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The Ebola virus: a review of progress and development in research

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ABSTRACT

The Ebola virus was identified in the year 1976 and has caused periodic outbreaks in West African countries. The disease has a case fatality rate up to 90%. Ebola has been classified as a biosafety level four pathogen and there is no currently approved vaccine or treatment for the virus. However, remarkable progress has been demonstrated by researchers in understanding the pathogenicity of the Ebola virus. Several animal models have been cultivated to develop diagnostics, vaccines and therapeutic drugs.

1. Introduction

For the past decade researches have been conducted in laboratories to better understand the biology and potential therapies of Ebola virus (EBOV)[1]. However, field based research in high risk populations such as impoverished villages much progress has not been accomplished. For instance, there have been outbreaks in the Democratic Republic of Congo in 2007, 2008 and in Uganda in 2007[2].

The EBOV belongs to the Filoviridae family[3] which affects both human and non-human primates (NHPs), causing severe hemorrhagic fever syndrome. The disease is characterized with symptoms and signs of fever, focal necrosis of the liver, kidney and spleen bleeding diathesis, fulminant shock resulting in death with a mortality rate reaching 90%[4,5]. The first two outbreak of the EBOV included illnesses such as fever, headache, vomiting and diarrhea. Nonetheless, during the early diagnosis of the EBOV, hemorrhagic manifestations were the most prominent features seen in patients who died[6]. The Filoviridae consist of three general names known as EBOV, Marburg virus (MARV) and Cuevavirus[7]. The disease is also considered to be a category A agent and potential bio-weapon agent[8].

The first outbreak of an unknown infectious disease (Marburg disease) was reported in Germany and Yugoslavia in the year 1967. An estimated 31 persons were affected in which 7 persons died. Eventually, a new strand of the virus was extracted from a patient and was traced back to velvet monkey imported from Uganda. The disease was named the 'Marburg disease' because it was located in the West German town of Marburg[9].

In 1976, an occurrence of hemorrhagic fever started to spread rapidly in Sudan and Zaire with tremendous level of deaths. Specimens were isolated from patients and tested which revealed that the virus resembled the MARV but had different reactive

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properties[9].

This paper aims to review various researches done, developments and progress made concerning the EBOV over the past several years.

2. Epidemiology

The EBOV has a case fatality rate of 30% to 90% and increased frequency in the African region due to weaker health infrastructure and services. The EBOV is sub-divided into five species: Zaire ebolavirus (ZEBOV), Sudan ebolavirus (SEBOV), Tai forest ebolavirus, Bundibugyo ebolavirus (BDBV), and Reston ebolavirus (REBOV)[10]. After the first case of the virus was discovered in 1967 in Germany, it appeared in Africa, two neighboring locations: Sudan and Zaire (SEBOV and ZEBOV), now in the Democratic Republic of the Congo[11]. Finally, it was named the EBOV after a small river located in the northwestern region of the Democratic Republic of Congo[12]. The third strain of the virus was discovered in 1994 and it was called the Cote d'Ivoire EBOV which was noted in the Tai forest[13]. The fourth strain of the virus was found in the equatorial Africa and it was called the BDBV[14]. Additionally, the last virus species was discovered in the Philippines and it was named the REBOV. The EBOV continues to be a plague for the occupants of West Africa, with increasing number of outbreaks seen in 2000[5]. The ZEBOV, SEBOV and BDBV has caused the most tremendous outbreak in sub-Saharan Africa. There have been outbreaks of the EBOV in countries such as Uganda, Sudan, Gabon, Democratic Republic of Congo and the Republic of Congo[15].Moreover, the emergence of the REBOV found in pigs raises public health concerns and food safety in the Philippines and can become a major problem in the near future[5]. The first few cases of the EBOV in Zaire occurred among factory workers and the reservoir animal host was unknown[6]. Eventually, an experiment conducted in the regions of Gabon and the Republic of Congo, suggested that fruit bats are believed to be the reservoir for EBOV[16]. And it is transferred to other hosts such as humans and gorillas[17]. Additional host of the virus are small rodents, duikers, NHPs and shrews. The current outbreak in Guinea, Liberia Sierra Leone and Nigeria showed that the greatest mode of contracting the virus is human to human transmission[18].

