INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

LONG-ACTING BETA2-AGONISTS VERSUS LEUKOTRIENE RECEPTOR ANTAGONIST AS ADD-ON THERAPY TO CORTICOSTEROIDS FOR CHRONIC ASTHMA MANAGEMENT IN PATIENTS OF KARACHI, PAKISTAN

Safila Naveed*, Safa Akmal and Sameea Zubair
Jinnah University for Women, Karachi, Pakistan
*Corresponding Author Email: safila117@yahoo.com

Article Received on: 18/12/13 Revised on: 06/01/14 Approved for publication: 28/01/14

DOI: 10.7897/2230-8407.050208

ABSTRACT
Asthmatic patients are usually maintained with inhaled corticosteroids but if symptoms are appearing we need to manage asthma with add on therapy either with LABA or leukotriene receptor antagonist. To estimate which maintenance therapy is more effective among LABA with CS or LTRA with CS and which combination is more prescribed in asthmatic patients of Karachi. We take 20 asthmatic patients from diff hospitals of karachi and find out the no of patients were taking corticosteroids mono therapy. Corticosteroids with long acting beta two agonist, corticosteroids with leukotriene receptor antagonist for long term management of asthma. Out of 20 patients 2 patients were the age of below 6 years and all are receiving corticosteroids for maintenance, 5 patients come in the age group of 6- 12 years and among them 1 patient was receiving corticosteroid mono therapy for maintenance, 1 patient was receiving combination of LABA with corticosteroid and 3 patient were receiving combination of LTRA's with corticosteroids and the adult patients i.e. of age above 12, receiving corticosteroid combination with montelukast. Asthmatic patients are usually maintained with corticosteroids, if not maintained than add on therapy is started LABA should be added with corticosteroid but if the symptoms still continued after giving LABA then LTRA should be started but according to our result LTRA is more prescribed as maintenance therapy because of severe side effects associated with LABA. However LTRA is less effective than LABA but it is safe for long tern maintenance and can be give prophylactically to prevent from asthmatic symptoms.
Keywords: Asthma, Corticosteroids, Long Acting Beta two Agonist, Leukotriene Receptor Antagonist.

INTRODUCTION

Asthma is a common chronic disorder of the airways that involves a complex interaction of airflow obstruction, bronchial hyper responsiveness and an underlying inflammation. This interaction can be highly variable among patients and within patients over time.[1]

Asthma is a global problem with an estimated 300 million affected individuals across the globe. In Pakistan Approximately 10 million people visit hospitals every year with symptoms of asthma while it's is estimated that is more common in developed countries. In Pakistan its prevalence is estimated to be 5 % of the total population, of which 5 % of the sufferers are children according to a recent study conducted in 2002. Three hundred million people across the world are afflicted with the disorder with 180 million deaths annually.[2] Asthma is a chronic disorder, in most of the patients once it occurs needs to be maintained throughout the life. Drugs for the relief of asthma are short acting beta 2 agonists along with corticosteroids, after relieving from severe symptoms asthma should be maintained for long term. The medication used for maintenance is long acting beta 2 agonist along with inhaled corticosteroids or leukotriene receptor antagonist with inhaled corticosteroids or corticosteroids as mootherapy. All levels of persistent asthma require daily anti-inflammatory treatment, and the safest, most effective treatment for patients who have persistent asthma is inhaled corticosteroids (ICSs). Although steroids may be given orally or parenterally, and numerous non steroidal medications are available for treating persistent asthma, ICSs are the treatment of choice. Even when ICSs are given daily over a long period of time, they have less toxicity than oral or parenteral steroids administered only occasionally. The exact mechanism of action by which ICSs decrease airway inflammation is not fully. However, the effect is believed to occur through a variety of pathways. ICS molecules do not need assistance to enter the respiratory epithelial cell, but they must bind to the glucocorticoid receptor to enter the nucleus of that cell. In the nucleus, the ICS-receptor complex promotes transcription of genes encoding proteins (IL-10) that decrease inflammation and inhibits transcription of genes encoding proteins (IL-4, IL-5, IL-13, and tumor necrosis factor-alpha) that increase inflammation. ICSs also reduce cytokine production of pro inflammatory cells, such as mast cells, eosinophils and T-lymphocytes. In addition, ICSs may increase the concentration of beta-adrenergic receptors on the airway smooth muscle cells and prevent down regulation by beta-adrenergic agonists. ICSs are indicated as first-line therapy for chronic treatment of patients who have all severities of persistent asthma and to reduce or eliminate the need for systemic corticosteroids (oral or parenteral) during acute asthmatic attacks. Persistent asthma requiring ICS treatment usually is apparent clinically. However, many physicians may not initiate ICS treatment because they do not recognize the subtle symptoms of persistent asthma, they fail to obtain pulmonary function tests when suspicion is adequate to warrant testing, or they miss the need for ICSs in the infant or young child whose asthma is hard to classify as persistent and who is too young for pulmonary function testing.[3] Long-acting inhaled beta 2-agonists are used on a daily basis to control moderate and severe persistent asthma. The Canadian Thoracic Society (CTS) and the U.S. National Asthma Education and Prevention Program (NAEPP) recommend using them only as an addition to inhaled corticosteroids.[4,5] Long-acting inhaled beta 2-agonists enhance the corticosteroids' anti-inflammatory action for controlling asthma and preventing asthma attacks. They should not be used as a substitute for inhaled corticosteroids.[4] They have a

