International Journal of Pharmacy Teaching & Practices 2016, Vol.7, Issue 1, 2657-2665.

A Review on Current Trends in the Management of Ebola Virus Disease

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Review Article

Please cite this paper as: Palanisamy Sivanandy, Shim Hui Sin, Ong Yee Ching, *et.al.,*. A Review on Current Trends in the Management of Ebola Virus Disease. IJPTP, 2016, 7(1), 2657-2665.

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Abstract

The Ebola virus created a ripple of fear when its number of cases rose rapidly and drastically in recent years. Ebola infection is transmitted in humans when contact closely with blood, organs or other body fluids of infected animals or secretions. It is often mortal as it affects vascular system of the body which simply denotes the ways blood travels throughout the body. Hence, this results in organ failure and serious internal bleeding. Standard supporting care in a hospital setting such as replenishment of fluid and electrolytes, ventilation support, pain control and nutritional support is initiated to the patients to manage the symptoms and prevent any complications of Ebola disease since there are no FDA-approved medications available. In terms of pharmacological drug therapy, Favipiravir has been shown to be efficacious and safe in treating the Ebola Virus Disease (EVD). Nevertheless, there are some preventive measures as well to decrease the risk of getting the disease.

Keywords: *Ebola, Haemorrhagic fever, Infection, Transmission, Bleeding, Virus.*

Introduction

The Ebola virus created a ripple of fear when its number of cases rose rapidly and drastically in recent years. While other diseases have since gained more international exposure, it appears that the Ebola virus has taken a backseat. Nevertheless, it is essential to note that it still continues to ravage certain countries and knowledge of the virus and its various elements will aid in being better informed of its symptoms and management of treatment. This review is an attempt to summarize various essential aspects of Ebola virus disease (EVD).

Ebola virus disease of the genus '*Ebola*' and family '*Filoviridae*'[1-3] is a negative sense, non-segmented individual stranded RNA virus that results in fever and bleeding of the internal organs in animals and humans.[1,2] As Ebola affects the body's vascular system which simply denotes the ways blood travels throughout the body therefore Ebola are said to be mortal. Hence, this results in organ failure and serious internal bleeding.[1]

The virus was first identified in Ebola River which is located in Congolese region and eventually the virus was named after it.[4] *Zaire Ebola virus* (EBOV), *Sudan Ebola virus* (SUDV), *Bundibugyo Ebola virus* (BDBV), *Taï Forest Ebola virus* (TAFV) and *Reston Ebola virus* (RESTV) are the 5 definite classes in genus Ebola virus.[5] However large EVD epidemic outbreaks in Africa have been predominantly associated with BDBV, EBOV, and SUDV.[5]

The typical clinical description of EVD includes an immediate onset of illness followed by nonspecific signs such as fever, myalgia, headache, sore throat, cough, vomiting, and diarrhoea.[6] The means of exposure of this Ebola virus may either be primary or secondary. Primary exposure relatively involves being present in an Ebola infection particular region and secondary exposure involves primate-to-human or human-to-human spreading.[7] In addition, close contact with the blood, organs, and other body fluids of infected animals or with the secretions are the ways of spreading Ebola infection in human being.[8] Apart from that, some bats that eats fruit also known to be a natural reservoir of Ebola infection.[8] Nevertheless, the duration between vulnerability to an infection and the presence of the early symptoms ranges from 2 to 21 days.[8]

Even though the Ebola virus exists longer than 35 years, the major outbreak started in West Africa in March 2014.[9] The current epidemic of Ebola virus (EBOV) infection in Africa involve many nations which includes Guinea, Sierra Leone, Senegal,

Liberia, Democratic Republic of the Congo and Nigeria and has not end.[10] The overall prognosis for patients with Ebola virus infection is bad.[7] Nevertheless, people who live for 2 weeks usually make a gradual improvement.[7] Currently, no particular treatment is available that has shown effectiveness in the Ebola haemorrhagic fever (EHF) treatment, also there are no Ebola virus vaccines commercially available.[7]