The virus is highly contagious which is transmitted to individuals in direct contact with bodily fluids from an infected person[19]. The risk of transmission is highest during the latent stage of the disease but the level of transmission decreases during the early stages even if there is a high risk exposure[6]. Persons that are at the greatest risk for infection of the EBOV during an outbreak are, scientists[20], health care workers, relatives and those in close contact with ill individuals and deceased patients. Basic hygienic practices can be cultivated in the prevention of the EBOV such as regular washing of hands and changing of attire before and after getting in contact with these animals. Moreover, the consumption of sick animals should be avoided[18].

Looking at the 2014 EBOV disease (EVD) outbreak in West Africa, as of September 14, 2014, a total of 4 507 probable and confirmed cases, including 2 296 deaths from EVD (Zaire species) had been reported from five countries in West Africa: Guinea, Liberia, Nigeria, Senegal and Sierra Leone. The World Health Organization Ebola Response Team analyzed a detailed subset of data on 3 343 confirmed and 667 probable Ebola cases collected from the five countries and found out that the majority of the patients are 15-44 years of age with 49% male. The case fatality rate was estimated at 70.8% (95% *CI*, 69-73) among persons with known clinical outcome of infection. The course of infection, including signs and symptoms, incubation period (11.4 d) and serial interval (15.3 d), is similar to that reported in previous outbreaks of EVD. Assuming no change in the control measures for this epidemic, the team projected that by November 2, 2014, the cumulative reported numbers of confirmed and probable cases will be 5 740 in Guinea, 9 890 in Liberia and 5 000 in Sierra Leone, exceeding 20 000 in total[21].

In the 2014 outbreak, the World Health Organization conducted a virological analysis to determine if there was any linkage between the EBOV in West Africa and the Democratic Republic of Congo. The epidemiological investigation and results concluded that the outbreaks in the Democratic Republic of Congo were completely separate and independent event from the cases reported in West Africa. The finding reassures investigators that the virus has not spread from West to Central Africa[22]. However, investigators have isolated 99 EBOV genomes from infected patients in Sierra Leone. Upon examination of the specimens, investigators concluded that there is rapid mutation of the virus which could have implication for the development of diagnostics, vaccines, and therapies of the EBOV. It was observed that the sequence of the virus has changed since the start of the outbreak and the researchers have not found any additional zoonotic sources of the virus in the outbreak strains. Additionally, it was mentioned that the EBOV can affect approximately 20 000 persons before it is contained[23]. Nonetheless, the typical symptoms seen in patients with the EBOV can be mistaken for other infectious diseases that are more common[2].

3. Transmission epidemiology

A published article in 1995 reported that two control NHPs were infected with the ZEBOV without direct contact with

inoculated challenged monkeys held in the same room. The most likely source of transmission can be aerosol, oral, or conjunctival exposure secreted from the infected monkeys[24]. An experiment examined the transmission of the EBOV from pigs to NHPs without direct contact. The inoculated piglets were inoculated with ZEBOV and placed in a room containing four cynomolgus macaques. The NHPs were housed in two levels of individual cages within the pig pen and separated by wire mesh to prevent direct interaction. The cages housing the NHPs were located to the side of an air exhaust system. During the cleaning of the cages, piglets were removed and precautionary measures such as preventing the water from coming into contact with the NHPs cage and the changing of disposable glove between procedures and animals. However, the NHPs were infected with the EBOV and the EBOV antigen were found in the respiratory epithelial cells in the lung of the NHPs. Due to the measures taken, suggestive modes of transmission can be inhalation or droplets inoculated in the eyes. Therefore, in such an environment which prevents direct contact can lead to the concept of airborne transmission[3].

