Vaccine 29 (2011) 1844–1849

Contents lists available at ScienceDirect

Vaccine

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

The effectiveness of trivalent inactivated influenza vaccine in children over six consecutive influenza seasons

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ARTICLE INFO

Article history:
Received 19 October 2010
Received in revised form 7 December 2010
Accepted 13 December 2010
Available online 31 December 2010

Keywords:
Influenza
Vaccine
Children

ABSTRACT

Objective: To estimate the effectiveness of two doses of trivalent inactivated influenza vaccine (TIV) over six consecutive influenza seasons in a small community in Japan.
Patients and methods: A prospective, non-randomized, observational study of TIV effectiveness was performed involving children aged 6 months to 6 years accessing pediatric services in Soma and Shinchi, Japan. The total number of children under observation was 14,788. Each fall from 2002 to 2007 TIV was offered to all children with an average uptake of 52.9%. Influenza rapid diagnostic tests were performed to all children with respiratory symptoms and a temperature >38 °C during each surveillance period. The efficacy of two doses of TIV was estimated by the relative risk of influenza illness and influenza associated hospitalizations and effectiveness by reduction in all respiratory illness in vaccinated and unvaccinated children.
Results: Influenza A occurred each year resulting in approximately one in five children in the unvaccinated group having an influenza A related clinic visit. For influenza A, two doses of TIV showed yearly efficacies that ranged from 42% to 69% with the highest efficacy during the 2002/2003 influenza season when the vaccine strains were well matched with the circulating viruses. The overall efficacy of two doses of TIV against influenza A and B associated illness was 52% and 59%, respectively. TIV also reduced the rate of the influenza associated hospitalizations attributable to both influenza A and B.
Conclusions: Vaccination with two doses of TIV was consistently effective in preventing influenza-associated clinic visits and hospitalizations.

1. Introduction

Influenza virus is a major pathogen which causes acute respiratory infections each winter and influenza is an important cause of morbidity and mortality among both children and adults. While influenza virus causes disease in all ages, influenza is associated with an annual excess number of hospitalizations among young children under 5 years of age [1]. Currently all children more than 6 months in Japan and the United States are encouraged to be immunized with trivalent inactivated influenza vaccine (TIV). TIV is efficacious (50–60%) in reducing the incidences of influenza in older children when efficacy is measured against documented influenza illness by culture, antigen detection or molecular methods [2–4]. TIV effectiveness in children is lower when estimated based on non-laboratory-confirmed outcomes such as influenza-like illness [5,6]. The data in children under 2 years are so limited that a Cochrane Review of Influenza Vaccination in Children published in 2008 reached the conclusion that there was no evidence of TIV efficacy under the age of 2 years [7].

In the present study we have defined the substantial and consistent efficacy of two doses of TIV in the prevention of influenza associated clinic visit and hospitalization in children 6 months through 5 years of age over six consecutive influenza seasons, 2002/2003 to 2007/2008, in a small Japanese region with cloistered medical care.

Abbreviations: TIV, trivalent inactivated influenza vaccine; HA, hemagglutinin; LAIV, live attenuated influenza vaccine; CI, confidence interval.

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doi:10.1016/j.vaccine.2010.12.049

