

New Research Studies Future Treatments on Marburg Virus

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ABSTRACT

Marburg virus disease (MVD), formerly known as Marburg haemorrhagic fever, is a severe, often fatal illness in humans. The virus causes severe viral haemorrhagic fever in humans. The identification of the natural reservoir of this virus should also foster the development health measures and prevention campaigns to the population to reduce the apparition and emergence of potential outbreaks of hemorrhagic fever. The emergence of Marburg virus (MARV) in Guinea and Ghana triggered the assembly of the MARV vaccine "MARVAC" consortium representing leaders in the field of vaccine research and development aiming to facilitate a rapid response to this infectious disease threat. While much is being investigated to devise a vaccine, it is important to educate Health Care Workers (HCWs) and close contacts facing the illness.

Keywords: Marburg, Virus, Pathology, Treatment. Diagnosis, Treatment, Future Research, etc

Introduction

Marburg virus is the causative agent of Marburg virus disease (MVD), a disease with a case fatality ratio of up to 88%, but can be much lower with good patient care. Marburg and Ebola viruses are both members of the Filoviridae family (filovirus). Though caused by different viruses, the two diseases are clinically similar. Both diseases are rare and have the capacity to cause outbreaks with high fatality rates. Two large outbreaks that occurred simultaneously in Marburg and Frankfurt in Germany, and in Belgrade, Serbia, in 1967, led to the initial recognition of the disease. The outbreak was associated with laboratory work using African green monkeys (*Cercopithecus aethiops*) imported from Uganda. Subsequently, outbreaks and sporadic cases have been reported in Angola, the Democratic Republic of the Congo, Kenya, South Africa (in a person with recent travel history to Zimbabwe) and Uganda. In 2008, two independent cases were reported in travellers who had visited a cave inhabited by *Rousettus* bat colonies in Uganda [1].

Marburg virus (MARV) is a highly pathogenic virus associated with severe disease and mortality rates as high as 90%. Outbreaks of MARV are sporadic, deadly, and often characterized by a lack of resources and facilities to diagnose and treat patients. There are currently no approved vaccines or treatments, and the chaotic and infrequent nature of outbreaks, among other factors, makes testing new countermeasures during outbreaks ethically and logistically challenging. Without field efficacy studies, researchers

must rely on animal models of MARV infection to assess the efficacy of vaccines and treatments, with the limitations being the accuracy of the animal model in recapitulating human pathogenesis [2].

Transmission

Initially, human MVD infection results from prolonged exposure to mines or caves inhabited by *Rousettus* bat colonies. Marburg spreads through human-to-human transmission via direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials (e.g. bedding, clothing) contaminated with these fluids.

Symptoms of Marburg Virus Disease

The incubation period (interval from infection to onset of symptoms) varies from 2 to 21 days.

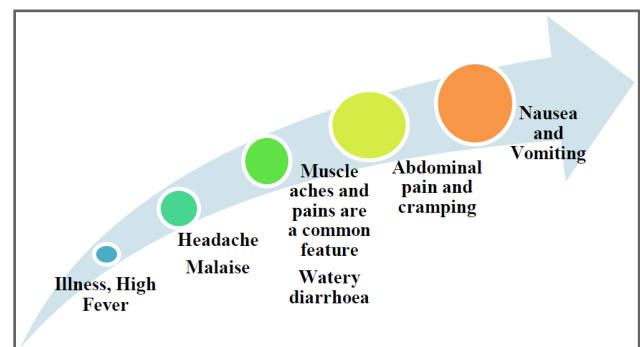


Figure 1: Symptoms of Marburg Virus

Diagnosis

It can be difficult to clinically distinguish MVD from other infectious diseases such as malaria, typhoid fever, shigellosis, meningitis and other viral haemorrhagic fevers.

