



Effectiveness of varicella vaccine as post-exposure prophylaxis during a varicella outbreak in Shanghai, China



Qiang-Song Wu¹, Jing-Yi Liu¹, Xian Wang, Yuan-Fang Chen, Qi Zhou, An-Qi Wu, Lan Wang*

Shanghai Xuhui Center for Disease Control and Prevention, Shanghai 200237, China

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ABSTRACT

Objectives: Varicella vaccine (VarV) is recommended as effective post-exposure prophylaxis (PEP) within 3–5 days to control outbreaks. However, the effectiveness of PEP at >5 days after exposure and the administration of a second dose to those with a history of one dose prior to exposure have not been fully examined. This study evaluated the vaccine effectiveness (VE) of PEP in preventing disease during a varicella outbreak in Shanghai, China in 2013.

Methods: Self-administered questionnaires were used to obtain the students' varicella history, vaccination status, and willingness to receive PEP. One dose of VarV was provided free of charge to eligible students. The VE of PEP was calculated as $[1 - \text{relative risk (RR)}] \times 100\%$. Analyses were restricted to grade 8 students, as no students from the other grades or teachers developed varicella during the outbreak.

Results: Twenty-seven varicella cases were identified, 16 (59%) of which were infected after the PEP campaign. Sixty-five students received one dose of VarV on day 13 or 19 after the index case. Attack rates were 28% (9/32), 16% (15/94), 0% (0/10), and 6% (3/55) among unvaccinated, one-dose Pre-PEP, first dose as PEP, and second dose as PEP recipients, respectively. Cases among second dose as PEP recipients tended to have less fever compared with unvaccinated or one-dose Pre-PEP recipients. Compared with unvaccinated students, the VE of first dose as PEP recipients was 100% and of the second dose as PEP recipients was 60% (95% confidence interval –72% to 91%).

Conclusions: Post-exposure vaccination should be given as soon as possible after exposure. Nevertheless, vaccination is still recommended even at more than 5 days post-exposure to control varicella outbreaks. © 2017 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Varicella, also called chickenpox, is a highly contagious disease in children that is characterized by itchy, red blisters on the skin (Simpson, 1952). Varicella vaccine (VarV) is widely available and is the most effective prevention and control measure against varicella. Since 1998, VarV has been licensed for use as a single dose for children aged 1–12 years in China. In 2012, it was reported that 78% of students aged 3–17 years in Shanghai, China, had received one dose of VarV, even though the vaccine was not included in the China National Immunization Program (Wu et al., 2013). A meta-analysis that included vaccine effectiveness (VE)

calculated from 42 studies published between 1995 and 2014, reported that a single dose of VarV was moderately effective at preventing all varicella (81%) and highly effective at preventing moderate and severe varicella combined (98%) (Marin et al., 2016).

Despite successful global varicella vaccination programs, varicella outbreaks in the school setting continue to occur, even with high one-dose VarV coverage (Centers for Disease Control and Prevention, 2004; Fu et al., 2015; Lopez et al., 2006; Lu et al., 2012). According to infectious disease surveillance data for the years 2005–2007, more than 80% of varicella infections in China occurred among children younger than 14 years old, and varicella outbreaks were most likely to occur in the school setting (97%) (Jin and Fen, 2007; Chao and Xiang, 2009).

Previous studies from Japan, the USA, and Israel on varicella household exposure in children have indicated that VarV is highly effective in preventing moderate or severe varicella disease (79–100%) if given within 3–5 days post-exposure (Arbeter et al., 1986;

* Corresponding author.

E-mail address: wanglan1974@126.com (L. Wang).

¹ These authors contributed equally to this study.

Mor et al., 2004; Takahashi et al., 1974; World Health Organization, 2014). The post-exposure use of VarV was first suggested in the USA in 1999 (Galil et al., 1999). In China, a varicella emergency vaccination program was started in Beijing in 2006, in Guangzhou in 2012, and in Shanghai in 2013 (Li, 2013; Ma et al., 2009). However, the estimated effectiveness of post-exposure prophylaxis (PEP) in preventing any varicella has varied from 9% to 100% (Arbeter et al., 1986; Asano et al., 1977; Mor et al., 2004; Ma et al., 2009; World Health Organization, 2014). In addition, the potential benefits of PEP at more than 5 days after exposure and the administration of a second dose of VarV after exposure to persons who have previously received one dose have not been fully examined.

During the 2013 varicella outbreak in a middle school in Shanghai, China, one dose of VarV was recommended as PEP even for students exposed more than 12 days previously in order to reduce disease transmission. In this study, an epidemiological investigation was conducted to assess the effectiveness of PEP given as first-dose VarV to unvaccinated students or as second-dose VarV to students who had received one dose of VarV.

