Clinical Infectious Diseases

BRIEF REPORT

Use of Postexposure Prophylaxis After Occupational Exposure to *Zaire ebolavirus*

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From September 2014 to April 2015, 6 persons who had occupational exposures to *Zaire ebolavirus* in West Africa received investigational agent rVSV-ZEBOV or TKM-100802 for postexposure prophylaxis and were monitored in the United States. All patients experienced self-limited symptoms after postexposure prophylaxis; none developed Ebola virus disease.

Keywords. Ebola virus; postexposure prophylaxis; vesicular stomatitis virus; TKM-Ebola.

Postexposure prophylaxis (PEP) after Ebola virus (EBOV) exposure can prevent infection or progression to severe EBOV disease (EVD) when administered promptly in nonhuman primates [1, 2]. Whether PEP prevents EVD after EBOV exposure in humans is unknown. Effective PEP is desirable to reduce progression to EVD after EBOV exposures, especially among healthcare personnel, who have a higher EVD incidence than nonhealthcare personnel [3].

A few individuals were evacuated from West Africa to the United States after potential EBOV exposures and received PEP through Food and Drug Administration–approved emergency investigational new drug (eIND) applications. Investigational PEP strategies include a recombinant vesicular stomatitis virus (VSV) vaccine that expresses a *Zaire ebolavirus* surface glycoprotein (rVSV-ZEBOV), a small interfering RNA known as TKM-100802, favipiravir (RNA polymerase inhibitor), and ZMapp (monoclonal antibody cocktail against EBOV glycoprotein).

There are limited human data about PEP use for potential EBOV exposures and symptoms experienced after PEP administration. Previous reports described rVSV-ZEBOV administration to 2 physicians and a laboratory worker with percutaneous EBOV exposures [4–6]. One report of healthcare personnel medically evacuated to the United Kingdom after potential EBOV exposure described 4 individuals given PEP, including favipiravir and monoclonal antibody cocktails ZMab, and MIL77 [7]. Of the 7 patients described in these case reports who received investigational PEP, none developed EVD. We describe PEP use among 6 persons monitored in the United States who experienced potential EBOV exposures during 2014–2015.

METHODS

This retrospective case series includes all persons who received PEP after a potential EBOV exposure in West Africa. Exposures occurring from September 2014 to April 2015, included suspected percutaneous exposure to blood or body fluids of a patient with EVD, direct contact with such a patient while wearing inappropriate or compromised personal protective equipment (PPE), or other exposure thought to be of sufficient risk to warrant medical evacuation and consideration of PEP. Decisions about medical evacuation, whether to initiate PEP, which investigational PEP agent to use, the duration of hospital monitoring, and clinical and laboratory monitoring of PEP recipients were made by clinicians at the treating facilities with input from public health authorities.

The rVSV-ZEBOV vaccine was made available under an eIND application to the Food and Drug Administration; the protocol specified a dose of 10^8 plaque-forming units (PFUs). TKM-100802 was also made available under an eIND application. All patients were monitored initially in US healthcare facilities. EBOV nucleic acid testing of blood specimens was performed at the US Army Medical Research Institute of Infectious Diseases using the EZ1 real-time reverse transcription polymerase chain reaction (RT-PCR) assay or at the Centers for Disease Control and Prevention (CDC) using the CDC Ebola Virus NP and VP40 Real-time RT-PCR assays. Clinicians who cared for PEP recipients were contacted to perform chart review using a standardized form to abstract patient characteristics, EBOV exposures, signs and symptoms after PEP administration, and laboratory results. Data were aggregated, and summary results are presented. Data for 1 case were published elsewhere [4]. This activity was determined to be nonresearch, not requiring institutional review board determination at CDC.

RESULTS

Six persons received PEP for a potential EBOV exposure assessed to be sufficiently high risk from September 2014 through April 2015. These included 3 nurses and 2 physicians working

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Table 1. Potential High-Risk Ebola Virus Exposures Experienced by 6 Personal Protective Equipment Recipients

