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Ebola Disease: Challenges for Medical Professionals

Mohsina FP[1,*], Nesar A[2], Mukim M[3,5], Roy S[4], Sharma P[3] and Faheem IP[1]

[1]Luqman College of Pharmacy, Gulbarga, Karnataka, India
[2]Rahul Sankriyayan College of Pharmacy, Azamgarh, Uttar Pradesh, India
[3]Kota College of Pharmacy, Kota, Rajasthan, India
[4]Amity Institute of Pharmacy, Amity University, Uttar Pradesh, Lucknow Campus, India
[5] Dr. A.P.J Abdul Kalam University, Indore, India

[*]**Corresponding author:** Mohsina FP, Luqman College of Pharmacy, Gulbarga, Karnataka, India; Tel: +91-8904588538; E-mail: mohsina.patwekar [at] gmail [dot] com

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Abstract

Ebola virus disease (EVD) is epidemically fast-growing disease. Ebola virus (EV) was discovered by Dr. Peter Piotin (1976, Zaire), who suspected yellow jack in blood of catholic nun. There are five strains of EV, but the Zaire strain is the most severe having case-fatality~90%. Its genome is a 19 kb long single-helix, (-) RNA. More than 28,000 cases and over 11,000 deaths occurred in West African (September 2015). EV transmitted to people from wild animals and spread frequently in the human with incubation period and infection of 2 to 21 days. First symptoms were appeared as sudden onset of fever, fatigue, muscles pain, headache, sore throat, gum bleeding, rectal bleeding, multi-organ disease with damaged vascular system and body's regulation was impaired. The defensive white blood cells as well as platelet count can be reduced while the liver biomarker enzymes are elevated in some patients. The EV may be treated intravenous fluids. However, innumerable probable treatments are under preclinical and clinical evaluation consisting of immunological therapies, blood products, and drugs therapeutics. Also, various vaccines are under clinical trials for safety testing, but till date no vaccines are approved for human use. There is a challenge to understand the differences among species of Ebola virus. Moreover, studies are required into the ecology of reservoir species and shedding procedures. Novel targets tactics required in the pathophysiology of EV infections with animals' study.

Keywords: Ebola virus disease; Ebola virus; Prevention; Management; Treatment

Introduction

The international community has responded to the Ebola outbreak in West Africa with an approach that could be described as 'top down'. Small groups of elite scientists, health policy makers, pharmaceutical company executives, and the staff of the World Health Organization (WHO), governmental agencies, and non- governmental institutions have decided how to implement interventions for outbreak control and containment and develop new Ebola vaccines and treatments. These 'top down' interventions have built Ebola treatment units and organized the delivery of supplies, communications, and surveillance that have been essential for outbreak control. However, they have had only a modest impact on the survival rate for individual patients. In most treatment units, overall case fatality rates have been 60% or greater, and they have been even higher in patients who have been treated in the community [1]. Ebola virus disease outbreak in West Africa sends an alarming message to all countries in the world, to increase the level of coordination and application of preventive measures globally to avoid a disastrous epidemic in the World, as the current situation in West Africa is critical especially after the WHO increased the alarming level to an emergency in public health all over the world [2] reported systematic review on MHPSS programs among communities affected by EVD. This study shows the need to increase efforts to systematically document and evaluate the implemented programs. Results also provide preliminary evidence about the value of culturally sensitive MHPSS programs and of the implication of local mental health professionals [3]. The first outbreak of Ebola virus was described in 1976 near the Ebola River in Zaire. The Ebola virus infected 318 cases and caused 280 deaths. Fever and bleeding were the main symptoms observed at that time;

therefore, the EVD was initially termed Ebola hemorrhagic fever. To date, there have been 33 sporadic outbreaks worldwide, including 23 human-to-human transmission epidemics, three laboratory-induced outbreaks, and seven animal-to-human transmission outbreaks [4]. The Ebola virus is spread easily through the use of filthy syringes and needles or when an infected person comes in a close proximity with the non-infected person [5]. As per the reports of WHO, till May 3, 2015 more than 26 628 cumulative cases of EVD and about 11020 mortality had occurred [6]. The continued upsurge in the new cases has been lowered in Liberia, Guinea, and Sierra Leone, showing the signs of reversal. Since there is no specific drug treatment for the EV, extensive research is urgently needed on new epidemiological features and EVD epidemic developmental patterns that will eventually aid in the guidance for the proper drug development, treatment and management of the EVD outbreak.

Modes of Conduction of Ebola

EVD can transmit directly through the close contact with infected saliva, blood, sweat, urine, and other body fluids including semen, vomit, feces, and breast milk. It can also transmit via contact with objects infected with the various body fluids of the diseased person [7,8]. Transmission is believed to occur via contact with mucous membranes and non-intact skin (i.e., rashes, cuts, etc.). Risk of infection by inhalation of contaminated aerosols by healthcare workers has not been documented but is assumed to be low at this point supported history evidence [9,10]. Soap, direct sunlight, bleach, or drying can directly inhibit the viral growth. The virus has a short life span on the surfaces that are directly in the contact with the sun [11].

