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Low Rates of Vaccination for Herpes Zoster in Older People Living With HIV

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Abstract

Herpes zoster (HZ) occurs at a higher age-specific rate in people living with HIV (PLWH) than in the general population. We implemented a quality improvement study to assess herpes zoster vaccine (HZV) usage among PLWH, assess HZV usage after additional reminders/prompts, and identify barriers to HZV among older PLWH. HZV rates in PLWH were determined in six institutions with varying payment structures. For the intervention, Part 1, PLWH eligible for HZV at the University of Colorado were identified, and providers were notified of patient eligibility. In Part 2, in addition to provider notification, an order for HZV was placed in the patient's chart before a clinic appointment. HZ vaccination rates ranged from 1.5% to 42.4% at six sites. Before the intervention, 21.3% of eligible University of Colorado patients had received HZV. An additional 8.3% received HZV with Part 1 and 17.8% with Part 2 interventions. At completion, a total of 53.2% of eligible patients had received HZV through routine clinical care or the interventions. Insurance coverage concern was cited as a common reason for not receiving HZV. Minor adverse reactions occurred in 26.7% patients and did not require medical care. HZV coverage was low at a majority of sites. Clinical reminders with links to vaccination orders or preplaced vaccination orders led to improved HZV coverage in our clinic, but published guidelines for use of HZV in PLWH and improvement in logistic or insurance barriers to HZV receipt are paramount to improved HZV coverage.

Keywords: HIV, frail elderly, herpes zoster, herpes zoster vaccine, immunization schedule

Introduction

Herpes zoster (HZ) results from the reactivation of latent varicella zoster virus (VZV). The occurrence of HZ is closely correlated with loss of VZV-specific T cell immunity, due to disease, immunosuppressive therapy, or immune senescence.[1] Consequently, among people living with HIV (PLWH) not receiving antiretroviral therapy (ART), HZ occurs at age-specific rates that are 10–20 times greater than the rate in the general population.[2] Even with reconstituted immune function (>200 CD4 T cells/μL) following initiation of ART, the prevalence and severity of HZ among PLWH remain approximately thrice greater than in the general population, with greater risk among those with no or recent initiation of ART and CD4 T cells less than 500 cells/μL.[3–5]

Live attenuated Oka/Merck zoster vaccine (HZV; Zostavax®) significantly reduces HZ incidence and morbidity among immunocompetent adults ≥50 years of age.[6–8] As PLWH were excluded from pivotal efficacy trials,[6,8] there are little safety data and no efficacy data for HZV in PLWH, although subsequent studies have supported both the safety and efficacy of the vaccine among PLWH.[9,10] The Advisory

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Committee on Immunization Practices (ACIP) does not provide HZV recommendations for PLWH, except to advise against administration if CD4 counts <200 cells/μL.[11] The primary care guidelines for management of PLWH suggest that HZV *can be considered in* PLWH (≥60 years, CD4 count ≥200 cells/μL).[12] Little is known, however, about HZV uptake among eligible PLWH. Consequently, we carried a two-part quality improvement study to: (1) assess HZV usage among eligible PLWH in different practice settings; (2) identify patients eligible for HZV; (3) assess HZV usage after additional reminders/prompts; (4) describe adverse reactions among HZV recipients; and (5) identify barriers to HZ vaccination of older PLWH.

Methods

This was a quality improvement project consistent with routine clinical care. Verbal or written consent was not required. The Institutional Review Board at the University of Colorado waived institutional review board review.

Preintervention: HZ vaccination rates

HZ vaccination rates were determined between December 1, 2014 and May 1, 2016 at six institutions with varying payment structures (i.e., three Department of Veterans Affairs (VA) Healthcare Centers, a Canadian academic center, a University-based clinic, and an urban safety-net hospital). Eligibility criteria included HIV infection, ≥60 years of age, and CD4 T cell count ≥200 cells/μL. Clinic directors at each of these sites were queried about the primary barrier to HZV use within their clinic.

