Can Influenza Vaccination Prevent Adverse Cardiovascular Events?


Study Overview

Objective. To determine whether influenza vaccination can prevent adverse cardiovascular events.

Design. Meta-analysis.

Study selection. A search to identify randomized clinical trials (RCTs) comparing influenza vaccine with placebo or standard care was conducted using Ovid MEDLINE, EMBASE, and the Cochrane Library Central Register of Controlled Trials from inception of these databases to August 2013. 71 potentially relevant studies were identified. After 59 studies were excluded, a total of 12 RCTs met inclusion criteria for final meta-analysis. In the primary meta-analysis were 6 RCTs of influenza vaccine vs. placebo or control involving 6735 participants with a mean age of 67 years followed for a mean duration of 7.9 months; 36.2% of the participants had a cardiac history. In the secondary meta-analysis were 6 RCTs of experimental vs. standard influenza vaccination involving 16,857 participants with a mean age of 72 years, with 30.2% having a cardiac history.

Main outcome measures. The primary endpoint was a composite of major adverse cardiovascular events (ie, cardiovascular mortality, hospitalization for myocardial infarction, unstable angina, stroke, heart failure, or urgent coronary revascularization). The authors performed a subgroup analysis of patients with and without recent acute coronary syndrome (ACS) within 1 year of randomization.

Main results. In the analysis of influenza vaccine vs. placebo or control, 95 of the 3238 participants (2.9%) treated with influenza vaccine developed a major adverse cardiovascular event compared with 151 of the 3231 participants (4.7%) treated with placebo or control within 1 year of follow-up (risk ratio [RR] 0.64, 95% confidence interval [CI] 0.48–0.86; \( P = 0.003 \); \( I^2 = 28\% \)). The absolute risk difference was 1.74% (95% CI, 0.81%–2.67%; \( P = 0.003 \)). This translates into a number needed to treat (NNT) of 58 (95% CI, 38–124) to prevent 1 major adverse cardiovascular event. In the subgroup analysis, 41 of the 400 (10.25%) patients with a recent history of ACS treated with influenza vaccine developed a major adverse cardiovascular event compared with 90 of the 389 patients (23.1%) with a recent history of ACS treated with placebo or control (RR 0.45, 95% CI 0.32–0.63; \( P < 0.001 \); \( I^2 = 0\% \)). The absolute risk difference for this subgroup was 12.9% (95% CI, 7.75%–18.0%; \( P < 0.001 \)) or a NNT of 8 (95% CI, 6–13). Other sub-
group analyses including comparison of stable coronary artery disease, cardiovascular mortality, and all-cause mortality were not statistically significant. In the secondary meta-analysis comparing more potent vaccine with a standard vaccine, there was a trend favoring more potent vaccine in prevention of major adverse cardiovascular events; however, the results were not statistically significant.

**Conclusion.** The use of influenza vaccine was associated with a lower risk of major adverse cardiovascular events. The benefit of influenza vaccination was most prominent in patients with recent ACS.

**Commentary**

Many studies have shown the benefits of influenza vaccine, especially in children as well as in patients with hematological malignancy or chronic obstructive pulmonary disease [1–3]. Despite various guideline recommendations and conventional wisdom, definitive evidence remains limited for certain subgroups, including the elderly or patients with asthma [4,5]. Previous observational studies and systematic reviews have suggested the biological possibility of influenza vaccination and reduction of cardiac complications [6–8]. In this meta-analysis, the authors tested the hypothesis that influenza vaccine could protect patients from adverse cardiovascular outcomes and found that influenza vaccination may prevent 1.7 adverse cardiovascular events for every 100 persons. This points to a significant public health benefit with influenza vaccination in addition to prevention of primary influenza illness [9].

The study has several limitations. First, readers should be aware of the confines of meta-analysis. Findings in meta-analysis are limited by the quality of the underlying studies and can only provide information about association and not causation. Second, the underlying studies do not distinguish between a matched and unmatched year between the circulating strain of influenza viruses and the vaccine used [10]. Finally, patients with a recent history of ACS in the subgroup analysis had a reported NNT of 8; this finding may be beyond biological plausibility, as pointed out in the accompanying editorial [9].

**Applications for Clinical Practice**

The results of the study by Udell et al indicate an association between influenza vaccination and lower risk of cardiovascular events. According to retrospective data, only 50% of the population received influenza vaccination in 2012–2013, a season with widespread influenza activity [9,11]. With a number needed to treat of just 55 as suggested by the authors, it is important to increase vaccination coverage. For health care practitioners, providing influenza vaccination for at-risk patients will be an important life-saving action for the 2013–2014 influenza season.

—Ka Ming Gordon Ngai, MD, MPH

**REFERENCES**


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