International Journal of Infectious Diseases 66 (2018) 51–55

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

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

Qiang-Song Wu[1], Jing-Yi Liu[1], Xian Wang, Yuan-Fang Chen, Qi Zhou, An-Qi Wu, Lan Wang*

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

ARTICLE INFO

Article history:
Received 11 July 2017
Received in revised form 22 October 2017
Accepted 23 October 2017
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Outbreak
Post-exposure prophylaxis
Vaccine effectiveness
Varicella vaccine

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 − relative risk (RR)] × 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.

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.

https://doi.org/10.1016/j.ijid.2017.10.016

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 − relative risk (RR)] × 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.

Results

Outbreak epidemiology

During the varicella outbreak from October 24, 2013 to December 4, 2013, 27 cases were reported. The mean age of the cases was 13.6 ± 0.3 years and 18 of them (67%) were male. The index case was a 14-year-old boy from class 2 of grade 8 who had previously received one-dose VarV. He developed a rash on the evening of October 24, 2013, approximately 10.5 years after varicella vaccination on March 5, 2002. The next day, he attended school and participated in the school Olympic day before he was sent home and clinically diagnosed with varicella. He had a generalized rash with <50 lesions and reported a fever of 38 °C. One case report peak occurred during this outbreak at approximately 2 weeks after the index case (Figure 1).

Study population

The outbreak was restricted to the four classes of grade 8 in the middle school, with 5–10 cases per class. All students in the four classes of grade 8 stayed on the third floor and performed a gymnastic show on the school Olympic day on October 25, 2013. All analyses were restricted to students in grade 8, as no varicella was reported in students in the other grades or their teachers. There were 191 students in grade 8 and none of them had had varicella before the outbreak. The mean age of the 191 students was 13.7 ± 0.3 years (range 12.9–14.7 years) and 50% were male. Among the 191 students, 42 (22%) were unvaccinated and 149 (78%) had previously received one dose of VarV before the outbreak according to their immunization records (Figure 2). Among one-dose recipients (n = 149), the mean time since vaccination before the outbreak was 11.8 ± 1.2 years (range 7.4–12.9 years).

Post-exposure prophylaxis

Before the PEP campaign, five unvaccinated students and six one-dose Pre-PEP recipients were diagnosed with varicella (2–3 cases per class). Among the 180 students from grade 8 who were eligible for one dose of VarV as PEP, a total of 65 received one dose of VarV on day 13 or 19 after the index case (Figure 2). The rate of PEP was 27% (10/37) among unvaccinated students and 39% (55/143) among one-dose recipients before the outbreak, which was not statistically significant (p = 0.20). After PEP, 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.

Disease characteristics

All cases had mild varicella. Among second-dose as PEP recipients, one out of three cases (33%) had fever. In contrast, fever was reported in 67% (6/9) of unvaccinated subjects and 53% (8/15) of one-dose Pre-PEP recipients (Table 1). There was no difference between one-dose Pre-PEP and second dose as PEP recipients with breakthrough varicella with regard to rash severity (p = 1.0), fever (p = 1.0), duration of rash (p = 0.53), or duration of isolation (p = 1.0) (Table 1).

VE of PEP

Among the 27 varicella cases, 11 (41%) were infected before the PEP campaign and 16 (59%) were infected after the campaign (Figure 2). After PEP, the incidence rate was 3.6 cases/1000 person-days, 2.3 cases/1000 person-days, 0 cases/1000 person-days, and 1.4 cases/1000 person-days among unvaccinated, one-dose Pre-PEP, first dose as PEP, and second dose as PEP recipients, respectively (Table 2). Compared to unvaccinated students, the effectiveness of the first dose as PEP was 100% and of the second dose as PEP was 60% (95% CI −72% to 91%) (Table 2). The incremental VE (second dose as PEP vs. one-dose Pre-PEP) was 38% (95% CI −127% to 83%).

