59 before treatment to 14.55 after 1 month and to 14.05 after 3 months, Table (2). Moreover, treatment the patients with zafirlukast reduced eosinophil count significantly from 0.32 before treatment to 0.30 after 1 month and to 0.27 after 3 months. Table (3). There is high significant increase in PEFR from 313.64 liter/minute before treatment to 335.33 liter/minute after 1 month and to 347.19 liter/minute after 3 months, (Table (3).

Also, there is a high significant increase in clinical assessment score from 65.8% before treatment to 69.67% after 1 month and to 71.07% after 3 months. While, there is a non significant change in ESR value of before treatment comparing with that of after 1 month and there is a non significant decrease in ESR after 3 months 14.31 than before treatment 14.98, (Table (3).

There is a significant decrease in eosinophil count from 0.34 before treatment with placebo to 0.33 after 1 month from starting treatment with placebo and 0.32 after 3 months. Table (4). There is a non significant decrease in PEFR from 308.46 liter/minute before treatment to 306.74 liter/minute after 1 month and there is a significant increase in PEFR to 315.03 liter/minute after 3 months than 308.46 before treatment with placebo, (Table (4).

Also, there is a non significant increase in clinical assessment score from 65.65% at before treatment to 65.98% after 1 month and to 65.79% after 3 months, table (4). While there is a non significant decrease in ESR from 13.72 before treatment to 13.13 after 1 month and there is a non significant

increase in ESR after 3 months 14.26 than before treatment 13.72, (Table 4).

There is a non significant difference in decrease of eosinophil counts after 1 month between montelukast and placebo table (5). While, there is a significant difference in decrease of eosinophil counts after 3 months between montelukast and placebo, (Table 6).

Also, there is a significant difference in value of PEFR after 1 month and after 3 months between montelukast and placebo (Table 5, 6).

There is a significant difference in improvement in clinical assessment score after 1 month and after 3 months between montelukast and placebo (Table 5, 6). There is a non significant difference in ESR after 1 month between montelukast and placebo table (5) and after 3 month table (6).

2-Comparsion between zafirlukast and placebo:

There is a non significant difference in decrease of eosinophil counts after 1 month between zafirlukast and placebo table (7). While, there is a significant difference in reduction of eosinophil counts after 3 months between zafirlukast and placebo (Table 8). Also, there is a significant difference in measurement of PEFR after 1 month (table 7), and after 3 months between zafirlukast and placebo. (table 8). Moreover, there is a significant difference in improvement in clinical assessment score after 1 month table (7), and after 3 months between zafirlukast and placebo (Table 8). While, there is a non significant difference in ESR after 1 month between zafirlukast and placebo table (7) and after 3 month table (8).

The clinical side effects (headache, worsening asthma, pharyngitis, sinusitis, upper respiratory tract infection, and gasterointestinal tract problem), occurring in 8.67% of all the study groups. The overall frequency of clinical adverse events was similar among the montelukast, and zafirlukast groups. Headache and upper respiratory tract infections and gastrointestinal tract problem including (nausea, epigastric pain, and diarrhea) were the most frequently reported adverse events, other side effects include worsening asthma, pharyngitis and sinusitis, (Table 10).

Discussion

Asthma is characterized by airway inflammation that manifests as reversible airflow limitation and airway hyperresponsiveness. Consequently, anti-inflammatory therapy plays a pivotal role in its management. Cysteinyl leukotriens are important pro-inflammatory and bronchoconstrictor mediators in the pathogenesis of asthma, while leukotriene receptor antagonists (LTRAs) demonstrate hybrid anti-inflammatory and bronchodilatory properties (14).

This clinical trial demonstrates that leukotriene receptor antagonists (LTRAs) provided clinical benefit during the 12-week treatment period by consistent and significant improvement of all asthma control variables compared with placebo.