Confirmation that symptoms are caused by Marburg virus infection are made using the following diagnostic methods:

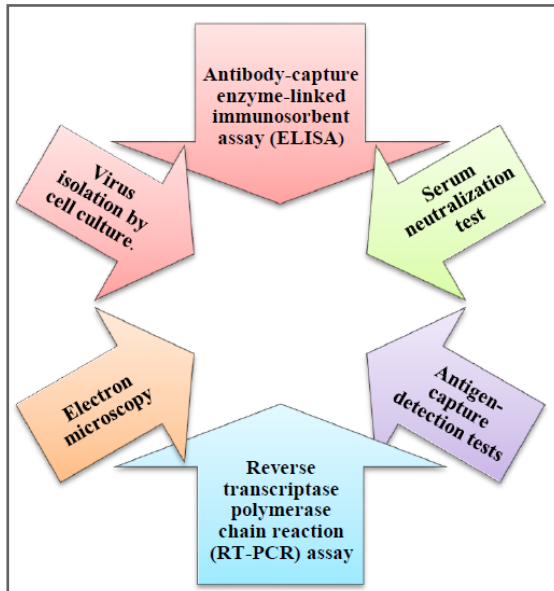


Figure 2: Diagnosis method of Marburg Virus

Samples collected from patients are an extreme biohazard risk; laboratory testing on non-inactivated samples should be conducted under maximum biological containment conditions. All biological specimens should be packaged using the triple packaging system when transported nationally and internationally.

Treatment and Vaccines

Currently there are no vaccines or antiviral treatments approved for MVD. However, supportive care rehydration with oral or intravenous fluids and treatment of specific symptoms, improves survival. There are monoclonal antibodies (mAbs) under development and antivirals e.g. Remdesivir and Favipiravir that have been used in clinical studies for Ebola Virus Disease (EVD) that could also be tested for MVD or used under compassionate use/expanded access. In May 2020, the EMA granted a marketing authorisation to Zabdeno (Ad26.ZEBOV) and Mvabea (MVA-BN-Filo) against EVD. The Mvabea contains a virus known as Vaccinia Ankara Bavarian Nordic (MVA) which has been modified to produce 4 proteins from Zaire ebolavirus and three other viruses of the same group (filoviridae). The vaccine could potentially protect against MVD, but its efficacy has not been proven in clinical trials.

Prevention and Control

Good outbreak control relies on using a range of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe and dignified burials, and social mobilization. Community engagement is key to successfully controlling outbreaks. Raising awareness of risk factors for Marburg infection and protective measures that individuals can take is an effective way to reduce human transmission.

Risk reduction messaging should focus on several factors:

- **Reducing the risk of bat-to-human transmission** arising from prolonged exposure to mines or caves inhabited by fruit bat colonies. During work or research activities or tourist visits in mines or caves inhabited by fruit bat colonies, people should wear gloves and other appropriate protective clothing (including masks). During outbreaks all animal products (blood and meat) should be thoroughly cooked before consumption.
- **Reducing the risk of human-to-human transmission in the community** arising from direct or close contact with infected patients, particularly with their body fluids. Close physical contact with Marburg patients should be avoided. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. Regular hand washing should be performed after visiting sick relatives in hospital, as well as after taking care of ill patients at home.
- **Communities affected by Marburg** should make efforts to ensure that the population is well informed, both about the nature of the disease itself and about necessary outbreak containment measures.
- **Outbreak containment measures** include prompt, safe and dignified burial of the deceased, identifying people who may have been in contact with someone infected with Marburg and monitoring their health for 21 days, separating the healthy from the sick to prevent further spread and providing care to confirmed patient and maintaining good hygiene and a clean environment need to be observed.
- **Reducing the risk of possible sexual transmission.** Based on further analysis of ongoing research, WHO recommends that male survivors of Marburg virus disease practice safer sex and hygiene for 12 months from onset of symptoms or until their semen twice tests negative for Marburg virus. Contact with body fluids should be avoided and washing with soap and water is recommended. WHO does not recommend isolation of male or female convalescent patients whose blood has been tested negative for Marburg virus [1].