Discussion

This study appears to be the first to present the potential benefit of administering a second dose of VarV as PEP to those who have received one dose during an outbreak in China. In this study, the VE of the second dose as PEP was 60% and the incremental effectiveness was 38% compared with unvaccinated students and one-dose Pre-PEP recipients, respectively. However, the difference in effectiveness between groups was not statistically significant, although this may be the result of the small sample size and the late start of the PEP campaign (>12 days after exposure). Moreover, cases among second dose as PEP recipients tended to have less fever. The results of this study add to the limited data regarding the potential benefit of administering a second dose of VarV after exposure to persons who have previously received one dose of VarV. Additional data are needed to better understand the benefit of administering a second dose of VarV to one-dose

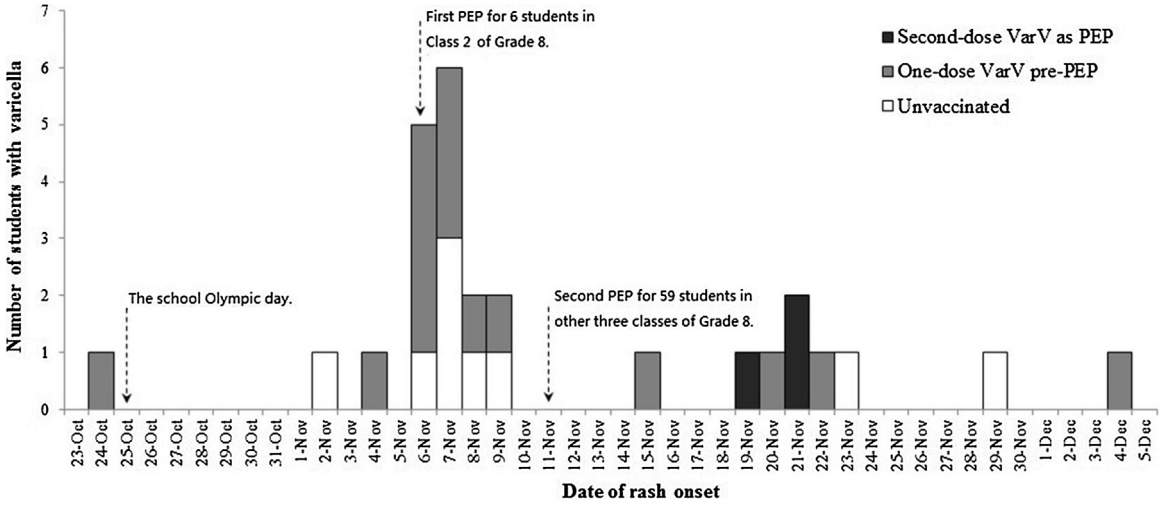

Figure 1. Distribution of cases by date of rash onset, and immunization and PEP status.

