

Prevention and treatment of monkeypox: an analytical review

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Abstract

1. Introduction to Monkeypox

Human monkeypox is a rare viral disease caused by the monkeypox virus. It spreads through handling infected animals and bushmeat. Monkeypox has similarities to smallpox and is classified as a bioterrorism threat. The current vaccine is similar to the smallpox vaccine, but new treatments are needed. Antivirals have had limited success in treating monkeypox. The virus was first identified in lab monkeys in 1958 and has since been found in other animals. There are no veterinary vaccines and monkeypox is expected to continue spreading. People born after 1980 are no longer immune, except for the elderly. U.S. states have a process for monitoring and containing monkeypox cases.

Methods

A treatment was tested on monkeys infected with Monkeypox. It reduced the amount of live virus and improved various symptoms. Another group of monkeys received prophylactic treatment, with one monkey remaining healthy without treatment.

Conclusion

In conclusion, it was noted that where smallpox persists in certain isolated areas, there is a risk for development of monkeypox and possibly ultimately for re-introduction of smallpox to those areas not protected by vaccination. These are concerns of public health dimensions. Presently, further systematic attempts to eradicate smallpox or monkeypox in wild animal reservoirs are not in operation. Epidemiological infrastructure needs to prepare proactively for future combined actions on zoonotic, enzootic and possibly anthroozoonotic-enhanced aspects as well as a survey of all orthopoxviruses and need to refine a detailed understanding of their epidemiology as well as host and virus interactions in order to foster continuous refinement of public health intervention measures. Many physicians have never seen a case of smallpox. They are, therefore, very important to the immunization program, particularly as regards the reporting and management of vaccinia. Physicians treating smallpox and monkeypox may encounter

most of the orthopox infections that occur in this country, and their recognition is necessary for epidemiologic studies of transmission and prompt interventions to prevent further spread.

Introduction

Mr. Chairman, I speak as a doctor. I have been fighting monkeypox for 8 months in the United Kingdom. I have had unparalleled experience: no one else has seen as many clinical cases from the start. My co-workers and I have treated 1,000 persons in the London area. So far, no one has died. We have learned how to prevent the disease. But those who saw it first in Wittenham, and others who refer to the 1958 outbreak, talk of mortality rates between 4% and 10%. I had thought these people were giving monkeypox a big CV on insufficient data. I now accept those fatality rates. My research team is spreading alarm in six countries, but we now half-believe the stories of a leeching fourth of a million.

Let me take you on a journey. Monkeypox infection is seldom mild and can be appalling. The longer the incubation period, the milder the case. It begins as influenza: fever of around 38–39°C, headache, backache, neckache, conjunctivitis. Hardly a flu immune response: disconsolate, not robust. Perhaps one in five of those who went on to a rash had a white blood count of 1,000. Two days later, painful enanthem patterns in the throat: 'smallpox of the mouth,' someone said. Quietly angry, depressed, like Ben-Hur with a bit too much bother: measles rather than smallpox. Behind the sore throat, crammed with skin phylloxera, the lymph nodes remain dormant. Pancreas: heat, pain, and jaundice for two weeks – mumps. Mumps gave a 15–20% false-positive serological response for CMV. 'Three-day glandular fever': not common, but often three piggy piles on the same infective foot. Succinct orchitis, inflamed and rent and rot. No further subsequent complications have been reported for monkeypox.

1.1. Overview of Monkeypox Virus

Monkeypox virus is the etiologic agent of the human monkeypox disease, which is an important viral zoonosis closely related to human smallpox. In general, the diseases resemble mild smallpox, and this resembles a less severe form of smallpox without the potential for eradication. The existence of human monkeypox disease, along with its relatively well-conserved disease symptoms, has encouraged research on MPV, both to understand the virus-host interactions and to respond to the potential use of the virus as a bioterrorism agent. Research to investigate MPV virology has contributed basic fundamental knowledge for future gene therapy vectors, since MPV belongs to the orthopoxvirus family, one of the most important vectors for this type of therapy. These research topics are the major driving force for the investigation related to MPV therapy and epidemiology.