Occupation	Exposure	PEP (Time From EBOV Exposure to Initiation)
Physician	Physician manipulated an intravenous cannula on a viremic patient with EVD; while wearing the same gloves, physician drew medication from an ampule and accidentally stuck the needle through both pairs of gloves	TKM-100802 (2 d)
Nurse	Nurse was providing patient care in an ETU, which included delivering medications and meals and cleaning up bloody emesis and broken glass medication ampules; nurse did not realize that an injury had occurred but when removing PPE noted a tear in a glove and found a bleeding laceration	rVSV-ZEBOV (3 d)
Other ETU worker	Worker picked up with ungloved hands a cardboard box that contained sharps, in the grass near an ETU that was being renovated, and a hollow-bore needle pierced the worker's hand; it is unknown whether the needle could have been contaminated with EBOV (ETU had not had a patient with EVD for about 2 wk)	rVSV-ZEBOV (24 h)
Nurse	Nurse broke a glass medication ampule while working in an ETU and continued to work for about 15 min before inspecting gloves; both layers of gloves had been penetrated, and blood was noted at the point of penetration	rVSV-ZEBOV (27 h)
Physician	A hollow-bore needle that was not contaminated with body fluids from a patient with EVD pierced contaminated gloves while physician was disposing of the needle in an overflowing sharps container	rVSV-ZEBOV (43 h)
Nurse	Nurse felt a sharp prick to a finger while turning a severely ill patient with EVD and an open draining wound; no needle or sharp found, and no skin puncture was noted initially, but a red pin-sized wound was found on the finger the next day	rVSV-ZEBOV (3 d)

Abbreviations: EBOV, Ebola virus; ETU, Ebola treatment unit; EVD, EBOV disease; PEP, postexposure prophylaxis; PPE, personal protective equipment.

Table 2. Characteristics of 6 Patients Receiving Postexposure Prophylaxis for Potential High-Risk Ebola Virus Exposures

Characteristic	Patients, No. (%)[a]
Male sex	4 (67)
Age, median (range), y	39 (36–45)
Occupational role at time of exposure	
Nurse	3 (50)
Physician	2 (33)
Nonhealthcare worker	1 (17)
Exposed by percutaneous injury	6 (100)
Type of sharp	
Hollow-bore needle	3 (50)
Broken medication ampule	2 (33)
Unknown	1 (17)
Sharp and PPE (glove) EBOV contamination status	
Noncontaminated sharp through contaminated PPE	2 (33)
Noncontaminated sharp through PPE recently cleaned with chlorine solution	1 (17)
Unknown sharp through contaminated PPE	2 (33)
Unknown sharp, no PPE	1 (17)
Activity at time of injury from sharp	
Medication administration	3 (50)
Disposing of sharps	2 (33)
Turning patient	1 (17)
Time from exposure to initial decontamination, range, min	5–15
Type of PEP received	
rVSV-ZEBOV	5 (83)
TKM-100802	1 (17)
Time from exposure to PEP initiation, range, d	1–3
Site of PEP initiation	
West Africa	2 (33)
Medical evacuation flight	4 (67)
Time from PEP administration to first sign/symptom, range	10 h–2 d

Abbreviations: EBOV, Ebola virus; PEP, postexposure prophylaxis; PPE, personal protective equipment.

[a] Data represent No. (%) of patients unless otherwise specified.

in Ebola treatment units (ETUs) when the exposures occurred and 1 nonclinician worker (Table 1). All potential EBOV exposures were confirmed or suspected percutaneous exposures that occurred in Sierra Leone; 5 occurred in ETU patient care areas, and 1 occurred outside a nearby ETU (Table 1). Three of the injuries involved hollow-bore needles, 2 involved broken medication ampules, and 1 occurred with an unknown sharp object. One person noticed the injury when removing PPE; the others recognized the injury immediately. No sharps were known to be contaminated with EBOV; however, the sharp penetrated potentially contaminated PPE in 4 PEP recipients. One PEP recipient was not wearing any PPE at the time of injury. Percutaneous injuries occurred while administering medication (3 injuries), disposing of sharps (2 injuries), and turning a patient with EVD in bed (1 injury). On recognizing the injury, all PEP recipients decontaminated the wound site within 15 minutes with a chlorine solution. All were medically evacuated to the United States within 2–3 days after injury.

Five patients received rVSV-ZEBOV at a dose of 10^8 PFUs in a 1-mL solution; 1 received multiple TKM-100802 doses at 0.3–0.5 mg/kg/d. The time from EBOV exposure to PEP initiation was 1–3 days. Two patients began PEP while in West Africa, 4 on the medical evacuation flight. PEP for human immunodeficiency virus was given to 4 individuals; the other 2 declined this intervention.

All PEP recipients were isolated in US healthcare facilities with at least standard, contact, and droplet precautions initially; the length of stay ranged from 3 to 19 days. All reported symptoms that began ≤1 day after PEP initiation (Tables 2 and 3). Of 5 who received rVSV-ZEBOV, the most commonly reported adverse effects were fever, headache, and nausea, each occurring in 4 patients. Fever among rVSV-ZEBOV recipients began 12–24 hours after rVSV-ZEBOV administration. Diarrhea was

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Table 3. Systemic and Local Reactions in 6 Patients Receiving Postexposure Prophylaxis for Potential High-Risk Ebola Virus Exposures

	Type of PEP Received	
Reaction	rVSV-ZEBOV (n = 5)[a]	TKM-100802 (n = 1)
Systemic		
Fever	4	Yes
Highest fever, °C	37.3–39.1	38.1
Myalgias	3	Unknown
Chills/rigors	3	No
Diaphoresis	3	No
Hypotension	1	Yes[b]
Malaise	2	No
Fatigue	3	Unknown
Headache	4	Yes
Dizziness	1	No
Arthralgia	1	No
Arthritis	0	No
Rash	1	No
Chest pain	1	No
Dyspnea	1	No
Hypoxia	1	No
Nausea	4	No
Vomiting	1	No
Diarrhea	2	No
Local		
Redness	0	Yes
Swelling	0	Yes
Pain	3	Yes
Thrombophlebitis	0	Yes

Abbreviation: PEP, postexposure prophylaxis.