Demographic characteristics of the sample were as follows, total study group 150 patients were included in the study to detect role of leukotriene receptor antagonists (montelukast and zafirlukast) in management of mild to moderate asthma. Eighty nine patients of them (59.33%) were from rural areas and 61 patients of them (40.66%) were from urban areas. This results may be due to the escalation of asthma over recent decades has been linked to an increase in environmental pollutants. In rural areas, the consanguineous marriage is predominant, which explain the genetic predisposition (15). This agree with Ring *et al*, who found that environmental factors from the physical, chemical, biological and psychological environment (characteristic of a modern or western society) influence the development of atopic sensitization and diseases (16).

In the present study, a high rate positive family history of allergic diseases because asthma have a familial predisposition and a genetic basis. However, sorting out the key genes in multifactorial disorders in which environmental and genetic factors are important has been difficult (17).

It is likely that clinical expression of asthma results from the complex interaction of many genetic loci and that variation in

each of these genes contributes to the diversity of phenotypes observed in asthma (17).

Peak expiratory flow rate exhibited significant increase compared with placebo, this is due to that montelukast, as a leukotriene receptor antagonists, improve lung function and, decrease inflammatory response , and this is in agreement with previous study done by Theodore, who found that montelukast, compared with placebo, significantly improve asthma control during a 12-week treatment period (18). Also, the present result agree with the study don by Noonan et al. While, there is a non significant relation between montelukast and ESR (19).

Percentage of clinical assessment score (number of diurnal symptoms attacks, number of nocturnal symptoms attacks, number of doses of β2-agonist, and effect of asthma on physical activity) exhibited significant increase compared with placebo, and this is in agreement with the study done by William Busse who found that Montelukast significantly decreased both daytime asthma symptoms and nocturnal awakenings in patients with mild asthma and with mild-to-moderate asthma (20).

Eosinophilia is a feature of airway inflammation associated with asthma. Leukotriene antagonists provide therapeutic benefit in asthma (21). In present study, it was found that a significant decrease in eosinophil counts compared with placebo, this is due to that montelukast, as a leukotriene receptor antagonists, decrease inflammatory response, and this is in agreement with the study done by Stelmach Livona, who found that montelukast, compared with placebo, significantly decrease eosinophils count over 6 weeks treatment period (22). Also, study done by Noonan MJ, *et al.* (23), and Altman LC, *et al.* who show significant decrease in blood eosinophil counts over time (24).

In the present study, Zafirlukast, compared with placebo, improve significantly the value of peak expiratory flow rate, this is due to effect of zafirlukast, as a leukotriene receptor antagonists, improving lung function and decrease inflammatory response. This finding is in agreement with the study done by Samy Suissa, who found that a daily regimen of zafirlukast added to as-needed inhaled ß-agonists is more effective than ß-agonists alone in treating mild-to-moderate asthma while there is a non significant relation between zafirlukast and ESR (25).

When zafirlukast treatment compared with placebo, there was a significant improvement in percentage of clinical assessment score (number of diurnal symptoms attacks, number of nocturne symptoms attacks, number of doses of β2-agonist, and effect of asthma on physical activity), this is due to that zafirlukast, as a leukotriene receptor antagonists, improve lung function, and this is in agreement with the study done by J.P. Seale, who found that zafirlukast improve, patient-reported endpoints, such as daytime asthma scores, night wakening and use of beta agonists (26), compared with placebo, also Spector SL, *et al.* found that Zafirlukast improved airway obstruction in a 6-week study (27).

There is a non significant difference between effect of montelukast and zafirlukast on measured parameters (PEFR, eosinophil count, clinical assessment score, and ESR), and this is in agreement with the study done by Riccioni, & others who found that significant improvement for both montelukast and zafirlukast on quality of life and there is no many differences between the two treatments (28, 29).

Another study done by Cohn J *et al* show that 5-lipoxygenase inhibitors (zileuton) improve daytime asthma symptom scores, nocturnal awakening, β-agonist use (30), and PEFR. Sahn S. *et al* who found the same result in the study on other leukotriene receptor antagonist (pranlukast) (31).

