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Prevalence of Montelukast Use as an Add-On Therapy among Iraqi Asthmatics on Treatment Attending Al-Kindy Teaching Hospital and Al-Zahraa Center of Asthma and Allergy

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Abstract

BACKGROUND: Montelukast (Singulair) is a cysteinyl leukotriene receptor antagonist, used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergic rhinitis and asthma, also used for exercise-induced bronchospasm.

AIM: This study was performed to determine the prevalence of Montelukast use as an add-on therapy among Iraqi asthmatic patients on treatment. Comparing the effectiveness of regimens with and without montelukast.

METHODS: This descriptive cross-sectional study was carried out on 73 Iraqi asthmatic patients on treatment of both sexes with age range (18-60) years old, attending Al-Kindy Teaching Hospital and Al-Zahraa Centre of Asthma and Allergy, Baghdad, for the period between February and March 2017. A questionnaire was specifically prepared to meet the objectives and was used to collect the data of the study.

RESULTS: There was a significant statistical reduction of frequency in asthmatic attacks after Montelukast treatment (p-value < 0.05). Out of 73 patients, 39 were males, and 34 were females, 46 were jobless, 37 were married, 63 were urban residents, 63 were educated. Prevalence of exacerbation factors was as following: infection was found in 60.3% of the patients, exercise in 57.5%, dust in 72.6%, smoking in 60.6%, food in 24.7%, others (stress, perfumes) in 20.5%. The prevalence of Montelukast use in this study was 46% (34 patients). Out of 34 patients using Montelukast, 28 were using inhaled salbutamol, 5 were using oral salbutamol, 15 were using inhaled corticosteroids, 9 were using systematic corticosteroids, 2 were using xanthines, and 6 were using ketotifen.

CONCLUSION: Montelukast was used as add-on therapy with the inhaled corticosteroids to reduce the required dose of inhaled corticosteroids also the use of Montelukast lead to reduced number of exacerbations which will be reflected on the use of inhaled salbutamol and systematic corticosteroids. Also, Montelukast was superior to xanthines and ketotifen as an add-on therapy.

Introduction

Asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, dyspnea, chest tightness, and coughing, especially at night or early morning [1]. An estimated 300 million people worldwide have asthma, with 250,000 annual deaths attributed to the disease [2]. This prevalence of asthma is expected to increase from 300 to 400 million by 2025 [3]. In Iraq, about 200,000 patients per year with asthma are either hospitalised or treated in an emergency room. Prevalence of asthma in the adjacent countries to Iraq includes 5.6 % in Saudi Arabia and 8.5 % in Kuwait [4], [5].

The major etiologic factors of asthma are a genetic predisposition to type 1 hypersensitivity (atopy) and bronchial hyperresponsiveness to a variety of stimuli. In asthma, all cells of the airway are involved and become activated. Included are eosinophils, T cells, mast cells, macrophages, neutrophils, epithelial cells, fibroblasts, and bronchial smooth muscle cells [6]. Activation of these cells leads

to release of proinflammatory cytokines and mediators [7]. The risk factors for development of asthma include genetics, prenatal tobacco smoke (maternal smoking), prenatal diet and nutrition, prenatal antibiotic use (maternal use), mode of delivery, family size and the number and order of siblings, exposure to environmental tobacco smoke, socioeconomic status, viral infections and antibiotic use [8]. Also, there is asthma-related to workplace exposures [9].

Montelukast (Singulair) is a cysteinyl leukotriene receptor antagonist used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies, also used for exercise-induced bronchospasm. It acts by blocking the action of leukotriene D4 (and secondary ligands, leukotrienes C4 and E4) on the cysteinyl leukotriene receptor 1 (Cys-LTR1) in the lungs and bronchial tubes by binding to it [10]. It is a controller drug that shouldn't be used for immediate bronchodilation. It is usually taken once a day with or without food.

