Available online at www.sciencedirect.com

ScienceDirect

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

Original Article

Use of immunization as strategy for outbreak control of varicella zoster in an institutional setting

Col V.K. Bhatti^a, Capt Lee Budhathoki^b, Col Mahadevan Kumar^c,
Maj Gurpreet Singh^b, Amol Nath^b, Maj Gen Velu Nair, AVSM, VSM^{*,d,*}

^a Col Health, HQ Northern Command, C/O 56 APO, India

^b Resident, Department of Community Medicine, Armed Forces Medical College, Pune 411040, India

^c Associate Professor, Department of Microbiology, Armed Forces Medical College, Pune 411040, India

^d Dean and Deputy Commandant, Armed Forces Medical College, Pune 411040, India

ARTICLE INFO

Article history:

Received 10 November 2013

Accepted 15 March 2014

Available online 24 June 2014

Keywords:

Outbreaks

Health care providers

Vaccination

Chickenpox

ABSTRACT

Background: Outbreaks of varicella gets reported often in India. However, outbreak in health care providers living in closed institutional setting and role of vaccination as post exposure prophylaxis for control of outbreak has not been studied extensively. This paper presents epidemiological investigation and control strategy undertaken in such scenario.

Methods: This is an epidemiological investigation of chickenpox in nursing students which highlights role of early identification and appropriate control strategy to prevent explosive outbreak in high risk vulnerable population. Vaccination of all susceptible in addition to isolation of cases, quarantine of suspects and proper screening for new cases was the major control strategy adopted.

Results: The index case was imported and all eight cases occurred within the incubation period of the case. Two cases occurred in students previously vaccinated for chickenpox. No second or third wave of infection occurred showing vaccination as effective tool in outbreak control strategy.

Conclusion: Early identification of cases and vaccination of all susceptible contributed to effective control of the outbreak.

© 2014, Armed Forces Medical Services (AFMS). All rights reserved.

Introduction

Chickenpox (Varicella) is an acute infectious disease caused by exposure to Varicella Zoster Virus (VZV) and is characterized by a maculopapular vesicular rash; fever and malaise. The clinical course is highly dependent on the age and immune

status of the patient. Children usually have a milder disease whereas adults can have severe disease. The incubation period varies from 10 days to 21 days with an average of 14–16 days.^{1,2} The period of infectivity ranges from one to two days before the appearance of rash till all vesicles crust, usually 4–5 days after the rash.^{1,2} With a secondary attack rate up to 90%,^{1,3} an outbreak of chickenpox in schools, barracks and

* Corresponding author. Tel.: +91 7875633494.

E-mail address: nairvelu2000@yahoo.com (V. Nair).

<http://dx.doi.org/10.1016/j.mjafi.2014.03.006>

0377-1237/© 2014, Armed Forces Medical Services (AFMS). All rights reserved.

institutions can be serious. Outbreaks of chickenpox get reported quite often in countries like India where vaccination is not part of the country's national immunization policy.

An outbreak of varicella occurred amongst nursing students in an institutional setting of a tertiary care hospital from 23rd November to 13th December 2012. An inbuilt Health Intelligence (HI) surveillance unit exists in the institution and based on the information obtained from the unit, investigation and control measures were initiated.

The students undergo training over a period of 4 years, with batch strength of 40 per year, therefore at any given time there are about 160 students undergoing training at the institute who reside in a hostel in rooms on a sharing basis ranging from two to six in each room with common dining hall facilities.

The institution has recently adopted a strategy to vaccinate first year students as part of the institutional vaccination policy enforced since September 2011 which lays down that all cadets and recruits will be vaccinated with two doses of vaccine, 4 weeks apart, on entry. After checking the VZ IgG level, two doses of vaccine were given on 9th October and 6th November 2012 to those negative for antibodies for IgG VZV antibodies.

This study reports the investigation and control strategy adopted during the outbreak.

Materials and methods

This is an epidemiological study of an outbreak amongst nursing students, the index case was reported on 23rd of November 2012. On reporting of the case, an alert was sounded by the HI division as the occurrence was in a nursing trainee who visits hospital wards for training activities. The case was admitted and kept in an isolation ward. A list of close contacts was prepared and standard daily screening of them implemented, as per protocol, along with advisory for avoiding visits to health care facility till further instructions.