4. Vaccines research

Previously, the development of a vaccine for the EBOV was disputed because the disease was rare and many companies had little interest. Due to frequent outbreaks of the EBOV, this has drawn attention for vaccine and treatment development for the bio threat pathogen. The development of a protective vaccine is not only recommended or needed by medical workers, first responders; but also by affected population. Currently, there is no licensed or approved vaccine or therapeutics for the EBOV while the disease is spreading quickly[5]. However, the U.S. Food and Drug Administration advise the public that fraudulent drugs on the market claiming to prevent or treat the EBOV is false[25].

The first attempt immunization process for the EBOV occurred in 1976, when an investigator accidently got pricked. The disease had similar features of the MARV as a result the investigator was given human interferon every 12 h for 14 d. The following morning, the patient temperature was normally but increased during the evening period. Therefore, dosage of convalescent serum was administered to the patient. However, no definite conclusion was made as to whether the serum administered was responsible for the results obtained[9]. The convalescent serum was extracted from Yambuku Ebola hemorrhagic fever epidemic in 1976 and the researcher survived[9,26]. In 1995, there was an outbreak of the EBOV in the Democratic Republic of the Congo[27]. A total of 316 cases of the Ebola were observed with an overall case fatality rate of 80%. A total of eight patients received blood transfusion from convalescent patients while only seven survived[28].

Numerous researches in filovirus infection have been utilized in animal models such as mice, guinea pigs, hamsters and NHPs[10]. Examples of NHPs used in filoviral models are African green monkeys, hamadryas baboons, cynomolgus macaques, and rhesus macaques[29]. The animal models adapted will increase scientist understanding of the pathogenesis of Ebola and Marburg hemorrhagic virus because human specimens are limited. Since the symptoms observed in the animal model are similar to humans, this practice will be most useful in evaluating the efficacy of vaccines and treatments developed[10].

Experimental vaccines and treatments must be deployed in clinical trials and it is required to meet the ethical guidelines for trials. Here are the following eight ethical principle for trials of an experimental treatment or vaccine: (a) collaborative partnership (involvement of the community in every aspect of the trials), (b) Social value (provide valid information and disseminate knowledge), (c) Scientific validity (feasible trials and randomly select patient with included supportive care), (d) Fair selection of study population (transparency in selection criteria), (e) Favorable risk-benefit ratio (minimize potential risk factor associated with the trial), (f) Independent review (public accountability with reviews from international organization), (g) informed consent (acquired written or orally consent from participates) and (h) Respect for recruited participants and study communities (ensure confidentially of patients and compensation for injuries during the research trial[30].

In early attempts to develop vaccines that can prevent the spread of the EBOV, animal models such as the guinea pigs or NHPs were vaccinated with formalin-fixed or heat-inactivated virion preparations[31]. The results were inconsistent; a study indicated that the guinea pigs were partially protected[32], while the other study revealed complete protection was attained from an inactivated EBOV vaccine in four of the five hamadryas baboons[33]. However, other studies have proven that the inactivated EBOV does not provide sufficient immunity against the lethal challenge administered to the hamadryas baboons[34]. The classical methods used were unsuccessful which led to the formulation of new vaccines, such as recombinant viral vector vaccines, DNA vaccines and virus-like particles (VLPs). The advantage of using the new approach: “more robust induction of both innate and adaptive immune responses, humoral as well as cellular, resulting in a better vaccines efficacy”[35].

5. Venezuelan equine encephalitis virus (VEEV)

The VEEV replicons particles that express glycoprotein (GP)

or nuclear protein (NP) of EBOV genes, in combination or separate protected mice and guinea pigs from lethal dosage of the virus[36]. However, a study concluded that the EBOV NP-expressing VEEV replicon alone protected mice not guinea pigs when immunized. Moreover, immunization with the expressing EBOV GP and NP, in combination or alone resulted in cynomolgus macagues not being protected from lethal infection of the EBOV[37]. A recent study revealed that the VEEV-based replicon particles provided protection against EBOV and Sudan Ebola virus (SUDV). However, the results obtained from this study are inconsistent and more research is needed[38].

