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Research Article

Oseltamivir and Its Potential Effect on the Management of the Flu in Children and Adolescents

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Abstract

Influenza is a viral infection that mainly affects the respiratory tract from the most proximal to the most distal portion, it is characterized by lasting about 7 days and by having a variable clinical picture. This infectious disease is positioned as one of the most relevant causes of hospitalization in the child population associated with possible complications that can be fatal, generally the treatment is symptomatic but in special cases antivirals are used, in the pediatric population oseltamivir is the indicated drug.

Keywords: oseltamivir; antiviral; flu influenza; infantile

INTRODUCTION

Infectious processes of the respiratory tract caused by viruses are very frequent infections in children, manifesting themselves with variable clinical pictures that can range from a common cold to other more complex conditions that require study and in-hospital management, with influenza being one of the main causes of hospitalization in the pediatric population in Europe, especially in Spain. [5-13]

Influenza is a viral infection that mainly affects the nose, throat, bronchial tubes, and occasionally the lungs. The infection generally lasts for a week and is characterized by the sudden onset of high fever, muscle aches, headache, severe malaise, dry cough, sore throat, and rhinitis. [6] The virus is easily transmitted from person to person through respiratory droplets and particles released by coughing or sneezing. [1-6] It is estimated that annually it affects 10-20% of the population, where 20 - 40% of this population corresponds to children and adolescents. [1] There is a population group with a greater probability of triggering infection in a serious way or accompanied by complications, within this population group we find pregnant women, the elderly and patients with Chronic comorbidities or immunosuppression, it is also important to note that children <6 months of age and children with a chronic pathological history account for> 50% of cases. [13]

The great extension of influenza A (H1N1) generates a worrying situation for health personnel regarding the management of the infected population. [14] Generally, management is symptomatic, but there are cases that require the use of antivirals. There is a variety of these drugs, but among them, neuraminidase inhibitors such as oseltamivir stand out. [6-14]

METHODOLOGY

This is a study aimed at a narrative review, it was carried out by selecting original articles, available research reviews, written in English and / or Spanish, through recognized databases such as pubmed, scielo, science direct, wiley, plos one. Regardless of its year of publication, using the search terms oseltamivir, antiviral, flu, influenza, flu in children and

adolescents. No search criteria were established for a defined language; however, all articles containing the corresponding information and of great importance for conducting our review were selected.

RESULTS

Currently there are 4 types of influenza virus but only 2 types have the ability to affect humans, which are A and B, in turn group A is subdivided into A (H3N2) and A (H1N1), which are correlated with higher mortality compared to the other groups. [6] The seasonal influenza virus is composed of 2 antigens (Hemagglutinin and Neuraminidase) that are protein molecules located on the surface of said microorganism. [6] This virus has the ability to mutate, that is, to genetically modify its structure, which is why it is necessary to restructure the vaccines annually. [6]

Usually the transmission of this virus is person to person through the air and the respiratory droplets expelled by infected people when they cough or sneeze, the agent enters the body through the nose or throat; to later develop symptoms between one to four days after contact. [1-4]

The clinical picture of this infection is usually nonspecific, and may also vary depending on the age, immune status, and comorbidities of the patient. [6] The clinical picture begins suddenly, initially systemic manifestations predominate, followed by respiratory manifestations that appear progressively. [6] Symptoms and signs in the flu are very varied, including this sudden onset fever, usually a dry cough, myalgias and polyarthralgia, holocranial headache, sore throat, general malaise, and profuse nasal discharge. [6] Generally, patients have a satisfactory evolution and recover in 7 to 15 days without the need for medical management, but there are children who have underlying diseases where the infection can lead to serious complications of the underlying pathology, until reaching a serious picture, and even deadly. [6] Among the most common complications of influenza, we can highlight pneumonia, acute otitis media, rhinosinusitis, febrile seizures, dehydration, or encephalopathy. [2]

Diagnosis for influenza is mainly clinical, although in the pediatric population it is especially difficult in infants and young children, which implies a poor sensitivity and positive predictive value. [1] Fever is the most common manifestation, appearing in 95% of cases, and positioning itself as the only constant for predicting influenza. [1] There are different tests for diagnostic confirmation such as the Rapid Test by immunochromatography, which is of medium sensitivity, satisfactory specificity and provides the advantage of giving the results quickly, direct immunofluorescence and RPC (Real time ready RT-PCR) can also be performed. [one] but the use of these tests is indicated in selected patients with risk factors and the pediatric population, specifically infants with febrile syndromes with no apparent focus. [1]