bronchodilator effect when broncho motor tone (the state of airway smooth muscle contraction or relaxation regulating airway calibre) is low, and a protective (or "airway stabilizing") effect with increased broncho motor tone. Long-acting beta agonists are not rescue medicines and do not relieve sudden asthma symptoms. They are often used in people who have asthma symptoms at night or used to prevent exercise-induced asthma symptoms. A LABA relaxes smooth muscle lining the airways of your lung and causes your airways to open up. As a result, you begin to experience fewer symptoms. The effects of a LABA can last 5 to 12 hours depending on how frequently you use this inhaler. Importantly, a LABA does not decrease any of the underlying inflammation associated with asthma. Long-acting beta-agonists may cause tremor, rapid heartbeat, palpitations, low potassium, elevated blood pressure, headache and dizziness or nervousness. Throat and upper airway irritation can also occur. Elderly patients and those with heart disease should discuss their condition with their regular doctor prior to using medications.[6] Leucotriene modifiers, including leucotriene receptor antagonists (LTRA), are a relatively new class of anti asthmatic drugs. Evidence exists that LTRA, by blocking the leucotriene receptors of the smooth airway muscles, reduce airway eosinophilic inflammation and alleviate symptoms of airway obstruction. Many clinical trials have shown LTRA to be effective in asthma therapy. They also have the advantage of being administered orally. However, as inhaled corticosteroids (ICS) are more effective than LTRA in reducing asthma exacerbations, ICS remain the first choice in asthma management whereas LTRA are recommended as an add-on therapy to ICS.[7] Montelukast is a prototype, selective, pharmacological antagonist of type 1 cysteinyl leukotriene receptors (CysLT1Rs). These G protein–coupled receptors recognize the CysLTs LTD4 and LTC4/LTE4 expressed on the plasma membrane of structural (epithelial, fibroblasts/myoblasts,smooth muscle) and inflammatory cells, including neutrophils, monocytes/macrophages, mast cells, basophils, dendritic cells, and lymphocytes.[8] Montelukast effectively antagonizes the proasthmatic/pro inflammatory activities of CysLTs and forms part of numerous international guidelines for asthma therapy.[9]

Methodology

The study was conducted in vicinity of Karachi, on the asthmatic patients. We focus on the medications given to the asthmatic patients particularly medications given for the maintenance for asthma. Patients are categorized according to the age group i.e. children of age below 6 years, age between 6 years-12 years and patients of age above 12 years. Then check for their medications i.e. patient is either is given with mono therapy of corticosteroids or combination of corticosteroids either with LABA or LTRA's.

