Mepolizumab for the Treatment of Chronic Asthma. A Meta-Analysis of Randomized Placebo-Controlled Trials

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INTRODUCTION
- Asthma is a progressive inflammatory disease which is a major cause of disability, health resource utilization and poor quality of life for those who are affected.
- Asthma is the most common chronic disease among children and young adults, particularly because of its early onset.
- It is estimated that more than 10% of asthma has an allergic background.
- About 50% of patients with severe asthma have allergic-asthmatic asthma.
- Current treatment for asthma suggested by Global Initiative for Asthma (GINA) guidelines includes several reliever and controller drugs, specially inhaled corticosteroids which reduce airway inflammation. Other drugs include β2 agonists and anti-leukotrienes.
- Interleukin-5 (IL-5) plays a key role in the pathogenesis of eosinophilic disorders including asthma.
- Mepolizumab is a fully humanized monoclonal antibody that binds to IL-5, and it may represent a useful therapeutic option to control exacerbations and improve quality of life in asthma patients with persistent airway eosinophilia and moderate to severe asthma.

OBJECTIVE
- To evaluate the efficacy and safety of mepolizumab compared to placebo in patients with chronic asthma.

MATERIALS AND METHODS
- Literature search was conducted in PubMed, Embase and ClinicalTrials.gov from inception to the end of January 2016
- An initial search using the MeSH Terms “mepolizumab,” “Asthma,” and “Randomized Controlled Trials” was followed by a search of related citations
- All studies examining efficacy and safety data for mepolizumab in the treatment of chronic asthma were included
- In addition, references of the included studies were screened for additional studies
- Two reviewers independently searched, extracted data and assessed risk of bias using the Jadad scale and differences adjudicated via consensus discussion.
- The primary outcomes included were eosinophil counts in blood and sputum, exacerbations, and forced expiratory volumes.
- Secondary outcome was adverse events due to mepolizumab.

RESULTS
- A total of seven RCTs (including one recently completed, unpublished trial) involving 1910 participants were included.
- The common adverse events reported with mepolizumab were: headache, chest pain, nasopharyngitis, erectile dysfunction, fatigue, rash, upper respiratory tract infection and sinusitis.

DISCUSSIONS
- Despite receiving high doses of inhaled or oral corticosteroids, up to 5% of asthmatics return with severe symptoms, frequent exacerbations, enhanced airway remodeling, and a greater mortality risk due to asthma.
- Around 20% to 40% of these patients with severe resistant asthma have persistent airway and tissue eosinophilia.
- The level of tissue eosinophilia has been correlated with asthma severity.
- Mepolizumab is a humanized monoclonal antibody against IL-5.
- Mepolizumab selectively inhibits eosinophilic airway inflammation and induces a significant reduction in severe asthma exacerbations, regardless of IgE levels in blood and sputum.
- However, early studies have demonstrated that mepolizumab does not modify pulmonary function.
- In clinical trials, mepolizumab was associated with a significant decrease in exacerbation rate, improvement in quality of life, and good safety profile.
- Thus, mepolizumab represents a useful and innovative therapeutic option in asthmatic patients with persistent airway eosinophilia.
- However, appropriate patient selection is essential to avoid treatment failure, because several studies confirm that in a specific subgroup of patients, eosinophils play an important role in exacerbations and mepolizumab therapy may have clinical benefit.
- Available literature demonstrates that anti-IL-5 treatment is safe for clinical use. It was very well tolerated in all clinical trials. The adverse event profile of Mepolizumab was comparable to placebo in large trials.

CONCLUSION
- Our findings indicates that mepolizumab significantly lowers blood and sputum eosinophil counts, and also effectively reduced asthma exacerbation frequency, but showed no significant improvement on functional airway outcome.
- Further larger randomized controlled trials are needed to confirm these findings.

REFERENCES