Original Article

Montelukast As An Add On Therapy In Asthma As Compared To Its Use In Asthma Associated With Concomitant Rhinitis Symptoms

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Summary:

Back ground: The use of Montelukast in mild and moderate asthma has been studied ,allergic rhinitis or rhinitis and asthma are strongly inter related, Montelukast has been used in both conditions, whether treating rhinitis will improve asthma control ,a point which has been stressed recently.

Objectives: To evaluate the effect of Montelukast in mild and moderate asthma according to Global INitiative For Asthma guidelines (GINA),and to compare its use in asthma alone and in asthma which is associated with persistant rhinitis symptoms.

Patients and methods: Seventy patients who fulfill the criteria of mild and moderate asthma according to Global INitiative For Asthma guidelines had been recruited from the consultation clinic of the respiratory diseases in Baghdad Teaching Hospital from the 111st.July 2009 to 31st. December 2010,patients were divided in to 2 groups : Group – 1 patients with asthma only which was subdivided into 2 sub groups: 1-a on salbutamol inhaler on need and 1-b on beclomethasone inhaler 800Mgm/day in addition to salbutamol inhaler on need.

Group- 2 patients with asthma and rhinitis which was sub divided in to subgroups: 2-a on salbutamol inhaler on need and 2-b on beclomethasone 800Mgmlday in addition to salbutamol inhaler on need.

Evaluation of day and night time symptoms, records of rhinitis symptoms and measurement of FEV1(Forced Expiratory Volume in 1st. second) and FEF 25-75%(Forced Expiratory Flow)were done to all patients .

Montelukast 10 mg/ day was given to all patients for 4 weeks,and reevaluation for day , night time symptoms , rhinitis symptoms and measurement of FEV1 and FEF 25-75% were done .

Results: There was a significant statiscal improvement in day , night time symptoms , FEV1 , FEF 25-75% and rhinitis symptoms after Montelukast treatment than before treatment (p value < 0.05), Montelukast use in asthma alone as compared to its use in asthma which was associated with rhinitis did not show a significant statiscal improvement in outcome response in day,night symptoms and in percentage of change in FEV1 and FEF25-75% (p value>0.05) .

Conclusion: Montelukast improved day , night time symptoms , FEV1 , FEF 25-75% in mild and moderate asthma ,it also improved rhinitis symptoms but Montelukast use in asthma alone as compared to its use in asthma which was associated with rhinitis did not show a significant statiscal imrovement in asthma control regarding day,night time symptoms,FEV1 and FEF25-75% values .

Key words: Montelukast, asthma, rhinitis

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Introduction:

Asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, In susceptable individuals,this inflammation causes recurrent episodes of wheezing,dyspnea,chest tightness and coughing,especially at night or early morning(1). The release of anti inflammatory mediators such as cytokines and cysteinyl leukotrienes, plays an essential role in the complex pathophysiology and symptomatology of asthma(2). The main mechanism of action of inhaled corticosteroids (ICS) is the inhibition of cytokines (3). There is a considerable evidence that cysteinyl leukotrienes have a potent effect on airway function inducing broncho-constriction and air way hyperresponsivness(4). Cysteinyl leukortienes are poorly inhibited by steroids (5). Adding a Montelukast,when a low to moderate dose of (ICS) donot provide sufficent disease control, by addressing another pathways of airway inflammation(6). Rhinitis is defined as inflammation of the nasal mucosa characterised by nasal discharge,blockage,sneezing and non purulent rhinorrhea,pruritis of the nose ,palate and the eyes,two or more symptoms occuring for more than 1 hour on most days.It can be further classi fied as intermittent (symptoms occuring on < 4 days out of 7 or for< 4weeks per year) or persistant(symptoms occuring at least 4 days out of 7 or for> 4 weeks per year)(7).

Patients and methods:

Asthmatic patients proved by history and clinical examination and reversibility testing of FEV1 improvement of 12% and more on salbutamol

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inhalation after 10 minutes were included in the study.

Asthmatic patients on sytemic steroid,aminophylline ,smokers and patiens younger than 16 years old were excluded from the study,patients with persistant rhinitis symptoms on antihistamines and intranasal steroids were excluded from the study too.

