The inactivated trivalent split-virus influenza vaccine was safe in stable asthma

American Lung Association Asthma Clinical Research Centers. **The safety of inactivated influenza vaccine in adults and children with asthma.** N Engl J Med. 2001 Nov 22;345:1529-36.

QUESTION

In patients with stable asthma, is the inactivated trivalent split-virus influenza vaccine as safe as placebo?

DESIGN

Randomized (allocation concealed*), blinded (clinicians and patients),* placebo-controlled crossover trial with follow-up to 14 days after each injection.

SETTING

19 centers in the United States.

PATIENTS

2032 patients who were 3 to 64 years of age, had stable asthma, and had been taking prescribed treatment for asthma within the preceding 12 months. Exclusion criteria included hypersensitivity to egg products or thimerosal, inability to use the peak flowmeter properly, lack of a telephone, a history of the Guillain-Barré syndrome, and influenza vaccination in the preceding 6 months. 96% of patients (mean age 30 y, 62% girls and women) received both vaccine and placebo injections and completed both of the 14-day postinjection diaries.

INTERVENTION

Patients were allocated in a crossover design to receive an injection of inactivated influenza vaccine and an injection of placebo 4 weeks apart.

MAIN OUTCOME MEASURES

The primary outcome measure was an exacerbation of asthma (defined as ≥ 1 of the following: ≥ 30% decrease in peak expiratory flow rate [PEFR] from the second-highest morning PEFR ["personal-best rate"] measured during the study, new or increased use of oral corticosteroids, unscheduled use of health care for asthma symptoms, and increased use of rescue medication) within 14 days after an injection. Secondary outcomes included a decrease of ≥ 20% in the PEFR from the personal-best rate during the 14 days after each injection, average morning PEFR, symptoms thought to be associated with the vaccine or placebo injection (rhinitis, sore throat, cough, headache, body chills, or fatigue), and the number of days without symptoms of asthma.

MAIN RESULTS

Analysis was by intention to treat. The rates of exacerbations of asthma within 14 days after vaccine or placebo injections did not differ (Table). The exacerbation rates were also similar in groups of patients defined according to age and severity of asthma. More patients reported body aches after the vaccine than after the placebo injection (25% vs 21%, $P < 0.001$). The vaccine and placebo injections did not differ for other secondary outcomes.

CONCLUSION

In patients with stable asthma, the inactivated trivalent split-virus influenza vaccine was as safe as placebo.

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*See Glossary.

Incidence of asthma exacerbations 14 days after vaccine and placebo injections†

Outcome	Number of patients	Vaccine injection	Placebo injection	Absolute difference (95% CI)
Exacerbations	1952	28.8%	27.7%	1.1% (-1.4 to 3.6)‡

†Exacerbations = new or increased use of oral corticosteroids, unscheduled use of health care for asthma symptoms, increased use of rescue medication, or ≥ 30% decrease in peak expiratory flow rate (PEFR) from the second-highest morning PEFR measured during the study.
‡Not significant.

COMMENTARY

In patients with asthma, infection with influenza can lead to bronchoconstriction and serious asthma exacerbations. Influenza is a common reason for hospitalization in children with asthma (1). Although immunization is effective in reducing exacerbations in patients with chronic obstructive pulmonary disease (2), concern has been raised about the role of immunization in patients with asthma. In a recent review (3), it was suggested that the lack of evidence of benefit and the potential harm associated with influenza immunization indicated the need for a cautious interpretation of the current guidelines, which include a consensus recommendation to immunize patients with asthma. A large randomized controlled trial was also recommended (3).

The study by the ALAACRC group is therefore welcome news. This large, multicentered, double-blind trial with a crossover design studied patients with stable asthma who were immunized against influenza with the inactivated trivalent split-virus vaccine. The investigators used rigorous methods and assessed patients for important clinical outcomes (i.e., exacerbations) and pulmonary function for up to 14 days. Overall, the results of this study indicate that influenza vaccination in adults and children with stable asthma is safe. However, myalgia seems to be a common adverse effect and patients should be warned accordingly. The study firmly supports the safety of vaccination for patients with asthma, and efforts should be made to increase immunization in this group.

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References

1. **Neuzil KM, Mellen BG, Wright PF, Mitchel EF Jr, Griffin MR.** The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. N Engl J Med. 2000;342:225-31.
2. **Poole PJ, Chacko E, Wood-Baker RW, Cates CJ.** Influenza vaccine for patients with chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2000;(4):CD002733.
3. **Cates CJ, Jefferson TO, Bara AI, Rowe BH.** Vaccines for preventing influenza in people with asthma. Cochrane Database Syst Rev. 2000;(2):CD000364.