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Influenza vaccine effectiveness against influenza-associated hospitalization in 2015/16 season, Beijing, China

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ABSTRACT

Background: Vaccination is recommended to prevent influenza virus infection and associated complications. This study aimed to estimate the influenza vaccine effectiveness (VE) against hospitalization in the 2015/16 season in Beijing.

Methods: Patients who were hospitalized in the 5 study hospitals between 1 Oct 2015 and 15 May 2016 were recruited. Influenza vaccination status was obtained for PCR-confirmed influenza patients and the selected controls who tested negative for the virus. Conditional logistic regression was used to estimate the influenza VE matching by calendar week, and adjusting for age, study sites, underlying medical conditions, smoking status, and hospital admissions over the past 12 months.

Results: The overall VE was −37.9% (95% CI: −103.3, 6.5) against laboratory-confirmed influenza-associated hospitalization. The 2015–16 seasonal vaccine was had −61.9% (95% CI: −211.9, 15.9), −5.4% (95% CI: −108.1, 46.6) and −45.2% (95% CI: −152.6, 16.5) effectiveness to prevent infection from A(H1N1)pdm09, A(H3N2) and influenza B, respectively.

Conclusions: Influenza vaccination did not show effective protection against hospitalization with influenza in 2015/16 season in Beijing.

1. Introduction

Vaccination is the most effective way to prevent influenza virus infections and the associated complications. In China, influenza vaccination is largely self-paid with all-age coverage as low as 2%, according to a previous study conducted by the Chinese Center for Disease Control and Prevention (China CDC) [1]. To encourage vaccination among residents of the city, the Beijing government has invested approximately 30.5 million RMB ($US 5.1 million) each year to provide free influenza vaccination to seniors (≥60 years) and all primary and secondary school students since 2007 [2].

Few studies have been conducted to examine the influenza vaccine effectiveness (VE) in Beijing. In the 2013–14 and 2014–15 seasons, we carried out a study in Beijing to estimate the influenza VE [3]. It was estimated that vaccination in the 2013–14 season reduced the influenza-associated hospitalizations by 47%, while the overall VE for the 2014–15 season was as low as 5% [3]. Influenza VE is associated with the degree of matching between vaccine strains and circulating strains [4]. Annual estimation of influenza VE is important for ongoing evaluation of the vaccine. The test-negative study design is preferred in using routinely collected patient data to provide continuous estimation of the influenza VE [5].

In this study, the data from an established hospital-based influenza surveillance system were used to estimate the influenza VE

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against laboratory-confirmed hospitalization, in Beijing, 2015–16 season.

2. Methods

2.1. Study setting and subjects

Our study was conducted in 5 hospitals located in 5 districts of Beijing from 1 October 2015 to 15 May 2016. Children and adults who were diagnosed any of the diseases listed in Appendix Table 1 and were admitted into the pediatric ward, respiratory care unit, or intensive care unit (ICU) in any of these hospitals were eligible for inclusion in the study. At the same time patients ≥5 years should also meet the influenza like illness (ILI) definition which was defined by the European Center for Diseases Control as presence of any of the four systemic symptoms (fever or feverishness, headache, myalgia or malaise) plus any of the three respiratory symptoms (cough, sore throat or shortness of breath). Patients were excluded if they (1) did not provide a consent; (2) could not communicate; (3) were not residents of Beijing (living in the city for ≥6 months); (4) were institutionalized; (5) had the onset of ILI symptoms >7 days prior to admission; or (6) had been hospitalized in the previous 30 days.

Attending doctors in each hospital screened for eligible patients every day, and all patients who met the above criteria and consented to be interviewed were recruited into the study. The doctors interviewed the patients using standard questionnaires within 24–48 h after admission. Patients' information was collected including patients' demographic characteristics, medical history, clinical procedure and treatment outcomes. As part of the surveillance, nasopharyngeal swabs were also collected from the recruited patients after obtaining their verbal consent. All of the samples were tested for influenza A and B viruses by the real-time RT-PCR.

The influenza season was defined in this study as the time period in which two or more recruited cases testing positive for influenza virus in two consecutive weeks. The influenza season identified in the study was from week 50 in 2015 through to week 17 in 2016. In estimation of the VE, we only included the inpatients that were recruited during the influenza season. Meanwhile patients enrolled before 1 November 2015 were excluded from the VE analysis because the influenza vaccine was not available in Beijing for the 2015–16 season until 15 October 2015.