Part 1: prompts for vaccination

Patients in the University of Colorado Infectious Diseases clinic were identified through Ryan White reporting records, and included in the analysis if they met the above criteria, and did not have active malignancy, use of immunosuppressive therapy, had not moved from the area, and had not died. Patients taking antiviral medications to prevent herpes simplex were asked to hold medication for 2 weeks following vaccination and, ideally, held therapy for at least 1 day before vaccination. Vaccination opportunities were chosen to coincide with a scheduled clinic visit. For Part 1 (December 2014 to May 2015), each provider was e-mailed weekly with a list of scheduled patients eligible for HZV. At the visit, the patient was alerted to his/her HZV eligibility and the appropriate vaccination facility, as determined by insurance (Medicaid or private insurance, in clinic; Medicare, at a retail pharmacy). If the vaccine was administered or prescribed, the patient was contacted within 7 days and completed a questionnaire regarding adverse reactions; up to three attempts by telephone and one query sent through the medical record were used before a patient was considered a nonresponder. If vaccine was not administered, the reason was recorded.

Part 2: enhanced prompts for vaccine

Additional eligible patients were identified for Part 2 (November 2015 to May 2016) through new clinic transfers and newly eligible patients turning 60 years of age. In addition to the Part 1 e-mail prompt, an order for HZV was placed in the electronic medical record before the scheduled visit. The provider then needed to sign or cancel the order at the visit. Other procedures were the same as described above for Part 1.

Results

Preintervention

Six clinics that provide care for PLWH provided vaccine uptake data: three VA clinics in major cities in the United States (Denver, Atlanta, and San Diego), one academic center in the United States (University of Colorado) and one in Canada (McGill University), and one urban safety-net clinic (Denver Health Medical Center). From December 1, 2014 to May 1, 2016 HZV coverage rates ranged from 1.5% to 42.5% (Table 1). Primary barriers to vaccination identified by clinic directors included lack of formal recommendations for HZV usage in PLWH (two of six clinic directors), concerns about insurance coverage/cost (two of six), logistic barriers [vaccine storage, availability, nonformulary consultation, second appointment needed (three of six)], or lack of electronic reminder (three of six).

Intervention

Before the intervention, 21.3% (37/174) of eligible PLWH in the University of Colorado Clinic had received HZV (Table 1). One hundred forty-four patients met the inclusion criteria for Part 1. In addition to those who had received HZV preintervention, 12 of the 144 (8.3%) eligible patients received HZV in association with the Part 1 intervention. For Part 2, 269 patients met the inclusion criteria; 95 had already received HZV as a result of routine clinical practice and/or the Part 1 intervention. An additional 48 (17.8%) of the 269 eligible patients were vaccinated in association with the Part 2 intervention. At the completion of Part 2, a total of 143 (53.2%) of the 269 PLWH meeting the inclusion criteria had received HZV in association with one of the interventions or routine clinical practice.

The mean age and CD4 count for eligible patients were 64.8 [standard deviation (SD) 4.25] years and 626 (SD 317) cells/μL in Part 1 and 63.7 (SD 4.48) years and 611 (SD 306) cells/μL in Part 2. In Part 1, the primary reason for not vaccinating (10 of 16 provider responses) was ''deferral to the next visit.'' During Part 2, insurance coverage (13 of 52 provider responses) and patient refusal (13 of 52 provider responses) were the most common reasons for not vaccinating.

Table 1. Preintervention Herpes Zoster Vaccination Rates from a Sampling of HIV Clinics in the United States and Canada

Clinic location	*Number of eligible patients*	*Number (%) of patients with documented receipt of HZV*
Atlanta Veterans Affairs	323	5 (1.5)
McGill University	375	9 (2.4)
Denver Health Medical Center	170	6 (3.5)
Denver Veterans Affairs	130	9 (6.9)
University of Colorado	174	37 (21.3)
San Diego Veterans Affairs	306	130 (42.5)
Total	1,478	196 (13.3)

HZV, herpes zoster vaccine.