The clinical adverse events occurred with similar frequencies with montelukast, zafirlukast and placebo treatments. Adverse events that occurred were generally transient and self-limited, and did not require discontinuation from study therapy. In Theodore F et al. study, it was found that montelukast was generally well tolerated with clinical adverse events occurred with similar frequencies with montelukast, (18).

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Table (1): The mean & SD of age (years) of the studied groups.

Groups of treatment	Mean ± SD
Montelukast	33.98 ± 11.54
Placebo	31.08 ± 9.70
Zafirlukast	31.21 ± 12.34

Table (2): Effect of Montelukast on measured parameters before & after 1 & 3 months of treatment.

Time(month) / Parameters	Mean ± SD		
	Before treatment	After 1 month	After 3 month
Eosinophil ($\times 10^9$/l)	0.38 ± 0.13	0.33 ± 0.11***	0.26 ± 0.09***
ESR(mm/hr)	15.59 ± 7.40	14.55 ± 7.20	14.05 ± 8.60
PEFR(liter/minute)	311.41 ± 46.4	337.50 ± 50.90***	349.0 ± 54.1***
Clinical Assessment %	65.57 ± 8.80	70.46 ± 7.80***	71.28 ± 7.20***

*** Significant at p<0.01*,

Table (3): Effect of zafirlukast on measured parameters before & after 1 & 3 months of treatment.

Time (month) / Parameters	Mean ± SD		
	Before treatment	After 1 month	After 3 month
Eosinophil ($\times 10^9$/L)	0.32 ± 0.12	0.30 ± 0.10***	0.27 ± 0.08***
ESR (mm/hr)	14.98 ± 7.07	15.49 ± 7.14	14.31 ± 6.44
PEFR (liter/minute)	313.64 ± 51.6	335.33 ± 59.4***	347.19 ± 57.98***
Clinical Assessment %	65.8 ± 8.23	69.67 ± 7.57***	71.07 ± 7.29***

Significant at p<0.05*.

Table (4): Effect of placebo on measured parameters.

Time (month) / Parameters	Mean ± SD		
	Before treatment	After 1 month	After 3 month
Eosinophil ($\times 10^9$/l)	0.34 ± 0.12	0.33 ± 0.11*	0.32 ± 0.12*
ESR (mm/hr)	13.72 ± 6.80	13.13 ± 6.4	14.26 ± 7.42
PEFR (liter/minute)	308.46 ± 43.9	306.74 ± 43.19	315.03 ± 39.73**
Clinical Assessment(%)	65.65 ± 8.7	65.98 ± 8.0	65.79 ± 7.22

Significant at p<0.05*, at p<0.01*

Table (5): Compares between the effect of montelukast and placebo on the measured parameters after one month

Drugs / Parameters	Mean ± SD		p-value
	Placebo	Montelukast	
Eosinophil ($\times 10^9$/l)	0.327 ± 0.11	0.332 ± 0.11	0.835 (NS)
ESR(mm/hr)	13.13 ± 6.4	14.55 ± 7.20	0.326 (NS)
PEFR(liter/minute)	306.74 ± 43.19	337.50 ± 50.90	0.003
Clinical Assessment%	65.98 ± 8.0	70.46 ± 7.80	0.009

Table (6): Compares between the effect of montelukast and placebo on the measured parameters after three months.

Drugs / Parameters	Mean ± SD		p-value
	Placebo	Montelukast	
Eosinophil ($\times 10^9$/l)	0.323 ± 0.12	0.258 ± 0.09	0.008
ESR (mm/hr)	14.26 ± 7.42	14.05 ± 8.60	0.908 (NS)
PEFR (liter/minute)	315.03 ± 39.73	349.0 ± 54.1	0.002
Clinical Assessment%	65.79 ± 7.22	71.28 ± 7.20	0.001

Table (7): compares between the effect of zafirlukast and placebo on the measured parameters after one month.