OUTBREAKS OF EVD

In September 1976, Dr. Piot received two vials of blood while working in a lab at the Institute of Tropical Medicine in Antwerp, Belgium.[11] The vials contain blood of a Belgian nun whom working in Zaire and recently became seriously ill.[12] Upon microscopic examination, he found a gigantic worm like structure present in the blood sample. He suspect that the worm could be Marburg virus due to similar shape and size observed.[11,12] Subsequently, the blood sample was sent to the CDC lab in Atlanta for further examination and confirmed that the sample contained a brand new haemorrhagic virus.[12] After the revelation, Dr. Piot and several Belgian scientists were on a flight to Zaire to investigate the new virus.[11,12] In a village of Yambuku, the team finally decided to name the virus after a river, which called the Ebola virus disease (EVD).[11]

The first outbreak of EVD occurred in South Sudan, the areas affected is Nzara and Maridi. The virus strain found was *Sudan ebolavirus*.[13,14] At the similar time, a second outbreak occurred in 1976, the area affected is Yambuku village, Zaire where *Zaire ebolavirus* strain was identified[13] However, the reason for virus occurred simultaneously in two distant areas with virtually no contact between of the virus was still remain unknown.[12] In 1979, a recurrent outbreak of *Sudan ebolavirus* occurred in similar site of South Sudan affected in 1976.[15] An increase of 12% of fatality rate reported when compared with year 1976.[14,15]

From 1989 to 1992, a new species of ebolavirus, *Reston ebolavirus* was discovered and spread to three different country by importing infected monkey from the Philippines.[16-19] The areas affected are Virginia, Pennsylvania and Texas in USA, Sienna in Italy and export primate facility area in Philippines.[16-19] *Reston ebolavirus* caused a serious illness on non-human primate but not in human.[16,18] Workers and researchers who get infected with *Reston ebolavirus* did not show any symptom of EHF.[16,18]

In November 1994, another new strain of Ebola virus was discovered on a chimpanzee in Ivory Coast.[20] An ethologist performed an autopsy on the chimpanzee and get infected by this new strain of virus, *Tai Forest ebolavirus*.[20] The ethologist subsequently develops EHF and treated in Switzerland.[20] *Tai Forest ebolavirus* is a non-fatal infection in human but highly fatal in chimpanzee.[20]

After 15 years epidemiologic silence of *Zaire ebolavirus* since 1979, an re-emerged outbreak of *Zaire ebolavirus* happened in the end of 1994. It occurred in Mekouka, Andock, and Minkebe gold mine camps in Gabon. Initially, it was thought as yellow fever, and finally recognize as *Zaire ebolavirus* in 1995.[21] A 60% of fatality rate reported in this outbreak. In May 1995, another outbreak of *Zaire ebolavirus* occurred in Kikwit, Democratic Republic of the Congo (formerly Zaire).[22] The fatality rate reported is 81%, which is similar to the epidemic happen in 1976.[13,22] The outbreak was rapidly terminated by health education efforts and used of barrier-nursing techniques.[22] Subsequently, two outbreaks of *Zaire ebolavirus* occurred in Gabon on different time length, January 1996 to April 1996 and July 1996 to January 1997. It happened in Mayibout and Booue area respectively. The fatality rate reported in both areas exceed 50%.[21]

From 2000 to 2001, an outbreak of *Sudan ebolavirus* occurred in Gulu, Masindi and Mbarara districts of Uganda.[23] A 53% of fatality rate reported and the outbreak resolved in February of 2001 as Uganda declared free of EHF at that time.[24] From October 2001 to December 2003, there were total of four outbreaks of *Zaire ebolavirus* occurred in both Republic of Congo and Gabon.[25-27] The fatality rate reported of these four outbreaks is greater than 75%.[25-27] In addition, the symptoms of EHF is first known in the Republic of Congo.[25]

In 2004, an outbreak of *Sudan ebolavirus* occurred in Yambio County of southern Sudan. It is a minor outbreak of 17 human cases, but a fatality rate of 41% reported.[28] In 2007, another outbreak of *Zaire ebolavirus* occurred in Kasai Occidental Province, Democratic Republic of Congo. In contrast, it is a large outbreak of 264 human cases and higher fatality rate of 71% reported.[29]