[a] Data in this column represent number of patients, unless otherwise specified.

[b] This patient's lowest blood pressure was 90/56 mm Hg while asleep; hypotension resolved without intervention.

reported in 2 rVSV-ZEBOV recipients, started 2 days after rVSV-ZEBOV administration in one and 1 day before it in the other. One rVSV-ZEBOV recipient vomited 4 days after PEP initiation, 1 had a rash that appeared 1 day after PEP initiation and lasted for 18 days, and 1 reported joint pain starting on the day of PEP initiation, resolving by the next day. Three rVSV-ZEBOV recipients reported pain at the injection site. In the TKM-100802 recipient, fever developed 48 hours after the first dose, with redness, swelling, pain, and thrombophlebitis at multiple injection sites. All patients had resolved symptoms by hospital discharge and were monitored through 21 days after their potential EBOV exposure.

No patients had laboratory evidence of EBOV infection. The EBOV glycoprotein, expressed by rVSV-ZEBOV, was detected in blood with RT-PCR in 4 of 5 rVSV-ZEBOV recipients. Three rVSV-ZEBOV recipients had detectable immunoglobulin M and G antibodies to EBOV glycoprotein after vaccination [4]. EBOV glycoprotein was not detected with RT-PCR in the blood of the TKM-100802 recipient. Among rVSV-ZEBOV recipients, EBOV nucleoprotein was not detected with RT-PCR in blood collected ≥3 days after exposure. Three rVSV-ZEBOV recipients underwent RT-PCR for VSV nucleoprotein in the blood, and all had VSV detected.

DISCUSSION

We describe 6 individuals who received PEP after potential EBOV exposures; none had RT-PCR evidence of EBOV infection, and none developed EVD. All patients reported symptoms after PEP administration that may have been attributable to PEP or to other factors, such as anxiety, stress, fatigue related to medical evacuation, or other medications, including PEP for human immunodeficiency virus.

Safety studies of rVSV-ZEBOV among healthy volunteers have shown that rVSV-ZEBOV is generally well tolerated; early reactogenicity symptoms are common, and rare occurrences of arthritis and vesicular dermatitis have been reported [8–10]. Although 1 of the 5 rVSV-ZEBOV recipients reported joint pain, none reported arthritis; 1 reported a rash. All PEP recipients' symptoms resolved by the time of hospital discharge. An ongoing ring vaccination trial, designed to examine use of rVSV-ZEBOV at a lower dose of 2×10^7 PFUs/mL for rapid preexposure prophylaxis rather than for PEP [11], may provide additional data on safety, efficacy in prevention of EVD, and duration of protection [12]. Additional vaccine trials that aim to immunize healthcare and other frontline workers before an EBOV exposure event are ongoing [13].

In the few reports of TKM-100802 for treatment of EVD, fever and rigors were described in 1 patient, the drug was discontinued in another owing to multiorgan system failure, and a third experienced hypotension after the initial infusion [14, 15]. The patient we describe who received TKM-100802 for EBOV PEP experienced fever and injection site reactions, and therapy was stopped after dose 5 of 7 because of these adverse effects.

This report is subject to limitations. The small number of PEP recipients makes it difficult to generalize any of the clinical findings. PEP was uncontrolled; therefore, we cannot determine whether rVSV-ZEBOV or TKM-100802 was effective in preventing EVD. Although the exposures described among PEP recipients were assumed to be high risk for the purpose of public health monitoring, it was not determined whether EBOV exposure actually occurred because no testing was performed on the sharps or PPE to document the presence of EBOV.

None of the PEP recipients reported here or elsewhere [4–6] developed evidence of EBOV infection, but it is unknown whether PEP prevented EVD. Although the effectiveness of PEP remains unclear from this small case series, high-risk exposures are likely to occur in the future, and timely PEP availability and administration may help reduce the risk of progression to EVD. Priorities for PEP research include using observational studies or clinical trials when feasible to determine the highest-risk EBOV exposures, the optimal time and "window period" for PEP, the safety profile of candidate PEP therapies, and the

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most effective interventions to prevent EVD after high-risk EBOV exposures.

Notes

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