Academic Sciences Asian Journal of Pharmaceutical and Clinical Research
Vol 5, Issue 2, 2012 ISSN - 0974-2441

Research Article

DRUG UTILISATION AND EVALUATION OF ADJUVANT THERAPY IN MILD TO SEVERE ASTHMA PATIENTS

A.ARUNSHIRWAIKAR[1], N.PREMKUMAR*. A.SARALA[2], K.BHASKARAN[3], P.L.RAJAGOPAL[4]

[1] College of Pharmacy, Gulf Medical University, Ajman, UAE,*Department of Pharmacology, Pariyaram Medical College, Kannur, Kerala, India,[2] Department of Medicine, Pariyaram Medical College, Kannur, Kerala, India,[3] Department of Pharmacology, Pariyaram Medical College, Kannur, Kerala, India,[4] Department of Pharmacognosy, Academy of Pharmaceutical sciences, Kerala,
Email: prem.n1977@gmail.com

Received: 12 January 2012, Revised and Accepted: 11 March 2012

ABSTRACT

Objective: The primary objective of this study was to determine drug utilization and evaluation of adjuvant therapy in mild to severe asthma patient and whether adjuvant therapy like montelukast, an oral leukotriene receptor antagonist and theophyline, provides additional clinical benefit with prescribed asthma therapy.
Study design: The present study was an open labeled study conducted for a period of two years with mild to severe asthma patients in a tertiary care hospital and Private clinics in North Malabar region of Kerala. A total of 64 patients with mild to severe asthma were included in this study.
Results: In these 64 patients, 12.5% received adjuvant therapy; in these 9.5% received montelukast.LTa added baseline PFT (1.59± 0.66) and 90th day follow-up PFT (2.66±0.67) showed improvement (1.07unit) and QoL improvement (27.46unit). LTa included asthma therapy had showed -0.62 units clinical improvement in pulmonary function test and -7.49 units quality of life, when compared to other adjuvant therapy like theophyline.
Conclusion: all treatments were well tolerated, adjuvant therapy in bronchial asthma patients was found to be minimal in this area, including montelukast add on asthma therapy, patients showed additional improvement in quality of life comparing with theophyline.

Keywords:

INTRODUCTION

Asthma literally means 'panting' derived from Greek word 'panos'. More than 2000 years ago, Hippocrates used the word asthma to describe episodic shortness of breath; however, the first clinical description of the asthmatic patient was made by Aretaeus in the second century. Asthma is a major, chronic airway disorder and is a serious public health problem in countries throughout the world. Asthma affects people of all ages, can be severe, and is sometimes fatal. Asthma is a complex process that result from airway inflammation and manifests as bronchoconstriction. Infiltration of the airway mucosa and lumen by activated inflammatory cells, along with release of mediators, can occur Leukotriene inhibitors, particularly leukotriene receptor antagonists, have been added in patients already taking inhaled GCS, with consistent improvements in lung function (Reiss *et al.,* 1998). An inhaled corticosteroid-sparing effect of one leukotriene receptor antagonist has been demonstrated in moderate to severe asthma, but these results are controversial (Robinson *et al.,* 2001).

The global burden of asthma is considerable. Its effect include reduced quality of life, lost productivity, missed school days, increased health care coast, the risk of hospitalization and even death. An estimated 13.9 million visits to physician offices and hospital outpatient department, 1.9 million emergency department visits and 484,000 hospital admissions were attributed to asthma in 2002.Roughly 14.7 million school days and 11.8 million work days were missed in the United States that year because of asthma[3]. Asthma is more common in children than adults. Chemical mediators known as leukotriene are believed to play a major role in this process. At present, inhaled corticosteroids (ICS) are the pharmacologic cornerstone of asthma management. However, asthma control may remain suboptimal when relying on ICS because of problems with compliance, poor inhaler technique and concerns about the side effects of steroids; additional agents are often required to control symptoms.

LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRA) SUPPORTING REVIEWS, montelukast, provide a safe and effective additional anti-inflammatory treatment option. There is particular benefit for patients with asthma and concomitant allergic rhinitis. Areas covered: Montelukast has been well studied through rigorous clinical trials. A thorough review of the literature has been undertaken to assess the evidence supporting the use of LTRAs. This review focuses on the role of montelukast not only as monotherapy but also as add-on therapy to ICS in the adult asthma population, as well as adult asthmatics with concomitant allergic rhinitis. In addition, there is often some discrepancy between the evidence generated in the idealized asthma patients recruited into randomized clinical trials and results obtained in the real-life setting. This review assesses recent clinical trials evaluating the real-life evaluation of montelukast, achieved mainly through open-label observational studies. Oral LTRA bring remarkable ease of anti-inflammatory treatment administration and symptom improvement with minimal side effects to the management of adult asthma. Basic asthma mechanisms and much-valued scientific groundwork has been identified by exploring target asthma treatment with anti-leukotriene therapy. This will have a significant impact in the future development of targeted asthma therapies as well as the current management of asthma and other inflammatory medical conditions. Recommendations from both national and international guidelines on the use of leukotriene receptor antagonists are broadly similar[5] .The new British guideline on the management of asthma is evidence-based, using well defined methodology[7] to evaluate all relevant published papers up to the end of September 2001. At step 3, inhaled long acting β_2 agonists are the first choice add-on therapy to low or moderate dose inhaled corticosteroids.