In December 2007, a new strain of Ebola virus discovered which contribute to the fifth species of Ebola virus, *Bundigyo ebolavirus*. This outbreak occurred in Bundibugyo District in western Uganda and a fatality rate of 25% reported.[30] After approximate 5 years silence epidemic of *Bundigyo ebolavirus*, it re-emerged in June 2012 in the Democratic Republic of Congo and reported to increase by 11.1% of fatality rate when compared to 2007.[30, 31]

From March 2014 to present, the outbreak of Ebola virus is the most serious outbreak with high fatality rate in the West Africa. The country affected are Guinea, Sierra Leone and Liberia. Guinea was the first country reported on 21st March 2014. The first case was found to be the death of a child in Gueckedou on December 6th, 2013.[24] There were estimate of 28602 numbers of human cases and 11301 of death numbers among these cases reported. This number of cases and death is

outweigh the sum of all the previous outbreak and contribute an Ebola crisis to the west Africa.[24]

EPIDEMICS

The first appearance of EVD in Nzara, a South Sudan's town in which local cotton factory workers were affected. It was becoming the source of transmission upon the referral to the Hospital of Maridi.[32,33] Nosocomial transmission served as the mode of exposure of Ebola virus to the hospital stuff.[34] Within four weeks, 220 cases were reported with 41 death.[34] By the end of outbreak in November, a total of 284 cases were recorded with 53% fatality rates.[34,35]

Zaire outbreak, the concurrent occurrence of EVD in 1976 affects Yambuku hospital. It is about 800 km from Nzara.[36] There were 318 cases reported and caused 88% fatality rates.[35]The source of infections were similar as Sudan outbreak, the nosocomial transmission where 27 % of the cases were receiving non-sterilize injection at the Yambuku hospital.[34,35]

The virus strain were therefore known as the Zaire and Sudan Strain.[3]Indeed, the outbreaks continued to spread in the central Africa and with more than 20 documented outbreaks prior to the 2014 Africa outbreaks.[34] From 1994 to 1997 there are reported several EVD in Gabon and Zaire and, Taï Forest ebolavirus (TAFV) was identified.[34,36] This was the only human Ebola infection cases in west Africa before the epidemic in 2014.[34]

Gulu district of northern Uganda was the largest outbreak before 2014 epidemic.[34,35] It was spreading to the nearby district with secondary transmission as of hospitalization and burial attendee of sufferers.[34,37] The outbreak spread to another hospital which is 150km apart when patient was transferred.[34] Sudan and Zaire were the identified viral strains and by the end of outbreaks there were reported cases of 425 with 224 deaths.[37] Meanwhile, in 2007*, Bundiuygiyo strain* was emerged and reported in Bundiuygiyo district with 147 cases.[35,36]

In 2014, EVD was caught in the eyes of the world because it caused the most serious outbreaks with highest fatality rate.[33] In the end of December 2014, the recorded infections was 20,171 with 7890 deaths among Guinea, Sierra Leone and Liberia.[35] Guinea was the first reported country 59% fatality rates.[34] Family members and health care workers were infected as of direct exposure.[34,35] This serve as the amplifier of the virus to the districts of Guinea. Indeed, spreading to the nearby countries, Sierra Leone and Liberia with case reported on March and May respectively.[35] It became the largest reported outbreaks by the middle of June with 103 reported cases more in comparison to the Uganda outbreak in 2000.[34,35] By early August, there were 1848 cases and 1013 deaths as all districts of these countries were infected.[35] WHO therefore declared this epidemic as international concern to public health emergency.[37]

PATHOPHYSIOLOGY

Ebola virus is a filovirus comprising of enveloped particle with negative stranded, non-segmented RNA molecule.[3] Ebola virus enters the host via mucosal surfaces or percutaneous route.[38,39] At the entry site into the body, Ebola virus selectively targets macrophages and dendritic cells, which both are essential in acquired and innate immunity in human.[40-42] Destruction of these cells causes incapability of mounting a sufficient immune response to the virus.[40]

When the infection is in the early phase, an adaptive mechanism is activated for the inhibition of human's immune system while allowing virus dissemination throughout the entire body.[40] The infected mobile dendritic cells and macrophages serve as a vehicle, carrying the virus to the regional lymph nodes through the lymphatic system where further replication occurs.[38,40,41,43] From lymph nodes, the virus travels via several routes which are the lymphatic channels and blood stream, reaching a variety of organ systems and in turn to the entire body.[39] Once the virus is spread to the liver, it will progress to hepatocellular necrosis, leading to a reduction in the levels of coagulation factors, resulting in haematological events such as reduced platelet production, abnormal clotting and increased bleeding.[38, 43]