6. Adenovirus vaccine

The adenovirus vector vaccine has been used in the development of vaccine against Ebola and evaluated in NHP model. The adenovirus expressing ZEBOV with GP (Ad-ZGP) is proven to protect mice, guinea pigs and NHPs against the Zaire Ebola challenge[39,40]. In the earlier years, the EBOV GP-expressing adenovirus-based vaccines (ADV) 5 and EBOV NP- expressing ADV5 protected cynomolgus macaques 100% against the virus challenge. This first generation of the ADV had one filovirus GP gene but the second generation ADV had the able to express multiple antigens on a single construct. When the second generation of the ADV, which expressed numerous filovirus GPs of EBOV, SUDV and MARV was administered to cynomolgus macaques inducted a 100% protection against the EBOV, SUDV and two strains of MARV[40]. Although the ADV is effective, there is a problem of pre-existing immunity of ADV which can limit the immunogenicity and clinical utility. Approximately, 60% of the general population and 85% of African population have the prevalence of antibody to ADV. For example: macaques showed no signs of protection from the lethal ebola challenge when they are pre-immunized and vaccinated with EBOV GP-expressing ADV5. A phase I clinical trial showed that the adenovirus serotype 5 expressing ZEBOV and SEBOV GP were safe for humans[41].

7. DNA vaccine

In a study conducted, EBOV DNA vaccine was successfully used in protecting mice and guinea pigs against the challenge. Another strategy used included four inoculation with DNA encoding ZEBOV GP and SEBOV GP, boost of adenovirus 5 expressing ZEBOV GP resulted in a cross protection in NHPs EBOV challenge[36]. Currently, there are no licensed DNA vaccines for human use. However, DNA vaccines encoded with EBOV GP, SUDV GP, and EBOV NP had been used in a phase 1 clinical trial in human which has proven to be safe and immunogenic[42].

8. Vesicular stomatitis virus

A single dosage of the vesicular stomatitis virus expressing EBOV GP generated complete protection of NHPs from homologous challenge but unsuccessfully for a heterologous SEBOV challenge[28]. One study has proved that EBOV GP expressed on the vesicular stomatitis virus vaccine, when is administrated orally or intranasal results in complete protection of the cynomolgus macaques from the Ebola challenge[43]. A multiple vaccine composed of the vesicular stomatitis virus expressing the GP of MARV, ZEBOV, and SEBOV generated complete protection in NHPs challenged with MARV, ZEBOV and SEBOV[44]. The vesicular stomatitis virus expressing EBOV GP was administered to mice 24 h before infection, 1 or 24 h post-challenge, all the mice survived. In guinea pigs, the outcome was 67%, 83% and 50% when administered prior to infection and 1 or 24 h post challenge, respectively. Furthermore, the importance of this vaccine post exposure is partially effective. In an experiment, NHPs infected with the homologous EBOV challenge was given the vesicular stomatitis virus expressing ZEBOV GP or SEBOV GP approximately 30 min after infection. The results indicated 50% and 100% protection from ZEBOV and SEBOV, respectively[45]. Moreover, an article published in 2008, evaluated NHPs protection capability against an aerosol challenge of the ZEBOV. All the monkeys immunized with the vesicular stomatitis virus were protected but the control species succumbed to the virus[46].

9. VLPs

VLPs mimic the structure of a virion but do not contain the genetic composition of an infectious virus. However, it is noninfectious and safer than replicating vaccines. The EBOV VLPs is expressed as GP, NP and VP40, usually in the presence of adjuvant. This was administered three times to NHPs which resulted in complete protection against the EBOV challenge. Another researcher examined the use of the ZEBOV vaccine without the VP40, the outcome concluded mice and guinea pigs were protected from the ZEBOV challenge. Furthermore, other vaccines such as the EBOV without VP30, an Fc portion of a human IgG fused to the EBOV GP have been studied in rodent models but more research is needed to determine the efficacy and safety of these vaccines in NHPs[36].

