Effectiveness of Antiviral Drugs *versus* Vaccine against MPOX Virus Infection

Mpox virus (MPXV), an enveloped double-stranded DNA virus member of the genus Orthopoxvirus (OPXV), previously transmitted *via* zoonosis, has been reported recently to spread *via* human-to-human route. This can occur through direct skin contact, respiratory droplets, or by unprotected contact with blood.

Following a series of consultations with global experts, WHO has recommended using a new term "mpox" as a synonym for monkeypox. Both names will be used simultaneously for one year while the term "monkeypox" is phased out.[1] The virus is currently spreading throughout many nations in regions where the virus has not previously been detected, including Europe, America, the Western Pacific, Eastern Mediterranean, and South East Asia. In areas of Africa that have previously recorded occurrences, such as Nigeria, the Democratic Republic of the Congo, and the Central African Republic, more cases than usual have been reported in 2022. Clinically, the virus has a similar manifestation as the smallpox virus; however, certain clinical features specific to mpox include generalised lymphadenopathy following the onset of fever. The incubation period of the disease ranges from 4 to 21 days and the illness is usually self-limiting. The infection can lead to several complications like secondary bacterial skin infections, corneal scarring, bronchopneumonia, and septic shock. The current understanding regarding mpox virus infection and its complications in humans has not been investigated to find a validated first line of treatment. There are several treatment options including vaccine and Vaccinia Immune Globulin (VIG) providing temporary and symptomatic relief but none of them offers complete protection. Although the vaccinia vaccine has been used globally as a preventive measure against mpox, clinical studies have yet to be done to prove its post-exposure efficacy in humans.[2]

Antiviral drugs may be a better choice in treating mpox. A recent clinical trial was conducted in 2021 to determine the efficacy and pharmacokinetics of antiviral brincidofovir (BCV), against mpox. The drug is a lipid conjugate of the nucleotide analog, cidofovir (CDV), with better cellular uptake and conversion to an active form and has a good renal biosafety profile as compared to CDV. The trial revealed that pre-exposure initiation of the BCV was found to be more efficient (57% survival rate) than on the day of exposure treatment (43% survival rate) and even more than those who received treatment a day after exposure (29% survival rate) following an intra-nasal challenge with MPXV. Moreover, delay in mortality was also noticed when BCV treatment was started before MPXV infection; for animals treated on the pre-exposure day, the average day of euthanasia was day 13 post-exposure, whereas the average euthanasia day for the other groups was approximately day 11 post-exposure.[3] Adler *et al.,* in their retrospective study conducted on 7 patients suffering from MPXV in the UK, revealed that the off-label use of Tecovirimat was associated with much shorter stay at the hospital, shorter duration of viral shedding, and illness with full recovery and no side effects reported while patients who received BCV did not show many potent clinical effects and also reported elevated transaminases, nausea and abdominal discomfort.[4] A clinical trial, conducted in 2006 to compare the post-exposure vaccine and antiviral therapy in an animal model, revealed that post-exposure antiviral treatment with CDV was associated with much-reduced mortality, reduced number of skin lesions, and a post-therapy significant amount of monkeypox virus-specific immunoglobulin in the serum.[5] A study conducted in Nigeria in 2018 elaborated that although the Centers for Disease Control and Prevention (CDC) proposes the use of both CDV and BCV against mpox infection, BCV has been reported to be less nephrotoxic than CDV.[6] A detailed review done to evaluate the efficacy and practicality of tecovirimat reported that around 50 animal studies have been conducted to date to determine the effectiveness of the drug against orthopoxvirus infections and it showed significant efficacy in treating lethal challenges specifically of MPXV in many of these studies.[7]

Pakistan's healthcare sector faced various obstacles during the COVID-19 pandemic due to lack of healthcare funds. It was tormenting for hospitals and healthcare organisations to ensure adequate staffing, ventilators, medical workers, hospital beds, and laboratory equipment.[8] With this new evolving MPXV pandemic, the nation's healthcare is not ready yet. Fortunately, no cases of mpox have been documented in Pakistan to date, but due to the increase of the mpox virus in non-endemic nations, national and provincial health authorities were obliged to issue a high-level alert because the virus could also spread in Pakistan.

Since viruses have no frontiers, the global community must act swiftly and cooperatively to fill knowledge gaps and stop the pandemic. Rapid case identification is essential to control infection in the absence of readily accessible prophylaxis or treatment. There are many diverse ways in which diseases can present, as is typical in clinical practice, and mpox is no exception. Given the previous studies and the rapidly changing demographics of the human mpox infection, antiviral treatment should be considered as a first-line management option besides vaccine and supportive management for a speedy recovery. More intensive trials should be carried out to find the best antiviral drug with maximum efficacy, minimum side effects, and better practicality for the treatment of MPXV.

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