Inactivated influenza vaccine decreased pulmonary function in asthma except when colds were considered


Question
In patients with asthma, is inactivated influenza vaccine safe when the occurrence of colds is taken into account?

Design
Randomised, double-blind, placebo-controlled crossover trial with follow-up to 2 weeks after the final injection.

Setting
9 respiratory centres and 2 asthma clinics in the United Kingdom.

Patients
299 patients between 18 and 75 years of age (mean age 52 y; 57% women) who had stable asthma. Exclusion criteria were hypersensitivity to eggs, chicken, or influenza proteins; pregnancy; a febrile illness at the beginning of the study; or treatment with an investigational drug during the 30 days before study recruitment. 262 patients (88%) completed the study; 255 (80%) had complete paired data.

Intervention
Patients were allocated in a crossover design to 0.5 mL intramuscular injection of vaccine and placebo separated by 2 weeks.

Main outcome measures
Exacerbation of asthma within 72 hours of injection, defined as a decline in early-morning peak expiratory flow (PEF) of > 20% compared with the lowest of the best 3 early-morning PEF values measured during the 3 days before injection. Secondary outcomes were colds coinciding with exacerbations; β2-agonist, antibiotic, and oral steroid use; and medical consultations and hospital admissions.

Main results
Analysis was by intention to treat. Among 255 patients with paired data, 11 had a decrease in PEF of > 20% after vaccine compared with 3 after placebo (P = 0.03) (Table). 8 patients had a moderate or severe decrease in PEF (> 30%) after vaccine compared with 0 after placebo (P = 0.008) (Table). When patients with colds were excluded, the groups did not differ for a decrease in PEF of > 20% (6 vs 3, P = 0.51) or > 30% (5 vs 1, P = 0.06) (Table). No differences existed between the groups for other secondary outcomes.

Conclusions
Inactivated influenza vaccine led to a decrease in pulmonary function in patients with asthma. However, this decrease was no longer statistically significant when concurrent colds were considered.


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*P value calculated from data in article.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Vaccine</th>
<th>Placebo</th>
<th>RRI (95% CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall in PEF &gt; 20%</td>
<td>4.3%</td>
<td>1.2%</td>
<td>267% (12 to 1111)</td>
<td>32 (15 to 289)</td>
</tr>
<tr>
<td>Excluding those with a cold</td>
<td>2.4%</td>
<td>1.2%</td>
<td>100% (45 to 624)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Fall in PEF &gt; 30%</td>
<td>3.1%</td>
<td>0%</td>
<td>Approaches infinity</td>
<td>33 (20 to 110)</td>
</tr>
<tr>
<td>Excluding those with a cold</td>
<td>2.0%</td>
<td>0%</td>
<td>Not significant</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

Inactivated influenza vaccine vs placebo at 2 weeks in asthma

PEF = peak expiratory flow. Other abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article.

Commentary
Nicholson and colleagues studied whether inactivated influenza vaccine affects pulmonary function in patients with asthma. Previous studies have suggested that influenza vaccine temporarily reduces pulmonary function in this group of patients. These studies were plagued by several problems, including failure to adjust for the presence of a concurrent cold.

In this study, it first appeared there might be a difference in PEF rates for all patients, in particular, for patients who received influenza vaccine for the first time. However, when patients with colds were removed from the analysis, no statistically significant (or, in my view, clinically important) differences were observed between the vaccinated and placebo groups. Nor were significant differences found between the 2 groups for the secondary end points.

In several studies, vaccine efficacy has been shown to be approximately 75% in healthy working adults (1). Even in elderly adults in whom vaccine efficacy is somewhat lower, the prevention rate is 56% for respiratory illness, 53% for pneumonia, 50% for hospitalisation, and 68% for death (2). Of note, influenza vaccine is effective in preventing 27% to 30% of deaths from all causes, not just those clearly identified as being caused by influenza (3).

I conclude from this study that influenza vaccine definitely prevents far more exacerbations of asthma than it causes. I would certainly recommend influenza vaccine for patients with asthma, assuming they have no strong allergy to egg protein and no allergy to other vaccine components.

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References