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Current Status of Oseltamivir Application and Its Future Development Trend

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Abstract. Influenza is a common respiratory disease with severe complications that can be fatal in severe cases. Oseltamivir is a drug that suppresses influenza disease, it can effectively reduce the symptoms of influenza patients but there are also some adverse effects that can affect the quality of life of patients and the psychological status of the treatment process. This article examines the side effects, mechanism of action, trends, and future prospects of oseltamivir, and draws conclusions about the drug's use in treating influenza. It provides direction and reference information for future research on this drug, discusses the limitations of its therapeutic efficacy and the challenges it will face. Liver enzyme levels should be carefully monitored and liver health should be carefully assessed when using oseltamivir to treat illnesses such as influenza. These studies will help provide better options for the treatment of diseases such as influenza. However, this paper has not addressed the limitations of whether oseltamivir has additional adverse effects in patients with hepatic and renal disorders, whether they can take the drug normally, and whether the dosage needs to be reduced compared to normal patients. In addition, even though oseltamivir is very effective against the influenza virus, it is not a perfect solution to all problems. It still has limitations and challenges to overcome in terms of viral suppression. In future studies, a deeper understanding of the mechanism of action, efficacy and safety of oseltamivir is needed to develop better anti-influenza drugs to serve patients.

Keywords: Oseltamivir; adverse effect; mechanism.

1. Introduction

According to the World Health Organisation (WHO), between 3 and 5 million people worldwide have been infected with influenza in the last five years, and between 2.9 and 650,000 people have died as a result of severe respiratory illnesses caused by the influenza virus and its accompanying complications [1]. In the 20th century, four major influenza virus epidemics were recorded, including the H1N1 pandemic of 1918 (also known as the Spanish virus), the H2N2 pandemic of 1957-1958 (Asian influenza), the H3N2 pandemic of 1968-1969 (Hong Kong influenza), and another H1N1 pandemic of 2009 (Mexican or swine flu) [2].

Influenza is a large infectious disease that affects people around the globe in some way. In humans, the majority of infections are caused by influenza A or B viruses, with a very small percentage of infections being caused by viruses. Influenza A viruses pose the greatest threat to human health due to their strong tendency to mutate antigenically and their potential for pandemic spread. It can range from an asymptomatic mild infection to an upper respiratory tract infection that can eventually lead to severe high fever, muscle pain, chills, pneumonia, coughing, and even life-threatening illness [3]. Globally, it affects a greater number of children and a slightly smaller number of adults than children.

Oseltamivir plays an important role in the suppression of both type A and type B viruses. In 1999, oseltamivir was approved by the U.S. Food and Drug Administration (FDA) for the treatment of uncomplicated cases of influenza within 48 hours of the onset of symptoms [4]. Gradually, it has been promoted for widespread use and value in clinical treatment. In 2010, oseltamivir was added to the WHO's list of essential medicines [1]. Oseltamivir has the ability to lower viral load, reduce the duration of fever, shorten the duration of illness, and reduce a range of complications and mortality associated with the influenza virus [5].

Antiviral drugs are the first line of defence against influenza strains, although other therapeutic approaches are available, including drugs that target host proteins involved in the viral life cycle [6]. In addition, human protein targeting is a promising therapeutic method for eliminating influenza and amplifying the effects of antiviral compounds [7]. Among several drug targets for influenza A, HA and NA are important antigenic glycoproteins necessary for viral proliferation [6]. Of all the NA inhibitors, oseltamivir and zanamivir [8] are the most widely used. The former is administered orally and the latter by inhalation [9]. The oral bioavailability of oseltamivir in humans is high usually up to 15 times higher (79%) than that of oseltamivir carboxylate [10].

However, because oseltamivir is an oral neuraminidase inhibitor, it is widely used to treat acute influenza [11]. Reduction of human endogenous neuraminidase activity by oseltamivir carboxylate (a metabolite of oral oseltamivir phosphate) may lead to delayed adverse reactions to neuraminidase inhibitors - not only inhibiting antibody and pro-inflammatory cytokine induction but also causing gastrointestinal bleeding [12].

