

Clinical Communications

Safe vaccination of patients with egg allergy by using live attenuated influenza vaccine

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Clinical Implication

- In our study, 68 patients with egg allergy were safely vaccinated with live attenuated influenza vaccine. This is the first study to determine the safety of live attenuated influenza vaccine in patients with egg allergy.

TO THE EDITOR:

There has been a long-standing controversy about influenza vaccination of patients with egg allergy. In recent years, 2 studies showed that intramuscular trivalent inactivated influenza vaccination (TIV) is safe in this population,^{1,2} which led to a change in vaccination guidelines. However, the US Centers for Disease Control³ and Health Canada⁴ officially recommend avoidance of intranasal live attenuated Influenza vaccine (LAIV) in patients with egg allergy because the vaccine contains trace amounts of egg proteins and no data are available in the literature concerning its safety. Besides avoiding the inconvenience and the anxiety related to intramuscular vaccines, LAIV offers a better protection against influenza than TIV in children 6 to 59 months of age⁵; the Canadian National Advisory Committee on Immunization recommends the preferential use of LAIV instead of TIV for influenza immunization in children 24 months old and older.⁴ When considering that, up to 2% of young children have egg allergies⁶ and that these patients often have other atopic-related comorbidities (eg, as asthma), the increased protection against influenza that can be achieved with LAIV is highly desirable.

We conducted a prospective cohort study to determine whether LAIV can be safely used in patients with egg allergy. The project was approved by the Ste-Justine Ethics Committee and Health Canada, and the trial was registered on the National Institute of Health's clinical trial Web site (240713). Between November 2013 and February 2014, 69 patients with egg allergy and 55 patients without a history of egg allergy aged 2 to 16 years were recruited. After obtaining signed parental consent, the patients were vaccinated with the 2013 to 2014 intranasal LAIV (FluMist; AstraZeneca, Mississauga, Ontario, Canada), which contained <0.24 µg of ovalbumin per dose, as provided by the US Centers for Disease Control.³ Patients were administered a questionnaire that collected information on previous influenza vaccination history, previous egg allergic reaction manifestations, and severity of allergy (Table I).

We defined egg allergy as a history of at least 1 sign or symptom of allergy (ocular, respiratory, gastrointestinal, or cardiovascular) that occurred within 1 hour of egg ingestion and persistent sensitization confirmed by a skin prick test response to egg at least 3 mm larger than that of the saline control within 10 to 15 minutes, specific IgE levels ≥ 0.35 kU/L (UniCAP; Pharmacia, Uppsala, Sweden), or specific IgE levels ≥ 0.1 kU/L (Immulite; Siemens Healthcare Diagnostics Munich, Germany.). Forty of 68 patients (59%) had mild asthma. Thirty patients had mild intermittent asthma, and 10 patients had mild persistent asthma, as previously defined.⁷ One patient with severe persistent asthma was excluded from the study. Eleven of 68 patients were accidentally exposed and reacted to egg within the year before vaccination. The age of worst reaction was on average 5.3 years before the vaccination. Twenty-four of 68 children (35%) included baked egg in their diet at the time of vaccination. The patients were examined before vaccination, were kept under observation, and were reexamined 1 hour later to evaluate symptoms and signs of anaphylaxis. The patients were followed up by telephone call 24 hours later to look for any delayed reactions. The primary outcome was anaphylaxis, as previously defined.⁸

Among the 68 patients with egg allergy included in the study, 52 had previously received TIV and 41 received the pandemic AS03-adjuvanted monovalent H1N1 vaccine in 2009. One patient who had rhinorrhea after TIV subsequently received the pandemic vaccine without any reaction. Another patient who reported conjunctival erythema and pruritus after the pandemic vaccine was later vaccinated with TIV without any reaction. Among the 68 patients with egg allergy, 10 received their first influenza vaccine during this study and 7 received 2 doses. No patients developed an allergic sign or symptom during the hour of observation. At the 24-hour follow-up, 7 patients (10%) reported nonspecific adverse reactions after the first vaccine dose, none of which required medical consultation or treatment (Table II) or were suggestive of an allergic reaction. All of the reported adverse reactions occurred in the evening or following morning after vaccination except for a patient with a nonpruritic peribuccal rash, which occurred 4 hours after vaccination and disappeared spontaneously in the evening. None of the 7 patients who received a second dose reported an adverse event at the 24-hour follow-up. Among the 55 patients in the control group (3 received 2 doses) vaccinated with FluMist, one reported ocular pruritus 15 minutes after vaccination, which spontaneously resolved within 1 hour without any treatment. At 24 hours, another patient reported nasal congestion.

Analysis of the data from our study indicates that LAIV is a safe alternative to TIV in children with known egg allergy. It was not surprising that there were no immediate IgE-mediated reactions after vaccination of the children with egg allergy because the quantity of ovalbumin in LAIV is comparable with that of TIV, which has previously been shown to be safe in patients with egg allergy.^{1,2} Moreover, systemic absorption of ovalbumin via intranasal vaccination is probably much lower than intramuscular administration; a recent study showed that intranasal peanut challenge of patients with documented peanut allergy and with much higher concentration of allergens than those present in

TABLE I. Description of patients with egg allergy or sensitized

Total no. patients	68
Age at FluMist vaccination (y), median (95% CI)	6.5 (5.6-7.3)
Age of first reaction (mo), median (95% CI)	12 (8.1-16)
Age of worst reaction (mo), median (95% CI)	12 (6.1-18)
Description of worst reaction to egg, no. (%)	
Cutaneous symptoms	52 (76)
Ocular symptoms	10 (15)
Respiratory symptoms	17 (25)
Gastrointestinal symptoms	21 (31)
Cardiac symptoms	7 (10)
Anaphylaxis	27 (40)
Epinephrine used	7 (10)
Egg skin prick test mean wheal diameter (mm) at time of vaccination, mean (95% CI) (n = 68)	11 (9.9-12)
Egg white specific IgE (Unicap) at the time of vaccination (kU/L), mean (95% CI) (n = 46)*	21 (12-31)
Egg white specific IgE (Immulate) at the time of vaccination (kU/L), mean (95% CI) (n = 52)*	34 (24-45)

*Some patients had both Immulate and Unicap specific IgE dosages.

TABLE II. Description of adverse reactions at 24-hour follow-up

Symptoms	Patients with egg allergy (n = 7)	Control group (n = 1)
Peribuccal rash	1	
Headache	1	
Nausea	1	
Nasal congestion	1	1
Abdominal pain	2	
Cough with fever	1	

LAIV was not associated with systemic reactions.⁹ Furthermore, systemic absorption of corticosteroids administered intranasally is much lower than when administered orally.¹⁰ Thus, the quantity of ovalbumin absorbed systemically after LAIV vaccination is probably much less than the 0.24 µg indicated in the product monograph. The increased number of delayed adverse reactions of patients with egg allergy compared with controls (7 vs 1) could be due to the increased awareness and surveillance of adverse effects by parents of children with egg allergy.

Many potential benefits could be obtained from using LAIV with patients with egg allergy, including better protection in a population with a high prevalence of asthma and atopy, and potentially a better vaccine coverage because of its less-invasive route of administration. Although these data are reassuring, multicentric studies over a few seasons are needed to confirm the safety of LAIV in these patients.

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