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High-dose influenza vaccine use among patients receiving hemodialysis in the United States, 2010–2013

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ABSTRACT

Background: Standard influenza vaccines may be of limited benefit to patients with end-stage renal disease (ESRD). These patients may benefit from high-dose influenza vaccine, currently indicated for patients aged ≥65 years. Studies in other populations have demonstrated that high-dose vaccine elicits a stronger immunological response. We compared vaccine uptake in the United States and predictors of receipt for high-dose and standard influenza vaccines.

Methods: Using data from the United States Renal Data System (2010–2013), we conducted a cohort study of 421,482 adult patients on hemodialysis. We examined temporal trends in uptake of high-dose or standard trivalent influenza vaccine each influenza season, and used multivariate logistic regression to assess the association between individual-level variables (e.g., demographics, comorbidities) and facility-level variables (e.g., facility size and type) with vaccine receipt.

Results: The proportion of patients with ESRD who were vaccinated with any influenza vaccine increased from 68.3% in 2010 to 72.4% in 2013. High-dose vaccines were administered to 0.9% of patients during the study period, and 16.7% of high-dose vaccines were administered to patients <65 years of age. Among patients aged ≥65 years, older patients (>79 vs. 65–69 years: OR, 1.29; 95% CI, 1.19–1.41) and patients at hospital-based versus free-standing dialysis facilities (OR, 2.31; 95% CI, 2.13–2.45) were more likely to receive high-dose vaccine, while blacks (vs. whites [OR, 0.66; 95% CI, 0.61–0.71]) and patients with longer duration of ESRD (>9 vs. 0 years: OR, 0.66; 95% CI, 0.55–0.78) were less likely to receive the high-dose vaccine.

Conclusions: While the overall influenza vaccination rate has increased, use of high-dose vaccine among patients with ESRD was very low. Being an older patient, living in the Midwest, and receiving care at hospital-based facilities were the strongest predictors of receiving high-dose vaccine.

1. Introduction

Prevention of influenza is important for patients with end-stage renal disease (ESRD) due to the risk of severe complications from influenza infections or influenza-related hospitalizations, mortality, and health care costs in this population. Yet, immunogenicity evidence demonstrates that patients with ESRD on chronic hemodialysis have inferior responses to the standard, seasonal trivalent influenza vaccine relative to the general population. Additionally, effectiveness studies suggest that the standard vaccine provides little benefit in preventing influenza-related outcomes in these patients [1–3].

High-dose inactivated influenza vaccine was licensed by the United States Food and Drug Administration in December 2009 for adults aged ≥65 years [4]; the rationale for introducing this vaccine was to induce higher antibody responses and to provide better protection than the standard vaccine among this high-risk population. The high-dose vaccine contains the same three strains as standard trivalent vaccines, but has four times as much antigen (60 vs 15 μg per strain). A postlicensure randomized controlled efficacy trial including almost 32,000 older adults showed that the high-dose vaccine was 24.2% (95% confidence interval [CI], 9.7–36.5%) more effective overall in preventing influenza

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infections than the standard vaccine [5] and was 22.1% (95% CI, 3.9–37.0%) more effective among patients with one or more high-risk comorbidity [6]. Similarly, a large, effectiveness study conducted in the general Medicare population showed that the high-dose vaccine was more effective than the standard vaccine in preventing probable influenza infection and influenza-related hospitalizations [7].

While influenza vaccine is recommended for patients on dialysis, neither the Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices, nor the Kidney Disease: Improving Global Outcomes Foundation have issued a recommendation stating a preference for the type of vaccine that should be administered in this population [8]. Yet evidence demonstrates that alternative vaccination strategies can elicit an antibody response greater than that provided by the standard vaccine [9]. Given the availability of high-dose influenza vaccine and the known poor immunogenicity of the standard dose among patients with ESRD on dialysis, we examined the national uptake of each type of influenza vaccine and quantified the association between individual- and facility-level variables and the receipt of high-dose versus standard influenza vaccine among patients receiving dialysis since the licensure of the high-dose vaccine in 2009.

2. Methods

2.1. Study population

Data for this study came from Medicare claims collected in the United States Renal Data System (USRDS) [10], which is a population-based registry of most patients with ESRD in the United States. The data included claims billed for dialysis treatment, hospitalizations, outpatient care, medication dispensings, preventive services (including vaccinations), and death.

