

Role of Leukotriene Antagonists in the Treatment of Asthma Exacerbations

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ABSTRACT

Background: Asthma is a condition known for symptoms like wheezing and breathing problems. Asthma exacerbations, which are episodes of deteriorating asthma symptoms and lung function, continue to be the most common causes of patient hospitalization. These exacerbations are frequently treated with a variety of drugs, including corticosteroids, inhaled bronchodilators such as beta-2 agonists, and anticholinergics.

Mast cells and eosinophils produce a substance called leukotriene, which causes vascular leakage and other inflammatory responses that result in airway edema and remodeling. Leukotriene receptor antagonists (LTRA), such as Montelukast, in addition to being used in managing chronic asthma, have been shown to be effective in treating asthma attacks.

Methods: PubMed/Medline, Google Scholar, and other online database resources were screened until January 2023. 512 articles about asthma exacerbation and its management were found, of which 10 were included in our review article.

Results: A previous study on 117 children aged 2–5 years found no significant difference in improving peak expiratory flow in asthma exacerbation treatment between the Montelukast and placebo groups. In another study on 93 children randomly assigned to the montelukast or no-controller group, montelukast was beneficial in asthma treatment.

Regarding adults, there was no difference between oral montelukast and traditional treatment for managing acute asthma attacks in a study of 100 patients, most of whom were nonsmokers and female. In another study consisting of five double-blind, randomized, placebo-controlled trials, Zafirlukast has been shown to successfully reduce the risk of asthma exacerbations when used as a control medication in patients with mild to moderate asthma.

Conclusions: More research is needed to identify the treatment that is most effective in controlling exacerbations and preventing the irreversible changes in the patient's airways that are linked to asthma.

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Introduction

Asthma is a known chronic condition seen in children and adults with symptoms such as wheezing, breathing difficulty, and chest discomfort which can negatively impact the quality of life and cause a financial burden in addition to increasing mortality [1].

World Health Organization reported that in 2019 asthma afflicted around 262 million individuals and accounted for 455,000 deaths. A variety of variables, such as respiratory infections, dust mites, cigarette smoke, outdoor air pollution, airborne irritants, pets, mold, and changes in weather, may all play a part [2].

Acute asthma exacerbations are episodes of deteriorating asthma symptoms and lung function. During an asthma attack, the airway primarily becomes swollen and inflamed. Given the importance of this problem, asthma exacerbation remains one of the most frequent reasons for patient hospitalization. It is essential to approach asthma management, which can control symptoms and reduce emergency department visits and hospitalization depending on disease severity and appropriate medical therapy [3].

The Global Initiative for Asthma (GINA) states that the asthma cycle of care should involve regular assessment, treatment modification, and review [4].

Corticosteroids, which have anti-inflammatory characteristics, are important in the management of asthma and they have been associated with a decrease in mortality. Therefore, Inhaled corticosteroids (ICSs) should be used regularly by asthma patients [5]. However, corticosteroids are not responsible for all inflammatory pathways. Proinflammatory mediators – Cysteinyl leukotrienes play a big part in systemic corticosteroid non-responsiveness [6]. Leukotriene is an inflammatory mediator that is produced by eosinophils and mast cells in the respiratory system and leads to inflammatory responses such as bronchospasm by contracting the smooth muscles, bronchial hyperresponsiveness, and increased vascular leakage leading to edema and airway remodeling. Its production can also be boosted by respiratory viruses, especially rhinoviruses, and allergens [7, 8].

During an asthma exacerbation, a great amount of leukotriene is released by inflammatory cells (*Inhaled Corticosteroids and Leukotriene Modifiers in the Acute Treatment of Asthma Exacerbations - PubMed*, n.d.). Consequentially, blocking their effects by using leukotriene receptor antagonists will cause bronchodilation and relieve the symptoms. (Balzano et al., 2002). Leukotriene antagonists, such as Montelukast, have been used successfully in the treatment of mild persistent asthma as well as moderate asthma as adjuvant therapy or to reduce the ICS dose and side effects related to its long-term use [9, 10]. In addition to their effectiveness in managing chronic conditions, they have also been shown to be effective in treating asthma attacks and raising the forced expiratory volume in one second (FEV1) [7].