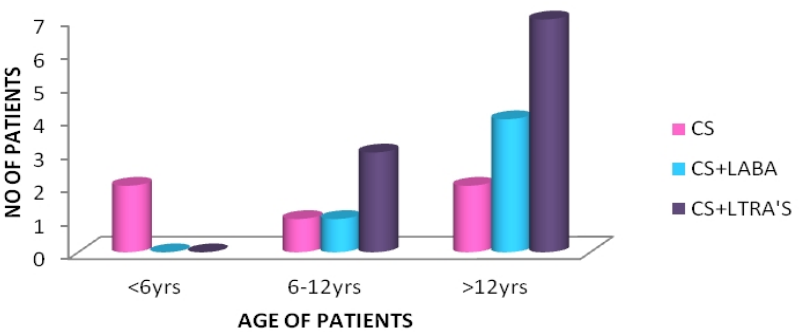

Figure 1: Prescribing maintenance medication in different age group

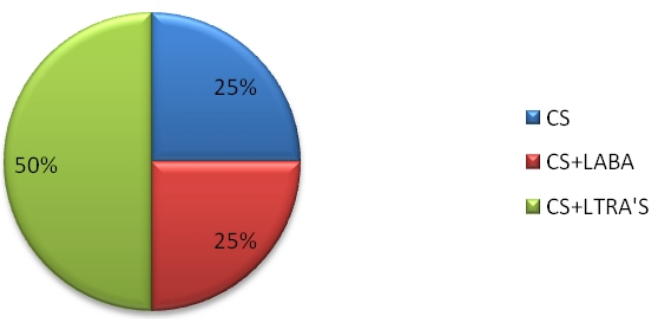

Figure 2: Prescribing maintenance medication given in asthma

CS = corticosteroids, LABA = long acting beta$_2$ agonist, LTRA'S = leukoterine receptor antagonists

RESULT

Out of 20 patients 2 patients were the age of below 6 years and all are receiving corticosteroids for maintenance, 5 patients come in the age group of 6- 12 years and among them 1 patient was receiving corticosteroid mono therapy for maintenance Figure 1. One patient was receiving combination of LABA with corticosteroid and 3 patients were receiving combination of LTRA's with corticosteroids and the adult patient's i.e. of age above 12, receiving corticosteroid combination with montelukast. In the chart below 50 % of patients were given with Corticosteroids with LTRA'S, 25 % of patients with corticosteroids with LABA and 25 % of patients are maintained with corticosteroids mono therapy Figure 2.

DISCUSSION

A stepwise approach to pharmacologic therapy is recommended to gain and maintain control of asthma in both the impairment and risk domains**,** patient with severe asthmatic effect needs to be treated with rapid acting b2 agonist along with corticosteroids Because asthma is a chronic inflammatory disorder of the airway, persistent asthma is most effectively controlled with daily long-term control medication directed toward suppression of airway inflammation.[10] Inhaled corticosteroids are considered the most potent and effective long-term control treatment and have been documented to reduce asthma severity symptoms and control, improve quality of life, improve lung function, prevent exacerbations, reduce emergent health services utilization, and reduce the risk of death due to asthma. They have been shown to more effectively improve asthma control compared to any other single controller agent. Patients who continue to experience asthma symptoms despite taking regular inhaled corticosteroids (ICS) represent a management challenge. Leukotriene receptor antagonists (LTRA) and long-acting beta$_2$-agonists (LABA) agents may both be considered as add-on therapy to inhaled corticosteroids (ICS). In asthmatics inadequately controlled on low doses of inhaled steroids, the addition of LABA is superior to LTRA for preventing exacerbations requiring systemic steroids, and for improving lung function, symptoms, and the use of rescue beta$_2$ agonist., but according to the results of this study conducted in karachi 10 patients were taking LTRA'S combination with corticosteroids however only 5 patients were given with combination of LABA with corticosteroids, and 5 patient's symptoms were sub sided by corticosteroid mono therapy. The efficacy of montelukast may be explained by its anti-inflammatory effect, which is the hallmark of asthma therapy. The importance of reducing eosinophilic inflammation was demonstrated in several studies. Despite the fact that this therapeutic principle seems to be addressed with montelukast, its impact on symptom reduction and quality of life is weaker compared with LABA, at least in the medium term. Long-acting beta agonists exert their therapeutic effect through sustained smooth muscle airway relaxation. In the light of the current safety discussion, montelukast may be a treatment alternative in asthma that is sub optimally controlled with ICS. The disadvantage of slower symptom relief with montelukast may be counterbalanced by possibly better long term safety. LABA has serious adverse effects such as cardiac problems, tachycardia and tremor, and they also affect serum potassium and glucose. Long acting beta$_2$ agonists increase the risk for asthma-related intubations and deaths, even when used in a controlled fashion with concomitant inhaled corticosteroids. At present, guidelines suggest that long-acting $b_2$agonists be added to inhaled corticosteroids in patients with moderate or severe asthma that is not well controlled with inhaled corticosteroids alone, but this approach might not in fact confer a meaningful health benefit compared with the use of other standard therapies. Long term trials are needed for a conclusive evaluation of the long term efficacy and safety of various alternative controller medications in patients with mild to moderate asthma. In those trials, possible efficacy relevant aspects such as patient age, co morbidities or ethnic group should be considered for study design and analysis. Also, patient acceptance and compliance for oral compared with inhaled preparations should be assessed in future studies as these factors may have a relevant impact on the difference between medium and long term studies.

