Vaccine 32 (2014) 5285–5289

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Influenza vaccine effectiveness against medically-attended influenza illness during the 2012–2013 season in Beijing, China

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ARTICLE INFO

Article history:
Received 28 April 2014
Received in revised form 8 July 2014
Accepted 22 July 2014
Available online 1 August 2014

Keywords:
Influenza
Vaccine effectiveness
Influenza-like illness
China

ABSTRACT

Background: Influenza vaccine coverage remains low in China, and there is limited information on the preventive value of local vaccination programs.
Methods: As part of influenza virological surveillance in Beijing, China during the 2012–2013 influenza season, we assessed the vaccine effectiveness (VE) of one or more doses of trivalent inactivated influenza vaccine (IIV3) in preventing medically-attended influenza-like-illness (ILI) associated with laboratory-confirmed influenza virus infection using a test-negative case–control design. Influenza vaccination was determined based on self-report by adult patients or the parents of child patients.
Results: Of 1998 patients with ILI, 695 (35%) tested positive for influenza viruses, including 292 (42%) A(H3N2), 398 (57%) A(H1N1)pdm09, and 5 (1%) not (sub)typed influenza viruses. The rate of influenza vaccination among all patients was 4% (71/1998). Among influenza positive patients, 2% (57/1303) were vaccinated compared to 4% (14/695) among influenza negative patients, resulting in VE for one or more doses of vaccine (adjusted for age, sex, week, and days since illness onset) against all circulating influenza viruses of 52% (95% CI = 12–74%). A significant adjusted VE for one or more doses of vaccine for all ages against A(H1N1)pdm09 of 59% (95% CI, 8–82%) was observed; however, the VE against A(H3N2) was 43% (95% CI, −30% to 75%). The point estimate of VE was 59% (95% CI, 19–79%) for those aged <60 years, but a negative VE point estimate without statistical significance was observed among those aged ≥60 years.
Conclusions: IIV3 conferred moderate protection against medically-attended influenza in Beijing, China during the 2012–2013 season, especially against the A(H1N1)pdm09 strain and among those aged <60 years old.

1. Introduction

Influenza contributes to high morbidity and mortality in China [1,2] and globally [3]. Although the Chinese Center for Disease Control and Prevention (CDC) recommends annual vaccination with the northern hemisphere trivalent influenza vaccine (as recommended by World Health Organization (WHO)), for young children, older adults, and other high risk groups [4], the vaccine coverage remains very low, with less than 2% vaccine uptake in the total Chinese population and around 10% among Beijing citizens [5], and there is limited information on influenza vaccine effectiveness (VE) in China [6,7]. In the capital city, Beijing, which is located in the temperate northern region of China, the influenza epidemic usually occurs from December to January [8]. Before each influenza season, trivalent inactivated influenza vaccine (IIV3) has been provided at no cost to school-aged children (aged 6–17 years old) and older adults (aged ≥60 years old) since 2007 and is available for an out-of-pocket fee to all other residents [5,9].

In order to examine the preventive value of our current influenza vaccine program, during the 2012–2013 influenza season, we evaluated the VE of IIV3 in preventing medically-attended influenza-like-illness (ILI) associated with laboratory-confirmed influenza virus infection using a test-negative case–control design,

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http://dx.doi.org/10.1016/j.vaccine.2014.07.083
0264-410X/

which has been extensively employed for the study of influenza VE [10,11].

2. Methods

2.1. Participants and laboratory detection

Influenza positive and negative patients were identified through influenza virological surveillance at 20 sentinel hospital-based ambulatory care clinics in Beijing, China from December 1, 2012 to January 31, 2013 which corresponded to a period of peak influenza circulation in the northern region of China [1,12,13]. According to previously described procedures of influenza virological surveillance of Beijing formulated by Beijing CDC [8], sentinel hospitals were requested to collect pharyngeal swabs each week from ≥20 patients with ILI (i.e., temperature ≥ 38 °C and either cough or sore throat) who visited the clinic within 3 days of illness onset. Respiratory specimens were collected from consenting patients by a trained nurse, placed in viral transport medium, stored in the refrigerator at 4 °C, and transported in a cool box with ice packs to 1 of 14 collaborating laboratories managed by Beijing CDC within 24 h after collection. Upon received by the collaborating laboratory, the respiratory specimens were immediately inoculated into Madin–Darby canine kidney (MDCK) cells, and subsequently cultured in an incubator at 33–35 °C. After incubation within a period of ≤7 days, influenza viruses in cell cultures were identified using hemagglutination assay (HA) and hemagglutination inhibition (HI) assays. All the assays were conducted in Biosafety Level 2 (BSL2) laboratories by well-trained staffs according to standard operating procedures of influenza issued by WHO Collaborating Centre for Reference and Research on Influenza in China [14].

In this test-negative case–control study, cases were ILI patients who tested positive for influenza by virus isolation, and controls were ILI patients who tested negative for influenza.

