Inactivated influenza vaccine prevented influenza in healthy adults

Ohmit SE, Victor JC, Rotthoff JR, et al. **Prevention of antigenically drifted influenza by inactivated and live attenuated vaccines.** N Engl J Med. 2006;355:2513-22.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Infectious Disease ★★★★★★☆ Public Health ★★★★☆☆☆

QUESTION

How effective are inactivated or live attenuated influenza vaccines in preventing influenza caused by circulating strains—whether they are antigenically similar or dissimilar to the strains included in the vaccines—in healthy adults?

METHODS

Design: Randomized placebo-controlled trial.

Allocation: Unclear allocation concealment.*

Blinding: Blinded (nurses administering vaccine and participants).*

Follow-up period: Influenza surveillance period from November through April.

Setting: 2 university sites and 2 community sites in Michigan, United States.

Patients: 1247 healthy adults 18 to 46 years of age (mean age 27 y, 62% women) who had not received an influenza vaccine for the 2004 to 2005 season. Exclusion criteria were any health condition for which the inactivated vaccine was recommended or contraindication to either vaccine.

Intervention: Inactivated influenza vaccine (n = 522) or matching placebo (n = 103) by intramuscular injection, or live attenuated influenza vaccine (n = 519) or matching placebo (n = 103) by intranasal spray.

Outcomes: Influenza A or B, confirmed by isolation of the influenza virus in cell culture or by an increase of ≥ 4 in serum antibody titer against a circulating influenza strain on hemagglutination-inhibition testing. Secondary endpoints included confirmation through isolation of the virus only, isolation of the virus or identification of the virus through real-time polymerase chain reaction (PCR), or PCR only.

Patient follow-up: 97% (intention-to-treat analysis).

MAIN RESULTS

The 2 placebo groups were combined for the efficacy analysis. The inactivated influenza vaccine had a higher rate of vaccine efficacy than did placebo for each influenza confirmation method (Table). The live attenuated influenza vaccine did not differ from placebo (Table). The inactivated and live attenuated vaccines did not differ for vaccine efficacy (Table).

CONCLUSION

The inactivated influenza vaccine prevented laboratory-confirmed influenza caused by circulating strains in healthy adults.

Source of funding: National Institute of Allergy and Infectious Diseases.

For correspondence: Dr. S.E. Ohmit, University of Michigan School of Public Health, Ann Arbor, MI, USA. E-mail sohmit@umich.edu.

*See Glossary.

Efficacy of inactivated vs live attenuated influenza vaccine vs placebo in healthy adults during the 2004 to 2005 influenza season†

Method of laboratory confirmation of influenza	Cumulative incidence of influenza			Percent relative reduction (95% CI)
	Inactivated	Live attenuated	Placebo	
Cell culture	1.3%	–	5.8%	77% (37 to 92)
	–	2.5%	5.8%	57% (–3 to 82)
	1.3%	2.5%	–	46% (–44 to 82)
PCR	1.9%	–	7.3%	74% (37 to 89)
	–	3.5%	7.3%	52% (–2 to 77)
	1.9%	3.5%	–	45% (–26 to 77)
Cell culture or PCR	1.9%	–	7.8%	75% (42 to 90)
	–	4.0%	7.8%	48% (–7 to 74)
	1.9%	4.0%	–	53% (–5 to 80)

†PCR = polymerase chain reaction. CI defined in Glossary.

COMMENTARY

The study by Ohmit and colleagues addresses the efficacy of intranasal live attenuated and injected inactivated influenza vaccines in a community-based trial. This comparison is of interest because in seasons with a mismatch between vaccine strains and circulating virus, the best approach to protect high-risk persons from influenza infection and its complications is unknown. Furthermore, the increased interest in universal influenza vaccination requires accurate data on efficacy in segments of the population at varying risk for complications (1).

Conventional wisdom suggests that a live vaccine that induces mucosal immunity by intranasal administration provides better protection of longer duration than does injected inactivated vaccine against a "drifted" circulating virus strain mismatched to the vaccine strain. A recent study showed superiority of live vaccine against matched and mismatched ("drifted") virus strains in a study of children 12 to 59 months of age (2). A previous trial comparing live with inactivated vaccine has, however, shown similar efficacy between the 2 (3).

The strength of the study by Ohmit and colleagues is the addition of laboratory-confirmed influenza infection to serologic evidence as an endpoint. A limitation is the inability to accurately assess the endpoint of serologic evidence of infection. About 30% of persons were excluded because the test for serologic response to vaccine was not obtained before the influenza season began.

The authors found that only the inactivated vaccine protected better than placebo against laboratory-confirmed influenza. The difference was particularly striking for type B influenza. A future study adequately powered to assess the relative protection against type A and type B viruses by the available vaccines would be valuable. This study re-emphasizes the need for investigations of efficacy of available vaccine formulations in populations with varying risk.

Bruno Granwehr, MD
University of Texas Medical Branch
Galveston, Texas, USA

References

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