Materials and methods

Outbreak setting

A varicella outbreak occurred in a middle school located in Xuhui District, Shanghai, China from October to December 2013. The school had a total of 707 students in grades 6–9. All grades were located in a four-story building, which included 16 classrooms. Each grade had four classes that were all located on the same floor.

Study definitions

A case of varicella was defined as an acute maculopapular vesicular rash without any other explanation in a middle school student, occurring between October 24 and December 25, 2013. In this study, students were classified as unvaccinated, one-dose Pre-PEP, first dose as PEP, and second dose as PEP recipients based on their varicella vaccination status. One-dose Pre-PEP was defined as students who had received only one-dose of VarV before the outbreak and refused PEP. First dose as PEP was defined as students with no VarV immunization history before the outbreak who received one dose of VarV as PEP during the outbreak. Second dose as PEP was defined as students who had received one dose of Pre-PEP and then received a second dose of VarV as PEP.

Data collection

Xuhui Center for Disease Control and Prevention conducted the outbreak investigation to identify varicella cases. Self-administered questionnaires and informed consent forms were distributed to the students' parents to obtain the students' varicella history, vaccination status, and willingness to receive PEP. The VarV status of these students was further verified through the school immunization records. Information on clinical manifestations and duration of isolation was collected by telephone interview with the parents. The severity of varicella was classified based on the number of skin lesions as follows: mild (<50 lesions), moderate (50–500 lesions), and severe (>500 lesions, or the presence of complications or hospitalization).

Outbreak control measures

Students with varicella were excluded from school until their lesions had crusted over. Their classmates were isolated from other

students by time-shifting the school dismiss, using specific stairwells, and prohibiting the use of public rooms. Moreover, school activities were suspended and classrooms, indoor play areas, and public rooms were disinfected daily during the outbreak.

According to the Shanghai Varicella Emergency Vaccination Program, which was started in 2013, one dose of VarV should be offered immediately to immunize all unvaccinated classmates with no varicella history once two varicella cases are detected in the same school class. All unvaccinated students at the school should be vaccinated when the varicella outbreak evolves into a public health emergency event (≥ 10 varicella cases within 7 days during an outbreak). A second dose of VarV is recommended for post-exposure administration for students with a history of one dose of VarV more than 5 years before the outbreak. One dose of VarV was provided as PEP at no cost to the students willing to receive the vaccination. Students with any acute illness or whose parents refused to allow them to be vaccinated were excluded from vaccination.

On November 6, 2013, six students in class 2 of grade 8 were vaccinated with VarV on day 13 of exposure. On November 9, 2013, the outbreak developed into a public health emergency event, as 15 students were infected from November 2 to November 8. On November 11, 2013, another 281 middle school students (59 from grade 8) were offered PEP vaccination on day 19 after the occurrence of the index case.

Statistical methods

Data were entered into EpiData 3.1 (The EpiData Association, Odense, Denmark). Statistical analyses were performed using SPSS for Windows version 12.0 (IBM Corp., Armonk, NY, USA). Varicella severity was compared between unvaccinated, one-dose Pre-PEP, first dose as PEP, and second dose as PEP recipients using Pearson's Chi-square test, Fisher's exact test, or the Wilcoxon rank-sum test, as appropriate. A p -value of <0.05 was considered statistically significant.

VE was calculated using the following formula: $[1 - \text{relative risk (RR)}] \times 100\%$ (Orenstein et al., 1988), where RR was the incidence ratio calculated from this outbreak investigation. VE of PEP was analyzed after stratifying students according to VarV immunization status, and the unvaccinated students were the control group. To calculate the VE of PEP, the at-risk period for each uninfected student who refused PEP began on the day of PEP (November 6, 2013 for students in class 2 of grade 8; November 11, 2013 for students in the other three classes). The theoretical basis for PEP relates to the ability of the vaccine to result in a rapid immune response within 4–7 days (Baba et al., 1978; Kamiya et al., 1977; Watson et al., 1995). It was assumed that it takes at least 4 days after vaccination to induce sufficient antibodies against varicella-zoster virus infection. Therefore, first dose PEP recipients and second dose PEP recipients within 4 days after varicella exposure were grouped as unvaccinated and one-dose Pre-PEP, respectively, during the outbreak. To calculate the at-risk period for students who received one dose of VarV as PEP, this began at 5 days after the day of PEP (November 11, 2013 for students in class 2 of grade 8; November 16, 2013 for students in the other three classes). Each PEP ended on December 26, 2013 (21 days after the date of rash onset for the last infected student, as 21 days is the maximum incubation period of varicella) or the date of rash onset for students who developed varicella. In addition, the additional reduction in varicella disease experienced by second dose as PEP recipients relative to one-dose Pre-PEP was assessed. A 95% confidence interval (CI) of VE excluding 0 was considered as statistically significant.

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