We used USRDS data from the years 2010 through 2013. Yearly cohorts were created for each influenza vaccination season (defined as August 1 through December 31). The analysis was structured by calendar year rather than full influenza season (which typically extends into the spring of the following year), allowing for the inclusion of the 2013 vaccination season since the vast majority of vaccinations (>98%) [11] are administered in the fall of each influenza season.

We created two analysis cohorts of patients with ESRD receiving hemodialysis for this study: (1) a cohort of all adults used in the descriptive uptake analysis and (2) a cohort of older patients indicated for the high-dose vaccine used in the predictive analysis. For both cohorts, patients were required to have Medicare as a primary payer and Parts A and B coverage to ensure capture of vaccine and comorbidity information. The uptake cohort of all adults included all eligible patients aged ≥18 years and required patients to receive regular in-center hemodialysis treatments from May 1 through July 31 of the given year; patients could enter multiple yearly cohorts if eligible each year. The predictive cohort of older adults was restricted to patients aged ≥65 years (because the high-dose vaccine is indicated only for patients aged ≥65 years) who had at least 6 months of regular in-center hemodialysis treatments prior to August 1; baseline covariates for the predictive modeling were measured during this 6-month period.

2.2. Variables

Medicare claims were searched for Current Procedural Terminology (CPT), Healthcare Common Procedure Coding System (HCPCS), and *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes for high-dose vaccine (CPT: 90662) and standard vaccine, which included all other non-high-dose vaccine formulations (CPT: 90654, 90656, 90658, 90660, 90661, 90672, 90673, 90688; HCPCS: G0008, G8482, Q2034, Q2035, Q2036, Q2037, Q2038, Q2039; ICD-9-CM procedure: 99.52). If a patient had more than one vaccine type in a given season, the first vaccine was used to define the patient's exposure group. Individual-level predictors included demographics, Medicaid eligibility as an indicator of low-income status, health status variables, comorbidities (see Supplemental Table 1 of ICD-9-CM codes), medications (measured using National Drug Codes [NDC]), variables related to functional status used as frailty markers, and other preventive tests and procedures such as pneumococcal vaccination. Facility-level variables included geographic region, facility type, affiliation, profit status, and size.

2.3. Statistical analysis

To understand overall patterns of vaccine uptake by year and vaccine type, vaccine administrations and characteristics of vaccinees in the all-adult, uptake cohort were described. We report the distributions of vaccine type and timing by influenza season, and we report frequencies of patients who received high-dose vaccine in multiple seasons.

Potential predictors of vaccine type were assessed in the predictive cohort restricted to patients aged ≥ 65 years with 6 months of baseline in-center hemodialysis. We used multivariable logistic regression to estimate the associations between patient- and provider-level variables chosen a priori and the receipt of high-dose influenza vaccine versus standard influenza vaccine. To examine changes in predictors of high-dose vaccine receipt over time, we stratified the analysis by yearly influenza season.

Analyses were conducted with SAS, version 9.3 (SAS Institute, Cary, North Carolina) and R version 3.4.0. This study was considered exempt by the Institutional Review Board at the University of North Carolina due to the deidentified nature of the data.

3. Results

We identified 421,482 unique patients with ESRD receiving dialysis across all study years; patients could contribute to multiple vaccination seasons, resulting in 1,000,204 unique patient-seasons. Among these patient-seasons, the mean age was 62.7 years (standard deviation, 14.3), 54.4% were aged <65 years, and 55.6% were male (Supplemental Table 2). In the uptake cohort of all adults, the yearly proportion of patients who were vaccinated with any influenza vaccine increased slightly over the study period from 68.3% in 2010 to 72.4% in 2013. High-dose vaccine use increased from 0.3% to 1.3% over the four years of the study; however, almost all patients who were vaccinated received the standard seasonal vaccine (Table 1, Fig. 1). Among patients aged ≥65 years of age, uptake of high-dose vaccine increased from 0.6% in 2010 to 2.5% in 2013. The majority of both standard vaccine and high-dose vaccine were administered in September and October; 97% of standard-dose vaccines and 93% of high-dose vaccines were administered by the end of October (Fig. 1). About 81% of dialysis clinics administered only standard dose vaccine, while 18% administered both standard and high-dose. Of note, 16.7% of high-dose vaccines were administered to patients aged <65 years. About 2% of patients received multiple standard-dose vaccines within a single influenza season; receipt of multiple doses of high-dose vaccines within a single season was rare. Among patients who were eligible across two consecutive influenza seasons, 59% received repeated standard-dose vaccines and <1% received repeated high-dose vaccines.

In the predictive cohort of older adults (≥65 years) who received either standard or high-dose vaccine, there were

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