Absence of Laboratory-confirmed Failures of High-dose Influenza Vaccine in an Elderly Population

Estimates of the limited effectiveness of conventional influenza vaccine in individuals 65 years of age and older have raised interest in the possibility of superior clinical protection with high-dose influenza vaccine.[1] We had an experience with high-dose vaccine in the 2010-2011 season in this population that offers some hope.

Taking into account the superior hemagglutinin antibody levels of high-dose vaccine[2] and the continuing stream of evidence correlating hemagglutinin antibody levels with clinical protection,[3] we made high-dose vaccine the routine vaccine for the elderly in the Veterans Health Administration's Nebraska-Western Iowa (NWI) Health Care System. Colleagues responsible for similar patients at other sites in our region's Veterans Integrated Service Network (VISN 23), however, overwhelmingly chose standard dose vaccine.

Our laboratory identified no positive tests for influenza among 7575 elderly who received high-dose vaccines in NWI. The 8 laboratories of our VISN 23 colleagues in Iowa, Minnesota, and the Dakotas documented 22 positive tests among 36,565 vaccines. The Minneapolis site did note that one of its positive tests occurred in a high-dose recipient. Chi-square calculations comparing positive lab tests in our setting (0 of 7575 vaccines) and our colleagues' use of standard-dose vaccine (21 of 36,565) gave 3.43 (one-tailed *P* 0.03). This report was reviewed by the institution using a process that determined that this did not require approval by our institutional review board.

These results suggest clinical benefit of high-dose vaccine. Nonetheless, this data set has limitations. Laboratory methods varied, as did decisions to order tests. Geographic variation in the impact of influenza may occur in VISN 23. Because this was an informal review of extant data, not a prospective research study, our data set is subject to errors in recording vaccination status and laboratory results. Conventional statistical methods, moreover, rest on the assumption of independence. This may not be valid in a community where vaccine-induced protection of 1 patient can influence the risk of influenza in an acquaintance.

Nevertheless, a Bayesian sensibility[4] would consider the prior expectation of superiority of a high-dose vaccine that produces higher levels[2] of antibodies correlated with protection[3] and give credence to our trend.

Our experience bolsters the view that, absent a randomized clinical trial, high-dose influenza vaccine is preferred for those 65 and older. Additionally, it hints at the value of conducting extensive observational studies, particularly in view of the similarity of results of observational studies and randomized clinical trials.[5]

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Commentary: Solid Evidence Is Lacking, But Signs Are Hopeful

As evidenced by the recent seasonal (2012-2013) outbreak of influenza, elders bear the brunt of this pathogen, both in terms of hospitalizations and death. Sixty-five percent of Wisconsin's influenza hospitalizations were for individuals aged 65 years or older. Despite widespread use of inactivated influenza vaccine (IIV) by this group (62% coverage rate for 2012-2013 in Wisconsin), recent estimates of vaccine efficacy are disappointingly low.[1]

High dose IIV was licensed in 2009, based on non-inferiority of the resulting antibody concentrations. However, we still lack good clinical evidence showing the anticipated superiority of this presentation. This is due in part to the very low prevalence of seasonal influenza in the wake of the 2009 influenza A (H1N1) pandemic, forcing extension of definitive effectiveness studies.

While awaiting the results of well-designed clinical trials, evaluations of experiences such as that presented by Bittner et al[2] are most welcome. Such reports provide some guidance to clinicians. Since adoption in 2010, the US Advisory Committee on Immunization Practices is increasingly using an evidence-based approach for vaccine recommendations using GRADE.[3] This report would likely be scored as level 4 evidence (very low quality). This simply means that conclusions likely are to change as more evidence is gathered. Science is an iterative process. As best said by Jacob Bronowski, "We are always at the brink of the known; we always feel forward for what is to be hoped."[4] Given the low efficacy of the current IIV in elders, we hope that Dr Bittner's conclusions are correct.

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