

Clinical Case Management Guidelines of Ebola Virus Disease (EVD)

Introduction

Ebola hemorrhagic fever (Ebola HF) is one of numerous Viral Hemorrhagic Fevers. It is a severe, often fatal disease in humans and nonhuman primates (such as monkeys, gorillas, and chimpanzees).

Ebola HF is caused by infection with a virus of the family *Filoviridae*, genus *Ebolavirus*. When infection occurs, symptoms usually begin abruptly. The first Ebolavirus species was discovered in 1976 in what is now the Democratic Republic of the Congo near the Ebola River. Since then, outbreaks have appeared sporadically.

There are five identified subspecies of *Ebolavirus*. Four of the five have caused disease in humans: Ebola virus (*Zaire ebolavirus*); Sudan virus (*Sudan ebolavirus*); Tai Forest virus (*Tai Forest ebolavirus*, formerly *Côte d'Ivoire ebolavirus*); and Bundibugyo virus (*Bundibugyo ebolavirus*). The fifth, Reston virus (*Reston ebolavirus*), has caused disease in nonhuman primates, but not in humans.

The natural reservoir host of ebola viruses remains unknown. However, on the basis of available evidence and the nature of similar viruses, researchers believe that the virus is zoonotic (animal-borne) with bats (fruit) being the most likely reservoir. Four of the five subtypes occur in an animal host native to Africa.

A host of similar species is probably associated with Reston virus, which was isolated from infected cynomolgous monkeys imported to the United States and Italy from the Philippines. Several workers in the Philippines and in US holding facility outbreaks became infected with the virus, but did not become ill. Ebola hemorrhagic fever (Ebola HF) is one of numerous Viral Hemorrhagic Fevers. It is a severe, often fatal disease in humans and nonhuman primates (such as monkeys, gorillas, and chimpanzees).

Transmission

Because the natural reservoir of ebolaviruses has not yet been proven, the manner in which the virus first appears in a human at the start of an outbreak is unknown. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal.

When an infection does occur in humans, there are several ways in which the virus can be transmitted to others. These include:

- direct contact with the blood or secretions of an infected person
- exposure to objects (such as needles) that have been contaminated with infected secretions

The viruses that cause Ebola HF are often spread through families and friends because they come in close contact with infectious secretions when caring for ill persons.



During outbreaks of Ebola HF, the disease can spread quickly within health care settings (such as a clinic or hospital). Exposure to ebola viruses can occur in health care settings where hospital staff are not wearing appropriate protective equipment, such as masks, gowns, and gloves.

Proper cleaning and disposal of instruments, such as needles and syringes, is also important. If instruments are not disposable, they must be sterilized before being used again. Without adequate sterilization of the instruments, virus transmission can continue and amplify an outbreak.

In Africa, confirmed cases of Ebola HF have been reported in:

- Guinea
- Liberia

- Sierra Leone
- Democratic Republic of the Congo (DRC)
- Gabon
- South Sudan
- Ivory Coast
- Uganda
- Republic of the Congo (ROC)
- South Africa (imported)

* Outbreak affected countries include Guinea, Liberia, Sierra Leone, and Lagos, Nigeria, as of 4-August-2014

I. Clinical case definition:-

(i) **Suspected case** :- Patient having history of travel or close contact with symptomatic person traveling from Ebola Virus Disease affected areas in the past 21 days, with high grade fever more than 101 degrees F, along with one or more of the following additional symptoms:-

- Headache
- Body ache
- Unexplained haemorrhage
- Abdominal pain
- Diarrhoea
- Vomiting

(ii) **Confirmed case:-** : A case with the above features and laboratory confirmed diagnostic evidence of Ebola virus infection at a BSL-3 facility by any one of the following:-

- Ig M (ELISA)
- Antigen detection
- RT-PCR

N.B

Diagnosing Ebola HF in an individual who has been infected for only a few days is difficult, because the early symptoms, are nonspecific to ebola virus infection and are seen often in patients with more commonly occurring diseases.

However, if a person has the early symptoms of Ebola HF and there is reason to believe that Ebola HF should be considered, the patient should be isolated and public health

professionals notified. Samples from the patient can then be collected and tested to confirm infection.

II. Case Management in Hospital

- (i) Isolate the patient
- (ii) Follow standard precautions including appropriate Personal Protective Equipments(PPE)
- (iii) Restrict visitors
- (iv) Avoid aerosol generating procedure
- (v) Implement environmental infection control measures.
- (vi) Proper disposal of potentially infected material following biohazard precautions.

III Treatment:

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Approach Considerations

1. Currently, no specific therapy is available that has demonstrated efficacy in the treatment of Ebola hemorrhagic fever
2. General medical support is critical and should include replacement of coagulation factors and heparin if disseminated intravascular coagulation develops. Such care must be administered with strict attention to barrier isolation. All body fluids (blood, saliva, urine, and stool) contain infectious virions and should be handled with great care.
3. Surgical intervention generally follows a mistaken diagnosis in which Ebola-associated abdominal signs are mistaken for a surgical abdominal emergency. Such a mistake may be fatal for the patient and for any surgical team members who become contaminated with the patient's blood.

There are no commercially available Ebola vaccines. However, a recombinant human monoclonal antibody directed against the envelope GP of Ebola has been demonstrated to possess neutralizing activity. This Ebola neutralizing antibody may be useful in vaccine development or as a passive prophylactic agent. Work on a vaccine continues.