10. Treatments

10.1. Recombinant nematode anticoagulant protein c2 (rNAPc2)

Coagulation disorders are one of the significant aspects of filovirus infection. In the instance of a filoviral infection, the tissue exhibits an important role in triggering bleeding complication in NHPs. When the organs are affected, this results in coagulation inhibitor depletion which in turn causes dissemination intravascular coagulation. In the dissemination intravascular coagulation, the tissue factor (a substance present on a cell but not in contact with blood) combines with factor VII for clotting formation[47]. However, the rNAPc2 inhibits factor VII and the tissue factor whereby providing partial post exposure protection to rhesus macaques during a filovirus infection. The NHPs that were treated with rNAPc2 had a longer survival time than the untreated control. The rNAPc2 provides a mark increase in survival rate for a NHP that is 100% affected with the filovirus infection. Lastly, rNAPc2 can be useful in the fight against other viral hemorrhagic fevers because it targets the disease process. It can be referred to as having a suitable pharmacokinetic and safety profile in humans. However, the clinical efficacy of rNAPc2 needs to be confirmed[48].

10.2. Recombinant human activated protein C (rhAPC)

It was observed that EVD and severe sepsis had similar clinical features such as fever, increased production of tissue factor and elevated levels of nitric oxide. The most common factor prominent in severe sepsis was deficiency in protein C. However, patients having severe sepsis treated with rhAPC resulted in improved survival. Taking into account the similarity between sepsis and EVD, the investigators decided to use the same procedure for improving survival from EBOV. As a result, the investigators decided to use NHPs to test the theory[49]. The activated protein C is generated from protein C, it was recognized that infected NHPs have decreased level of protein C when infected with EBOV. This is because the infection targets protein C which is produced in the liver[48]. Therefore, experiments were conducted to demonstrate the efficiency of rhAPC in protecting NHPs from the EBOV. This resulted in 14 rhesus macaque infected with the lethal EBOV challenge and 11 were administered the rhAPC, 30-60 min after the challenge for 7 d. The outcome concluded that 2 out of 11 were protected from the lethal EBOV challenge. The survival rate in treated NHPs was prolonged than the untreated[50]. This product was created as a single dose post exposure treatment but since the treatment does not target the virus, there may be merit in analyzing the treatment in conjunction with a direct antiviral[38].

10.3. RNA interference (RNAi)

RNAi represents a powerful process which inhibits gene expression with a regulated enzyme-mediated process. RNAi has been used for a number of years in the prevention of viral replication against number of viruses such as the HIV-1, hepatitis B virus, influenza A virus and herpes viruses. The small interfering RNA targeted the polymerase L protein of the Zaire Ebola, which formulated a stable nucleic acid-lipid particle. This phenomenon protected the guinea pig shortly after infected with the EBOV. This treatment was then tested in rhesus macaques, which targeted EBOV L, VP24, and the VP35 formulated in stable nucleic acid-lipid particles. Eventually, three of the monkeys were given four doses and as a result two survived the infection. However, eleven monkeys were given seven doses and all survived the infection. The purpose of the investigation using the rhesus macaque model was to represent the worst case scenario such as accidental exposure of a laboratory worker or a first responder to a high dosage of the ZEBOV, which has occurred several times in the past. Generally, the progression of Ebola viral disease is slower in humans than in NHPs, suggesting that the therapeutic window could be larger in humans than infected rhesus macaques[50].

10.4. Phosphorodiamidate morpholino oligomers (PMOs)

At the point in time, most researchers focused on therapeutic strategies that bolstered the host immune response or inhibiting viral replication. As a result, two researchers decided to use a different approach; a substance called PMO. PMO exerts a hindrance of gene translation by blocking ribosomal assembly. As such, the EBOV specific is combined with the PMO which targets the viral mRNA in acquiring the VP24 and VP35. This has resulted in the protection of mice in pre-exposure and post-exposure from the lethal Ebola challenge[51]. Afterwards, AVI-6002 was developed which is known as the combination of PMOs against EBOV VP24 and VP35 which is currently in phase I clinical trials. These PMOs, provided 30-60 min of post exposure, approximately more than 60% of rhesus macaques were protected from the Ebola infection. The PMO has been tested in humans and it was considered to be safe and can be produce in large amounts[52].

