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Single-dose varicella vaccine effectiveness in school settings in China☆

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ABSTRACT

Background: Varicella vaccine has been available in the private sector in China for a decade as a single-dose regimen, but varicella vaccine effectiveness (VE) has not been fully examined in school settings yet.
Methods: A matched case–control study was carried out in elementary schools and daycares in Tai'an prefecture, Shandong province, China. Clinical diagnosis of varicella and breakthrough disease was used for this study. Four controls were randomly selected from classmates; two from classmates of the case and two from another class of the same grade without cases. Vaccination status, date of vaccination, and vaccine product received if vaccinated were collected from home and clinic immunization records. Vaccination status of all students in schools/daycares with varicella cases from home immunization records or parental recall was used to calculate vaccination coverage.
Results: The overall varicella VE was 83.4% (95% confidence interval 71.4–90.3%). Receipt of varicella vaccine five years or more years before the outbreak was significantly associated with breakthrough varicella (odds ratio = 4.7, $P < 0.001$), while age at vaccination (<15 vs. ≥15 months) was not (odds ratio = 1.5, $P = 0.62$). Varicella vaccination coverage was 41% with substantial variation across schools (range of 0–93.8%).
Conclusions: Single-dose varicella vaccine is highly effective in school settings. Maintaining limited vaccination coverage might shift varicella disease burden to older individuals, who are more prone to develop severe outcomes if varicella occurs.

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1. Introduction

Varicella (chickenpox) is a highly contagious disease caused by infection with varicella zoster virus (VZV), and is characterized by a generalized pruritic vesicular rash. Although varicella is usually self-limiting and resolves within a week, severe complications, including death, can occur [1].

Varicella vaccines are now widely available as the most effective measure for prevention and control of varicella. In China, varicella vaccine first became available in 1998. Five vaccines are currently licensed in China for single dose use in persons 12 months and older: Varilrix® (GlaxoSmithKline) and four domestic vaccines (Baike, Changsheng, Keygen, and Shanghai). The five varicella vaccines have similar concentrations of Oka strain VZV: >1995 plaque forming unit/dose (0.5 mL) in Varilrix, and >2000 plaque forming unit/dose (0.5 ml) in the domestic vaccines. The five vaccines have the same temperature requirement (2–8 °C) for cold-chain storage and transportation. Currently, varicella vaccines are only available for private purchase in China and vaccination coverage varies substantially by regional level of economic development [2–5]. Although their immunogenicity and safety have been assessed previously in randomized clinical trials [6–13], the effectiveness of these vaccines in China have not yet been fully examined in school settings, the most likely places for intense varicella exposure as a consequence of decreasing family sizes in China [14]. A matched case–control study was carried out in schools and daycares to examine the post-licensure effectiveness of varicella vaccines in school settings in Shandong Province, China.

☆ The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, U.S. Department of Health and Human Services.

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Table 1
Characteristics of the cases and the controls by exposure status in 44 schools, Tai'an prefecture, China, 2010–2011.

	Cases, No. (%) (n = 180)	Controls, No. (%) (n = 679)	P value
Sex			0.15
Male	97 (53.9)	328 (48.31)	
Female	83 (46.1)	351 (51.69)	
Age in years: mean (SD)	7.4 (2.2)	7.3 (2.1)	0.66
Having any underlying disease			1.0
Yes	1 (0. 6)	5 (0.74)	
No	179 (99.4)	674 (99.26)	
Type of school			0.33
Elementary school	118 (65.6)	471 (69.37)	
Daycare	62 (34.4)	208 (30.63)	
Varicella vaccination status			<0.001
Vaccinated	18 (10.0)	232 (34.17)	
Unvaccinated	162 (90.0)	447 (65.83)	
Varicella vaccine product[a],[b]			0.30
Baike	3 (16.7)	80 (34.637)	
Changsheng	12 (66.6)	123 (53.25)	
GlaxoSmithKline	0 (0.0)	1 (0.43)	
Keygen	1 (5.6)	15 (6.49)	
Shanghai	2 (11.1)	12 (5.19)	
Age at vaccination[a]			0.62
<15 months	3 (16.7)	37 (92.50)	
≥15 months	15 (83.3)	195 (92.86)	
Year since varicella vaccination:			
Mean (SD)[a]	4.1 (2.3)	2.9 (2.0)	0.01

[a] Single-dose varicella vaccine recipients only.
[b] One control with missing information on varicella vaccine product received.

2. Methods

2.1. Study population

The China Center for Disease Control and Prevention (CDC) and Tai'an CDC conducted a case–control study in schools and daycare centers in five counties of Tai'an prefecture, Shandong province, from 3/2010 to 6/2011. A case of varicella was defined as an acute generalized maculopapulovesicular rash without other apparent cause [15]. Breakthrough varicella was defined as a case that developed >42 days after vaccination [15]. Although varicella was not a notifiable disease in Tai'an prefecture during this period, 248 elementary schools and daycare centers in five counties of Tai'an prefecture agreed to report varicella cases to the local department of health, whose staff enrolled eligible case-patients and controls and interviewed parents/guardians. Informed consent for study participation was obtained from parents/guardians. For each enrolled case-patient from an elementary school, two classmates sitting directly around the case were randomly selected, and another two students from a class of same grade without any varicella cases were also randomly selected as controls. Each control group was analyzed separately with the cases to calculate vaccine effectiveness and finding no difference, the controls were grouped together. For each case from a daycare center, two controls were selected from the case-patient's classroom and another two controls were randomly selected from daycare attendees of the same age from a classroom without cases.

2.2. Data collection

Parents/guardians of the participants were interviewed using a standard questionnaire to collect information on sociodemographics, underlying diseases, prior varicella history, and recent possible VZV exposure. Case and control candidates with prior varicella history were excluded. For enrolled cases and controls, vaccination status, date of vaccination, and vaccine product received if vaccinated were collected from immunization records at home or in the immunization clinics. Date of rash onset and prior varicella history were collected from parents or clinic records. For evaluation of vaccine coverage in the schools and daycare centers under study, the vaccination status and prior varicella history were collected from immunization records at home or parental recall and vaccination coverage was calculated after the outbreak was over and excluded those with prior disease history.

2.3. Statistical analyses

We defined varicella VE as [1 − odds ratio (OR)] × 100%, where OR was calculated from conditional logistic regression for the matched case–control study. Vaccine product-specific VEs could only be calculated for the Baike and Changsheng vaccines due to the small number of participants who had received the other vaccine products. We used previously described methods to assess VE changes with time since vaccination [16]. For pairs in which either or both the case and the controls had received varicella vaccine, we defined the time since vaccination as the time interval between the date(s) of vaccination and the rash onset date of the matched case. For assessing vaccination status of controls, we used the date of rash onset in the case as the reference date. Thus, controls who received varicella vaccine after the disease onset date of the matched case were defined as unvaccinated. We performed all analyses with SAS version 9.2 (SAS Inc., Cary, NC).

China CDC Ethics Committee reviewed and approved this protocol.

3. Results

3.1. Characteristics of the study participants

There were a total of 180 cases reported from 44 schools and day cares and 679 controls enrolled. Half (434, 50.5%) of the 859 participants were female. The majority of participants were elementary school students (589, 68.6%) with a mean age of 7.3 years (range: 1.3–12.4). Five participants reported having underlying medical conditions of asthma and eczema. More than half of the cases (97/180) reported a VZV exposure, 93 (95.9%) of which were at school. Of the 250 (29.1%) vaccinated cases and controls, 135 (54.0%) received Changsheng vaccine and 83 (33.2%) received Baike