Corticosteroids effect is mediated by their ability to inhibit the production of inflammatory cytokines, potentiation of effects of B-agonists, but their most important action is inhibition of infiltration of asthmatic airways by lymphocytes, eosinophils, and mast cells [11]. The beta-2 adrenergic agonists are potent bronchodilators that are widely used in the management of bronchial asthma. These agents act by binding to the beta-2 adrenergic receptors on the smooth muscle of bronchial tissue, relieving bronchospasm and reducing airway resistance [12].

There are three important methylxanthines (theophylline, theobromine and caffeine). Methylxanthines act by inhibiting several members of phosphodiesterase family enzymes, especially PDE4. Inhibition of PDE4 results in higher concentration of cyclic adenosine monophosphate (CAMP). CAMP is responsible for relaxation of airway smooth muscle [13].

Ketotifen is a controller drug which inhibits the release and activity of mast cell and basophil mediators, including histamine, neutrophil, and eosinophil chemotactic factors, arachidonic acid metabolites (prostaglandins and leukotrienes) [14]. Oral ketotifen has been used in patients with asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis.

This study was performed to determine the prevalence of Montelukast use as an add-on therapy among Iraqi asthmatic patients on treatment comparing the effectiveness of regimens with and without montelukast.

Material and Methods

This descriptive cross-sectional study was carried out on 73 Iraqi asthmatic patients on treatment (patients taking Montelukast were included in the study), of both sexes with age range (34.18 ± 14.84), attending Al-Kindy Teaching Hospital and Al-Zahraa Centre of Asthma and Allergy, Baghdad, for the time period between February and March 2017. Patients were excluded if they have the pregnancy, metabolic disease, and psychiatric condition. The diagnosis of facial palsy was a clinical diagnosis done by an internal medicine specialist. After obtaining the formal approval from the Scientific and Ethical Committee in Al-Kindy College of Medicine, University of Baghdad, a questionnaire was specifically prepared to meet the objectives and was used to collect the data of the study. After obtaining verbal consent from each patient, an interview using the questionnaire was conducted. The data were prepared as frequencies, relative frequencies, charts, mean ± Standard deviation, Chi-square test and paired sample t-test were used for statistical analysis using SPSS program version 17. P-value < 0.05 was used as level of significance.

Results

Seventy-three patients participated in the study. Data from all of them were included in the analysis.

Table 1 shows the number and percentage of asthmatic patients in each demographic characteristic like gender, occupation, marital status, address, and educational level.

Males and females were nearly equal in number; jobless patients were more than patients who have a job, urban residents were much more than rural ones, married and unmarried patients are much nearly equal, educated patients were much more than non-educated ones.

Table 1: No. of asthmatic patients in different demographic characteristics

		Frequency	Relative frequency (%)
Gender	Male	39	53.4
	Female	34	46.6
Occupation	Job	27	37
	Jobless	46	63
Address	Rural	10	13.7
	Urban	63	86.3
Marital status	Married	37	50.7
	Unmarried	36	49.3
Educational level	Educated	63	86.3
	Uneducated	10	13.7

Table 2 shows the number and percentage of asthmatic patients in each age group. Age groups were (18-25), (26-40), (41-54), and (55-60) (years). The group which contained the largest number of patients was (18-25) years. The group which contained the least number of patients was (41-54) years.

Table 2: Number of asthmatic patients in different age groups (years)

Age groups (years)	Frequency	Relative frequency (%)
18-25	35	47.9
26-40	15	20.5
41-54	10	13.7
55-60	13	17.8
Total	73	100.0

Table 3 shows the number and percentage of asthmatic patients in each disease duration category. Disease duration categories were, < 15 years, (16-30) years, (31-44) years, (45-58) years. Disease duration category which contained the largest number of asthmatics was (< 15 years). Disease duration category which contained the least number of asthmatics was (45-58) years.

