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Research Article

Cidofovir as a Potential Antiviral Agent against Monkeypox A Systematic Review

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ABSTRACT
Background: There are a number of large and complex viruses in the poxviridae family. Among these viruses are orthopoxvirus under which monkeypox virus (MPXV) falls. Monkeypox virus is transmitted through either getting exposed to contaminated objects or direct contact with infected humans or animals. For its treatment, specifically two antiviral drugs are used which are tecovirimat and cidofovir. In AIDS patients, cytomegalovirus (CMV) retinitis is present which is treated by using cidofovir.
Objective: To evaluate the effectiveness of cidofovir in treating monkeypox
Study design: A systemic reivew
Methodology: This is a comprehensive study which was performed by using a number of research studies conducted by different authors. The information was gathered through searching different research articles based on monkeypox and cidofovir. The outputs which were assessed were a negative MPXV PCR test, plague suppression, symptom relief without side effects, MPXV replication, and prevention of mortality and morbidity.
Results: The research studies that were included in this article were all related to monkeypox and cidofovir which were published between 2002 and 2024. Initially, there were more than 300 studies but after deleting the duplicate ones, 200 were left. Among these 200 articles, only a few were selected after screening titles and abstract.
Conclusion: It was found that cidofovir is an effective drug to treat monkeypox.

INTRODUCTION

There are a number of large and complex viruses in the poxviridae family. Among these viruses are orthopoxvirus under which monkeypox virus (MPXV) falls [1,2]. Monkeypox virus is transmitted through either getting exposed to contaminated objects or direct contact with infected humans or animals [3]. In a number of countries, monkeypox is referred to as a public health emergency [4]. A study states that 80,850 cases of monkeypox were reported from all around the world till November 2022 [5].

As monkeypox is a rare disease and people are not aware of it, they tend to neglect treatment of this virus and delay its management [6]. As it is not a common disease and its awareness is also very low, the cure and treatment of monkeypox is still difficult to detect. Doctors provide medicines related to the presenting concerns and focus on symptom relief care as a therapeutic approach [7]. For its treatment, specifically two antiviral drugs are used which are tecovirimat and cidofovir. Several DNA viruses such as adeno, papilloma, herpes, polyoma, and poxviruses are inhibited by zidovudine.

In AIDS patients, cytomegalovirus (CMV) retinitis is present which is treated by using cidofovir. Cidofovir and tecovirmat are the two antiviral drugs on which there is very limited research done [8]. There are also no clinical trials being conducted on the observation of these antivirals' therapeutic applications. There are a number of research studies conducted on animals which shows that diseases caused by poxiviruses are treated well by using tecovirimat [9]. Moreover, it is very effective if it is given early when the infection is detected. A few animal studies also state that cidofovir can be used to treat

monkeypox [10]. However, not much data is revealed on using cidofovir for treating monkeypox in humans. Therefore, this study was performed to evaluate the effectiveness of cidofovir in treating monkeypox.

METHODOLOGY

This is a comprehensive study which was performed by using a number of research studies conducted by different authors. The information was gathered through searching different research articles based on monkeypox and cidofovir. Some key words for this research were "antivirus" AND "cidofovir" AND "monkeypox". A number of publications were a part of this study which were only English-language complete-text publications. Manual searching for more research articles was also done. Articles in which a case was reported and cidofovir's antiviral activity in treating monkeypox were included. Repetitive publications were excluded. All the publications that were a part of this study were approved by the ethical committee.

The outputs which were assessed were a negative MPXV PCR test, plague suppression, symptom relief without side effects, MPXV replication, and prevention of mortality and morbidity.

RESULTS

The research studies that were included in this article were all related to monkeypox and cidofovir which were published between 2002 and 2024. Initially, there were more than 300 studies but after deleting the duplicate ones, 200 were left. Among these 200 articles, only a few were selected after screening titles and abstract. Table number 1 shows the characteristics of cidofovir that were gathered from different studies.

