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ORIGINAL ARTICLE

Risk of Herpes Zoster and Disseminated Varicella Zoster in Patients Taking Immunosuppressant Drugs at the Time of Zoster Vaccination

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Abstract

Objective: To determine the risks associated with zoster vaccine when administered to patients taking immunosuppressant medications.

Patients and Methods: Patients enrolled in 1 of 7 managed care organizations affiliated with the Vaccine Safety Datalink between January 1, 2006, and December 31, 2009, were eligible. The exposure of interest was zoster vaccination in patients with current or remote immunosuppressant drug use. The primary outcomes were disseminated varicella zoster virus (VZV) and herpes zoster in the 42 days after vaccination. Automated data were collected on immunosuppressant drugs and baseline medical conditions. A logistic regression model using inverse probability treatment weights was used to estimate the odds of developing VZV or herpes zoster.

Results: A total of 14,554 individuals had an immunosuppressant medication dispensed around the time of vaccination, including 4826 with current use and 9728 with remote use. Most patients were taking low-dose corticosteroids. No cases of disseminated VZV were found in the current or remote users. The risk of herpes zoster was elevated in the 42 days after vaccination in current vs remote users (adjusted odds ratio, 2.99; 95% CI, 1.58-5.70).

Conclusion: We found that patients taking immunosuppressant medications at the time of vaccination had a modest increased risk of herpes zoster in the 42 days after vaccination. The development of herpes zoster within 42 days after vaccination suggests that this is more likely due to reactivation of latent zoster virus than dissemination of the vaccine-derived varicella virus. These findings support the current zoster vaccination guidelines.

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Zoster vaccine live (Zostavax) is indicated for the general adult population older than 50 years to reduce the burden of disease associated with reactivation of latent varicella zoster virus (VZV).[1] In clinical trials and observational studies, the zoster vaccine has been shown to reduce the incidence of herpes zoster and postherpetic neuralgia.[2-4] Zoster vaccine, however, is not recommended for all individuals.

Live virus vaccines are generally contraindicated in immunocompromised patients, including those with human immunodeficiency virus, those with active malignancies receiving chemotherapy, and those receiving immunosuppressive drugs or corticosteroids.[5] The evidence suggests that varicella vaccination has, on rare occasions, been associated with "disseminated vaccine virus (Oka VZV) without other organ involvement," and in patients with demonstrated immunodeficiencies, the vaccine virus can disseminate to other organs (lung, liver, and central nervous system).[6] Recently, Tseng et al[7] reported a case of disseminated Oka VZV without other organ involvement after zoster vaccination.

For patients with immune-mediated diseases, the recommendation is frequently made to vaccinate before initiating immunosuppressant drug therapy.[8-12] The rationale for this

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recommendation is 2-fold. First, compared with the general population,[13] patients with diseases such as rheumatoid arthritis, inflammatory bowel disease, and systemic lupus erythematosus are at increased risk for herpes zoster.[14-19] Second, there is concern that immunosuppressant medication use in these patients could place them at even higher risk for herpes zoster.

Studies evaluating the risk of herpes zoster in patients who were receiving anti–tumor necrosis factor, corticosteroids, or methotrexate for immune-mediated diseases (mostly rheumatologic) have yielded conflicting results, with some reporting increased[20] and others no increased[21,22] risk. Although these studies focused on the risk of herpes zoster in treated patients with rheumatologic conditions, many patients are receiving corticosteroids and immunosuppressant agents for a variety of inflammatory and other conditions. We are aware of only 1 study that evaluated the safety of the zoster vaccine in patients with immune-mediated diseases, and most patients in this study were not being treated with immunosuppressant drugs.[23]

The current recommendation for patients taking corticosteroids is that the zoster vaccine is safe when taking low-dose or short-term courses of therapy (<20 mg/d of prednisone for <14 days).[12] Patients receiving high-dose corticosteroids (≥20 mg/d of prednisone for ≥14 days) should not receive zoster vaccination until corticosteroid therapy has been stopped for at least 1 month.[12] There is, however, little empiric evidence, and these recommendations are largely based on expert opinion. To better understand the potential risks associated with administration of the zoster vaccine to patients receiving corticosteroids and other immunosuppressant drugs, we undertook a study within the Vaccine Safety Datalink (VSD). The goal was to characterize this population of patients and to evaluate the risk of disseminated VZV and herpes zoster after administration of the zoster vaccine in patients who were currently receiving immunosuppressant medications.

METHODS

Setting and Patients

The VSD represents a collaboration between the Centers for Disease Control and Prevention and several managed care organizations (MCOs) across the United States.[24] Each MCO in the VSD maintains a standard set of data files on all members in their respective institutions. These files include information on vaccinations, demographic characteristics, health plan enrollment, outpatient clinic visits, emergency department visits, hospitalizations, mortality, and birth data.[24]

Study participants were members enrolled in 1 of 7 MCOs affiliated with the VSD. Adults aged 18 years and older who received the zoster vaccine between January 1, 2006, and December 31, 2009, were eligible for inclusion. In addition, patients needed to have 12 months of continuous membership in the MCO before and 6 months after the vaccination date. The study was approved by the institutional review board at each of the participating MCOs.

Exposure

The exposure of interest was zoster vaccination in patients with current or remote immunosuppressant medication use. Outpatient pharmacy records for patients vaccinated with the zoster vaccine were screened for immunosuppressant drugs dispensed in the 12 months before and up to 5 days after vaccination. Information on outpatient pharmacy prescriptions for immunosuppressant drugs included the date dispensed, generic name, strength, quantity, and days of supply. Most patients (>90%) with 12 months of continuous membership in their MCO have a drug benefit that provides an incentive to obtain their prescriptions in a network pharmacy, ensuring high prescription capture rates. The immunosuppressant drugs included the oral corticosteroids and a group of "other immunosuppressant drugs," including nonbiological disease-modifying antirheumatic drugs (DMARDs) and oral antirejection drugs (Supplemental Table 1, available online at http://www.mayoclinicproceedings.org). The daily dose of corticosteroids was determined using the strength of the tablets, quantity, and days of supply; the potencies of the various corticosteroids were converted to prednisone equivalent values.

We defined immunosuppressant drug use as current if the drug was dispensed between 30 days before and 5 days after vaccination or if the days of supply crossed into this time window. This definition of current use was based

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