Table 3: Disease duration (years) and no. of asthmatic patients in each category

Disease duration (years)	Frequency	Relative frequency (%)
< 15	33	45.2
16-30	26	35.6
31-44	11	15.1
45-58	3	4.1
Total	73	100.0

Figure 1 shows the percentage of asthmatic patients who have certain exacerbation factors like infection, exercise, dust, smoking, food and others (stress, perfumes). Most prevalent one was dust while the least prevalent factors were other factors (stress, perfumes).

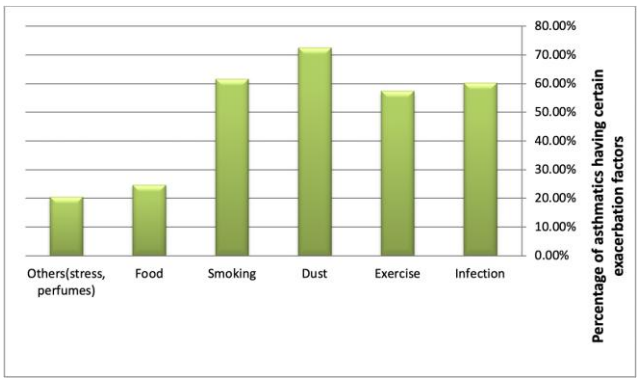

Figure 1: Prevalence of exacerbation factors

Figure 2 shows the percentage of asthmatics who use Montelukast versus those who don't use it.

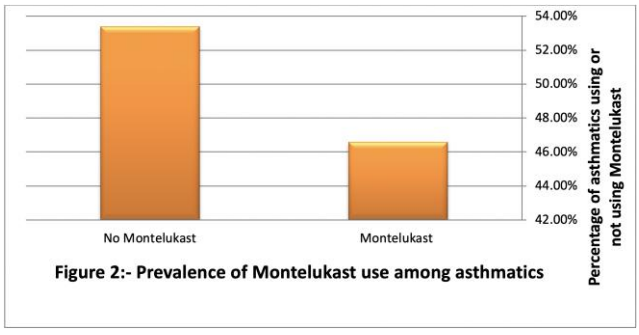

Figure 2: Prevalence of Montelukast use among asthmatics

Table 4 shows the number of asthmatics who use Montelukast in different age groups, versus those who don't use it. The age groups were (18-25), (26-40), (41-54), (55-60) years.

Table 4: Montelukast use in different age groups (years)

Age groups (years)	Montelukast use		Total
	Yes	No	
18-25	10	25	35
26-40	6	4	10
41-54	8	7	15
55-60	10	3	13
Total	34	39	73

Table 5 shows the number and percentage of asthmatic patients who use certain drugs with Montelukast, also shows the number and percentage of asthmatics who don't use these drugs with Montelukast. Most of the patients used inhaled salbutamol with Montelukast. The very small percentage used xanthines with Montelukast.

Table 5: No. of asthmatic patients using other drugs with Montelukast

		Frequency	Relative frequency (%)
Inhaled salbutamol	No	6	17.6
	Yes	28	82.4
Oral salbutamol	No	29	85.3
	Yes	5	14.7
Systematic corticosteroids	No	25	73.5
	Yes	9	26.5
Inhaled corticosteroids (ICS)	No	19	55.9
	Yes	15	44.1
Xanthines	No	32	94.1
	Yes	2	5.9
Ketotifen	No	28	82.4
	Yes	6	17.6

Table 6 shows the mean of asthmatic attacks/month before Montelukast use and the mean of asthmatic attacks/month after Montelukast use. The asthmatic attacks/month were significantly reduced after Montelukast use, as p-value was < 0.05.

Table 6: Comparison between the frequency of asthmatic attacks before and after Montelukast use in terms of means

	mean of attacks/month
Attacks/month before Montelukast use	6.47 ± 2.415
Attacks/month after Montelukast use	2.29 ± 1.169

Discussion

In Table 1, most of this study asthmatics were living in urban areas, urban areas are known to have more industrialization and pollution, and this agrees with a study done by Hirshon J. et al., (2006), in which Maryland showed the highest rates of emergency department visits for asthma in urban areas [15].