CONCLUSION

By our study we conclude that the addition of montelukast to ICS improves control of mild to moderate asthma compared with ICS mono therapy. However, montelukast as add-on therapy to ICS is less effective than the addition of salmeterol with regard to most clinical outcomes, at least in the medium term. Because of the possibly better long term safety profile of montelukast compared with salmeterol, montelukast may be considered as an add-on treatment alternative in patients sub optimally controlled with ICS. These findings indicate that asthma treatment guidelines should be reassessed to clarify whether the current recommendations require modification.

REFRENCES

1. Essen Zandvliet EE, Hughes MD, Waalkens HJ, Duiverman EJ, Pocock SJ, Kerrebijn KF. Effects of 22 months of treatment with inhaled corticosteroids and/or beta-2-agonists on lung function, airway responsiveness, and symptoms in children with asthma. The Dutch Chronic Non-specific Lung Disease Study Group. Am Rev Respir Dis 1992; 146: 547-54. http://dx.doi.org/10.1164/ajrccm/146.3.547
2. Haahtela T, Jarvinen M, Kava T, Kiviranta K, Koskinen S, Lehtonen K. Comparison of a beta 2-agonist, terbutaline, with an inhaled corticosteroid, budesonide, in newly detected asthma. N Engl J Med 1991; 325: 388-92. http://dx.doi.org/10.1056/NEJM199108083250603
3. Dodds WN, Soler NG, Thompson H. Letter: Deaths in asthma. Br Med J 1975; 4: 345. http://dx.doi.org/10.1136/bmj.4.5992.345-c
4. Lougheed MD. Canadian Thoracic Society asthma management continuum—2010 consensus summary for children six years of age and over, and adults: Canadian Respiratory Journal 2010; 17(1): 15–24.
5. National Institutes of Health. National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma NIH Publication No 2007; 08–5846.
6. Salpeter S, Buckley N, Ormiston T, Salpeter E. Meta-analysis: effect of long-acting -agonists on severe asthma exacerbations and asthma-related deaths. Ann Intern Med 2006; 144: 904–912. http://dx.doi. org/10.7326/0003-4819-144-12-200606200-00126
7. Montelukast as add-on therapy to inhaled corticosteroids in the treatment of mild to moderate asthma: a systematic review , S Joos, A Miksch, J Szecsenyi, B Wieseler, U Grouven, T Kaiser, A Schneider; 2007.
8. Peters GM and Henderson WR. Leukotrienes. N. Engl. J. Med 2007; 357: 1841–1854. http://dx.doi.org/10.1056/NEJMra071371
9. Rabe KF. State of the art in beta2-agonist therapy: a safety review of long-acting agents. Int J Clin Pract 2003; 57: 689–697.

Cite this article as:

Safila Naveed, Safa Akmal and Sameea Zubair. Long-acting Beta2-agonists versus leukotriene receptor antagonist as add-on therapy to corticosteroids for chronic asthma management in patients of Karachi, Pakistan. Int. Res. J. Pharm. 2014; 5(2):41-43 http://dx.doi.org/10.7897/2230-8407.050208

Source of support: Nil, Conflict of interest: None Declared