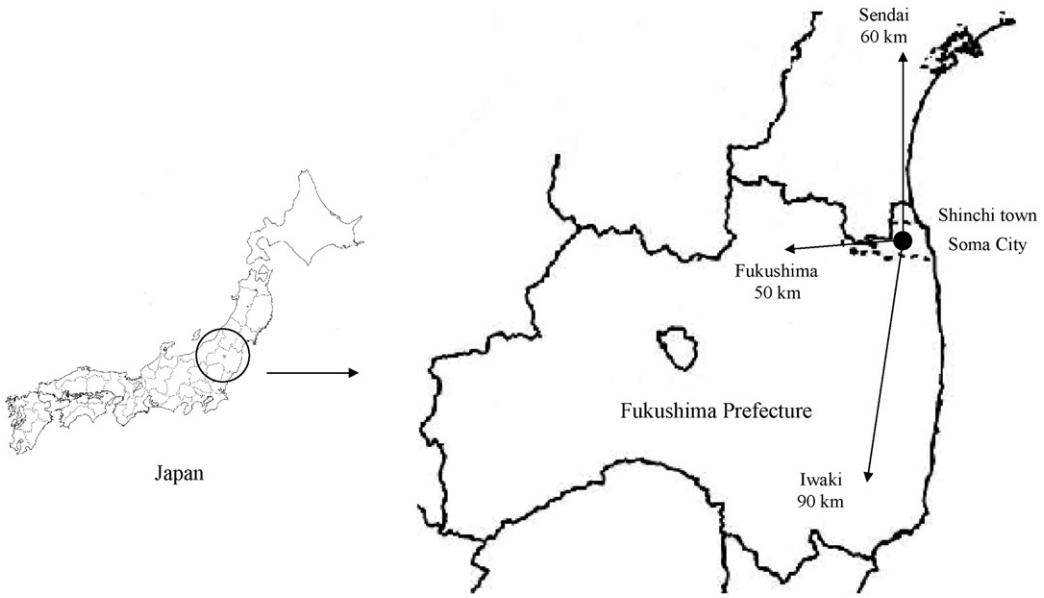

Fig. 1. The geography of Soma and Shinchi in Japan.

2. Patients and methods

2.1. Soma Study location and population

Soma city and Shinchi town form a contiguous, relatively isolated set of communities in Fukushima Prefecture, Japan. There is only one hospital in this area that admits children, two clinics serving exclusively children and 22 other clinics where children can be seen. There are no other major hospitals within 50 km of this area (Fig. 1). For these reasons, it is assumed that almost all vaccination and primary care for illness would occur locally in these facilities. Fukushima Prefecture has a population of approximately two million of which just less than 50,000 live in the Soma area. The Soma Study actively offers influenza vaccination to all children in the area and is organized by the Department of Pediatrics, Soma General Hospital with the cooperation of all of clinics and the Soma Medical Association. All clinical and demographic information on children was recorded whenever they visited a medical facility and this was correlated with their history of vaccination in the previous fall. It was not readily possible to link records from consecutive years to segregate high risks in the analysis, to determine the impact of distant vaccination or prior natural infection on influenza associated illness, or to determine if the same individuals either accepted or refused vaccination on a yearly basis.

2.2. Vaccine

In this study commercially available TIVs in Japan containing 30 μg/ml of hemagglutinin (HA) for each of the recommended H1N1, H3N2 and B components were administered each fall to children (Table 1). In Japan two doses of vaccine 3–4 weeks apart are recommended each season regardless of previous receipt of TIV. The subcutaneous dosage is 0.1 ml (3 μg of each strain's HA) for children 6–11 months of age and 0.2 ml (6 μg of each strain's HA) for 1 to <6 years of age. Vaccine components were decided yearly by National Institute of Infectious Diseases, Japan based on World Health Organization recommendations.

2.3. Influenza detection

Influenza rapid diagnostic tests which detected and differentiated between influenza A and B[1] were performed to all patients having acute respiratory infectious symptoms with >38 °C of fever during each surveillance period. The use of nasal swabs, method of sample collection and performance of the antigen test were standardized between all medical facilities before the Soma Study was started though the choice of rapid test was made by the local facility. The children with positive antigen detection were considered to have influenza virus infection and information of these children was reported weekly by all the clinical facilities to the Department of Pediatrics, Soma General Hospital. The total number of children seen with febrile respiratory disease and tested for influenza was available for 2007–2008.

2.4. Occurrence of influenza in Fukushima Prefecture and data on circulating strains

In Japan, through the National Epidemiological Surveillance of Infectious Diseases, clinically diagnosed influenza cases are reported weekly by approximately 5000 influenza sentinel clinics all over the country. A portion of clinical samples obtained from patients diagnosed as having influenza because of their clinical symptoms or on the basis of a positive rapid diagnostic test are provided to prefectural or municipal public health institutes for virus isolation and antigenic characterization. As one part of this surveillance network, Fukushima Prefecture has 80 sentinel clinics which weekly report the occurrence of influenza to the Fukushima Institute of Public Health. The data from the Fukushima Institute of Public Health was used to describe circulating viruses in the

[1] Tests used included Espline Influenza A&B-N, Fujirebio Inc., Tokyo, Capillia Flu A + B, Alfresa Pharma Corporation Tokyo, Poctem influenza A/B, Otsuka Pharmaceutical Co., Ltd., Tokyo, Rapid Testa FLU Stick Kyorin Pharmaceutical Co., Ltd., Tokyo, Quick chaser Flu A, B, Mizuho medy Co., Ltd., Check Flu A·B Alfrese Pharma Corporation, Tokyo, Quick Ex-Flu, Denka Seiken Co., Ltd., Tokyo, Clearview Exact Influenza A&B, Inverness Medical Japan Co., Ltd., Tokyo, Prolast Flu, Mitsubishi Chemical Medience Corporation Tokyo, or Quicknavi flu, Otsuka Pharmaceutical Co., Ltd., Tokyo.