10.5. MB-003 monoclonal antibody cocktail

Recently, antibodies have proven to be efficacious for post-

exposure treatment against the EBOV in NHPs. Protection was seen in rhesus macaques when passive transfer of macaque hyperimmune globulin was inoculated 2 days post-exposure. Another case concluded that a cocktail of three murine monoclonal antibodies successfully provided 100% protection in cynomolgus macagues administered within the first day but 48 h after, the cocktail provided 50% protection against the lethal EBOV challenge. Lastly, a mixture of three monoclonal antibodies (MB-003) produced in a plant called the *Nicotiana benthamiana*. This product provided 100% or 65% protection from the lethal Ebola challenge with no clinical manifestation, when administered 1 or 2 days post-exposure respectively[53].

10.6. ZMapp

ZMapp, being developed by Mapp Biopharmaceutical Inc., is an experimental treatment, for use with individuals infected with EBOV. It has not yet been tested in humans for safety or effectiveness. The product is a combination of three different monoclonal antibodies that bind to the protein of the EBOV. Previous experiments have demonstrated that antibodies are crucial for the survival of patients from the EBOV. Therefore, research was conducted to determine a treatment that was superior to both MB-003 and ZMab, which can be used in an outbreak among communities, health care workers and laboratory workers. The therapeutic treatment would be an upgraded antibody derived from MB-003 and ZMab. The study used a combination of ZMapp 1 (c13C6+c2G4+c4G7), ZMapp 2 (c13C6+c1H3+c2G4) and Zmapp 3 (c13C6+c1H3+c4G7). The best results were in the following order: ZMapp 1 (4 out of 6 survived), ZMapp 2 (3 out of 6 survived) and ZMapp 3 (1 out of 6 survived). Eventually, the study proceeded to use ZMapp 1 and 2 on rhesus macaques to demonstrate which one of the treatments was superior. The NHPs were administered ZMapp 1 (Group A) and 2 (Group B), three days post infection. There was a 100% survival rate in the Group A and 5 out of 6 survived in Group B. As a result, ZMapp 1 was carried forward to be tested in rhesus macaques with the trademark being Zmapp. All the animals with ZMapp survived the lethal challenge[54]. At the time of the review, ZMapp was not tested in humans but dosages were given to Ebola victims. Two American doctors and two Liberian health workers were administered the treatment and they did survive. Unfortunately, a priest and a Liberian doctor given the treatment died. Additionally, a fifth health worker is now being treated with ZMapp. However, there is limited supply of the treatment and it has been exhausted. It must be noted that ZMapp is an experimental therapeutic treatment that is currently undergoing investigation[55].

10.7. Other experimental treatments

A potential vaccine developed is being used in a human trail with a total of 60 persons from the Oxford area in the United Kingdom. If the resulted outcome is proven successful, the vaccine would be tested with volunteers in Gambia and Mali. This procedure will account for the potential difference between the European and West African hemisphere. The researcher stated that the vaccine is safe because “the vaccine takes a gene from the Ebola and puts in it a virus Carrier”[56].

The Chinese researchers have developed a JK-05 which is a micro-molecular chemical which was approved to be manufactured for emergency use only. It contains a RNA polymerase of the virus which inhibits the virus replication. The drug has proven to be successful in resisting the replication of the EBOV in animal and experimental testing. It has been tested for approximately five years and has passed clinical testing[57].

11. Discussion

The EBOV causes a highly lethal hemorrhagic fever and the most dangerous specie is the Zaire Ebola (ZEBOV), with a mortality rate of 90%[5]. The most prominent reservoir for the EBOV is the fruit bat. When the virus was first identified in 1967 and over the years the number of strains increased to five species (ZEBOV, SEBOV, Cote d’Ivoire ebolavirus, BDBV, and REBOV)[9,10]. The symptoms of the EBOV can be mistaken for other diseases that are similar in nature[2]. The vast majority of persons at risk for the EBOV have been residents of rural Central Africa. Some of the reasons associated with outbreaks of the EBOV are limitation in health surveillance and inadequate preventative measures[10]. Recently, researchers have suggested that close contact with infected individual[19], and the latest possibly that the virus is airborne contributes to the high infectivity of the EBOV[3].