Ebola virus is protected from the host interferon (IFN) response. This is because of its encoded VP24 and VP35 proteins.[44] The efficient reproductive replication of Ebola virus is due to its ability to inhibit the production of type 1 IFN and also signalling by the action of proteins such as VP24 and VP35 proteins.[45] This inhibition not only revoke an important early response of the immune system anti-viral arm but also hyper-inflammatory cytokine responses. Subsequently, resulting in an enhanced replication of the virus and a widespread throughout multiple tissues.[45]

In fact, monocytes and macrophages direct infection leads to release of inflammation related cytokines. In addition, the presence of fever due to cell damage and the host immune response to the virus.[42] This infection of the macrophages leads to the expression of tissue factor on their cell surface which then the coagulation cascade is activated resulting in a consumptive coagulopathy, which is also known as disseminated intravascular coagulation (DIC).[38] DIC is induced, as evidenced by thrombocytopenia, decreased protein C concentrations, generation of fibrin degradation by-products and depletion of clotting factors. As a result, there are blockages in small blood vessels due to the widespread deposition of microthrombi subsequently leads to extensive hypoxemic infarcts

in affected tissues in organs such as spleen, liver and kidneys.[45]

In addition, the rapid replication of Ebola virus in macrophages and monocytes causes a substantial release of reactive oxygen species (ROS) and pro-inflammatory cytokines which results in a few conditions such as disseminated intravascular coagulation, endothelial cell dysfunction and vasomotor collapse.[44] Furthermore, Ebola virus does not infect lymphocytes directly but causes lymphocytes to undergo apoptosis at a high rate.[38] This apoptosis and the infected antigen presenting dendritic cells cause impairment to the adaptive immunity development and Ebola specific $CD8^+$ and $CD4^+$ T cells where these cells provide protection to the host from Ebola virus infection.[44] As a result, this impairment further weakens the host immune system.[38] Ultimately, the combination of inflammatory factors, virus-induced impairment and cell damages causes the host immune system to be overwhelmed and consequently leading to death.[39]

SIGN AND SYMPTOMS

Patients infected will generally have abrupt onset of fever typically 8 to12 days (incubation period has a mean of 9 to 11 days).[46] Initial signs and symptoms are nonspecific which include elevated body temperature and malaise.[46] In the early course of the disease, EVD is often confused with other infectious diseases including typhoid fever, malaria, and bacterial infections (for example, pneumonia).[46]

After about 5 days of illness, patients can progress from initial nonspecific symptoms to gastrointestinal symptoms which includes severe watery diarrhoea (up to 10 litres per day), abdominal pain, nausea and vomiting.[46] The other symptoms including shortness of breath, chest pain, headache and confusion might develop. Conjunctival infection and incidence of hiccups have also been reported.[47]

The incidence of haemorrhages can be severe but this is only present in less than half of patients. Bleeding usually manifest later this is commonly manifested as blood in the stool (6 percent), ecchymosis, petechiae, oozing from venepuncture sites and mucosal haemorrhage.[48]

Macropapular rash is also observed by day 5-7 of illness and this is associated with varying severity of erythema. This is a valuable differential diagnostic feature for EBV and this is followed by desquamation in survivors.[48] The signs and symptoms reported from West Africa include: fatigue (76%), fever (87%), diarrhoea (66%), vomiting (68%), and a loss of appetite (65%).[46]

A more severe clinical signs early during infection is usually observed in patients with fatal disease.[46] These patients will die typically between days 6 and 16 of complications due to multiorgan failure and septic shock (mean of 7.5 days from onset of symptom to death). Some patients may have fever for days in nonfatal cases and typically around day 6, the conditions will improve[46] when humoral antibody respond is noted.[48] Patients who survive have a prolonged convalescence. Women may experience spontaneous miscarriages. There is also clinical findings that shows a high death rate for children of mothers who are infected.[48]

DIAGNOSIS

Ebola virus is detected in blood only after onset of symptoms, accompany with the rise in circulating virus in patient's body. After symptoms start, the virus may take up to 3 days to reach detectable levels.[47]

