Efficacy of esomeprazole for treatment of poorly controlled asthma

Study Type: MOE
Purpose: Whereas asthma and GERD often coexist at the rate of 32 to 84% and about half of the asthma patients have reflux symptoms, this study compared the efficacy of esomeprazole vs placebo on asthma symptoms in patients poorly controlled with no documented GERD disease. Is esomeprazole superior?

Study Duration: 4 year trial

Trial Design: Randomized, double-blinded, placebo-controlled trial, intention-to-treat, multicenter (19 Centers), 2-8 week run-in period to do pH testing and asthma diaries

Medications: esomeprazole 40 mg twice daily vs placebo

Patients: n = 412 out of 5,475 eligible patients, 42 years old, mostly female, 50% white, ~20% former smokers, BMI 32, 17 years old age of onset, ~60% used beta-agonist more than two times per week, 100% on inhaled steroids, Baseline scale scores (see outcomes below): House-Brackman (3.6); Mark 3 Health Utility (0.79); Derriford (73); Brief Pain Inventory (13) – therefore patients had paralysis, but facial appearance was not disfiguring and pain was minimal

Inclusion Criteria: > 18 years old, asthma, confirmed diagnosis, at least 8 weeks of inhaled steroid, poor control defined by a screening test (JACQ), episode of unscheduled medical care in the previous yr

Exclusion Criteria: smoking within last 6 months, FEV1 of < 50% predicted, reflux or PUD surgery, had clinical indication for PPI, had used antacid drug in last mth, meds that interact with PPI, pregnancy

Primary outcome: rate of episodes of poor asthma control (decrease of morning peak flows 30% for 2 days, an urgent visit, need for oral steroids)

Secondary outcome: spirometry, multiple scales to assess asthma symptoms

1. Are the results valid?
   * Randomized? Yes
   * Double-blinded? Yes
   * Placebo-controlled? Yes

2. What were the results?

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Esomeprazole</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma episodes</td>
<td>2.5%</td>
<td>2.3%</td>
<td>NS</td>
</tr>
<tr>
<td>&gt; 30% drop in peak flow</td>
<td>2.1%</td>
<td>1.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Night Awakening with &gt; 1 event</td>
<td>52%</td>
<td>55%</td>
<td>NS</td>
</tr>
<tr>
<td>New use of steroids</td>
<td>21%</td>
<td>24%</td>
<td>NS</td>
</tr>
<tr>
<td>Various asthma scores</td>
<td>---</td>
<td>---</td>
<td>NS</td>
</tr>
</tbody>
</table>

3. Will the results help me?
   * Trials are inconclusive on the association of GERD and asthma.
   * This trial adds to the body of information by excluding patients with documented GERD.
   * There was no benefit of asthma control in patients treated with esomeprazole that do not have major GERD symptoms.
   * There was no benefit in nocturnal awakenings, asthma symptom scores, QOL, and lung function.
   * Ambulatory pH monitoring did not identify a responsive group to treatment.
   * Very few adverse events.

Conclusion: The weight of evidence indicates that PPI should not be prescribed in asthma patients that do NOT have symptoms of GERD.