Table No. 1:

Characteristics	Cidofovir
Mechanism of action	DNA polymerase inhibitor
Mpox EC50	27–78 μM
How is it supplied	375-mg/5-mL vial for injection
Treatment duration	There is limited data available on this. For monkeypox virus, 5 mg/kg was given as the first dose.
Hepatic dose adjustment	None
Dosing (IV)	5 mg/kg IV once a week for 2 weeks; no definitive dosing data in poxviruses
Dosing (PO)	N/A
Availability of IV/PO	IV only
Adverse reaction of this drug	Vomiting, nausea, nephrotoxicity, rash, hypersensitivity

Table number 2 shows an overview of pox virus infection.

Table No. 2:

Poxvirus	Monkeypox virus
Year discovered	1958
Incubation period	3 to 34 days
Total cases up till now	More than 80,000
Disease type	Self-limited disease
Symptoms	Headache, fever, Skin or anogenital lesion rash
Antivirals to use	Cidofovir, Brincidofovir, Tecovirimat
Transmission route	Close contact with monkeypox lesions, scabs, and rash
Vaccines	ACAM2000, JYNNEOS

Table number 3 shows a summary of cidofovir.

Table No. 3:

Antiviral inhibitors	Cidofovir
Date on which it was	June 1996

approved	
Pharmaceutical form	Solution of infusion
Indication approved	Human cytomegalovirus retinitis in AIDS Patients
Effects	Vomiting, rash, headache, nausea, fever
Mechanism of drug action	Inhibits the DNA synthesis mediated by the viral DNA polymers
Dose recommended	5 mg/kg once a week for 2 weeks during treatment 5 mg/kg once in every 2 weeks after treatment
Drug interaction	It should not be administered with Tenofovir and Probenecid

DISCUSSION

By performing this study, it was revealed that cidofovir, which is an antiviral drug for orthopoxvirus infections, prevents the monkeypox virus from growing and multiplying [11]. When monkeypox virus is diagnosed to someone, it is best to provide cidofovir in the early stages so that it would work best and efficiently [12]. Even if it is provided a little late after the disease has occurred, it can still reduce symptoms. CMX001 is the lipid version of cidofovir which is used in mice to help them prevent weight loss [13]. Cidofovir has been tested on both normal and monkeypox-resistant viruses. Lab tests were performed on monkeypox-resistant viruses where it was found that they needed higher doses of cidofovir in order to be controlled. It is very crucial to understand that these resistant viruses are dangerous and cidofovir might not always work on them [14]. In order to test cidofovir for monkeypox virus, monkeys and mice have been used. A number of studies were conducted to evaluate the use of cidofovir immediately or within 24 hours for monkeypox virus after it was diagnosed [15-18]. However, the association between times to therapy is unclear in these models and human infection. When cidofovir was tested on mice and it was stopped at a certain point, the mice that survived had antiviral T-lymphocytes and virus-specific serum antibodies. It was found that cidofovir is found to be effective in improving outcomes in patients who are infected by monkeypox virus. In some studies, other antivirals have also been tested for synergy with cidofovir in monkeypox [19]. Some other reasons for which combination therapy is used is its ability to work well with lower doses as well, reduce drug resistance, and reduce side effects. Intravenous cidofovir is used to treat human poxvirus infections. According to the study of Mondi et al., the viral levels steadily decreased and health was completely restored within 4 to 18 days of therapy [20]. The limitations of this study were that the sample size was small, there was a need for a control group, impracticality of sampling patients, and heterogeneity of the population. Therefore, antiviral drug efficacy cannot be determined. There were numerous studies that stated intravenous cidofovir relieving symptoms within 48 hours. Although longer time was taken to clear the virus from the blood, skin lesions were improved by using cidofovir after the first dose. The levels of creatinine stayed in the normal range, showing no signs of toxicity. This allows the treatment to be called safe.

CONCLUSION

It was found that cidofovir is an effective drug to treat monkeypox.

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This study was conducted without receiving financial support from any external source.

Conflict in the Interest

The authors had no conflict related to the interest in the execution of this study.

Permission

Prior to initiating the study, approval from the ethical committee was obtained to ensure adherence to ethical standards and guidelines.

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