Pathophysiology

Ebola virus is an infectious, transferable, intra-cellular organism having either RNA or DNA as a genetic background. The filamentous filovirus is a single stranded RNA, enveloped organism having 80 nm non-segmented RNA molecules with a length up to 1400 nm. It encodes about 7 main genes: nucleoprotein, RNA-dependent RNA polymerase (L), VP 24, VP 30, VP35, VP40, and GP. The genomes of the five distinct Ebola viruses (BDBV, ZEBOV, REBOV, SEBOV and TAFV) vary in sequence and therefore the number and site of gene overlaps. Among all, viral transactivation and replication is mediated by VP30, nucleoprotein, VP35 as well as RNA polymerase. The viral budding and transmission is mediated by VP40 matrix protein while nucleo capsid development is associated with minor matrix protein called VP24. Interferon signaling is obstructed by both the matrix proteins that are VP24 and VP40. The GP is a surface protein represented as a trimeric spike embracing two subunits GP1 and GP2 [12]. The lifecycle of EV is divided into following phases:

- Attachment of virus to the cell surface
- Penetration of virus
- Uncoating
- Replication and viral expression
- Maturation
- Viral exocytosis

Scientific Aspects of Ebola

Extensive weakness, fever, and diarrhea are the main symptoms of EVD. Elevated transaminases, maculopapular rash, thrombocytopenia, lymphopenia are also main abnormalities associated with the EVD. Nearly half of the patients experience these bleeding problems mildly while severe bleeding problems are relatively rare. It is vital to have a thorough history of travelling. The viral incubation time is classically 5-7 days [13]. Once it is suspected that it is the Ebola virus, the diagnosis must be confirmed. In the absence of effective healing strategies, the analysis and diagnosis of the infection play an important role. Molecular techniques including polymerase chain reaction (PCR) are the main diagnostic tools. Blood samples usually present positive PCR results a day before the clinical manifestation occur. The PCR testing is sensitive and specific real time and it can give results within hours. The exchange of information in real time, about the PCR results, is completely essential to improve the response capacity. The primary detection of antigen could be employed as a confirmatory diagnosis test for instantaneous analysis. Secondary assays involve the antibodies detection including IgG and IgM that are generally significant for the epidemiological surveillance. Furthermore, confirmed deep-rooted diagnosis continues to be a vital procedure for contact search to overcome the various difficulties for reintroducing the survivors in the community. Ebola infected patients require an urgent and fast treatment as well as efficient basic support in order to visualize the difference between survival and mortality rate in the infested patient [14].

Managing Personnel

Managing contact tracing personnel is another major challenge. Hiring a sufficient number of appropriately trained staff, especially in heavily affected areas, has been hindered by limited education and managerial proficiencies in the population that necessitates the establishment of job-explicit training [15]. Furthermore, contact tracing employees can be erroneously perceived to have an augmented danger of obtaining EVD, leading to stigmatization. Guinea and Liberia have employed media resources for depicting the employees as

the heroes. Another major apprehension in retentive employees is security; some of the societies have banned the entry of contact tracing employees, occasionally intimidating physical fierceness [16]. In response, in Liberia, security forces have been employed to accompany contact tracing personnel into communities [17].

