

## DOGMA DETECTIVES CASE # 02-20-13-01 ATROVENT VS. MAGNESIUM

For patients with an acute exacerbation of reactive airways disease, which medication -- Atrovent (Ipratropium Bromide) or Magnesium Sulfate -- has more literature / research in support of its use by demonstrating beneficial patient outcomes?

There is a reasonable body of evidence that magnesium has a beneficial bronchodilatory effect when used in conjunction with inhaled beta-agonists for patients with ASTHMA. It is more effective when used in patients experiencing more severe attacks – basically its role is to help “bridge the gap” until steroids start to become effective around 1-2 hours after administration. The effect of magnesium is about 30-40 minutes in length. It is unlikely to have any beneficial effect in mild to moderate attacks. For COPD the data is less clear, but there may be a slight benefit.

The data for atrovent shows a modest improvement in moderate to severe ASTHMA attacks, with greater benefit in children and better if more than one dose is used. There is strong evidence in the ability of Atrovent and other inhaled anticholinergic agents to reduce and prevent severe COPD exacerbations when used in the long term. For acute COPD exacerbations, there is no definitive data to show an added benefit from adding atrovent to beta agonists, but given the low risk of side effects, it is still commonly used.

Neither one of these treatments has significant side effects for the patient (as long as magnesium is given over 20-30 minutes to avoid hypotension).

Read more to see the literature this conclusion is based upon...

### Magnesium

Beneficial in severe ASTHMA when used in conjunction with beta-agonists.

Meta-analysis shows modest benefit in children with moderate to severe asthma exacerbations  
<http://adc.bmj.com/content/90/1/74.short>

This is another meta-analysis that reviewed 27 studies, and 7 trials (665 patients; 5 trials of adult and 2 of pediatric patients, with 6 from the United States and 1 from India). It showed that the use of intravenous magnesium sulfate reduces the rate of hospital admissions and improves pulmonary function in patients with severe acute asthma treated in the emergency department.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1070764/>

When it comes to COPD exacerbations, the literature is less clear. Again it works as an adjunct, and may be beneficial, but the effect likely is not as great as it is in severe asthma.

<http://europepmc.org/abstract/MED/16948990/reload=0;jsessionid=ggKQmSij6mh1ZkOBNVFk.0>  
<http://europepmc.org/articles/PMC1726289/pdf/v021p00203.pdf>

### Atrovent

The data here is a bit more modest, but there likely is a small benefit to its use in acute asthma exacerbations, especially when severe, with a slightly better effect in children over adults.

This meta-analysis reviewed 40 identified trials, 13 were relevant and eight of these were of high quality. The conclusion of the authors is, "A single dose of an anticholinergic agent is not effective for the treatment of mild and moderate exacerbations and is insufficient for the treatment of severe exacerbations. Adding multiple doses of anticholinergics to beta2 agonists appears safe, improves lung function and would avoid hospital admission in 1 of 12 such treated patients. Although multiple doses should be preferred to single doses of anticholinergics, the available evidence only supports their use in school-aged children with severe asthma exacerbation. There is no conclusive evidence for using multiple doses of anticholinergics in children with mild or moderate exacerbations."

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000060/abstract>

This was a study involving nearly 400 adult patients, showing no benefit adding atrovent in adult patients.

<http://journal.publications.chestnet.org/article.aspx?articleid=1069948>

This article pooled the results of multiple studies in adults, showing a slightly beneficial effect, mostly in more severe exacerbations.

<http://journal.publications.chestnet.org/article.aspx?articleid=1080662>

This meta-analysis also showed a slight statistical benefit, and since atrovent has few deleterious side effects is supportive of its use.

<http://www.sciencedirect.com/science/article/pii/S0196064499702660>

Atrovent has good data that in the long term management of COPD, it reduces exacerbations and hospitalizations. Many long term COPD medications have an anticholinergic component.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1525-1497.2006.00507.x/full>

In the acute COPD exacerbation, there is no data to show a benefit for atrovent. See the following Cochrane data review / meta-analysis. Given its lack of significant side effects, its use does not have to be avoided, but its limitations in the acute phase should be recognized.

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003900/abstract>