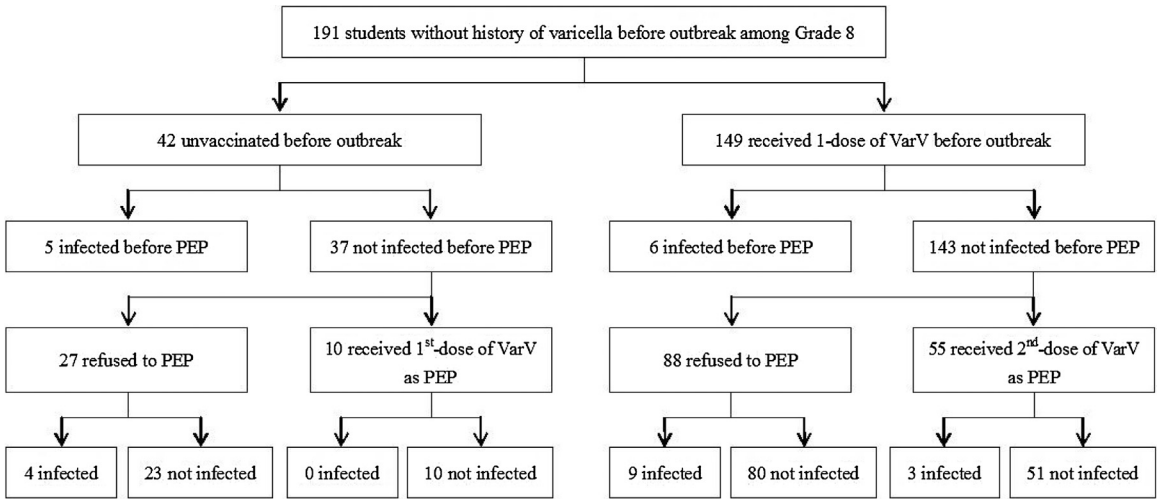

Figure 2. Varicella vaccination, case, and PEP status in students of grade 8 during a varicella outbreak in Shanghai, China.

Table 1
Disease severity of varicella according to varicella vaccine status.

Characteristic	Unvaccinated ($n=9$)	One dose Pre-PEP ($n=15$)	Second dose as PEP ($n=3$)	p-Value[a]	p-Value[b]	p-Value[c]
>50 lesions, %	0	0	0	1.0	1.0	1.0
Fever, %	67	53	33	0.68	0.52	1.0
Rash duration, median (range)	6 (5–9)	5 (3–9)	4 (4–7)	0.04	0.19	0.54
Duration of isolation, median (range)	16 (15–19)	15 (13–19)	15 (14–17)	0.04	0.25	1.0

PEP, post-exposure prophylaxis.
[a] Comparing one-dose Pre-PEP versus unvaccinated.
[b] Comparing second dose as PEP versus unvaccinated.
[c] Comparing second dose as PEP versus one-dose Pre-PEP.

Table 2
Effectiveness of PEP during a varicella outbreak in a middle school in Shanghai, China.

VarV vaccination status	Number	At-risk period (person-days)	Case	Incidence density (cases/1000 person-days)	RR (95% CI)	VE (95% CI) %
Unvaccinated	27	1123	4	3.6	Reference	
One-dose Pre-PEP[a]	88	3896	9	2.3	0.65 (0.20–2.09)	35 (−109 to 80)
First dose as PEP	10	410	0	0.0	–	100.0
Second dose as PEP[a]	55	2086	3	1.4	0.40 (0.09–1.72)	60 (−72 to 91)

PEP, post-exposure prophylaxis; VarV, varicella vaccine; RR, relative risk; CI, confidence interval; VE, vaccine effectiveness.
[a] Compared with one-dose Pre-PEP recipients, the incremental effectiveness of the second dose as PEP was 38% (95% CI −127% to 83%).

recipients after exposure, as varicella outbreaks in the school setting have become an increasing challenge even with high one-dose VarV coverage.

The incremental effectiveness calculated in this study differs from one report showing a high efficacy of second-dose vaccination for outbreak control (Nguyen et al., 2010). Nguyen et al. (2010) reported an incremental effectiveness of 76% during an outbreak in a Philadelphia elementary school. The discrepancy between the results of the two studies may be explained by different reference groups and methods for calculating the at-risk period. The start date began in the infectious period of the first case in the study by Nguyen et al. (2010), whereas it began on the day of PEP in the present study. Therefore, cases from one-dose recipients who were infected before the PEP campaign were also included when calculating the incremental effectiveness in the Philadelphia outbreak, which likely overestimated the incremental VE of PEP. Moreover, the one-dose VarV coverage rate was higher (97%) in the Philadelphia outbreak compared with that in the present study (78%), and the rate of second-dose VarV as PEP was higher than that in the present study (65% versus 38%). The effectiveness of the second dose of VarV as PEP might vary among populations with lower one-dose vaccine coverage or PEP uptake, or outbreaks with later PEP implementation.