Moreover, the strain of the virus identified in West Africa is completely different from the virus identified in the Democratic Republic of Congo confirming the fact that the virus was not transferred from West to Central Africa[22]. However, research has demonstrated that the EBOV has mutated over the years[23]. Different animal models such as mice, guinea pigs, hamsters and NHPs have been used to determine the efficacy and effectiveness of vaccines and treatments against the lethal EBOV[10]. Researchers have to develop models that accurately reflect diseases that affect humans. This is critical in order to understand the pathogenesis of the EBOV as there is limited access to human tissue. The most useful model that demonstrates similar symptoms that occurs in humans, such as shock and

hemorrhage is the NHPs. Therefore, this model is the most beneficial in evaluating the efficacy of vaccines and treatments being developed. However, the use of smaller animals is crucial for preliminary evaluation of vaccines and therapeutic treatments against the virus because of ethical concerns when dealing with NHPs. Additionally, the testing of experimental Ebola vaccine or treatment must be conducted in clinical trials, but when the trials are demonstrated it must comply with the standard ethical principles[30].

Examples of candidate vaccines tested on animal models are the VEEV, vesicular stomatitis virus, DNA vaccine, adenovirus vector vaccine and VLPs. The following are pre-exposure vaccination: the adenovirus type 5, vesicular stomatitis virus, VLPs and the recombinant EBOV. The post exposure treatments include rNAPc2, RNAi, recombinant human activated protein, PMO, MB-003 antibody cocktail[10,38,39,42,43,50]. And hence, there are other treatments such as, ZMapp and JK-05[55,57].

The ADV was used in the mouse and NHP model. It was able to protect mouse and NHP 100% from the EBOV with approximately two dosages[40]. According to the records on DNA vaccines, four injections were administered to mice and guinea pigs which resulted in 100% protection from the EBOV[42]. The candidate vaccine that has the potential of preventing the EBOV and as a post-exposure treatment in mouse, guinea pigs and NHP is the vesicular stomatitis virus vaccine with a 100% protection in the NHPs and mouse[45]. Additionally, the VLP has provided 100% protection in NHPs and mouse with 2 to 3 dosages from the EBOV[36].

The treatments rNAPc2 and recombinant human activated protein that were administered daily resulted in 33% and 20% protection in rhesus macaque respectively. On the other hand, the RNA treatment provides a percentage range of 25% to 100% protection according to the dosage administered to guinea pigs and NHPs. Moreover, the amount of dosage administered to guinea pigs will determine the percentage of protection observed in NHPs whereas providing a 100% protection in mouse[48-50]. Additionally, the PMO used as a post-exposure treatment showed promising efficacy in reducing the mortality of NHPs. The most recent treatments are the monoclonal antibody cocktail, ZMapp and JK-05. The monoclonal antibody cocktail is considered to be effective in protecting NHPs from the EBOV when administered post-exposure within 1 or 2 days of infection. The latest development of the experimental drug is ZMapp which has been administered to one nurse and two doctors. The patients were showing improvement but the product has not been distributed to the general public. However, ZMapp has already been exhausted and would need a couple of months in producing large quantity of this treatment. The Chinese government has a drug named JK-05 which has passed pre-clinical and clinical safety test but it is restricted for emergency cases only[55-57]. Lastly, there is no clinically approved vaccine available for humans but the population has been warned about fraudulent products being sold on the market.

12. Conclusion

The EBOV is significantly affecting a vast majority of persons in West Africa and much progress has been made in the understanding of the EBOV replication. Tremendous amount of experiments have been conducted to develop drugs and vaccines which can prevent the spread of this dreadful virus. Animal models such as mice, guinea pigs, hamsters and NHPs have been used to test the effectiveness or safety of the vaccines or drugs developed. Advances have been made in the development of drugs/vaccines for the EBOV but there is a need for more research in the development of a vaccine or drug that is efficacious to tackle all the various species of the EBOV.

Conflict of interest statement

We declare that we have no conflict of interest.

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