In Figure 1, the infection was an exacerbation factor in more than half of the asthmatics in this study, this agrees with a study done by K G Nicholson et al., (1993), in which it was concluded that respiratory infections especially viral infections are commonly

associated with asthmatic exacerbations [16]. Half of this study asthmatics were complaining from exercise as an exacerbation factor. Exercise-induced bronchospasm has been reported present in as few as 40% and as many as 90% of patients with asthma. In current study 34 patients were taking Montelukast, and Montelukast provided significant protection against exercise-induced bronchospasm as soon as 2 hours after a single oral dose, with persistent benefit up to 24 hours [17]. Majority of this study asthmatics were complaining from dust as a triggering factor for asthmatic exacerbations, according to a study conducted by Woong Park, Hee Lim (2005), it was concluded that dust events impact on the respiratory symptoms of subjects with bronchial asthma, and ambient air pollution, particularly elevated particulate matter < 10 um in diameter, might be one of the aggravating factors [18]. Smoking was an exacerbation factor in more than half of the study asthmatics, A finding that agrees with a review conducted by Stapleton, Howard-Thompson (2011)

In Table 5, the majority of asthmatics who use Montelukast were also using inhaled salbutamol, but a quarter of asthmatics who use Montelukast was not using inhaled salbutamol. According to a systematic review done by Zhang, Jia (2014), it was found that in comparison with placebo, adults with chronic asthma receiving Montelukast had significantly reduced number of exacerbations and this would be reflected on the use of inhaled salbutamol [20]. Only a small percentage of asthmatics were using oral salbutamol in addition to Montelukast, the difference in percentages between those using inhaled salbutamol and those using the oral one maybe due to the fact that oral salbutamol is less effective, having slower onset and more side effects than inhaled salbutamol [21]. More than half of the asthmatics using Montelukast, were not using inhaled corticosteroids. According to a study conducted by Andrew McIvor, Kaplan (2009), it was concluded that Montelukast is an effective alternative to inhaled corticosteroids in patients with mild asthma only. Others, who use Montelukast with inhaled corticosteroids, can use lower doses of inhaled corticosteroids in the presence of Montelukast. This agrees with previous studies, such as one performed by AL-Salami, Zaid (2011). Most of this study asthmatics using Montelukast, were not using xanthines, only very small percentage (5.9%) were using xanthines in addition to Montelukast. According to a study conducted by Shah (2004), it was concluded that the use of Montelukast along with inhaled bronchodilators and corticosteroids has a superior effect than addition of an oral sustained – release theophylline (a xanthine), on clinical and pulmonary function parameters in patients of chronic bronchial asthma [24]. Only a few asthmatics were using ketotifen with Montelukast (17.6%). According to a study performed by Al-Hamdani (2010), ketotifen and Montelukast were compared to each other and in conclusion, both ketotifen and Montelukast showed significant changes in asthma symptoms and pulmonary function tests after one month of treatment, but the changes were more significant with Montelukast group compared with ketotifen group and this indicated that Montelukast was more effective than ketotifen in treatment of asthmatic patients [25].

In Table 6, asthmatic attacks/month were significantly reduced after the use of Montelukast, this result agrees with a systematic review done by Miligkos, Bannuru (2015), in which it was found that the administration of Montelukast to adults and adolescents with asthma significantly reduced the risk of an exacerbation (asthmatic attack) and improved asthma control compared with placebo [26].

In conclusion, montelukast can be used as an add-on therapy with the inhaled corticosteroids to reduce the required dose of inhaled corticosteroids to reach the sufficient control, also the use of Montelukast lead to reduced number of exacerbations which will be reflected on the use of inhaled salbutamol and systematic corticosteroids. Also, Montelukast has a superior effect than xanthines and ketotifen as an add-on therapy.

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