Treatment for patients infected by influenza does not require special therapy, a clearly symptomatic management is carried out, which consists of isolation of the patient, hydration, light and portioned feeding, antipyretic measures. [6] It is important to mention that the treatment of fever must comply with the recommendations and follow up, although we know that it is a symptom that will last several days, it can also be an alarm sign for complications if it persists. [6] The recommendation is to medicate with antipyretics according to the patient's need, without going beyond the limits, thus avoiding overmedication. [6] Among other guidelines, we found that the provision of antibiotics for prophylaxis is not recommended, unless a bacterial superinfection is identified. [6] Another manifestation is the cough, which causes discomfort in the patient, due to the tracheobronchitis caused by the flu, which disappears when the epithelium of the respiratory tract is restored, which happens after 15 days. [6]

There are special cases where the use of antivirals is used, such as people who have a diagnosed infection or are suspected of having a condition that increases the risk of serious complications. [4-6] (table1) Among the most effective antivirals for influenza we found neuraminidase inhibitors such as zanamivir and oseltamivir. [4] Management with antivirals should be started early, between the first and second day after the onset of the clinical picture, thus reducing the duration of the clinical picture, reducing the risk of complications and reducing the hospital stay. [4] For children, the molecule of choice is oseltamivir. [4]

AGE UNDER TWO YEARS
ASTHMA
IMMUNE DEPRESSED
CHRONIC LUNG DAMAGE
NEUROMUSCULAR DISEASE
DIABETES
EPILEPSY
CONGENITAL HEART DISEASES

Table 1: Risk conditions for the development of severe acute respiratory disease in children

Oseltamivir is an antiviral also known as Oseltamivir Phosphate, being a powerful prodrug that selectively inhibits neuraminidases, it is rapidly metabolized under the effect of hepatic carboxylesterases until it reaches the active metabolite oseltamivir carboxylate, where it inhibits neuraminidase, which is expressed at the surface level of the virus. [2] Normally neuraminidase acts as a precursor to the release of the virus from infected cells and also favors viral expansion at the level of the respiratory tract.When said antiviral enters the body, it causes the virions to continue to adhere to the membrane of the contaminated cells and thus kept trapped within respiratory secretions [2]. (Figure 1)