Fulfilling the GINA (Global INitiative for Asthma) criteria for mild and moderate Asthma,124 patients attending the respiratory consultation clinic in Baghdad Teaching Hospital from 1st of July 2009 to 31st of December 2010 were included in the study,54 patients from the above 124 patients did not attend or completed 4weeks treatement of Montelukast and were excluded from the study

Seventy patients were included in the study who had completed 4 weeks of Montelukast treatment: females were 44(62.9%) and males were 26(37.1%)

From the 70 patients, 37(51.9%) patients had asthma a lone and 33 (48.1%) patients had asthma with persistant rhinitis based on symptoms(serum IgE and skin testing were not available).

The seventy patients were classified into 2 major groups:

Group I: Asthmatic patients without symptoms of rhinitis:37patients (51.9%),who were divided into 2 subgroups:

1-a 21 patients (30%),who are on short acting B2-agonist salbutamol on PRN (on need) basis(step I GINA criteria).

1- b 16 patients(22.8%),who were on a dose of inhaled beclomethasone of 800 Microgram/day,in addition to salbutamol inhalation on PRN basis(step 2 GINA criteria).

Group2: Asthmatic patients with persistant rhinitis symptoms:33 patients (48,1%),who were subdivided in to 2 subgroups:

2-a 16 patients (22.8%) on salbutamol inhalation on PRN basis.

2-b 17 patients (24.3%) on a dose of beclomethasone 800 Microgram/day.

All the 70 patients were fully assessed by history, asthma day, night time symptoms and were examined and and categorized according to GINA criteria.

Record of rhinitis symptoms was done

FEVI(Forced Expiratory Volume in First second in Litre and FEF 25%-75%(Forced Expiratory Flow)in Litre per second were done to all patients, peak flow rate variability testing was not done because peak flow meters were not always available. 10 mg Montelukast /day were added to treatment of the above groups and were followed after they had completed 4 weeks of therapy.

All the 70 patients were reassessed regarding their asthma day and night symptoms response and were classified in accordance with major GINA guidelines changes into controlled,partialy controlled and uncontrolled .

FEV1,FEF 25-75% were reassessed after treatment.

Rhinitis symptoms were assessed in their response as improved or un improved.

Statiscal analysis: Descriptive statistics (mean± SD) describing respiratory parameters and analysis using paired and unpaired t-test for difference. P value less than 0.05 was considered significant.

Results:

All groups had a better outcome response after 4 weeks of Montelukast treatment than before treatment ($P<0.05$). However, complete, partial and no response percentages were distributed evenly for asthmatics unrelated to the presence or absence of rhinitis for day and night symptoms ($P>0.05$) as in table(1). Improved rhinitis response was observed in (81.3%) of asthmatics on salbutamol treatment after one month of Montelukast administration (statistically significant than before Montelukast treatment $P<0.05$), and (82.4%) in asthmatics on salbutamol and beclomethasone after one month of Montelukast (statistically significant than before Montelukast treatment $P<0.05$). However, no significant statiscal difference was observed between the two groups ($P>0.05$).

Table (1): Outcome response of day and night symptoms after Montelukast treatment

Symptoms	Groups and subgroups	Response			Total number
		Complete	Partial	No	
Day symptoms	1-a	9 (42.9%)	8 (38.1%)	4 (19.0%)	21
	2-a	10 (62.5%)	4 (25.0%)	2 (12.5%)	16
	1-b	9 (56.3%)	5 (31.3%)	2 (12.5%)	16
	2-b	11 (64.7%)	5 (29.4%)	1 (5.9%)	17
Night symptoms	1-a	9 (42.9%)	9 (42.9%)	3 (14.3%)	21
	2-a	10 (62.5%)	4 (25.0%)	2 (12.5%)	16
	1-b	10 (62.5%)	3 (18.8%)	3 (18.8%)	16
	2-b	11 (64.7%)	5 (29.4%)	1 (5.9%)	17

Table(2) showed that comparison of values of FEV1 and FEF25-75% before an after 4 weeks treatment of Montelukast which showed a significant statiscal improvement ($P<0.05$) .