The diagnosis of Ebola virus is carried out in two ways. This involves detection of viral particles and measurement of host-specific immune responses to infection in infected individuals.[48] Acute infection is diagnosed by using primary assays which are RT-PCR and antigen detection ELISA. Nucleic acid and antigen can be detected from day 3 up to 7–16 days in patient's blood after onset of symptoms.[48]

The most commonly used assays for antibody detection are IgM capture ELISA and direct IgG and IgM ELISAs.[48] IgM antibodies can appear as early as 2 days after symptoms start and disappear between 30 and 168 days after the infection. Between day 6 and 18, IgG-specific antibodies will develop after onset of disease and it will persist for many years. A rising IgG titre or IgM constitutes for a strong presumptive diagnosis; while recent infection is indicated by increasing IgG titres, decreasing IgM or both in successive paired serum samples.[48]

MANAGEMENT

Currently, there are no FDA-approved medications available to cure the EVD or for post-exposure prophylaxis in person who have been exposed to the virus but not yet become ill.[49, 50] Hence, standard supporting care in a hospital setting such as replenishment of fluid and electrolytes, ventilation support, pain control and nutritional support is initiated to the patients to manage the symptoms and prevent any complications of Ebola disease.[24, 50] Since the survivors from Ebola outbreak are able to produce infectious virions for prolonged duration, strict barrier isolation is required throughout the illness.[51, 52] All healthcare personnel must apply the appropriate personal protective equipment, including wearing surgical mask and gloves.[24] A infected mother's breast milk should not use to feed to her child as well.[51]

Patients often experience dehydration and hypovolemic shock due to high frequency of vomiting and diarrhoea, where this is responsible for the high mortality rate in Ebola outbreaks.[53] Monitoring of body temperature, blood pressure, respiratory rate and fluid input/output are essential,

yet it is difficult in resource-poor setting.[51, 53] Therefore, in these setting, when crystalloid or colloid solution (e.g., 0.9% sodium chloride solution) is given intravenously to a patient, a few of critical measurement such as urine frequency, colour, along with the evaluation of skin turgor is assist in guiding volume replenishment.[50, 53] In severe cases, the volume of fluid replacement can be up to 10L/day.[53] However, intravenous fluid therapy should be monitored closely as aggressive fluid resuscitation can contribute to the development of pulmonary oedema.[50] Ventilation support is an optimal option once the patient has establishes respiratory failure with pulmonary oedema.[50]

In addition, symptomatic management is necessary to relieve the patients from fever and pain; nausea and vomiting; and diarrhoea.[52] Paracetamol and opioid analgesics (e.g., morphine) is the first line agent to treat fever and pain respectively. Non-steroidal anti-inflammatory (NSAIDs) drugs are not recommended in pain management as the risk of bleeding could be increased.[24, 50, 51]

Nutrition is complicated by the patient's nausea, vomiting, and diarrhoea. Good hydration is to be ensured with good amount of protein supplement.[51] Oral or intravenous anti-emetics (e.g., ondansetron, metoclopramide) is administrated to the patient to control the severity and frequency of vomiting. While Anti-motility agents (e.g. loperamide) is used to control diarrhoea, and decrease fluid and electrolyte losses.[50, 52] The recovery from Ebola requires months, and delays might be expected before normal activities can be resumed completely. The virus will present continuously for few weeks even after the resolution of clinical sickness.[51]

However, in March 2014, when there is a large outbreak in West Africa, a number of potential pre-existing medicines were consider for re-purposing to treat Ebola, including antiviral and monoclonal antibody, which had demonstrated efficacy with promising in-vitro activity against the virus family Filoviridae.[50, 54] Attention is focusing on the existing drugs as they were readily available in the market, and their characteristic and safety was known.[50]

The first clinical trial of experimental Ebola drugs, ZMapp was launched in year 2015 to obtain it's efficacy and safety data, cooperated with the Liberian government, the National Institute of Allergy and Infectious Diseases (NIAID).[55,56] ZMapp is a combination of three specific humanised mice monoclonal antibodies.[54] It is designed to arrest the progression of EVD within the body by targeting the glycoprotein presents on the surface of Ebola virus.[50, 51] These monoclonal antibodies are manufactured in tobacco plants. Tobacco is an ideal plant for the development of antibodies as it can grow rapidly in a less expensive way, where one growth cycle takes only about two months.[57]