In this study, our goal was to review the role of leukotriene antagonists in the treatment of asthma exacerbations.

Result

According to the study, it showed that population of severe asthma with co existing non-ABPA and non-CF bronchiectasis; who were given LTRA therapy increased the beneficial effects in biological therapy. This in turn, as we can see further in the study, showed to improve the clinical control of asthma and also reduced the

inflammation assessed by FeNO biomarker. In different types of asthma included in the study, like aspirin-exacerbated, elderly asthma, smoking asthma, obesity associated asthma along with asthma comorbid with allergic rhinitis, LTRA therapy proved to be advantageous because of the reduction of FeNO biomarker. LTRA therapy acts on both eosinophilic and neutrophilic inflammatory pathway to control asthma exacerbation [11].

For control of asthma, LTRA are effective significantly in older females. LTRA and xanthine were considered as an alternative but were less preferred as compared to ICS-LABA [12].

Zafirlukast 20mg twice daily reduced the risk of asthma exacerbation along with the need of other anti-asthmatic therapies in mild to moderate asthma patients. This study also showed, the patients on Zafirlukast had less withdrawal symptoms compared to the group that were given placebo [13]

Montelukast therapy on study population had significant benefit in quality of life by improving overall symptoms of asthma. In the study, 125 patients (18.01%) had one or more adverse effects. The adverse events were headache (5.6%), fever (2.2%), fatigue (5.2%), abdominal discomfort (2.6%), URTI (1.4%), rash (1%) [14].

The study showed, Montelukast therapy significantly improved the overall quality of life except emotional function. Montelukast can be considered alternate or as an add-on to ICS/LABA in uncontrolled asthmatic patients. 1.8% participants withdrew the study due to adverse events [9].

In adult patients with mild to moderate persistent asthma, Montelukast improved quality of life Montelukast when administered once daily, was feasible and had upper hand to long term side effects of steroids. In 4 week trial, the mean \pm SD of overall QOL on AQLQ-S improved from 3.74 \pm 0.88 to 5.06 \pm 0.89 for montelukast group and from 3.58 \pm 0.92 to 4.71 \pm 0.97 for placebo group (p=0.02) [15].

In preschool children with asthma symptoms persisting more than once a month but less often once a week, Montelukast was proved to be an effective treatment. During study, 13 patients on Montelukast and 23 patients in no controller group experience asthma exacerbations respectively [15].

The study found, no beneficial effect of oral Montelukast over conventional treatment in management of asthma exacerbation in hospitalized patient admitted for 3-5 days. The treatment didn't show marked difference in symptoms, PEF, discharge rate, FEV1 and length of hospital stay between the subject and control group.

For diverse primary care patients, LTRA was considered equivalent to corticosteroids in first line therapy and to LABA as an add-on therapy. No significant difference was observed in real world effectiveness between LTRA and inhaled corticosteroids as first line controller therapy [16].

In mild to moderate cases of asthma leading to exacerbation was reduced significantly by treatment with Zafirlukast 20mg twice daily. The withdrawal was half in group treated with Zafirlukast than the placebo group [17].

Discussion

In both adults and children, montelukast significantly reduces the episodes of acute asthma exacerbations.

With different classes of drugs such as corticosteroids, bronchodilator, monoclonal antibodies being used in the treatment of Asthma, Leukotriene antagonists have their own unique role in the management. In a systematic review and meta-analysis, compared with placebo, leukotriene receptor antagonists lowered exacerbations in patients with chronic mild-to-moderate asthma either in the first line or add-on regimens. However, montelukast treatment was inferior to ICS and ICS plus LABA but with lower adverse effects [18].

Regarding pulmonary function tests in the adult population, there is a significant clinical improvement in the peak expiratory flow (PEF) as well as the forced expiratory volume in one second (FEV1) when comparing LRTA with placebo [19]. However, in the pediatric population, a study conducted in China in children aged 2 to 5 years demonstrated no significant differences in the values of FEV1 at admission and at discharge and PEF [20]. This finding is consistent with other studies, which also aimed children, and showed no benefit in FEV1 after taking montelukast [21].