Supportive Care

1. Supportive therapy with attention to intravascular volume, electrolytes, nutrition, and comfort care is of benefit to the patient. Intravascular volume repletion is one of the most important supportive measures.
2. Survivors can produce infectious virions for prolonged periods. Therefore, strict barrier isolation in a private room away from traffic patterns must be maintained throughout the illness. Patient's urine, stool, sputum, and blood, along with any objects that have come in contact with the patient or the patient's body fluids

(such as laboratory equipment), should be disinfected with a 0.5% sodium hypochlorite solution. Patients who have died of Ebola virus disease should be buried promptly and with as little contact as possible.

Pharmacologic Therapy

1. Nucleoside analogue inhibitors of the cell-encoded enzyme S-adenosylhomocysteine hydrolase (SAH) have been shown to inhibit *Zaire ebolavirus* replication in adult BALB/c mice infected with mouse-adapted Ebola virus. Inhibition of SAH indirectly inhibits transmethylation reactions required for viral replication. Treatment response was dose-dependent. When doses of 0.7 mg/kg or more every 8 hours were begun on day 0 or 1 of infection, mortality was completely prevented. Even when the drug was given on day 2, 90% survived.
2. Smith et al found that in rhesus macaques infected with a lethal dose of Ebola virus, treatment with interferon beta early after exposure led to a significant increase in survival time, though it did not reduce mortality significantly. These findings suggest that early postexposure interferon-beta therapy may be a promising adjunct in the treatment of Ebola virus infection.
3. Passive immunity has been attempted by using equine-derived hyperimmune globulins and human-derived convalescent immune globulin preparations. In *Ebolavirus* -infected cynomolgus macaques, use of human recombinant interferon alfa-2b in conjunction with hyperimmune equine immunoglobulin G (IgG) delayed but did not prevent death. Equine IgG containing high-titer neutralizing antibodies to Ebola virus protected guinea pigs and baboons but was not effective in protecting infected rhesus monkeys.

During the 1995 outbreak in Kikwit, DRC, human convalescent plasma was used to treat 8 patients with proven Ebola disease, and only 1 patient died. Subsequent studies could not demonstrate survival benefit conferred by convalescent plasma products. The survival of these patients suggests that passive immunity may be of benefit in some patients.

4. Four laboratory workers in Russia who had possible Ebola exposure were treated with a combination of a goat-derived anti-Ebola immunoglobulin plus recombinant human interferon alfa-2. One of these patients had a high-risk exposure and developed clinical evidence of Ebola virus infection. All 4 patients recovered.
5. A recombinant human monoclonal antibody directed against the envelope glycoprotein (GP) of Ebola virus has been demonstrated to possess neutralizing activity. This Ebola virus-neutralizing antibody may be useful in vaccine development or as a passive prophylactic agent.
6. DNA vaccines expressing either envelope GP or nucleocapsid protein (NP) genes of Ebola virus have been demonstrated to induce protection in adult mice exposed to the virus. These vaccines were administered by coating gold beads with DNA

expressing the genes for either GP or NP, and they were delivered by skin particle bombardment using a PowderJect-XR gene gun. Both vaccines induced measurable antibody responses detected by enzyme-linked immunosorbent assay (ELISA) and induced cytotoxic T-cell immunity.

7. Other experimental therapies that use available drugs, though not approved by the US Food and Drug Administration (FDA) for treatment of Ebola virus infection, may be considered. Agents that may reduce mortality without directly effecting viral replication include activated protein C— and a recombinant nematode anticoagulant protein (NAP) that inhibits activated factor VII-tissue factor complex. NAP resulted in attenuation of the coagulopathy associated with decreased fibrinolysis and fibrin deposition with a resultant decrease in the severity of the systemic inflammatory response syndrome.
8. In a rhesus macaque model of Ebola hemorrhagic fever, which carries a mortality approaching 100%, Geisbert et al administered recombinant nematode anticoagulant protein, a potent inhibitor of TF-initiated coagulation.-One third of the monkeys given the nematode anticoagulant protein survived a lethal dose of Ebola virus, whereas 16 of the 17 (94%) control animals died.

(This <http://emedicine.medscape.com/article/216288-treatment#aw2aab6b6b3> approach targeted the hemorrhagic disease component of the infection rather than the virus itself.)

Diet and Activity

Nutrition is complicated by the patient's nausea, vomiting, and diarrhea.

Good hydration with good amount of protein supplement

Recovery often requires months, and delays may be expected before full resumption of normal activities. Weight gain and return of strength are slow. Ebola virus continues to be present for many weeks after resolution of the clinical illness. Semen from men recovering from Ebola infection has been shown to contain infectious virus, and Ebola has been transmitted by sexual intercourse involving recovering men and their sex partners. Any individuals who were exposed to infected patients should be watched closely for signs of early Ebola virus disease.

In short

- Fluid and electrolyte balance
- Management of complication symptomatically
- Maintaining Oxygen status and Blood Pressure
- Treat for any complicating infection and co-morbid condition.

IV. Prevention :

- Health Education and awareness about the disease
- Soap water cleaning easily kills Ebola Virus
- Use of Standard Operating Procedures (SOPs) for prevention of disease
- Safe disposal of dead body with proper precaution for prevention of transmission of EVD.

Disposal of waste material and dead Body

Specimen collected, waste material should be packed in triple packaging system which consist of primary receptacle(sealable specimen bag) wrapped with absorbent material, secondary receptacle (watertight, leak pro0f) and an outer package.

Person handling the dead body must be heavily protected. Burial is the preferred method of disposal. Cultural and religious procedures may be addressed too.. local health authority must ensure burial ground for safe disposal . like away from drinking/ ground water resources, habitat etc. Burial depth should be atleast 1.5 meter above ground water level with atleast 1 meter covering of soil. If coffins not available , corpus should be wrapped in plastic sheeting to keep the remains separate from soil. Individual burial grave preferred.

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