In terms of pharmacological drug therapy, Favipiravir (T-705), a potent broad spectrum antiviral pyrazinecarboxamide derivative against RNA virus is proved to be efficacious and safe in treating the EVD.[58] Through intracellular phosphorylation and ribosylation, an active manifestation of Favipiravir, T705RTP will selectively inhibit the RNA replication and infectivity by inducing viral mutagenesis. Potential risks of drug injection can be prevented as favipiravir can be taken orally.

Brincidofovir (CMX001), an acyclic nucleotide analogue of cidofovir which has potent in-vitro activity against double-stranded DNA viruses' infection was being used to treat several types of infection such as smallpox. It is found to be beneficial and useful for EBV patients.[58, 59] BCV can interfere RNA polymerase of Ebola virus through inhibition of viral replication so it has been used as part of the regimen for EVD therapy but its tolerability, safety and antiviral activity in EVD patients are yet to be investigated and tested in the phase III clinical trials.

Another novel nucleoside analogue, BCX4430 that inhibit the DNA polymerase's function of Ebola virus is also being produced for potential administration in human with high risk of exposure to Ebola virus infection mainly by intramuscular route.[64] Pharmacokinetics data suggests that administration of BCX4430 through intramuscular route provides a more favourable therapeutic level compared to oral route. It can protect the guinea pigs against the lethal Ebola virus infection by inhibiting the viral messenger RNA.[65] Promising results suggest that BCX4430 confers complete protection to the mice infected with Ravn and Marburg viruses even when treatment was being administered 48 hours after the infection.[59,65]As it does not incorporate into human DNA or RNA, it is said to have an accepting adverse effect profile.[59]

Small interfering RNA (siRNA) technology was being introduced into the anti-Ebola field. TKM-Ebola is a formulation of siRNA that binds to specific sequence of viral messenger RNA.[58] It is being encapsulated in lipid nanoparticles or complexed with polyethylenimine to facilitate the cellular delivery as well as to prevent subsequent the production of EVD of three key viral proteins. Phosphorodiamidate morpholino oligomers (PMOs) which composes of AVI-6002 and AVI-6003 is another synthetic third generation anti-sense oligonucleotide-based drugs applied in EBV therapy which sterically hinder mRNA processing.[60] This DNA oligomer agent will block the viral gene expression of filovirus by forming stable complexes after recognising specific single-stranded DNA or RNA viruses. The use of such molecules in targeting EVD as post exposure therapy is reported to be safe and generally well tolerated after receiving the dose through parenteral route in phase 1 clinical trial. Nevertheless, these drugs are prone

to have more genetic variations of virus compared to antivirals that target viral proteins such as antibodies due to the high mutation of RNA viruses at nuclei acid level.[60]

There are several new compounds that have been identified to have anti-Ebola activity. For instance, benzylpiperazine adamantane diamide derived compound can prevent viral glycoprotein from binding to the NPC1 and hence inhibiting the EBV entry into the cell. Toremifene and clomiphene which are selective estrogen receptor modulator that found to act as potential NPC1 and EVD inhibitor.[61] Clinically approved ion channel inhibitors like amiodarone, dronedarone and verapamil are recently being discovered to have anti-Ebola effect with proven efficacy in pseudo assay results by interfering the cell signalling pathway that functions to control and coordinate the viral entry. Amiodarone in particular can block the entry of filovirus with the dose of 1.5 to 2.5 mg/mL during the anti-arrhythmic therapy in human.[61, 62] Licensed anticoagulant includes recombinant human activated protein C (rhAPC) and recombinant nematode anticoagulant protein c2 (rNAPc2) can resolve coagulation diathesis caused by lethal Ebola infection and mainly used as a post-exposure treatment for EVD.