The effects of LTRA are proven to be more effective in older and female patients than in the younger population [22-25].

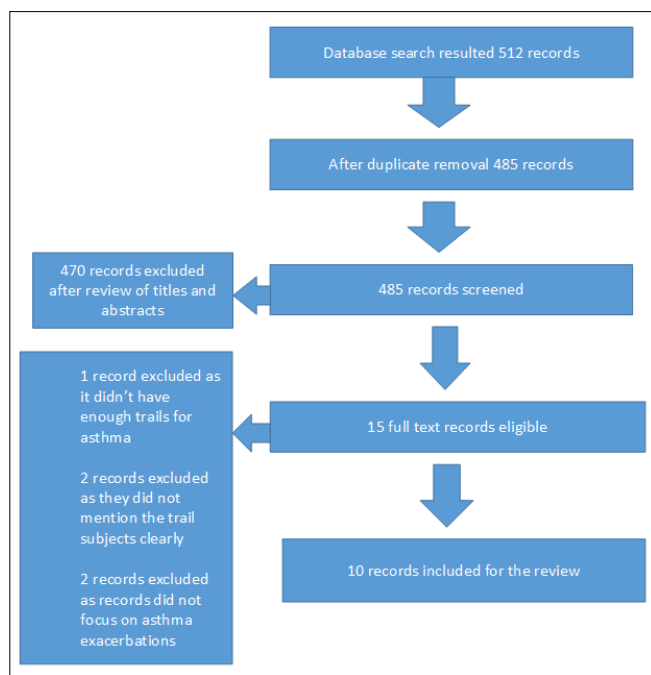


Figure 1: Flow Chart Showing the Records Selection

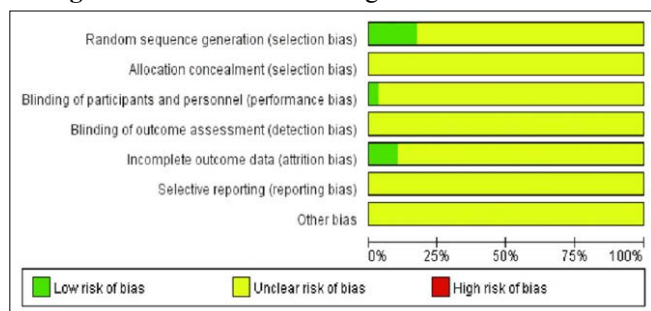


Figure 2: Possible Bias In Randomized Controlled Trials

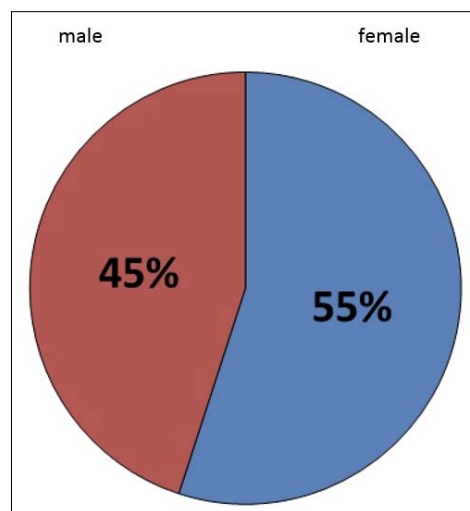


Figure 3: Distribution of Participants on Basis of Gender

Conclusion

LTRA therapy are useful in treating Asthma Exacerbation, but they aren't superior to ICS with or Without LABA. Usage of LTRA reduce Inflammation associated with Asthma and reduces chances of Exacerbation along with Less Side Effects. This is quite helpful in older and female patients than In young age group. Certain studies proved that LTRA with ICS is also an effective therapeutic treatment but effects of LTRA proved more effective in the elderly patients. However Further Clinical research is needed to determine which therapy can prevent Irreversible Changes of airways associated with asthma.

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