As no varicella was identified in 10 unvaccinated students who received the first dose of VarV as PEP during this outbreak, the VE of PEP in first-dose students was 100%. The time from exposure to vaccination in this study was more than 12 days, and 91% of students received one dose of VarV as PEP at 19 days after exposure, which is longer than reported in other published studies (within 3–5 days) (Arbeter et al., 1986; Asano et al., 1977; Brotons et al., 2010; Getaz et al., 2010; Mor et al., 2004). Previous studies on PEP were conducted in children aged 1 month to 13 years (Asano et al., 1982, 1977; Mor et al., 2004; Salzman and Garcia, 1998; Takahashi et al., 1974; Watson et al., 2000), and the mean age in the present study was 13.7 years. This study provides support for the recommendation of the Advisory Committee on Immunization Practices to administer VarV during varicella outbreaks as PEP, even if more than 5 days have passed since exposure (Marin et al., 2007). However, the sample size of unvaccinated students was small in this study and thus the VE of PEP may have been

overestimated. These findings support the need for additional evaluations in which people receive VarV as PEP more than 5 days after exposure during an outbreak.

Several limitations of this study should be considered when evaluating the VE of PEP. First, a clinical case definition that did not require laboratory confirmation was employed. Moreover, it could not be determined whether rashes in PEP students were caused by wild virus or VarV. In this study, any rash after one dose of VarV as PEP was considered to have been caused by wild virus, which may have led to an underestimation, not an overestimation of the VE of PEP. Second, the number of days of transition from unvaccinated to first dose as PEP, or from one-dose VarV to second dose as PEP vaccine immunity was inferred and not confirmed by antibody immune response testing. It was assumed that vaccine-induced immunity could develop as early as 5 days after PEP. This is the shortest period given the rapid immune response identified in previous studies (4–7 days), and thus may have led to an underestimation of the VE of PEP. Third, it was assumed that all students were exposed to varicella during the outbreak. Although the calculation was restricted to students in grade 8, it is possible that not all students had the same exposure to the index case. However, 11 students were identified as varicella-positive before the PEP campaign, with 2–3 cases per class in grade 8. Therefore, the other cases may have been exposed to these students from the other three classes of grade 8 before PEP.

In conclusion, VarV was effective in preventing a varicella outbreak in a middle school in China, even when administered more than 5 days after exposure to varicella. Before the implementation of a two-dose VarV schedule, the administration of a second dose of VarV may be worthwhile for persons who have previously received one dose, even if it does not offer sufficient protection as PEP. Future studies on administering first-dose or second-dose VarV as PEP during varicella outbreaks are warranted.

Conflict of interest/funding

None.