Inspired by the use of oseltamivir as a treatment for influenza, and in view of the continuing threat posed by the influenza virus to human beings around the world, in this report, I will look at the advantages of oseltamivir in the treatment of the disease and the side-effects of taking the drug, its development and approval process, clinical trials, the search for targets for oseltamivir, comparisons with similar drugs that inhibit the influenza virus, and the applications of the drug and its future directions. The analysis will be carried out in the following aspects.

2. Oseltamivir

2.1. The Introduction of Oseltamivir

Oseltamivir is an antiviral medication usually used to treat acute uncomplicated clinical symptoms caused by influenza A or B in adults and children older than 2 weeks of age. For infants under 2 weeks of age, it is uncertain whether oseltamivir can be used to treat influenza as its safety and efficacy have not been demonstrated in this population [3]. It has been found that newborns are at risk of pneumonia when infected with influenza B. Oseltamivir given within 48 hours of onset of illness is effective in reducing the risk of pneumonia [13]. However, many healthcare organisations recommend its use for people who develop complications or are at high risk of complications within 48 hours of the first symptoms of the infection. This is good for preventing viral infections in people at high risk, but this is not effective in the general population. The Centers for Disease Control and Prevention (CDC) recommends that clinicians treat low-risk patients who present to the clinic within 48 hours of the first symptoms of the infection as indicated [1].

The indications, mechanism of action, dosing regimen, major adverse reactions, contraindications, monitoring strategies, and potential toxicities of oseltamivir are being widely followed and monitored. The goal is to provide healthcare providers with the knowledge necessary to effectively guide patient treatment and ultimately optimise outcomes against influenza and related viral infections [3]. Oseltamivir is taken by mouth, either as a pill or as a liquid [1]. Oseltamivir, which selectively inhibits influenza neuraminidase, an enzyme essential for viruses, was originally administered as oseltamivir phosphate and is rapidly converted in vivo to a highly bioavailable, site-penetrating active metabolite, the oseltamivir carboxylate, for the purpose of inhibiting viral replication [14]. The pharmacokinetics of oseltamivir and oseltamivir carboxylate are dose-proportional in twice-daily therapy after repeated administration of up to 500 mg [14]. This property is highly reliable and can be applied to a diverse patient population, including young children and elderly patients as well as patients with renal or hepatic impairment [14].

2.2. Adverse Effects

Common adverse reactions to oseltamivir, a class of anti-influenza medication (occurring in more than 1% of the population), include nausea and vomiting. Trials have been conducted specifically to

verify the side effects associated with oseltamivir [1]. In the study, which was age-segregated, the number of adult participants was 28, and 22 of them experienced vomiting after taking oseltamivir, a drug that increases the risk of nausea. In the younger children's group, 1 in 19 children taking oseltamivir vomited. So, in the treatment of children, oseltamivir also induces vomiting [1].

Abdominal pain, diarrhoea, headache, insomnia and dizziness are also common adverse effects associated with oseltamivir use, and the high incidence of these adverse effects should be cause for alarm [3]. Adverse reactions such as conjunctivitis, rhinorrhoea, hypersensitivity, gastrointestinal bleeding, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and loosening of the epidermis, confusion, seizures, and neuropsychiatric events may also occur in a small number of patients, and the probability of these occurring is relatively low (less than 1%) [3].

In addition, oseltamivir has the potential to cause hepatotoxic reactions. In a small number of patients, the drug may lead to phenomena such as liver damage and jaundice [3]. The mechanism by which this occurs may be related to an immunoallergic reaction. Although such cases are rare, they need to be of great concern to doctors and patients.

When administering oseltamivir therapy, care should be taken to monitor the patient's liver function and serum enzyme levels, as well as the monitoring and management of adverse reactions [3]. In addition, as influenza itself may cause symptoms such as elevated serum enzymes and jaundice, doctors need to fully consider relevant factors and assess the possibility of adverse reactions when conducting etiological analyses. Taken together, adverse reactions to oseltamivir should be considered a clinically significant but rare cause of liver injury [3]. The side effects of oseltamivir on the heart are not known: it may reduce cardiac symptoms, but it may also induce serious arrhythmias and requires further experimental verification [1]. The side effects of this drug may be related to individual differences and the dosage of the drug, and different patients may react differently to its use. For example, when some people use Oseltamivir in poor health, more pronounced side effects can occur. The dosage should be controlled and not used in conjunction with other viral suppressive drugs to avoid drug-drug interactions that could lead to more serious adverse effects.