Drugs / Parameters	Mean ± SD		p-value
	Placebo	Zafirlukast	
Eosinophil ($\times 10^9$/L)	0.327 ± 0.11	0.30 ± 0.10	0.130 (NS)
ESR (mm/hr)	13.13 ± 6.4	15.49 ± 7.14	0.100 (NS)
PEFR (liter/minute)	306.74 ± 43.19	335.33 ± 59.4	0.010
Clinical Assessment%	65.98 ± 8.0	69.67 ± 7.57	0.026

Table (8): Compares between the effect of zafirlukast and placebo on the measured parameters after three months.

Drugs / Parameters	Mean ± SD		p-value
	Placebo	Zafirlukast	
Eosinophil ($\times 10^9$/l)	0.323 ± 0.12	0.269 ± 0.08	0.016
ESR(mm/hr)	14.26 ± 7.42	14.31 ± 6.44	0.976 (NS)
PEFR(liter/minute)	315.03 ± 39.73	347.19 ± 57.98	0.005
Clinical Assessment%	65.79 ± 7.22	71.07 ± 7.29	0.002

Table (9): Compares between the effect of montelukast and zafirlukast on the measured parameters after one month .

Drugs / Parameters	Mean ± SD		p-value
	Zafirlukast	Montelukast	
Eosinophil ($\times 10^9$/l)	0.30 ± 0.10	0.332 ± 0.11	0.201 (NS)
ESR (mm/hr)	15.49 ± 7.14	14.55 ± 7.20	0.536 (NS)
PEFR (liter/minute)	335.33 ± 59.4	337.50 ± 50.90	0.854 (NS)
Clinical Assessment%	69.67 ± 7.57	70.46 ± 7.80	0.631 (NS)

Table (10): Clinical side effects of the drugs occurring in 8.67% of treated patients.

Side effect	Montelukast Number & %	Zafirlukast Number & %
Headache	3 (6%)	4 (8%)
Worsening asthma	1 (2%)	2(4%)
Pharyngitis	1 (2%)	2 (4%)
Sinusitis	1 (2%)	1 (2%)
Upper respiratory tract infection	3 (6%)	3 (6%)
Gastrointestinal tract problem	2 (4%)	3 (6%)

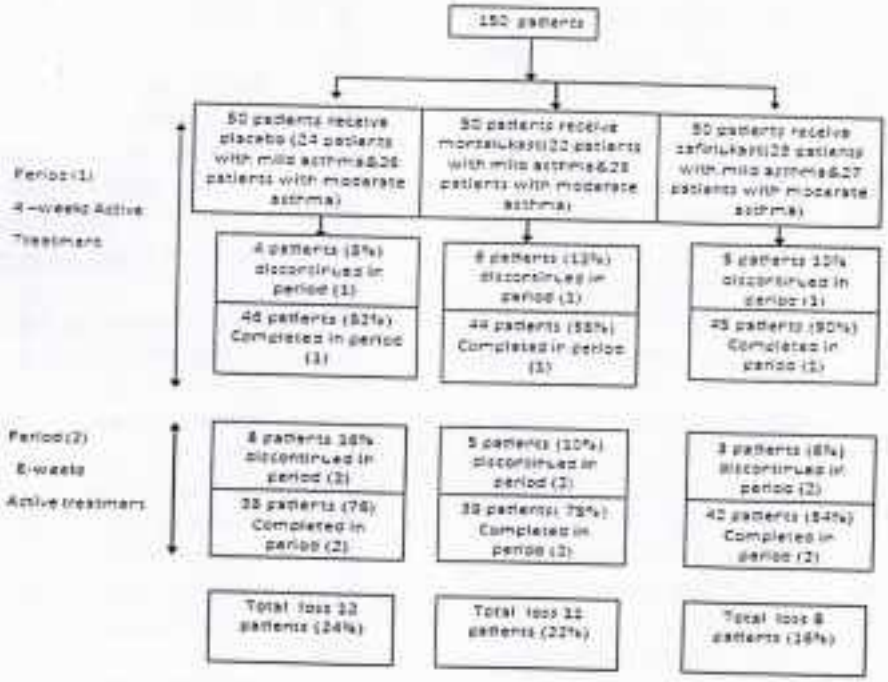

Figure (1): Study profile of the 150 asthmatic patients.