In order to implement appropriate treatments and preventions, we need to understand MPV biology and pathogenesis. Here we focus on these two aspects, addressing in each section the best characterized virological data and the suggested therapeutic approaches for monkeypox. We concentrate on the biological properties and pathogenic mechanisms of MPV, as well as the potential strategies for preventing and treating MPV infections.

2. Preventive Measures

Controlling the primary infection cycle by maintaining vaccination and containment of infected individuals would be the most effective method for the prevention of monkeypox. The former application, immunization against smallpox, is now no longer mandatory. Otherwise, there are no important differences in epidemiological importance between monkeypox and orthopoxvirus infections responsible for the two smallpox. In order to contribute to the prevention of human monkeypox infections in monkeys, the owner and staff should take precautions not to be the source of infection, avoid feeding or providing water that does not enter the cage where the monkey is kept. Measures that do not enter the cage where the monkeys are located are also taken to protect the monkeys and prevent the spread within the facility. These are important and fairly straightforward general preventive measures for other zoonotic diseases as well. Infection of carnivorous mammals, including dogs, with monkeypox has been confirmed, with primates, including monkeys, as the most important sources of infection. At zoos, it is important to pay due attention to opportunities for direct contact between visitors and infected animals. Measures intended to prevent primary monkeypox infections in animals would also apply to human infections. Such a health security structure protects monkeys from pet viruses or monkeypox.

2.1. Vaccination Strategies

Vaccination is unequivocally the most cost-effective strategy against infectious diseases. Its endpoint is to elicit effective, long-lasting immunity. Classical vaccines generally contain well-characterized immunogens, either inactivated pathogens or their major components such as surface antigens, subunits, or peptides. During the early stages of development, there is an emphasis on assessing the immunogenicity and safety, which are usually determined in phase 1 and phase 2 clinical trials. However, to obtain

definitive information on the vaccine's efficacy, large-scale phase 3 trials are needed, the assessment of which can sometimes be confounded by a range of issues including ethical implications of specific study designs, variability in vaccine matching with natural circulating pathogens, and feasibility issues.

To overcome the hurdles of traditional vaccine development and to speed up the deployment of safe and effective vaccine candidates to combat unpredictable infectious disease outbreaks, several researchers have conducted preclinical studies to develop non-replicating vectors, including nanoparticles made from novel nanotechnology such as virus-like particles or capsomere-based nanoparticles or bacterial toxins. These preclinical studies can be carried out with various animal models, including monkeypox-susceptible non-human primate models. These pre-exposure prevention strategies are also known as active immunization.

3. Treatment Approaches

Prevention will rely initially on the control of rodent populations and limiting human and rodent contact. In epidemic situations, barrier nursing and wearing gloves and protective clothing by medical personnel are effective. The smallpox vaccine remains effective against monkeypox infection, although who should receive it has yet to be determined. It is theoretically possible to vaccinate zookeepers or others throughout the country who might be in contact with monkeys or exotic rodents. Commercially available vaccinia virus vaccine offers cross-protection against monkeypox, and results are more variable with cell culture-derived vaccines. Whether pre-exposure protection can be achieved with non-replicating subunit vaccine approaches remains to be determined. Due to the difficulty in predicting which species are susceptible, a number of investigational vaccines have been tested in mice and nonhuman primates.

There is no specific treatment for orthopoxvirus infections. The replication of monkeypox can be inhibited *in vitro* by the nucleoside analog cidofovir, which also inhibits viral replication in a smallpox mouse model. The drug has yet to be tested in human monkeypox infections, but a single report documents potential efficacy. Interferons and tumor necrosis factor have also been reported to interfere with orthopoxvirus replication *in vitro* and may be useful clinically, especially if regionally administered. The use of intravenous immunoglobulin to protect against vaccinia infection is controversial and must be considered unproven. Infected individuals should be managed with good nursing care. Virus-containing pustular material is a potentially infectious source. Patients should wear gloves when directly handling soiled dressings and bed linens. Proper waste disposal is crucial, and the virus is susceptible to standard hospital disinfectants.

