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P: In patients with acute asthma presenting to the ED

I: Does the use of leukotriene inhibitors plus typical standard of care meds.

C: Compared to standard of care management alone (steroids, B-agonists, Mg).

O: Associated with improved outcomes, decreased admissions, decreased return rates

Background:

Meta-analysis and randomized controlled studies have shown that leukotriene inhibitors (LTI) (Zafirlukast (Accolate), Montelukast (Singulair), Zileuton (Zyflo)) are able to reduce asthma severity and ED visits in chronic asthma, but reduced symptoms to a less extent than those taking inhaled corticosteroids. The effects of LTIs on the acute management of asthma are less well studied.

Leukotrienes produce bronchospasm, increased bronchial hyperresponsiveness, mucosal edema, mucus production, and recruitment of eosinophils to the airway, and airway smooth muscle cell proliferation. The production and release of leukotrienes are not affected by corticosteroids.

The antileukotriene agents are generally safe and well tolerated and the most common adverse effects include headache, pharyngitis, abdominal pain, dyspepsia, and cough. Currently there are no IV formulations for the LTIs.

Search strategy:

Medline asthma and leukotriene inhibitor and emergency medicine

Medline asthma and leukotriene inhibitor and emergency

Medline asthma and leukotriene inhibitor and emergency room

Medline and acute asthma and leukotriene inhibitor

Medline asthma and Singular and emergency medicine

Medline asthma and Singular and emergency

Medline asthma and Singular inhibitor and emergency room

Cocaine data base: leukotriene and asthma

Relevant papers:

Author, journal, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Ferreira MB, et al. Allergy Immunology 2001 Portugal	20 adults with asthma exacerbation who presented to the ER	Randomized to either 10mg Montelukast PO or placebo	Steroid use and ER stay	10mg Montelukast reduced need for steroids and aminophylline vs. placebo (p=0.03) 10mg Montelukast reduced ER stay (2.5 vs. 2.9 hours) and improved peak flows vs. placebo (not statistically significant)	Only patients who "it appeared unnecessary to give systemic steroids" were included. Low sample size
Reiss TF, et al. Thorax 1997 USA	22 asthmatic patients	Randomized double blind, three period, crossover trial to receive 100mg	FEV1	Montelukast increased FEV1 8.5% verses placebo	Low sample size

		Montelukast PO, 250mg Montelukast PO, or placebo			
Cylyl AK, et al. Respiratory Medicine 2003 Turkey	70 acute asthmatics (FEV1 40-80% predicted)	Randomized to receive either Montelukast 10mg PO+prednisolone (1mg.kg) IV, prednisolone (1mg.kg) IV, or placebo prior to receiving 100mcg Terbutaline NEBs Q1 hour	1. PEFR 2. Need for rescue medication	Prednisolone and prednisolone+montelukast both had significantly improved PEFR compared to placebo. Prednisolone+montelukast were better than prednisolone alone but this did not approach statistical significance.	We don't routinely use Terbutaline anymore and getting systemic steroids in the ER is currently the standard of care.
Dockhorn RJ et al. Thorax 2000 USA	51 asthmatic patients were monitored at home for 24 hours; 4-14 days in between dosages	Double blind, single dose, three period, crossover study to receive IV Montelukast (7mg), oral Montelukast (10mg), or placebo in a randomized fashion	1. Percent change from baseline in FEV1 2. max percentage change in FEV1 3. percentage change at different time points	1. no statistical difference between IV and PO Montelukast; both showed statistical improvement in percent change from baseline in FEV1 vs. placebo 2-3. No statistical difference between IV and PO Montelukast but the mean percentage change in FEV1 was greater for IV than PO especially in the first hour. Both PO and IV Montelukast showed stastical improvement in FEV1 over placebo	IV Montelukast had a faster onset of action than PO by 1-2 hours. Both formulations lead to improved outcomes vs. placebo. Patients in study were not acute asthmatics.
Camargo, CA, et al. American Journal of Critical Care Medicine 2002 USA	201 patients randomized, double-blind, parallel-group pilot study with adults with mod to severe asthma who presented to the ER	Received standard asthma therapy plus either IV Montelukast (7 or 14mg) or matching placebo	FEV1 response and β -agonist use	IV Montelukast improved lung function (FEV1) beginning at 15 minutes and persists for over 24 hours. Montelukast patients also required less β -agonists. No significant difference was observed between the 7 or 14mg dosing.	Didn't use Atrovent in their asthma therapy
Silverman RA, et al. Chest 2004 USA?	641 patients presenting the ER with asthma.	Randomized double blind trial in which patients either got Zafirlukast 160mg PO, Zafirlukast 20mg PO, or placebo. In patients discharged from the ER; those who got Zafirlukast in the ER were sent home with Zafirlukast 20mg PO BID plus standard	1. ER disposition 2. ER returns for asthma	Zafirlukast 160mg reduced the relative risk of an ED admission by 34% (absolute risk 5.1%) verses placebo (p = 0.052), while the 20mg dose did not have an effect on ED disposition. The addition of Zafirlukast 20mg BID for 28 days by the ER physician for outpatient management had an 18% relative reduction (5.3% absolute reduction) in treatment failures (i.e. ER asthma returns) (p = 0.047).	Patients were admitted or discharged at 4 hours. LTRI medication compliance was not measured.

		of care, and those who got placebo in the ER just got standard of care			
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Comments:

There have only been a few studies looking at LTIs in the acute exacerbation of asthma in the emergency room setting. All studies above have indicated that LTIs can improve asthma symptoms and potentially reduce asthma admissions. None of the studies listed above have mentioned adverse effects or clinical worsening with the use of LTIs in acute asthma.

Montelukast has been shown to improve pulmonary function within 1 hour of ingestion. Previous pharmacokinetics have shown that 7mg Montelukast IV is thought to be comparable to 10mg PO but based on the above mentioned studies, higher doses of the PO formulation may result in improved clinical responses. The IV formulation appears to have a faster onset of action but appears to have a similar clinical effect to the PO formulation within approx 1-2 hours.

Clinical bottom line:

All the studies looking at Montelukast or Zafirlukast use in the Emergency room for acute asthma showed there was benefit to their use (improved FEV1, admission rates, asthma exacerbation scores, decreased β -agonist use) and none showed any clear adverse effect. The optimal drug, dose, and route are not clearly demonstrated. Clinicians can consider using: Montelukast (Singulair) 10mg PO or Zafirlukast 160mg PO, once in the emergency room, along with Albuterol, Atrovent, and steroids for patients with acute asthma exacerbations.

References: see above