Influenza and Pneumococcal Vaccines in Asthmatic Patients: Benefits and Risks

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Objectives

• Review current influenza and pneumococcal vaccine recommendations for patients with asthma including the rationale for these recommendations

Asthma is a major risk factor for influenza hospitalization

Increased H1N1 infection rate in asthma SUBJECTS

• 161 children aged 4-12 years followed through influenza season:
  - 95 with asthma
  - 66 without asthma
• Provided 8 weekly nasal mucus samples analyzed for respiratory viruses
• URI and asthma symptoms, morning PEFR and albuterol use recorded


Faculty Disclosure Information

• I have not had a financial interest or other relationship with the manufacturers of the products that will be discussed in my presentation.
• This presentation will not include discussion of pharmaceuticals or devices that have not been approved by the FDA.
• I will not be discussing unapproved or "off-label" uses of pharmaceuticals or devices.
Increased H1N1 infection rate in asthma

RESULTS

- 34% of children infected with H1N1
  - with asthma (41%)
  - without asthma (24%)
  - OR, 2.2; 95% CI, 1.1-4.4; P = 0.03
- Rates of loss of asthma control:
  - H1N1 38%
  - rhinovirus, 21%
  - combination rhinovirus and H1N1, 44%


CDC

- Recent studies show vaccine can reduce the risk of flu illness by about 60% among the overall population during seasons when most circulating flu viruses are like the viruses the flu vaccine is designed to protect against.

http://www.cdc.gov/flu/about/qa/vaccineeffect.htm

Does IV cause asthma exacerbations?

<table>
<thead>
<tr>
<th>Event</th>
<th>No. of Exacerbations in Asthma Subjects</th>
<th>Primary Infection</th>
<th>Secondary Infection</th>
<th>Absolute Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>New or increased medical conditions</td>
<td>79</td>
<td>2.0</td>
<td>2.0</td>
<td>0.0 (-0.8 to 0.8)</td>
<td></td>
</tr>
<tr>
<td>Without IV drug administration</td>
<td>79</td>
<td>2.0</td>
<td>2.0</td>
<td>0.0 (-0.8 to 0.8)</td>
<td></td>
</tr>
<tr>
<td>Without IV drug use</td>
<td>79</td>
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<td>2.0</td>
<td>0.0 (-0.8 to 0.8)</td>
<td></td>
</tr>
<tr>
<td>With IV drug administration</td>
<td>75</td>
<td>2.0</td>
<td>2.0</td>
<td>0.0 (-0.8 to 0.8)</td>
<td></td>
</tr>
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<td>2.0</td>
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<td></td>
</tr>
<tr>
<td>With IV drug administration and use</td>
<td>75</td>
<td>2.0</td>
<td>2.0</td>
<td>0.0 (-0.8 to 0.8)</td>
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</table>


Does LAIV cause asthma exacerbations?

- Some studies have shown a small increased rate of wheezing episodes after receipt of LAIV, particularly in children under age 3 years
- This risk has not been consistently shown across studies or across influenza seasons in the same study
- Most studies administering LAIV to children age 2 years and older with asthma have not shown exacerbations

CDC

- ACIP recommends against use in the following:
  - children aged 2 through 4 years whose parents or caregivers report that a health-care provider has told them during the preceding 12 months that their child had wheezing or asthma or whose medical record indicates a wheezing episode has occurred during the preceding 12 months
  - persons with asthma


Influenza vaccination of egg-allergic patients

- Patients who have IgE-mediated egg allergy have a theoretical risk of anaphylaxis if injected with influenza vaccines containing egg protein.
- Withholding influenza vaccine from egg-allergic recipients has very real risk, namely the morbidity and mortality associated with the disease.
Influenza vaccine contains measurable quantities of egg protein (ovalbumin); does this cause systemic reactions when injected into egg-allergic patients?

- 28 published studies involving 4300 egg-allergic subjects getting influenza vaccine without any serious reactions (no respiratory distress or hypotension), and with only a low rate of minor reactions (hives, mild wheezing).
- So, the answer appears to be no.

But what about patients with severe egg allergy?

- Most studies have specifically included patients with histories of severe anaphylaxis (n = 656) with egg ingestion and these patients also tolerate the vaccine.
- So, even these patients do not appear to be at risk of serious reaction.

Why are there no serious reactions being reported?