Whole blood collected from patients in the convalescent phase of infection or sometimes called convalescent sera or convalescent whole blood (CWB) is being employed as an empirical treatment for some EVD cases. Convalescent immune plasma was used to treat eight EVD patients during the outbreak in Kikwit, Democratic Republic of the Congo in which seven patients survived from the disease, suggesting a therapeutic benefit.[59] Patient who has been recovered from EVD can become a potential blood donor for CWB and donor's blood group as well as transfusion transmissible infections must be screened to ensure the administration of safe blood products in context of an Ebola outbreak. Only patients with confirmed EVD preferably in the early stage should be considered for CWB transfusion.[63] One unit of CWB (collected in a 350/450 mL blood collection bag) should be transfused for adult patients using standard transfusion procedure. Depending on the blood volume, a dose of 10 mL/kg could be used for pediatric CWB transfusion. Slow intravenous transfusion should be considered in every patients should be completed within 1 to 4 hours of commencement. Vital signs of acute transfusion reaction should be monitored closely and carefully particularly during the first 15 to 20 minutes. Measurement Ebola antibody level and viral load should be done by carrying out blood test to assess the effectiveness of this intervention. Some toxicity-related problems like transmission of contaminated or undetected pathogens to the EVD patients or acute lung injury might be identified after receiving convalescent sera-based therapy.[60]

The development of anti-EVD vaccines is paramount to prevent the spread of Ebola virus. The standard of EVD prevention packages must be implemented in order to prevent exposure of research participants to risk of EVD infection.[66] The prevention package includes providing effective personal protective equipment (PPE) and implementing protocols regarding working conditions.[66] The transmission of multidrug-resistant bacterial organisms (MDROs) from the clothing and hands of healthcare personnel to patients could be prevented by PPE.[70] Care should be given to the PPE requirements of those wearing prescription glasses and the use of respirators when performing procedures that could cause aerolisation of infectious particles.[66]

Revised recommendations were announced by Centers for disease control and preventions regarding the variety of PPE required for caring of the patient with EVD, and instruction on the processes for wearing and taking off PPE.[70] They should wash their hands or use an alcohol-based sanitizer at multiple time points upon the removal of PPE. In order to reduce breaches in protocol, there should be a trained observer to supervise the donning and removal processes.[67] There are some characteristics for the optimum protective equipment for Ebola virus: (1) be impermeable to fluid, (2) cover all skin, (3) be easy to put on, (4) be easier to take off, (5) give best comfort for healthcare workers, and (6) be easier on disposal.[67]

The infection control associated with the care of patients with EVD comprises of the utilization of an appropriate facility, provision of medical care in PPE, secure transport, laboratory preparation of specimens, waste disposal, and provisions for care outside the biocontainment facility.[68, 70] Biocontainment facilities should be designed to allow healthcare personnel to treat patients with EVD while decreasing the possibility of secondary transmission. All healthcare providers must abide by safe and effective practices, participate in drill exercises, as well as show competency in infection control practices.[68] In addition, solid medical waste produced in the care of patients with EVD must be sterilised and disposed of in a safe manner.[68]

There are some prevention measures to decrease the risk of developing EVD: (1) restrict the movement of people and goods from epidemic areas, (2) Engage with prominent community leader to reduce demoralising perceptions, anxiety and stigma, (3) adopt a multi-disciplinary method such as social mobilization, case identification and management and infection control, (4) establish surveillance response systems through effective collaboration, cooperation from stakeholders, funding, and cutting-edge research for vaccine development.[69] The division of responsibilities is not limited to individuals, communities, nation, but it is through worldwide concerted efforts in controlling EVD effectively and reducing the impact of future Ebola outbreaks.

Conclusion

The review conclude that the efficient control and prevention of Ebola epidemic require adequate political support from the government as well as the establishment of a robust public health infrastructure and medical reserve. Strengthening of contact tracing and quarantine policies are also important for the prevention of EVD. There should be a well-designed disease surveillance system when a suspected case is reported. Given the elevated case-fatality rate and the absence of effective treatment, it is sensible to evade research ethics and develop the promising future of experimental vaccines.[71] The collection of clinical and epidemiological information of Ebola should be vigorous and systematic in the endemic affected areas.

It seem to be a daunting task to control the Ebola outbreak as it happens continuously in West Africa, making EVD an important public health issue in Africa. Tremendous efforts need to be focused on the development of promising vaccines and drugs. While public health prophylaxis is vital concern to prevent the transmission of EVD.A cooperation between the governments of different country and medical systems is required to achieve the prevention goal.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.