Adding a leukotriene receptor antagonist represents a second line option. For patients at step 4 who remain inadequately controlled on these combinations of treatments, possible interventions include increasing the inhaled corticosteroid dose to 2000 µg daily or adding on a leukotriene receptor antagonist, a long acting oral $\beta_2$agonist, or a sustained release theophyline. Unfortunately no clinical trials of the benefits and safety of combinations of add-on therapies exist to guide management. Two papers published in this month's Thorax provide new information about several issues relating to the use of leukotriene receptor antagonists as add-on therapy to inhaled corticosteroids in adult asthma[8,9].The clinical efficacy of pharmacological drugs for asthma depends on their ability to decrease symptoms, improve lung function, and reduce asthma exacerbations.[7] The leukotriene receptor antagonist montelukast has been shown to improve symptoms and lung function" and several short to medium term studies have reported modest inhaled corticosteroid sparing effects[11,12]. The ability of montelukast to influence exacerbation rates in adults has not previously been assessed. The leukotriene receptor antagonist zafirlukast administered at an unlicensed dose of 80 mg twice daily to patients with severe persistent asthma receiving high dose inhaled

corticosteroids at a dose of 1200 µg daily for 6 weeks reduced exacerbations, improved symptoms, lung function and reduced β_2 agonist usage." A Cochrane systematic review of published and unpublished randomized controlled trials identified up to 2001 concluded that there was insufficient evidence, using the rate of exacerbations of asthma requiring rescue systemic corticosteroids as the primary outcome measure, to support the use of leukotriene receptor antagonists as add-on therapy to inhaled corticosteroids compared with doubling the dose of inhaled corticosteroid[14].

In this issue of Thorax Vaquerizo and colleagues[8] report the results of a 16- week randomized controlled trial in 639 adults with asthma inadequately controlled on inhaled budesonide at doses ranging from 400 µg to 1600 µg daily. Patients were randomized to receive either montelukast 10 mg or placebo and to continue on a constant dose of inhaled budesonide. The group receiving montelukast showed improvements in the primary end point (mild asthma exacerbation days) and in various secondary end points including symptom score, β_2 agonist use, and morning PEF. The results were independent of budesonide dose. This large well conducted study provides good evidence that the addition of a leukotriene receptor antagonist to low, moderate, and high doses of an inhaled corticosteroid reduces mild asthma exacerbations and improves other indices of asthma control. The efficacy of montelukast in reducing the rate of severe exacerbations was not addressed in this study. Previous studies have found that the efficacy of leukotriene receptor antagonists is less than that of inhaled long acting β_2 agonists as an add-on treatment to inhaled corticosteroids when assessed by changes in symptoms and lung functions '

A randomized trial of inhaled salmeterol in a dose of 50 µg twice daily compared with zafirlukast in a dose of 20 mg twice daily found that the long acting inhaled β_2 agonist was more effective in improving symptoms and lung function in adult patients with persistent asthma, the majority of whom were receiving inhaled corticosteroids[15]. A 12-week comparison of fluticasone 200 µg plus salmeterol 100 µg daily with fluticasone 200 µg plus montelukast 10mg daily[16] found that the former combination produced greater improvement in asthma control. A long term trial is indicated comparing the effectiveness of leukotriene receptor antagonists and inhaled long acting $\beta_2$agonists alone and in combination as add-on therapy to low to moderate doses of inhaled corticosteroids, with asthma exacerbation rates as the primary outcome measure.

METHODS

This was an open labeled study conducted for a period of two years with mild to severe asthma patients in a tertiary care hospital and Private clinics in North Malabar region of Kerala. A total of 64 patients with mild to severe asthma and age between 25-50 years were included in this study, in these 45 males and 19 were females. Pulmonary function tests(PFT) and Health related quality of life (HRQoL) were assessed in the beginning of the study for baseline and on every 15th, 30th,45th , 60th and 90th day, PFT, HRQoL and prescribed various asthma medications was documented. Adjuvant therapy like montelukast, an oral leukotriene receptor antagonist and theophyline provides additional clinical benefit were assessed with the help of PFT and HRQoL at end of the follow-up. Drug utilization of adjuvant therapy in asthma patients were assessed and documented.

