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Letter to the Editor

Can a smallpox drug treat monkeypox? Compassionate use of tecovirimat for monkeypox infection

Dear editor,

The monkeypox outbreak during the coronavirus disease 2019 (COVID-19) pandemic has given rise to the concern of multiple viral pandemics. Though COVID-19 has been around for three years by now, mass immunization and precautionary measures have played a pivotal role in tackling an emerging global panic. However, recently an unprecedented outbreak of monkeypox has occurred in areas that are not endemic to the disease. This has given rise to the concern that the world is most likely to enter a stage of a new viral pandemic, which is not only alarming but has also urged the healthcare professionals to speed up the research regarding its prevention and treatment much more effectively. The causative agent behind this disease has been around for decades and was first discovered in 1958 in Copenhagen, the virus is a double-stranded deoxyribonucleic acid (DNA) agent that belongs to the *Orthopoxvirus genus* of the *Poxviridae* family [1,2]. As of August 2022, more than 39,000 cases of monkeypox have been reported in Europe and North America, whereas the past cases have been limited to patients with international travel history or through African animal imports [3,4]. The mode of transmission is via contact with infected skin, body fluids, or respiratory droplets [3]. Though the disease reflects a milder form of smallpox, it can cause severe illness including ocular damage, soft-tissue superinfections, and excruciating anogenital lesions [1,2].

An observational analysis of individuals attending a sexual health clinic in the United Kingdom (UK) by Girometti et al. reported a total of 54 confirmed cases, all in men having sex with men [5]. Similarly, an international case series across 16 countries reported that 98% of cases were patients who were bisexual or gay thus indicating that the current outbreak involves a different clade of monkeypox than the one which is the source of infection in the Democratic Republic of Congo (DRC) [6]. The population affected (men who have sex with men) and clinical manifestations such as substantial anogenital and oral mucosal involvement also differ from the cases in countries endemic to this disease. In the current scenario, an antiviral drug, tecovirimat, which received approval for smallpox under "Animal Rule" can result in better clinical outcomes in monkeypox treatment [7]. The drug is currently available for clinical use under an expanded-access protocol (https://www.cdc.gov/poxvirus/monkeypox/clinicians/obtaining-tecovirimat.html). However, the question of "how the access to a drug, whose safety and efficacy in humans have not been established can be managed?" still stands. The Animal Rule pathway allows approval of drugs for life-threatening conditions when it's not possible to conduct efficacy studies in humans due to ethical issues or not feasible to evaluate the effectiveness of drugs via field trials [7]. The evidence supporting efficacy is based on results from adequate and well-controlled studies in animal models of the disease of interest. Since the research involving the variola virus is only limited to laboratories located in the United States and Russia, it imposes a significant challenge in conducting studies involving this virus. Moreover, smallpox is an eradicated disease, and based on all of these factors, efficacy of tecovirimat for smallpox was established on data received from studies in animal models using related orthopoxviruses. The safety points in humans were assessed by analyzing and evaluating the adverse reactions in healthy volunteers who received tecovirimat treatment. Subsequently, the comparison of plasma concentrations of the drug in healthy volunteers with those in animal models at a concentration showing full effectiveness against monkeypox and rabbitpox was used as a parameter to devise a recommended dose of tecovirimat [7].

There have been cases reporting the use of tecovirimat in the treatment of monkeypox illness however, the available data is not sufficient to demonstrate any significant efficacy [8,9]. Animal studies can serve as an alternative, but their results cannot be directly compared with human clinical trials. In contrast to smallpox, monkeypox remains endemic in some regions of the world where randomized controlled trials (RCTs) can be conducted, and subsequently, safety data can be obtained from infected individuals rather than healthy volunteers. In the wake of the current outbreak and the difference in disease from its usual presentation, there is a need for an RCT in the United States and Europe to assess the efficacy and safety of this drug in the treatment of monkeypox illness. Though the National Institute of Health (NIH) is already working in collaboration with the Acquired Immunodeficiency Syndrome (AIDS)) Clinical Trials Group to develop a US-based RCT to assess this drug and provide data for clinical and regulatory decision-making, the preliminary results from an uncontrolled cohort suggested that oral tecovirimat was well tolerated by all the patients with monkeypox infection [10,11]. The preliminary data is a good indication of the promising efficacy and safety of this drug for monkeypox however only large scale RCTs can provide a more reliable conclusion.

Declaration of Competing Interest

The author declare they have no conflict of interest.

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