One case each was reported on 6th and 7th December 2012. These two cases were within the incubation period of the initial case and gave history of contact with the first case. An epidemiological investigation was undertaken and notification was immediately done to the hospital authorities. Aggressive control measures were instituted as the risk of explosive outbreak of cases in close settings is very high and in this situation cases being trainees who visit various units in the tertiary care institute there was an impending risk of outbreak spilling over to individuals (patients and other staff) in the hospital setting.

First and foremost susceptible population at risk was identified; "Susceptible individuals" were regarded as people without prior history of chickenpox or no history of vaccination for varicella.

Case definitions used in this outbreak were as under:

A clinical case/possible case was defined as one with acute onset of diffuse (generalized) maculopapular vesicular rash having fever without apparent cause occurring from 23rd November to 24th January 2013 in a student with no prior history of chickenpox.

Breakthrough case of varicella was defined as a vaccinated person who develops varicella more than 42 days after vaccination.

A probable case was one which met clinical case definition, was not lab confirmed, and was not epidemiologically linked to another probable or confirmed case.

A confirmed case was one that was laboratory confirmed or a case which meets clinical case definition and was epidemiologically linked to a confirmed or a probable case.

Close contact were any one with close indoor contact like residing in same room or having face-to-face contact.

Confirmation of cases was done, epidemiological case sheet generated for each case and line listing was done. Blood sample for VZ IgM antibodies was taken from all cases on admission. Search for primary case was done for the index case. A spot map was prepared of the hostel and the all blocks where the cases and contacts resided and contact tracing was done. All cases that occurred were admitted and kept in isolation ward and quarantine done for close contacts. Health education for case identification and reporting was given. Meal timings of the students in each year were changed to minimize contacts and other group gatherings were withheld. Ventilation of individual rooms was improved by ensuring the windows were opened. Chickenpox screening drill was implemented every morning and evening for all residing in the hostel. Hospital training visits were stopped and only training activities in class rooms were permitted.

To determine potential VZV vaccine-related complications and to differentiate Varicella Zoster Virus (VZV) wild-type strains from an attenuated varicella vaccine, PCR targeting the ORF 38 segment was carried out which was further sequenced to differentiate the vaccine strain from wild-type VZV. Amplicon 600 bp in size for ORF 38.

Scrapings from the vesicles were taken. A sterile beveled hypodermic needle was used to de-roof vesicle and using a swab moistened with Viral Transport Media (VTM), the base of the opened lesion was scrubbed and placed in VTM tube and sent immediately to Virology Department where centrifugation was done at 4000 ×g, the sediment was used for extraction of DNA using spin column method (QIAGEN GmbH, Hilden, Germany) as per manufacturer's instructions. Similarly DNA of the OKA Strain was also extracted from the vaccine vials that had been used for vaccinating the patient (OKAVAX, Sanofi Pasteur India Ltd).

PCR was carried out in a 25 µL reaction volume with primers targeting the ORF 38 region of the VZ virus. Briefly the reaction cocktail consisted of 0.5 µM of each primer with 1.5 mM MgCl₂, 0.2 mM dNTPs, 0.2 U of Taq polymerase and 5 µL of template. Cycling conditions of the PCR were as follows, initial denaturation at 95 °C for 5 min followed by 35 cycles of denaturation at 95 °C for 1 min, a 1 min annealing step at a temperature of 60 °C and an extension step at 72 °C for 1 min followed by a final extension step at 72 °C for 5 min. On electrophoresis in a 1.5% agarose gel the amplified products were visualized with an UV transilluminator after staining with 0.05% ethidium bromide.

The amplicons were sequenced in an Capillary Electrophoresis System (ABI 3730 xl) using a Prism BigDye Terminator Cycle sequencing Kit (Applied Biosystems, Foster City, USA) as per manufacturer's instructions. Sequencing results were

analyzed using the Blast software on the website of the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov). Sequence has been submitted to Gen Bank under Accession number KF153936.

The HI division also undertook surveillance for occurrence of any cases in the patients admitted or relatives. All cases were managed with Tab Acyclovir 800 mg QID along with symptomatic treatment upon diagnosis. All susceptible nursing students were given two doses of vaccination at interval of 4 weeks with the first dose given within 4 days of 6th December 2012 as part of the outbreak control strategy. A total of 64 students were vaccinated.

Results

Occurrence of isolated cases of chickenpox amongst nursing cadets staying in the hostel of a nursing college was normal. Occurrence of three cases within a span of 2 weeks was in excess of the expected number as per last three years of incidence thus being labeled as an outbreak. The outbreak lasted for 20 days with the total number of cases being eight.