References

Arbeter AM, Starr SE, Plotkin SA. Varicella vaccine studies in healthy children and adults. Pediatrics 1986;78(4 Pt. 2):748–56.
Asano Y, Hirose S, Iwayama S, Miyata T, Yazaki T, Takahashi M. Protective effect of immediate inoculation of a live varicella vaccine in household contacts in relation to the viral dose and interval between exposure and vaccination. Biken J 1982;25(1):43–5.
Asano Y, Nakayama H, Yazaki T, Kato R, Hirose S. Protection against varicella in family contacts by immediate inoculation with live varicella vaccine. Pediatrics 1977;59(1):3–7.
Baba K, Yabuuchi H, Okuni H, Takahashi M. Studies with live varicella vaccine and inactivated skin test antigen: protective effect of the vaccine and clinical application of the skin test. Pediatrics 1978;61(4):550–5.
Brotons M, Campins M, Mendez L, Juste C, Rodrigo JA, Martinez X, et al. Effectiveness of varicella vaccines as postexposure prophylaxis. Pediatr Infect Dis J 2010;29(1):10–3.
Chao YO, Xiang NJ. Varicella epidemiology in China, 2007. Dis Surveill 2009;24(3):172–4.
Centers for Disease Control and Prevention. Outbreak of varicella among vaccinated children—Michigan, 2003. MMWR Morb Mortal Wkly Rep 2004;53(18):389–92.
Fu J, Wang J, Jiang C, Shi R, Ma T. Outbreak of varicella in a highly vaccinated preschool population. Int J Infect Dis 2015;37:14–8.
Galil K, Mootrey GP, Seward J, Wharton M. Prevention of varicella. Update recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1999;48(RR-6):1–5.
Getaz L, Siegrist CA, Stoll B, Humair JP, Scherrer Y, Franziskakis C, et al. Chickenpox in a Swiss prison: susceptibility, post-exposure vaccination and control measures. Scand J Infect Dis 2010;42(11–12):936–40.
Jin LM, Fen ZJ. Analysis of the epidemic situation of chickenpox from 2005 to 2006 in China. Disease Surveillance 2007;22(4)251–2 +5.
Kamiya H, Ihara T, Hattori A, Iwasa T, Sakurai M, Izawa T, et al. Diagnostic skin test reactions with varicella virus antigen and clinical application of the test. J Infect Dis 1977;136(6):784–8.
Li T. Varicella emergency vaccination seemed instrumental in declining chickenpox incident in Guangzhou, Southern China. Rev Inst Med Trop Sao Paulo 2013;55(3).
Lopez AS, Guris D, Zimmerman L, Gladden L, Moore T, Haselow DT, et al. One dose of varicella vaccine does not prevent school outbreaks: is it time for a second dose?. Pediatrics 2006;117(6):e1070–7.
Lu L, Suo L, Li J, Zhai L, Zheng Q, Pang X, et al. A varicella outbreak in a school with high one-dose vaccination coverage, Beijing, China. Vaccine 2012;30(34):5094–8.
Ma R, Sun MP, Sun M, Hou WJ, Jiang GY, Peng XH, et al. Effectiveness on post-exposure vaccination of varicella and its influencing factors in elementary schools in Beijing. Chin J Epidemiol 2009;30(6):559–63.
Marin M, Guris D, Chaves SS, Schmid S, Seward JF, Advisory Committee on Immunization Practices CfDC, et al. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2007;56(RR-4):1–40.
Marin M, Marti M, Kambhampati A, Jeram SM, Seward JF. Global varicella vaccine effectiveness: a meta-analysis. Pediatrics 2016;137(3)e20153741.
Mor M, Harel L, Kahan E, Amir J. Efficacy of postexposure immunization with live attenuated varicella vaccine in the household setting—a pilot study. Vaccine 2004;23(3):325–8.
Nguyen MD, Perella D, Watson B, Marin M, Renwick M, Spain CV. Incremental effectiveness of second dose varicella vaccination for outbreak control at an elementary school in Philadelphia, pennsylvania, 2006. Pediatr Infect Dis J 2010;29(8):685–9.
Orenstein WA, Bernier RH, Hinman AR. Assessing vaccine efficacy in the field: further observations. Epidemiol Rev 1988;10:212–41.
Salzman MB, Garcia C. Postexposure varicella vaccination in siblings of children with active varicella. Pediatr Infect Dis J 1998;17(3):256–7.
Simpson RE. Infectiousness of communicable diseases in the household (measles, chickenpox, and mumps). Lancet 1952;2(6734):549–54.
Takahashi M, Otsuka T, Okuno Y, Asano Y, Yazaki T. Live vaccine used to prevent the spread of varicella in children in hospital. Lancet 1974;2(7892):1288–90.
Watson B, Rothstein E, Bernstein H, Arbeter A, Arvin A, Chartrand S, et al. Safety and cellular and humoral immune responses of a booster dose of varicella vaccine 6 years after primary immunization. J Infect Dis 1995;172(1):217–9.
Watson B, Seward J, Yang A, Witte P, Lutz J, Chan C, et al. Postexposure effectiveness of varicella vaccine. Pediatrics 2000;105(1 Pt. 1):84–8.
World Health Organization. Varicella and herpes zoster vaccines: WHO position paper, June 2014. Wkly Epidemiol Rec 2014;89(25):265–87.
Wu QS, Liu M, Li SS, Zhou Q, Liu JY. Coverage and protective effects of varicella vaccination for students in Xuhui District of Shanghai. Chin J School Health 2013;34(4):465–7.