Seventy-five percent of 60 vaccinated patients through Part 1 and 2 participated in a postvaccination survey. Seven (15.6%) patients reported minor pain or swelling at the injection site. Three patients (6.7%) noticed local itching or rash, and two (4.4%) reported gastrointestinal symptoms. No patients reported a visit to a medical provider for adverse vaccine reactions.

Discussion

HZ vaccination rates were low at the majority of surveyed sites, with the exception of one VA site which exceeded national averages and is staffed by several champions of HZV who had been involved in the Shingles Prevention Study. There are likely many reasons for failure to vaccinate, including competing priorities in this complex patient population, lack of clinical guidelines, storage requirements for HZV, and the complexities and limitations of insurance coverage. For Medicare beneficiaries, HZV must be billed to Part D medication coverage and administered at a retail pharmacy, with variable reimbursement.[13] Vaccine administration at retail pharmacies may impede documentation. Indeed, baseline receipt of HZV at the University of Colorado was higher than expected, in part, due to direct patient reporting of receipt of HZV that was not previously documented in the medical record. Notably, concerns about safety or immunogenicity were not a primary reason for failure to vaccinate.

Within the University of Colorado clinic, 21.3% of patients had received vaccination before the intervention. An additional 8.3% of eligible participants were vaccinated with provider notifications alone and an additional 17.8% with both provider notification and a pended order. By the end of Part 2, despite an increase in the number of eligible patients during the intervention time period, a total of 53.2% of eligible patients had received HZV, more than double the 2013 HZV utilization rates (24%) in the U.S. general population.[14] In this small, single-site study population, we observed no serious adverse reactions to HZV, similar to published HZV safety data for this population. Numerous interventions to increase vaccination rates in the general population have shown variable efficacy: a meta-analysis of interventions aimed at increasing influenza vaccination in patients ≥60 years of age found that direct reminders to providers were most effective.[15,16] Increases in vaccination rates for interventions deemed successful were similar to the rates of improvement found in our project.[15]

Further data on the long-term clinical efficacy and formal guidelines for use of HZV among older PLWH may improve provider motivation: in a survey of 336 HIV care providers between October 2008 and January 2009, shortly after FDA approval of HZV, lack of safety data (72%) and lack of formal Infectious Disease Society of American guidelines for HZV usage in PLWH (56%) were identified as the most common major barriers to HZV administration.[17] A new candidate adjuvanted HZ subunit vaccine[18–20] appears to have markedly greater efficacy in immunocompetent adults and markedly greater immunogenicity in immunocompromised patients compared with HZV. As it is nonreplicating, it likely poses minimum risk for immunocompromised patients. Safety and efficacy data from these studies may soon provide greater impetus for vaccination in the general population and, ultimately, among PLWH.

Our study does have limitations. The capture of vaccination at other sites often did not include patient report or outside records, thus may have underestimated actual receipt of HZV. In addition, receipt of HZV may have differed in a private practice HIV clinic or a practice where patients were primarily followed by an internist or family practice provider rather than an HIV provider.

In summary, HZV coverage was generally very low among eligible patients in a sampling of HIV clinics. Although the safety and efficacy data with the HZ subunit vaccine may provide greater provider impetus, many barriers to HZV will still impede vaccination rates. Clinical reminders with links to vaccination orders and preplaced vaccination orders led to improved HZV coverage in our clinic, but provider motivation and decreasing barriers to HZV receipt are paramount to improved HZV coverage. Even 10 years after approval of HZV, formal published guidelines for its use in PLWH are still lacking, and this remains a barrier to routine vaccination in many clinical settings, including many of the sites surveyed in our study. Increasing HZV uptake has the potential to markedly decrease HZ morbidity and mortality among PLWH.

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