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Medications used in Monkeypox Disease – A Review

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Abstract

Monkeypox is a zoonotic viral disease similar to smallpox, caused by the monkeypox virus. With the recent global outbreaks, there is an increasing need to understand effective treatments for this infection. This article reviews the current evidence on antiviral treatments and other therapeutic strategies for monkeypox.

Keywords: Monkeypox; Smallpox; Virus; Treatment

1 Introduction

Monkeypox virus belongs to Orthopoxvirus, discovered in the 1950s, which causes zoonotic diseases in humans. After the eradication of the smallpox virus, the monkeypox infection has slowly but steadily spread globally, so much so that WHO declared monkeypox "a public health emergency of international concern" (PHEIC).[1–3]

Monkeypox virus spreads through droplets as well as sexual contact in humans. It can spread if infected animal bites, scratches, and consumption of bushmeat. The clinical manifestations are rash, fever, chills, and lymphadenopathy. Diagnostic tests for orthopox virus are viral cultures, immunohistochemistry, RT-PCR, and Anti-Orthopoxvirus immunoglobulins (IgM/IgG).[3,4]

2 Treatment strategies

2.1 Symptomatic supportive therapy

The majority of people who get affected with monkeypox heal without medical intervention. Oral/intravenous rehydration treatment is recommended for patients suffering from gut issues.[3]

2.2 Primary prevention with vaccines

a. Modified Vaccinia Ankara (MVA) vaccine

MVA vaccine is live and nonreplicating. It is marketed with the trade name Jynneos. It is administered in two dosages, either as 0.5 mL subcutaneous or 0.1 mL intradermal injection, given four weeks apart.[5]

MVA has minimal safety issues, so it is considered for immunizing patients on long-term treatment for skin disorders and immunocompromised individuals. After the vaccination, the recipient may experience headache, muscle pain, injection site pain and inflammation of lymph nodes. These symptoms resolve within a few days. FDA approved it under EMERGENCY USE AUTHORIZATION (EUA) in August 2022. [5]

b. ACAM2000

ACAM2000 was developed as a part of the U.S. "Strategic National Stockpile" as a precaution for smallpox bioterrorism threat management strategy. [6] US-FDA approved it in 2007 as a smallpox vaccine. Because of the recent threat of rampant monkeypox spread, clinical trials are being undertaken to evaluate ACAM2000's utility against monkeypox infection. [7]

At present, it is reserved only for those at high risk with an intact immune system and who are not pregnant. ACAM2000 is given as a single dose, but for those at high-risk booster dose is recommended every three years. It is administered "percutaneously with multiple puncture technique". Common adverse effects include pain at the injection site, lymphadenitis, and constitutional symptoms.

ACAM2000 is a replication-competent vaccine; the vaccinia virus can spread to the unvaccinated individual through close contact with the vaccine inoculation site or exudative secretions from the site of vaccinated individuals. Hence vaccine site care must be taken so that the spread to immunocompromised patients and pregnant ladies does not occur.

c. Aventis Pasteur Smallpox Vaccine (APSV)

APSV is also a replication-competent vaccinia virus vaccine as MVA, which is still at the investigational stage. It is a reserve vaccine, which means to be made available under an Investigational New Drug or Emergency Use Authorization to be utilized if and when approved vaccines are exhausted or hard to procure. [8]

2.3 Secondary prevention with drugs against monkeypox virus

The drugs approved for the management of smallpox have undergone clinical trials to determine their utility against monkeypox infection. All these drugs were developed based on animal models. Even though several human studies are available for the safety of these drugs, no efficacy studies are available. [9]

a. Tecovirimat

US-FDA approved Tecovirimat in 2018 for the treatment of variola virus-causing human smallpox disease. [10] The mechanism of action is inhibition of the VP37 protein present in the Orthopox virus; which in turn blocks the interaction of the virus with the host cell. It leads to the inhibition of entry of the virus into the host cell and effectively stops spread of infection. Tecovirimat is contraindicated in pregnancy and breastfeeding.

Table 1. Treatment regimen of Tecovirimat

Sl. No	Weight band	No. of 200 mg capsules to be consumed	Treatment duration
1.	40 – 120 kg	Three capsules twice daily	For 14 days
2.	>120 kg	Three capsules thrice daily	

b. Cidofovir

Animal studies have shown the effectiveness of Cidofovir against smallpox infection. Presently, significant clinical data regarding efficacy against monkeypox infection is unavailable. Cidofovir gets metabolized to cidofovir diphosphonate, which selectively inhibits viral DNA synthesis leading to the suppression of viral replication. [11]

Cidofovir can cause nephrotoxicity; thus monitoring renal functions with each dose is essential; patients must receive intravenous saline for rehydration to prevent nephrotoxicity. Other adverse effects are the risk of neutropenia, metabolic acidosis, hepatic impairment, and pancreatitis. [11]

c. Brincidofovir

The pharmacological profile of brincidofovir resembles cidofovir but with fewer side effects. Brincidofovir, being a lipid conjugate gets converted to cidofovir after it enters the cell, which in turn gets converted into cidofovir diphosphonate. It leads to selective inhibition of viral DNA, resulting in the suppression of viral replication.

Brincidofovir causes hepatotoxicity, so liver function tests have to be monitored. It must be discontinued if alanine transaminase (ALT) remains consistently high i.e., >10 times the upper limit of normal. It harms the fetus, should be avoided in pregnancy. It can also be detected in breastmilk. FDA approved brincidofovir under the trade name Tembexa to treat smallpox on June 4, 2021 but its utility against monkeypox is currently under trial. [9]

d. Trifluridine

Trifluridine is intended to be used in the treatment and prevention of corneal as well as conjunctival involvement in individuals with eye lesions caused by the monkeypox virus. Trifluridine inhibits intracellular thymidylate synthetase enzyme, leading to interference with virus replication and ultimately reducing the viral load. The dosage schedule is topical drops or eye ointment preparation to be applied four hourly for a duration of seven to ten days. They can be utilized

in hepatic and renal impairment patients. At present, trifluridine is undergoing clinical trials for its utility against monkeypox infection in humans. [9,12]

2.4 Vaccinia immunoglobulin

It is approved for the treatment of complications of immunisation using replication-competent vaccinia virus vaccines of smallpox. [9] It can also be used in immunocompromised patients and patients who are recently exposed to monkeypox infection. [13]

3 Conclusion

The sudden resurgence of the monkeypox virus and sporadic cases beginning to appear in nonendemic areas is a matter of concern. This situation needs the implementation of a strict surveillance system for international travellers and strict quarantine policies to mitigate the spread of disease. The administration of vaccines and medications against the monkeypox virus may help in the management of this condition.

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