2.2. Data collection

Nurses at sentinel hospitals recorded the patient's sex, age, illness onset date, specimen collection date, and influenza vaccination status within the prior 6 months. Receipt of one or more doses of influenza vaccine was documented from self-report of adult patients or the parents or guardians of child patients. The composition of influenza vaccines for the 2012–2013 influenza season recommended by WHO contained the following: A/California/7/2009 (H1N1)pdm09, A/Victoria/361/2011 (H3N2) and B/Wisconsin/1/2010-like virus [15]. The reporting form was sent along with respiratory specimens to the collaborating laboratory.

2.3. Data analysis

Unadjusted and adjusted odds ratios (OR: the odds of influenza vaccination among cases divided by the odds of influenza vaccination among controls) were estimated using unconditional univariate and multivariate logistic regression models (adjusting for sex, age, interval between illness onset and specimen collection, and month of illness onset), and VE was calculated as 100% × (1 − odds ratio) [10,11]. Stratified VE estimates were also calculated by age groups and by influenza virus type. All statistical tests were 2-sided, and statistical significance was defined as $p < 0.05$ or the lower bound of the 95% confidence interval (CI) for VE > 0. Using a case–control study design, we calculated that 527 cases were needed to detect VE of 60% with two controls for each case and a vaccination rate of 5% among controls (80% power, $\alpha = 0.05$) [5,16,17]. Although our all ages VE model exceeded this goal, stratified analyses by age did not, and these are presented as exploratory analyses to aid in comparisons and hypothesis generation. Analyses were carried out by using the SPSS 16.0 statistical package (SPSS Inc., Chicago, IL, USA).

This study was approved by the institutional review board and human research ethics committee of Beijing CDC.

3. Results

From December 1, 2012 through January 31, 2013, a total of 3748 patients with ILI participated in the influenza virological surveillance in Beijing, and 1213 (32%) were tested positive for influenza viruses. Of 3748 patients with ILI, 1998 (53%) with complete surveillance documentation that included influenza vaccination status were included in this test-negative case–control study (Fig. 1). Among 1998 patients, 695 (35%) tested positive for influenza viruses, including 292 (42%) A(H3N2), 398 (57%) A(H1N1)pdm09, and 5 (1%) not (sub)typed influenza viruses. No influenza B viruses were identified in the patients during this period. The proportion of females was 50% (997/1998), and approximately 62% (1246/1998) were 18–59 years. The median interval between illness onset and sample collection was 1 day, and 97% (1938/1998) of the participants, respiratory specimens were collected within 3 days of illness onset.

There were statistically significant differences in age group and interval between illness onset and sample collection between influenza-positive patients and influenza-negative patients, but not in sex (Table 1). The rate of influenza vaccination among all patients was 4% (71/1998), and differed by sex and age group (Table 1).

Among influenza positive patients, 2% (57/1303) were vaccinated compared to 4% (14/695) among influenza negative patients, resulting in an unadjusted overall VE for one or more doses of vaccine against all circulating influenza viruses of 55% (95% CI, 19–75%) and an adjusted overall VE for one or more doses of vaccine of 52% (95% CI, 12–74%) (Table 2). Age, week, and days from illness onset to specimen collection were statistically significant contributors to the multivariate model (data not shown).

In secondary analyses, we observed a significant adjusted VE for one or more doses of vaccine for all ages against A(H1N1)pdm09 of 59% (95% CI, 8–82%); however, the VE point estimate for one or more doses of vaccine against A(H3N2) was 43% (95% CI, −30% to 75%) (Table 2). The point estimates of VE were 16% (95% CI, −774% to 92%) for those aged 6–35 months, 53% (95% CI, −2% to 78%) for those aged 3–17 years, 78% (95% CI, −89% to 98%) for those aged 18–59 years, and −395% (95% CI, −3773% to 37%) for those aged ≥60 years, though confidence intervals for all subgroups overlapped with zero. Nonetheless, combining all patients under age 60 years old, we observed a significant VE of 59% (95% CI, 19–79%). In sensitivity analyses, the overall VE estimates were unchanged when those aged 6–35 months, who are recommended to receive two doses of influenza vaccine, were excluded; similarly, results were unchanged when patients enrolled >3 days since illness onset were excluded (Table 2).

4. Discussion

In our study of ambulatory patients with ILI (i.e., temperature ≥ 38 °C and either cough or sore throat) in Beijing, China, during two months when A(H3N2) and A(H1N1)pdm09 viruses co-circulated and matched with 2012–2013 IIV3 vaccine strains [18,19], we estimated that 2012–2013 IIV3 conferred 52% (95% CI, 12–74%) protection against medically-attended ILI attributed to influenza virus infection.

Our estimated VE for one or more doses of vaccine of 59% (95% CI, 8–82%) against A(H1N1)pdm09 is similar to VE estimates