RESULT AND DISCUSSION

The study population consisted of 64 patients of these 39 males and 25 females. Of these 64 patients, 56 patients were treated with β_2 agonist± steroids, 8(12%) were received adjuvant therapy (LTa and theophyline) shown in fig: 1 .All the three treatments had shown variable degrees of improvement in PFT and QoL from the baseline. Patients who were administered adjuvant therapy (LTa) had a baseline PFT of 1.59 and at 90th day was increased to 2.66 and baseline QoL 59.80 and at 90th day was reduced to 32.34and showed a decrease of 27.46 units had showed clinical improvements of 1.07 units in PFT and 27.46 units in QoL has been shown inFig:2 and Fig:3.Patients who were received without adjuvant therapy had improved only 1.69 units in and 34.95 units in QoL has been shown in table:1.LTa included asthma therapy had showed -0.62 units clinical improvement in Pulmonary function test and -7.49 units quality of life ,when compared to other adjuvant therapy like theophyline. Asthma therapy with theophyline had shown less improvement in lung function and quality of life when compared to other asthma therapies.

Table 1: Adjuvant therapy assessment during the study

Effectiveness assessment variables	Parameters	Baseline data	15th day	30th day	45th day	60th day	90th day
Pulmonary Function Parameters	Asthma therapy+LTa	1.59 ± 0.66	1.75 ± 0.67	1.88 ± 0.63	2.05 ± 0.68	2.42 ± 0.70	2.66 ± 0.67
	Asthma therapy+ Theophyline	2.07 ±0.80	2.25 ± 0.69	2.33± 0.66	2.45 ± 0.72	2.53 ± 0.78	2.68 ± 0.74
	Asthma therapy	2.25 ± 0.80	2.33 ± 0.69	2.45± 0.66	2.51 ± 0.72	2.79 ± 0.78	2.94 ± 0.74
SGRQOL Scores	Asthma therapy+LTa	59.80 ± 17.17	48.21 ± 17.01	39.52 ± 14.82	44.80 ± 21.11	35.47 ± 14.84	32.24 ± 14.12
	Asthma therapy+ Theophyline	59.33 ± 19.77	44.38 ± 19.14	35.49 ± 14.75	41.57 ± 24.31	29.25 ± 14.53	25.48 ± 13.48
	Asthma therapy	51.36 ± 19.89	31.30 ± 15.55	24.99 ± 11.96	31.27 ± 22.39	19.17 ± 10.62	16.39 ± 9.27