Prevention and dealing with future MVD outbreaks, comprehensive research to combat looming threats must be conducted along with establishing complete surveillance systems. Emphasis on primary prevention at the community level would be the foremost way to control the upsurge [3]. The identification of the natural reservoir of this virus should also foster the development health measures and prevention campaigns to the population to reduce the apparition and emergence of potential outbreaks of hemorrhagic fever [4]. The aetiological agent was identified as an RNS-virus and was named Marburg virus. It was detected in the blood, urine, throat-washing and seminal fluid [5].

The emergence of Marburg virus (MARV) in Guinea and Ghana triggered the assembly of the MARV vaccine “MARVAC” consortium representing leaders in the field of vaccine research and development aiming to facilitate a rapid response to this infectious disease threat [6]. Combining MR186-YTE with remdesivir beginning 6 dpi, significant protection (80%) is achieved, thereby extending the therapeutic window. These

results suggest value in exploring combination therapy in patients presenting with advanced filovirus disease [7].

It is crucial to identify the host of the virus and educate the populations that are greatly at risk of the disease. While much is being investigated to devise a vaccine, it is important to educate Health Care Workers (HCWs) and close contacts facing the illness. Stopping the transmission remains the best measure that can be taken [8]. Risk of acquisition of filovirus infections primarily follows from only close personal contact and generally only in later stages of illness. Evidence that more distant contact or that contact with people incubating the disease poses any risks [9]. A calcium channel blocker developed for treating angina, was identified as a potent inhibitor of filoviruses in vitro, including Marburg viruses, in vivo [10].

Material & Method

We conducted this research paper by observing the different types of reviews and research, as well as conducting and evaluating literature review papers.

Result & Discussion

In our research, we found that Marburg virus is the causative agent of Marburg virus disease (MVD), a disease with a mortality rate of up to 88%, but which can be greatly reduced with good patient care. Transmission initially, human MVD infection results from prolonged exposure to mines or caves inhabited by rosette bat colonies. Marburg is spread through human-to-human transmission through direct contact (through broken skin or mucous membranes) with the blood, secretions, organs, or other bodily fluids of infected people, and through contact with surfaces and materials (such as Clinical studies for Ebola virus disease (EVD) with Remdesivir and Favipiravir which have been used) which may also be tested for MVD or may be used under compassionate use/expanded access. Increasing awareness of risk factors for Marburg infection and protective measures that individuals can take is an effective way to reduce human transmission. Based on further analysis of ongoing research, the WHO recommends that male survivors of Marburg virus disease practice safe sex and hygiene for 12 months from the onset of symptoms or until their semen tests positive for Marburg virus within two weeks. The bar does not test negative. WHO does not recommend isolating male or female healthy patients. Whose blood has been tested negative for Marburg virus.

Conclusion

In our research, we concluded that Marburg is spread through human-to-human transmission through direct contact (through broken skin or mucous membranes) with the blood, secretions, organs, or other bodily fluids of infected people, and through surfaces and materials. Ebola virus diseases (EVD) with Remdesivir and Favipiravir through exposure to (e.g. clinical studies) which may also be tested for MVD or may be used under compassionate use/expanded access. Whose blood has been tested negative for Marburg virus. Research about these viruses is ongoing. This drug is targeted against the nucleocapsid protein of the virus, and the company has reported infection protection in monkeys ranging from 83%-100% when given four days after the monkeys were infected with Ebola. a lipid nanoparticle that interferes with the RNA replication of this virus. It too has shown

protection against Marburg virus infection in monkeys. This drug is termed TKM-Marburg (also termed NP-718m-LNP).

Future Aspect

Research about these viruses is ongoing. Sarepta Therapeutics has been developing the RNA- interfering drug termed AVI-7288. This drug is targeted against the nucleocapsid protein of the virus, and the company has reported infection protection in monkeys ranging from 83%- 100% when given four days after the monkeys were infected with Ebola. This drug is undergoing a phase 1 safety trial that began in May 2014. Another company, Tekmira Pharmaceuticals from British Columbia, has a lipid nanoparticle that interferes with the RNA replication of this virus. It too has shown protection against Marburg virus infection in monkeys. This drug is termed TKM-Marburg (also termed NP-718m-LNP) [11].

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