The index case had been on leave from 9th to 18th November 2012 at her native place. She gave no history of contact with an apparent case of varicella during her leave.

At the time of the outbreak a total of 156 training students were present in the institute. Out of these 67 students gave a reliable history of having had chickenpox in early childhood. 25 students gave reliable history of having been vaccinated for varicella. A total of 64 students were labeled as susceptible and at high risk for getting chickenpox in the current outbreak (Fig 1).

All the eight cases were females in the age group 18–22 years. 62.5% had fever as first symptom while 25% had rash (Table 1). 75% developed fever and 50% had malaise along the course of illness. 62.5% had less than 50 lesions in body and 37.5% had localized lesions. None of the cases had any complications due to illness. The 2 cases who got illness despite being vaccinated got disease within 42 days of vaccination (33 and 34 days respectively) and had a very mild disease with lesions being less than 50 in number.

Fig. 1 – Percentages of students with history of chickenpox, vaccination and those susceptible to chickenpox.

Table 1 – Demographic and clinical characteristics of cases.

Demographic/clinical characteristics (n = 8)	
Mean age in years	19.87 years (18–22)
Gender (% female)	8 (100%)
1st Symptom	
Fever	5 (62.5%)
Rash	2 (25%)
Body ache	1 (12.5%)
Fever	6 (75%)
Rash (Generalized)	8 (100%)
<50 in number	5 (62.5%)
50–249 in number	3 (37.5%)
Malaise	4 (50%)
Complications	Nil

Maximum cases i.e. five out of eight cases were from first year with one case each from rest of the batches. The breakdown of cases as per year of training batch is as Fig. 2.

Epidemic curve (Fig. 3) shows that all cases occurred within the incubation period of the index case with median IP of 18 days and there were no second or third wave of infection.

Place distribution by spot map method showed that five of the eight cases resided in the same building and two out the remaining three resided in another common building.

Results of antibody testing for VZV IgM showed that six of them had positive titer while the two vaccinated cases had negative titer.

Sequences generated from the DNA isolated from the lesions of the patient showed a match with the wild-type strain.

The surveillance activity of the admitted patients and other hospital staff that had come in contact of the trainee students showed occurrence of no case.

Discussion

This outbreak occurred among trainee health care workers (HCW) living in an institutional setting. Occurrence of outbreak in this setting highlights how vulnerable people living in hostels, barracks and in crowded areas are regardless

Fig. 2 – Distribution of cases as per training batches.

Fig. 3 – Epidemic curve: index case reported on 23rd November with peak of epidemic from 8th to 10th December as four cases were reported.

of the knowledge of the disease. HCW are considered as high risk population and vaccination is highly recommended to them.⁴ However only 25 trainees had history of prior vaccination and of these 21 were vaccinated as part of the institutional policy. This goes on to show how only few HCW are vaccinated in developing countries where there is no vaccination policy for them. The role of IEC in highlighting the importance of vaccination can thus be a good preventive strategy.

Nursing staff play a very crucial role in disease like chickenpox. Firstly, they are a vulnerable population since they come across patients of chickenpox everyday and are involved in their daily care, making them a close contact. However since the period of communicability starts before the clinical symptoms, this same staffs become potential source of infection to a large number of patients in addition to the household contacts. This can have serious implications in the health of the patients especially in pregnant, premature infants born to susceptible mothers and patients who are immune compromised.⁴

The recommended strategy for control of outbreaks of chickenpox in institutional settings is to vaccinate all persons without evidence of immunity within 3–5 days of exposure to varicella rash. Health care workers should also be furloughed from work from days 8 to 21 post exposure since they are potentially infectious in this period. Although post exposure vaccination should be given as soon as possible but it is still indicated more than 5 days post exposure as it induces protection against subsequent exposures. Those who have received one dose of vaccine and exposed to varicella should receive second dose within 3–5 days if 4 weeks has elapsed since first dose. All those who have already received two doses of varicella vaccine must also be monitored from day 8 to 21 after exposure to determine clinical status. All should be instructed to immediately report fever, skin lesions and systematic symptoms.² Keeping the recommendations and the potential of the outbreak

spilling out of control and into patient facility aggressive control measures were instituted to include notification, isolation of cases, preparation of list of susceptible, contact tracing, quarantine of contacts, furloughing of contacts from visiting wards of patients, screening for new cases, avoiding group activities, IEC activities, early treatment of cases and vaccination of the susceptible population within 72 h of outbreak.