- Manufacturers of injectable trivalent influenza vaccine (IIV) report the maximum amount of ovalbumin < 1 mcg per 0.5 mL dose.
- The measured amounts in independent laboratories are usually much lower than the claimed amounts.

What about LAIV?

- Although the intranasally-administered live attenuated influenza vaccine (LAIV) contains a low amount of ovalbumin, all published studies to date have evaluated the injectable inactivated influenza vaccine (IIV), and thus IIV rather than LAIV should be used for egg-allergic recipients.
- Also LAIV should not be used in children with asthma, which often coexists with egg allergy.

What about non-egg-based IIV?

- Two non-egg-based influenza vaccines have recently been approved by the FDA for use in patients 18 years of age and older.
- They should not be used in patients under age 18 because some influenza vaccines have been found to be less immunogenic in certain age groups and others have been found to have higher rates of adverse reactions in certain age groups, and the risk of the egg-based vaccines in egg-allergic patients is minimal.
Guillain-Barré syndrome

- "Swine flu" vaccine administered in 1976 associated with increased risk GBS (1 additional case per 100,000 over background rate of 1 to 2 cases per 100,000).
- Subsequent years influenza vaccines have shown no consistent increased risk (if any, 1 per million).
- Specific attention was paid to the potential for GBS after the 2009 pandemic influenza A (H1N1) vaccine campaign and no increased rate was found.

GBS continues to be reported in temporal association with influenza infection itself.
- Previous GBS has risk of a recurrence.
- Persons who developed GBS within 6 weeks of influenza vaccination should avoid subsequent immunization.
- However, individuals with a history of GBS unrelated to influenza infection or vaccination who would benefit from immunization can be vaccinated.

Asthma increases the risk of invasive pneumococcal disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (N=191)</th>
<th>Controls (N=595)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 2</td>
<td>104 (54.8%)</td>
<td>51 (8.5%)</td>
<td>2.5 (1.6-3.9)</td>
</tr>
<tr>
<td>Age 2-5</td>
<td>13 (6.8%)</td>
<td>24 (3.9%)</td>
<td>1.3 (1.0-1.8)</td>
</tr>
<tr>
<td>Age 6-10</td>
<td>10 (5.2%)</td>
<td>20 (3.0%)</td>
<td>1.0 (0.5-2.0)</td>
</tr>
<tr>
<td>Age 11-19</td>
<td>15 (7.8%)</td>
<td>25 (4.0%)</td>
<td>0.9 (0.4-2.4)</td>
</tr>
<tr>
<td>Age 20-34</td>
<td>13 (6.8%)</td>
<td>29 (4.7%)</td>
<td>1.3 (1.0-1.8)</td>
</tr>
<tr>
<td>Age 35-44</td>
<td>9 (4.7%)</td>
<td>21 (3.0%)</td>
<td>1.1 (0.6-2.2)</td>
</tr>
</tbody>
</table>

* # Hospitalization or ED visit or any antibiotic use ≥3 antibiotic courses in 7 yr.


PCV13

<table>
<thead>
<tr>
<th>Dates</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
<th>6th</th>
<th>7th</th>
<th>8th</th>
<th>9th</th>
<th>10th</th>
<th>11th</th>
</tr>
</thead>
<tbody>
<tr>
<td>2MCV4-2MCV5-PCV13</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Cochrane

• 25 studies (18 RCTs involving 64,852 participants and seven non-RCTs involving 62,294 participants)
• Meta-analysis of the RCTs found strong evidence of pneumococcal polysaccharide vaccine (PPSV23) efficacy against invasive pneumococcal disease (OR 0.26, 95% CI 0.14 to 0.45).

Injection Site Reactions

| Number Followed for Safety | PNEUMOVAX 23§ | PNEUMO-23§ | Pneumovax® 23
|---------------------------|----------------|-------------|-----------------
| Number of Subjects        | 643 (P)       | 541 (P)     | 587 (E)        |

Rare Reports of Anaphylaxis;
2 with positive skin tests


Summary

• Patients with asthma are more likely to get influenza and more likely to be hospitalized with influenza
• Influenza vaccine is approximately 60% effective at preventing influenza
• LAIV should not be given to (especially very young) children with asthma
• ILV can be safely administered to patients with egg allergy under observation

Summary

• Patients with asthma are more likely to get invasive pneumococcal disease
• Pneumococcal vaccine (PPSV23) is approximately 75% effective at preventing invasive pneumococcal disease and should be given to all adults 19 through 64 years of age with asthma (and all adults aged 65 and older)