Table (2): Lung function test values in asthmatics before and after Montelukast treatment

Montelukast	**Lung function test**	**Groups and sub groups**			
		1-a	2-a	1-b	2-b
Before	FEV1	1.88±0.5	1.90±0.4	2.06±0.5	2.09±0.8
	FEF25-75%	1.50±0.6	1.84±0.6	1.59±0.5	1.68±0.9
After	FEV1	2.54±0.8	2.34±0.4	2.75±0.5	2.88±0.7
	FEF 25-75%	2.19±1.1	2.16±0.7	2.34±0.7	2.54±0.9

Since all four groups showed a significant statistical difference in the pulmonary function tests performed before and after one month Montelukast treatment (Table 2), percentage of change (perentage of change=reading(before-after)/after×100) was calculated to compare the effect of treatment among all patients groups (Table 3)

Although no statistical difference in response percentage was evident (P>0.05) among all asthmatic groups, however, there was a clinical difference in response in asthmatics with rhinitis on beclomethasone after one month of treatment with Montelukast had 45.4% better FEV1 results and 76.3% better FEF25-75% results than the other groups

Table (3): Percentage of change in FEV1 and FEF25-75% after Montelukast treatment Among different groups of patients

Groups and subgroups				
Lung function test	1-a	2-a	1-b	2-b
FEV1	36.4±29.4%	39.1±35.4%	26.6±22.4%	45.4±40.3%
PEFR	52.1±60.9%	51.2±31.2%	30.2±62.2%	76.3±72.5%

Discussion:

The incidence of female to male ratio was 2:1 ,this relative increase in females could be explained by the exclusion of smokers from the study.The percentage of patients with rhinitis was 48.1% from the total number of patients. There was a significant statiscal improvement in day and night time symptoms(table 1) and a significant statiscal improvement in FEV1 and FEF 25-75% (table 2) than before treatment in all groups when Montelukast was added and this agrees with studies done by Drazen et al (8), Wenzel et al (9),Philip et al(10) , Price et al(11) and Murray (12). This study showed an improvement in the response percentage of day and night time symptoms table(1), but it showed that complete,partial and no response percentages were distributed evenly for asthmatics unrelated to the presence or absence of rhinitis , which was not statiscally significant(p value > o.o5) , similarly FEV1 and FEF 25-75% values though they showed an improvement after Montelukast treatment table(2) ,the presence or absence of rhinitis did not show a statiscal significant difference in the percentage of change values (p value >0.05) table (3),the result of this study is supported by Peters - Goldens review who stated that patients with both asthma and allergic rhinitis are any likely to benefit from leukotriene modifiers than are patients without concomitant allergic rhinitis (13) , and the result of our study disagreed with other studies which stated that treating allergic rhinitis will improve asthma control as in a study done by Virchow and Bachert who studied adult patients with asthma and allergic rhinitis and evaluated the response to asthma day, night symptoms,allergic rhinitis symptoms improvement, the need for rescue medications and improvement in quality of life and they concluded that Montelukast improves rhinitis symptoms and asthma control and suggested the concept of one air way one disease (14),the last study involved a big number of patients in contrast to our study which recruited a small number of patients because of difficulties in following up patients , other studies which shared Virchow and Bachert view (15,16) who showed that adding Montelukast to the controller therapy of patients with mild to moderate asthma and allergic rhinitis improves asthma control. The best response was in the group who were on Montelukast and Beclomethasone and this could be explained by the additive effect of both beclomethasone and Montelukast as beclomethasone targets cytokines and Montelukast targets cysteinyl leukotriense and this agrees with a study done by Vaquerizo et al who stated that adding Montelukast to inhaled steroids typically leads to an improvement in asthma control (17). The rhinitis symptoms were improved on Montelukat as 81.3% in asthmatics on salbutamol and 82.4% in asthmatics on salbutamol and beclomethasone and this agrees with other studies by Togias et al(18) and by Lagos et al (19).

Conclusion:

Montelukast improved day ,night time symptoms , FEV1 and FEF25-75% values,but the response percentage regarding day , night time symptoms and the percentage of change in FEV1 and FEF25-75% values ,though they showed an improvement,but it was statiscally not significant in relation to the presence or absence of rhinitis symptoms.Rhinitis symptoms showed a significant statiscal improvement on Montelukast treatment.

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