Treatment

There is no precise remedy for EVD. Since till date there is no efficacious vaccine or any antiviral drugs are available, the therapeutic management of EVD patients is a major threat. The management is basically relied on the survival support, control of organ failure as well as on providing the symptomatic relief that focuses on the supply of adequate nutrition and hydration along with antibiotics, and antimalarial drugs if essential. Remdesivir developed by Gilead Sciences in 2017 as a treatment for Ebola virus infection [18]. Severe isolation of diseased individual along with limited nursing support is another crucial step that can help to prevent the disease transmission. In the cases where there is an extensive disease transmission danger from dead bodies, individual defensive instruments as well as sanitization for surface cleansing should be employed along with the safety guidelines recommended by CDC directions [19]. Such type of investigation was not repeated in further outbreaks as in vitro assay indicated that antibodies against Ebola had no neutralizing action. Furthermore, monoclonal antibodies to the GP of Ebola virus exhibited defensive and healing properties in mice but they were unable to protect NHP [20,21]. The animal studies suggest that Ebola specific immunoglobulin of equine origin has little activity in hiding viraemia and slowing disease onset in NHP. Goat immune-globulins were evaluated in pre-clinical test on laboratory animals and were administered to scientist assumed of gaining infection with EHF during their investigational work. It was suggested that these immune-globulins might be beneficial for the emergency cure of persons inadvertently infected with EHF [22]. The Ebola virus reproduction was shown to be hindered in vitro by a series of nine nucleoside analogue inhibitors of S-adenosyl homocysteine hydrolase and carbocyclic 3-deazaadenosine was shown to avert death in mice infected with the Ebolavirus [23]. Various clinical aids like injections, catheters and parenteral interventions etc. should be reduced to avert trauma and the increased challenge of disease spread. Several drugs specially aspirin, non-steroidal anti-inflammatory drugs, anticoagulant therapies, and steroids should be contraindicated [24]. The recommendations of WHO for treatment at home have been comparatively effective if specialized care is not available [25]. Extensive researches are registered whose primary aim is to discover an effective the rapeutic for safe and efficient management of the EVD patients. Presently, RNA inhibitor drugs (TKM-Ebola), nucleoside analogs, monoclonal antibodies (ZMapp), antisense-based (AVI-7537) drugs and phosphorodiamidatemorpholino oligomers are the major drug categories that are under clinical evaluation for their action against EVD. Favipiravir is a potential repurposed candidate that can suppress viral growth by inhibiting viral replication. Another hopeful candidate is ZMapp consists of three monoclonal antibodies obtained from plant of tobacco. The main target of the drug is inhibition of viral replication, especially the expression phase as the virus enters the host cellular machinery [26]. Additional drug, that is also effective against yellow fever and Marburg is BCX4430. The drug possesses good antiviral activity as it is capable of targeting a major enzyme present in the EV. In preclinical studies the drug has shown significant effective results in suppressing the infection when administered within 2 days of infection [27]. The repurposed use inhibitors of angiotensin-converting enzyme as well as statins and blockers of angiotensin receptor have been recommended as supportive treatment for improvising and encouraging the immune system of the diseased person. Ebola virus is normally considered as a conceivable biological weapon, thus there is a crucial need to develop effective antiviral drugs and vaccines [28]. Reiter RJ et al., 2020 reported on the utility of melatonin as a treatment for virus-mediated diseases. Of special note are the data related to the role of melatonin in influencing Ebola virus disease. This infection and deadly condition has no effective treatment and the published works documenting the ability of melatonin to attenuate the severity of viral infections generally and Ebola infection specifically are considered. The capacity of melatonin to prevent one of the major complications of an Ebola infection, i.e., the hemorrhagic shock syndrome, which often contributes to the high mortality rate, is noteworthy. Considering the high safety profile of melatonin, the fact that it is easily produced, inexpensive and can be self-administered makes it an attractive potential treatment for Ebola virus pathology [29].

Ebola Record 2014-2015

This epidemic may be a tragic illustration of the importance of improving global health security. Every day, the transmission of the disease remains unchecked and therefore the likelihood of spreading to unaffected countries increases. It is also important to mention that the epidemic is occurring in West Africa, where there had not been an Ebola outbreak before. Ebola has grasped the level where it can be regarded as an endemic ailment due to a very insufficient and delayed global response. For the medium term, the risk of constant spread of the epidemic should be taken into account and the possibility that the Ebola become endemic in West Africa shall be assumed, a perspective never contemplated before. If this happens, West Africa could become a reservoir for the virus to spread to other parts of Africa and beyond [28]. The typical

efforts "to control the outbreak" aren't enough any longer for such an enormous epidemic. What is required is action at an enormous scale, a humanitarian strategy and a mixture of typical public health measures with efficient and secure procedures, which include supplies and human resources, among others [30]. Moreover, a proper response requires an appreciation of the culture of societies in the affected countries and the implementation of interventions with the consent of the population [31]. Paradoxically, in the first world there is an "urgency to delete "everything related to Ebola [32]. At the same time, there is a conviction that as Western Africa is not the whole world, but only a piece of the planet plagued by a deadly epidemic, it has now become a threat because the disease has the potential to spread to other countries, including the rich ones[33,34]. The self-preservation gregarious instinct prevented honest souls in real time disclosure of what was happening [35]. The greatest protection in contradiction of an epidemic is to prevent the transmission at a point where it initiated, and this may be accomplished with the support of the finest healthcare services. Africa is known to have no well-equipped health care services for preventing the epidemic in this public health crisis [36,37]. We have to be one step further from this outbreak, but at this time we are five steps behind [38-40].

Conclusion

Tracing process, as prompt and efficient contact tracing is important for the identification, control, and elimination of EVD, any delay or inefficiency may result in ongoing response efforts and failure to get to zero cases. Although contact tracing challenges could also be hooked in to each country's unique socioeconomic, geopolitical, and cultural context, there are common issues encountered throughout the West African region. Underlying a number of these challenges is the novelty of EVD in the region, which has contributed to the fear, stigma, and community EVD misperceptions. Liberia, Nigeria, Senegal, and Mali were able to overcome these challenges, successfully eliminating EVD. The ongoing support and continuing efforts of the West African ministries of health and in- country staff to identify and address these challenges, and learn from these successes, will improve contact tracing efforts in West Africa. Ultimately, this will lead to a halting of EVD transmission in the region and the prevention of large-scale EVD outbreaks in the future.

Conflict of Interest

We declare that we have no conflict of interest.

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