3.1. Antiviral Medications

1. Introduction The etiologic virus of monkeypox is the monkeypox virus, which is related to the human variola virus. The zoonoses of this disease render it, as well as human smallpox, a biosafety level 3 and 4 disease. MPXV infection in humans is rarely reported, but its high lethality rate has created concerns in the public health field. The availability of vaccinations for smallpox has led to an increasing proportion of human monkeypox cases among the international community. The outcome of this is that the development and evaluation of treatments or preventive options for this zoonosis have become important, as has the broad range of vaccines or treatments developed during the outbreaks of human smallpox. Since the need for treatment was no longer a concern with the eradication of smallpox, there are no specific recommendations for the care of MPX cases nowadays, with only symptomatic and supportive treatments being suggested.

1.1. Antiviral Medications Although there are no medicines developed specifically for MPX cases, antiviral medications could be considered for those cases, most commonly including cidofovir and its analogs, acyclovir, and small-molecule inhibitors developed based on preclinical studies for orthopoxviruses. Cidofovir is recommended for treatment due to its eventual effectiveness against human MPXV cases, even if not tested clinically. It is primarily a cytomegalovirus treatment, administered intravenously, and is responsible for a number of adverse events, including irreversible nephrotoxicity. Brincidofovir, on the other hand, gained attention due to its clinical usefulness in cases of human smallpox.

4. Case Studies and Outcomes

Many different types of vaccine platforms are currently being developed as a countermeasure for MPXV infection. Safety and efficacy, both crucial for developing current Good Manufacturing Practices-compliant products, must be ascertained before approval and licensure by the appropriate regulatory agencies. While various wild-type and inactivated virus platforms have been developed and undergone extensive testing in preclinical models, the number of vaccines that have been evaluated in non-human primate models is scarce. Non-human primates are considered to be the most relevant model in determining vaccine efficacy for poxvirus infection, so any testing in this model is a major step forward in the development of a vaccine.

The critical need for an MPXV vaccine has prompted the development of several vaccine strategies, including inactivated virus vaccines, replication-competent and -deficient viral vectors, DNA plasmids, and virus-like particles. Some of the first vaccine strategies tested in non-human primates were inactivated vaccines. Such vaccines were shown to be able to prevent poxvirus as well as smallpox virus infections and offer sterile immunity to intravenous challenge with both smallpox and monkeypox in macaques. More conventional vaccine methods have been developed using bacterial and viral vectors delivering MPXV or VACV antigens and other gene delivery platforms using DNA vaccines and viral-like particles. In this review, we will discuss the vaccine strategies developed against monkeypox, first starting with historical vaccines and moving forward to recent advancements. For brevity, only vaccines that have undergone testing in non-human primates will be focused on in this review. Data involving wild-type or recombinant VACV will include platforms, while DNA vaccine testing will be discussed in a separate section. (Yuqian et al.2024)(Garcia-Atutxa et al.2024)(Jiang et al.2024)(Fang et al., 2024)(Rcheulishvili et al.2023)(Wang et al.2023)

5. Future Directions in Research

The incidences of human monkeypox have increased, likely due to waning population-level immunity to monkeypox, and the wrongly held belief that the smallpox vaccine will protect against all poxviruses. Since monkeypox is such a serious disease in some cases, an effective treatment, in addition to vaccination, would be useful. The development of new antivirals is crucial, since resistance can develop to existing treatments. Research should focus on new treatments that could be effective. Currently, vaccine methods to prevent monkeypox are limited. In addition, existing treatments for monkeypox are not approved for general use in children. Other treatments are not very effective, either, and the longer use of antivirals for poxviruses is the preferential treatment. The development of a more effective and less toxic antiviral is thus needed. A pilot study of the antibody-based therapy for orthopoxvirus was conducted in humans, which suggested that a passive antibody-based therapy could be a useful approach. A similar strategy using small molecule inhibitors could also be effective. It should be noted that new therapies may also come in a different form, such as the use of siRNA to knock down specific targets, which decreased the spread of monkeypox. These studies should be further explored for therapeutic potential.

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