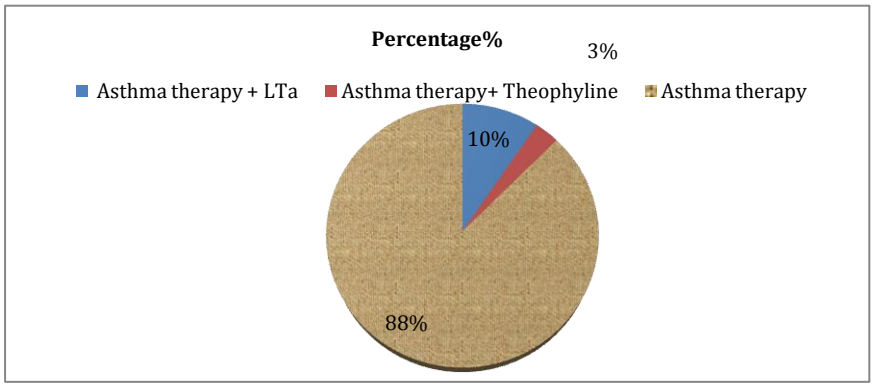

Fig 1: Drug Utilizations in asthma treatment

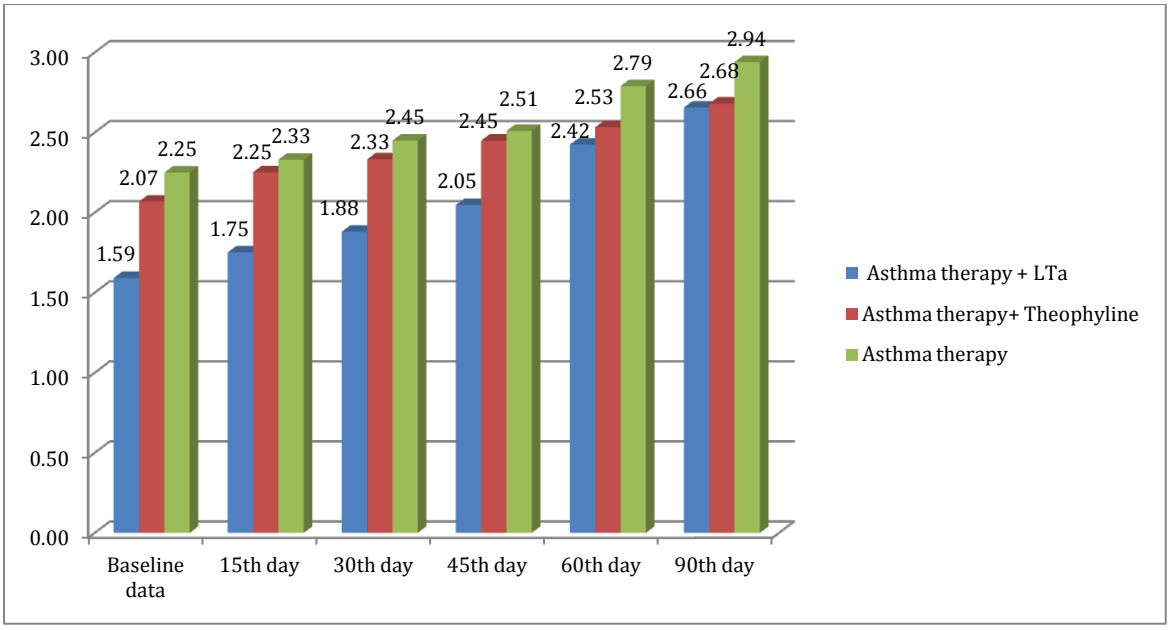

Fig: 2 Pulmonary Function Parameters

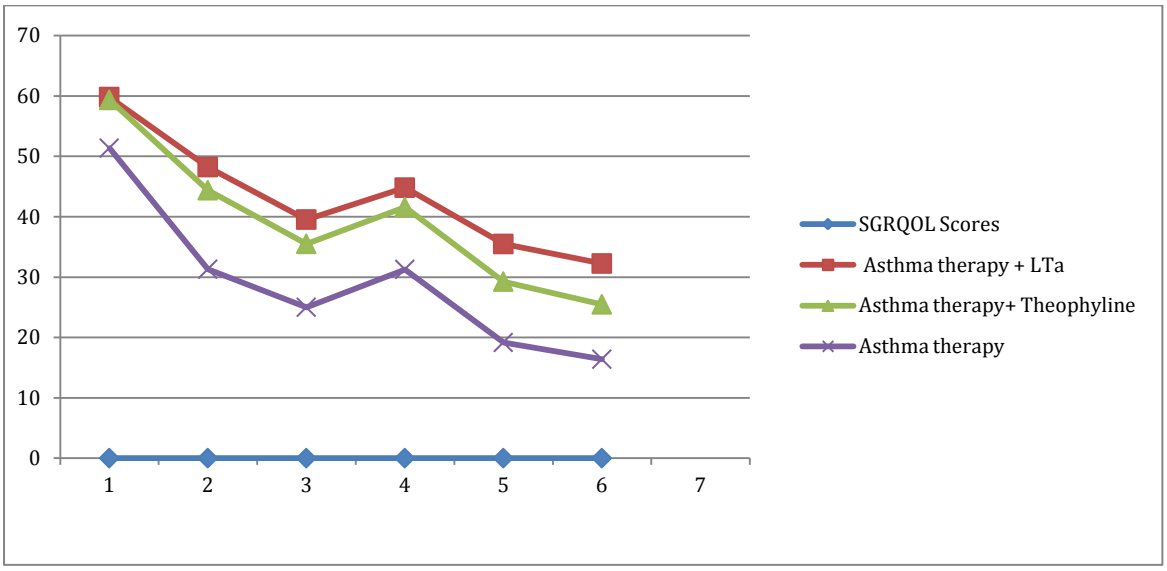

Fig 3: Quality of life parameters

CONCLUSION

All treatments were well tolerated, adjuvant therapy in bronchial asthma patients was found to be minimal in this area. Including montelukast add on asthma therapy, patients showed additional improvement in quality of life comparing with theophyline.

RECOMMENDATION

Leukotriene receptor antagonists add as adjuvant therapy in bronchial asthma treatment with mild to moderate patients. Health related quality of life assessment could be added as a standard way of evaluation of treatment outcomes especially in case of disease like asthma.

ABBREVIATION

Pulmonary Function Test (PFT)

Health Related Quality of life (HRQoL)

Leukotriene receptor antagonist (LTa)

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