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Joint Corticosteroid Injection Associated With Increased Influenza Risk

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Abstract

Aging and immunocompromising conditions or medications may reduce influenza vaccine effectiveness. The high-dose vaccine has been used to improve vaccine response in patients 65 years and older. Because of systemic immunosuppressive effects, oral corticosteroids may reduce vaccine effectiveness; however, despite over half a century of use, no data are available regarding the effect of joint and bursa corticosteroid injection on influenza vaccine effectiveness. The aim of this retrospective study was to determine whether joint corticosteroid injection was associated with reduced influenza vaccine effectiveness. During the 5 influenza seasons between August 1, 2012, and March 31, 2017, a total of 15,068 major joint corticosteroid injections were given to patients residing in Olmsted County, Minnesota. Vaccinated patients receiving a major joint corticosteroid injection (n=4804) were at increased risk (relative risk, 1.52; 95% CI, 1.20-1.93) for developing influenza compared with vaccinated control patients. Women younger than 65 years were at the highest risk, suggesting that perhaps the high-dose vaccine should be considered for this group to enhance protection when possible.

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Influenza is a major global public health issue with significant risk for morbidity and mortality. Annual vaccination can provide important protection; however, the efficacy of influenza vaccination depends on the generation of protective antibodies by the host immune system. Because of poorer immune response to vaccination, patients 65 years and older are routinely administered the high-dose influenza vaccine to improve efficacy. In immunosuppressed individuals, the humoral immune response may be compromised, resulting in less effective immune response to vaccination. Intraarticular corticosteroid injection is known to cause transient suppression of endogenous cortisol production,[1] and corticosteroids (CSs) are known to cause immunosuppression by multiple mechanisms.[2] Despite well over a half century of use to treat inflammatory, crystalline, and degenerative arthritis,[3] no data exist regarding the risk of intraarticular or bursa CS injections and susceptibility to influenza infection.

The aim of this retrospective study was to determine the rate of influenza in patients receiving a hip, knee, or shoulder CS injection just before or during 5 influenza seasons spanning August 1, 2012, to March 31, 2017. Vaccinated and unvaccinated patients receiving CS injections and a control group of vaccinated patients not receiving a joint CS injection were evaluated.

METHODS

The influenza vaccine is administered between the months of October and March at our institution (Mayo Clinic in Rochester, Minnesota, Olmsted County); thus, these months were defined as "influenza season." Patients who received an influenza vaccination at our institution during a given influenza season were defined as "vaccinated," and those who did not were termed "unvaccinated."

A retrospective chart review was conducted to identify all patients residing in Olmsted County who were vaccinated at our institution between October 1, 2012, and March 31, 2017. We also identified all patients who received a major joint CS injection (defined as hip, knee, shoulder joint, or bursa, *Current Procedural Terminology* codes 20610 and 20611) in the weeks before and during each influenza season spanning August 1, 2012, to March 31, 2017. August 1 was used for CS injection data collection to ensure that patients receiving a major joint CS injection a

few weeks before their influenza vaccination were included. Only those patients who were receiving CS injections between August 1 and March 31 of each year were included, whereas those between April 1 and July 31 were not. The location of the joint injected, the CS administered, and the CS doses were recorded for all injections.

The control group included patients 50 years or older receiving an influenza vaccination (but not a joint CS injection) at our institution between October 1, 2012, and March 31, 2017. Influenza diagnosis was based on clinical findings and recorded in the diagnosis section of the clinical visit note as "influenza," "probable influenza," or "influenza like illness." Inclusion criteria included residence within Olmsted County, medical care at our institution, defined influenza vaccination status, and defined joint CS injection status. This study was approved by the Mayo Clinic institutional review board.

The CS dose equivalents were calculated in relation to methylprednisolone acetate using the following conversions: betamethasone 6 mg = methylprednisolone acetate 40 mg and triamcinolone acetonide 40 mg = methylprednisolone acetate 40 mg.

Statistics

For comparisons between multiple groups, χ^2 test was used for categorical data and ANOVA test was used for ordinal data; for within-group comparisons (baseline cohort vs patients with influenza), unpaired *t* test was used for ordinal data and χ^2 test was used for categorical data. *P* values of less than .05 were considered statistically significant. Multivariate logistic regression was performed for clinical and demographic variables. *P* values of less than .05 were considered statistically significant.

RESULTS

A total of 43,236 patients 50 years or older were vaccinated during the influenza seasons between August 1, 2012, and March 31, 2017. During these 5 influenza seasons, a total of 15,068 patients received a major joint CS injection (hip, knee, or shoulder): 10,264 were unvaccinated and 4804 were vaccinated. Table 1 presents baseline characteristics of the groups including comorbidities associated with immunosuppression or immunosuppressive treatment. At baseline, the mean age of the control cohort was more than that of cohorts receiving joint CS injection ($P<.001$), and the percent of female patients was lower in the baseline control cohort than in patients receiving joint CS injection ($P<.001$). The most common comorbidity at baseline in all groups was diabetes mellitus. The overall percent of patients with rheumatoid arthritis in all groups was small, but statistically higher in the patients receiving joint CS injection ($P<.001$). This was expected given that joint CS injection has been a well-utilized treatment for painful rheumatoid arthritis.

Multivariate analysis of the groups together showed that joint CS injection was an important predictor for developing influenza ($P=.002$). Multivariate analysis of the control group alone showed that neither age ($P=.07$) nor sex ($P=.97$) was a significant factor for predicting influenza. In contrast, for patients receiving joint CS injections, multivariate analysis showed that both age less than 65 years ($P=.001$) and female sex ($P=.002$) were significant predictors of influenza. Looking at all vaccinated patients, including the control group and the vaccinated joint CS injection patients, multivariate analysis showed joint CS injection to be the most important predictor of influenza ($P=.002$).

To determine important risk factors for influenza within each group, baseline cohorts were compared with patients with influenza from their respective group. The control baseline cohort average age was not different from the average age of those who developed influenza ($P=.21$). Similarly, the percentage of females was not different between the control baseline cohort and the control patients with influenza. In contrast, for joint CS injection patients (vaccinated and unvaccinated), significantly more females developed influenza. In the joint CS injection baseline cohorts combined, 63.4% (weighted mean) were females and this rose to 73.1% (weighted mean) in patients with influenza receiving joint CS injection ($P<.001$). This finding suggests that for females, joint CS injection was a particular risk factor for the development of influenza.

Age was also an important factor for developing influenza in vaccinated patients receiving joint CS injection. There was a notable difference between vaccinated and