The new strategy applied in this setting before the outbreak occurred was to vaccinate all fresh students with negative VZ IgG levels but three cases developed disease despite having positive levels on IgG on qualitative estimation thereby implying that the qualitative kit used for estimating IgG is not a very sensitive and reliable kit thus may have given false positive results. It can thus be advised that in high risk unvaccinated population like HCW, history of prior disease as well as IgG status should be taken into consideration and absence of one should make the candidate a subject to vaccination.

Vaccine effectiveness with two doses of VZ vaccine in adult approaches about 99%.^{1,3} Role of vaccine in post exposure prophylaxis suggests it is about 90% effective in preventing disease when given within three to five after exposure.¹ Since the second and third wave did not occur in this case also, the vaccine effectiveness can be considered high and vaccination as a control strategy very effective.

Disease severity in most of cases was mild. Factors like early initiation of Acyclovir and vaccination (two post vaccination cases) may be the reason for it.^{3,5} Disease severity is said to be less in vaccinated person than in unvaccinated.³ In the present outbreak also these two cases had very mild disease thus emphasizing the point that with vaccination the disease severity become less hence immunization may be an effective tool to reduce the disease severity.

Transmission of chickenpox occurs among close contacts during period of infectivity.^{1,2} The index case was from first year so the probability of transmission of the disease to susceptible close contacts of first year is maximum as they share the hostel, classroom and have common training activities hence although maximum first year trainees were vaccinated, maximum cases also occurred in them.

Cost benefit analysis in developed countries like US and Spain has showed that vaccination program to all children is justified so the benefit of vaccinating HCW need not be over-emphasized and this has also been seen to be a cost effective strategy.^{3,6,7}

Conclusion

Early identification of cases by a robust surveillance mechanism and prompt action helped in the control of the outbreak. Isolation of cases, quarantine of contacts and preventing all suspects from giving care to patients prevented the spread of the disease to other nursing students and to the vulnerable patients to whom they were providing care. As a result, no cases of chickenpox were reported within

the time under surveillance from the patients. Well established HI division of the Community Medicine Department and availability of vaccines were major strengths in this case. Vaccination of all the susceptible was done and perhaps this action prevented further cases and early termination of the outbreak which would have otherwise simmered for a considerable period of time. It has been shown in the present approach of control strategy of using immunization during an outbreak coupled with other standard measures to be an highly effective tool especially so in preventing subsequent waves of disease.

Recommendations

All health care institutions should have a well functioning surveillance system. The existence of such system helped in the identification, management and the control of outbreak in a swift and efficiently manner. A proper vaccination policy for health care workers for infectious disease like chickenpox is a must as they can acquire as well as transmit the disease in Health Care Settings. Failure to protect them can result in serious health and safety implications to themselves and to the patient they care for.

Conflicts of interest

All authors have none to declare.

Acknowledgment

We acknowledge the faculty of College of Nursing, all the nursing cadets and Mr. Atul Khajuria, PHD scholar of Dept of Microbiology, AFMC for their contribution in this study.

REFERENCES

1. Park K. *Park's Textbook of Preventive and Social Medicine*. In: 22nd, ed. Jabalpur: M/s Banarsidas Bhanot; 2013.
2. Lopez AS, MHS, Marin M. Strategies for the control and investigation of Varicella outbreaks 2008 [Internet]. Centers for Disease Control and Prevention [Cited 2013 Nov 3]. Available from: <http://www.cdc.gov/chickenpox/outbreaks/manual.html>.
3. *Weekly Epidemiological Record: WHO Position Paper on Varicella Vaccines*. World Health Organisation; 1998;73(32):241–248.
4. CDC. Immunization of Health-care Workers. Recommendations of the advisory Committee on immunization Practices (ACIP) and the hospital infection control Practices Advisory Committee (HICPAC). MMWR Recomm Rep 1997 Dec 26; 46(RR-18).
5. Dunkle LM, Arvin AM, Whitley RJ, et al. A controlled trial of acyclovir for chickenpox in normal children. *N Engl J Med*. 1991 Nov 28;325(22):1539–1544.
6. Díez Domingo J, Ridao M, Latour J, Ballester A, Morant A. A cost benefit analysis of routine varicella vaccination in Spain. *Vaccine*. 1999 Mar 17;17(11–12):1306–1311.
7. Gray AM, Fenn P, Weinberg J, Miller E, McGuire A. An economic analysis of varicella vaccination for health care workers. *Epidemiol Infect*. 1997 Oct;119(2):209–220.