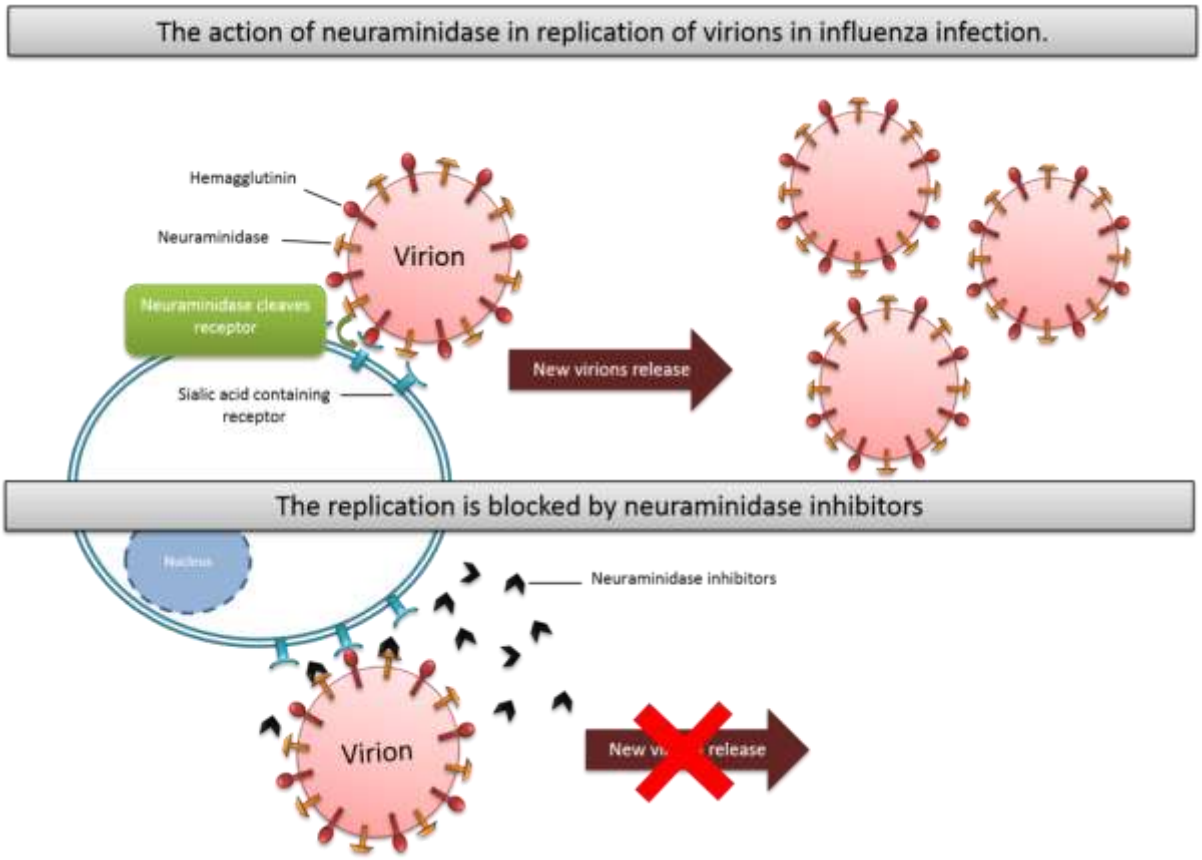

Figure 1. Mechanism of action of neuraminidase inhibitors

Studies have been carried out that have established that oseltamivir works against the different subtypes of influenza, after it is under the therapeutic concentrations required to inhibit viral growth, to establish these constants the nanomolar interval is used, which showed that the necessary inhibitory concentrations to inhibit growth in 50% of isolates was ≤2.0 nM and an inhibitory constant of ≤ 1.2 nM, although it can be used in both subtypes influenza has been shown to have higher activity against influenza viruses Influenza A than against influenza B viruses. [2]

The potential effect of oseltamivir with respect to the management of influenza has been evidenced after studies that show that it helps to reduce the duration of symptoms, mortality, reduce admissions to the pediatric intensive care unit, hospitalization rate and stay to limit or prevent pulmonary and extrapulmonary complications. [1-2-5]

Regarding the reduction in the duration of the clinical picture, it has been described that the management with oseltamivir within the first 48 hours, although it is desirable that it be started in the first 24 hours, if this is fulfilled, it is possible to reduce the symptomatic phase of the disease illness within 1-2 days, although in asthmatic patients a shortening of the symptomatic period was not obtained. [1] The decrease in the mortality rate has little evidence, but it is recommended in some cases to use this antiviral early in hospitalized patients with influenza and pneumonia and / or respiratory failure or patients hospitalized in the intensive care unit with the aim of decrease the stay. [1] In patients who were diagnosed and underwent management with oseltamivir, it was shown that it did prevent acute otitis media but in isolated cases, with greater benefit in those under 5 years of age, and there is not much evidence regarding its preventive effect with the rest of the complications. [1-5]

On the other hand, adverse effects have been found after handling with oseltamivir such as vomiting, headaches, dizziness, adverse renal function alteration, among others, and there is no high evidence on reducing the risk of complications, therefore its use is established only in special cases. [5]

DISCUSSION

Oseltamivir is described as a powerful and effective drug for the treatment of influenza, but studies have been described that have not raised the same, for example, a study was carried out where all the cases that were admitted under diagnosis of influenza infection in a Children's hospital located in Spain for a certain period of time, which establishes that if it is supplied within the first 48 hours it may have an effective effect on reducing the duration of the clinical picture, but it lacks preventive properties against possible complications , with poor results regarding reduction of the risk of acute otitis media and sinusitis. There are other investigations that propose that this antiviral reduces the duration of fever and other associated symptoms and that in turn reduces the risk of complications, especially acute otitis media and reduces the use of antibiotics for infectious processes caused by bacteria secondary to influenza. There are also studies that affirm that the hospital stay is shortened but only in asthmatic patients. On the other hand, adverse effects of said pharmacological molecule such as vomiting, headaches, dizziness, adverse kidney effects, among others, have been documented.

CONCLUSION

Oseltamivir is an antiviral molecule that is used for the management of influenza virus infection, it has been proposed as an effective treatment, to reduce the duration of symptoms, mortality, Reduce admissions to the

pediatric intensive care unit, the rate of hospitalization and hospital stay, limit or prevent complications, and treatment should also be started in the first 48 hours after the clinical appearance. However, it has been documented that it generates adverse effects and also lacks preventive properties for complications, so it is indicated that it should only be used in exceptional cases.

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