2.3. Mechanism of Action and Pharmacokinetics

An antiviral drug, Oseltamivir is a neuraminidase inhibitor. It interferes with the viral replication process by selectively and competitively inhibiting the neuraminidase enzyme activity of the influenza virus [1]. The drug is a phosphorylated prodrug form that needs to be hydrolysed in vivo to the activatable oseltamivir carboxylate form in order to exert pharmacological activity. Oseltamivir interferes with the process by which viral progeny is shed from infected host cells and spread to new host cells. Oseltamivir delays viral release, shortens the duration and amount of the virus, and significantly reduces the duration of symptoms of influenza virus, ranging from 0.5 to 3 days [3].

The mechanism of influenza virus resistance is a complex mutational process that primarily involves antigenic drift and deflection of antigenic surface proteins such as HA (hemagglutinin) or NA (neuraminidase). Antigenic drift is the process by which point mutations cause small modifications in key viral epitopes. Antigenic shift, on the other hand, refers to the complete exchange of HA or NA genes [3]. Antigenic shift occurs primarily in influenza A viruses because they have large animal hosts. Antigenic transfer is one of the common causes of pandemic outbreaks of influenza viruses [3].

In practice, doctors should pay attention to monitoring the progress of the disease, carry out rational drug therapy, and avoid overdose or drug abuse in patients [3]. In addition, the study of viral mutation and drug resistance mechanism is also one of the important directions for future drug research and development, in order to better control and prevent the spread and pandemic of the influenza virus [3].

Oseltamivir has a bioavailability of more than 80% when administered orally and is extensively metabolised to its active form when it first passes through the liver [1]. It has a volume distribution of about 23-26 litres [1]. The half-life of the drug is approximately 1-3 hours, while the half-life of

its active carboxylate metabolite is 6-10 hours. More than 90% of the oral dose is excreted in the urine as the active metabolite [1].

3. The Future of Oseltamivir

Oseltamivir, a potential antiviral agent against type A-B, COVID-19, offers an effective approach to treating patients with COVID-19 [15], with a reduced mortality rate in patients consuming the drug, and a lower chance of death than in patients who do not receive antiviral drugs [15]. Its cost is also relatively low, as can be deduced from the statistics of most U.S. pharmacies. Oseltamivir is available in three sizes of oral capsules. Oseltamivir 30 mg oral capsules cost about $26.93 USD for a supply of 10 capsules; oseltamivir 45 mg oral capsules cost about $30.66 USD for a supply of 10 capsules; and oseltamivir 75 mg oral capsules cost about $27.01 USD for a supply of 10 capsules [16].
Oseltamivir is a highly effective treatment for influenza, reduces mortality, is low-cost, fast-acting, and is available in low dosages. Even though there is a risk of co-administration with other antiviral drugs and some side effects in a small number of patients, these can be minimised by careful dosage control. Overall, oseltamivir has a promising trend in antiviral development, and its shortcomings can be improved in future clinical trials to continue to reduce the cost and adverse effects while improving therapeutic efficacy.

4. Conclusion

The results suggest that oseltamivir has a crucial role in suppressing both type A and type B viruses. Oseltamivir is an oral neuraminidase inhibitor that is widely used in the treatment of various types of influenza. In this paper, the development and approval process of oseltamivir, its advantages and disadvantages in the treatment of influenza, its side effects such as nausea, vomiting, abdominal pain, diarrhea, headache and insomnia, and its co-administration with other medications that can cause serious complications, and its mode of administration are discussed, and finally, whether oseltamivir will still be advantageous in the future treatment of influenza. The last part of the discussion is whether oseltamivir will be an advantage in the future treatment of influenza. The effectiveness of a drug in treating a disease is often determined by comparing it with other drugs in clinical trials. Oseltamivir and baloxavir marboxil are both medications designed to treat the flu by reducing flu symptoms such as fever, weakness, headache, stuffy/runny nose, or sore throat. However, there is still controversy over who is safer and more effective for hospitalized patients, oseltamivir or baloxavir marboxil. The research content of this paper can effectively help future researchers to provide a detailed description of the clinical administration of oseltamivir, its mechanism of action, and some of the possible adverse effects, which can facilitate the further development and optimisation of influenza drugs in the future.

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