The study protocol was approved by the Ethics Committee of the Beijing CDC.

2.2. Definition of vaccination status

In Beijing, only the trivalent inactivated influenza vaccine (TIV) was available for the 2015–16 season. The 2015–16 influenza TIV was composed of A/California/7/2009 (H1N1)pdm09-like virus, A/Switzerland/9715293/2013 (H3N2)-like virus, and B/Phuket/3073/2013-like virus (a B/Yamagata lineage strain).

The Beijing Health Bureau of the Beijing Government has set up a vaccination registry covering all residents in the city since 2009. As required, vaccination history was recorded for residents receiving a vaccination, including influenza vaccine regardless of whether it was self-paid or free. In this study, we used the information recorded in the registry to determine patients' vaccination status in the main analysis. We also collected self-reported vaccination status from each patient using the questionnaire in which the patient's vaccination status was classified as vaccinated, not vaccinated and unknown. Vaccination data collected from the two sources were compared in the later analysis. A patient was defined as vaccinated if he/she received a TIV in the current influenza season ≥14 days before developing the ILI symptoms reported upon admission. Children who missed one of the two doses of the vaccine but was vaccinated ≥14 days before the ILI onset were also categorized as vaccinated. Patients who reported having a contraindication to influenza vaccination or received a TIV within 14 days before symptom onset were excluded from the study.

2.3. Outcome definitions

The swab specimens were tested in the district CDCs' laboratories using the standardized method and reagents. The multiplex real-time PCR was performed for each sample to detect the presence of: influenza A (H1N1 and H3N2), influenza B (B/Yamagata and B/Victoria lineages). RNA extraction was performed with 140 μL samples using QIAamp Viral RNA Mini Kit (Qiagen, Copenhagen, Denmark) according to the manufacturer's instruction. The yield RNA was finally eluted using 50 μL RNase-free water. The viral detection was completed by rRT-PCR using AgPath-ID One-Step RT-PCR kit (Applied Biosystems, Grand Island, USA) and 7500 Fast Real-Time PCR System (Applied Biosystems) using 5 μL of RNA according to manufacturer's instruction and the WHO's protocol [6]. All reactions were run in duplicate. Only those samples that had Ct value lower than 35 or higher than 37 in duplicated tests were regarded as positive or negative, respectively. Otherwise a retest would be performed to get a confirmed positive or negative result.

Patients who tested positive for influenza virus by real-time RT-PCR were classified as influenza cases, while those with a negative testing result were controls.

2.4. Population vaccine coverage

The age-specific resident population data were derived from the Beijing Statistical Yearbook 2015. [7] Resident population was defined as people who had continuously lived in the city for over six months per year. The age-specific influenza vaccination coverage data among the general population in the city were exported from the Beijing Expanded Program on Immunization Information Management System.

2.5. Statistical analysis

We used conditional logistic regression models to estimate the odds ratios (ORs) of vaccinated patients testing positive for influenza by virus type/subtype compared with unvaccinated patients, matching on calendar weeks and adjusting for age groups, study sites (different hospitals), underlying conditions (cardiovascular disease, chronic obstructive pulmonary disease, asthma, diabetes, immunodeficiency or organ transplant, renal impairment, rheumatologic disease, neuromuscular disease, cirrhosis or liver disease, neoplasm, autoimmune disease and hematological disease), smoking status, hospitalizations over the previous 12 months. The VE was calculated as 100% x (1-adjusted OR). Age and study sites were included as categorical variables in the model. The VE estimates were provided for overall influenza (including virus type A and B) as well as by virus type/subtype including A(H1N1)pdm09, A (H3N2) and B separately. Age-specific VEs were estimated to investigate any potential differences in vaccine protection across age groups.

In the sensitivity analysis, we redefined the vaccination status by using both the self-reported and registration records. To be specific, self-reported vaccination history was used when a patient's influenza vaccination record in the current season could not be found in the registry, while the vaccination status was treated as missing if cases reported a unknown vaccination history in the self-reported questionnaire, and at the same time no influenza

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