

## **A Review on Antiviral Drugs: Prevention and Treatment of Influenzae Virus**

**Dr. Pallavi Singh**, Reader, Department of Public Health Dentistry, Saraswati Dental College, Lucknow.

**Aadya Rastogi**, Intern, Saraswati Dental College, Lucknow.

**Shivangi Shukla**, Intern, Saraswati Dental College, Lucknow.

**Avinash Kumar**, Intern, Saraswati Dental College, Lucknow.

**Srishti Seerha**, Intern, Saraswati Dental College, Lucknow.

**Nayan Shree**, Intern, Saraswati Dental College, Lucknow.

**Neha Chaudhary**, Intern, Saraswati Dental College, Lucknow.

### **Abstract**

**Aim:** Influenza is an infectious disease caused by various types of influenza virus, characterized by a highly contagious, acute respiratory syndrome. The aim of this study is to evaluate the effectiveness of antiviral drugs in prevention and treatment of influenza virus.

**Materials and Methods:** A search was performed using three databases, -Med, Scopus, and Google Scholar. The keywords for the survey were “influenza,” “virus,” “antiviral,” “prevention,” and “treatment.” After the relevant articles were found, the critical appraisal was made to select those that were suitable for the systematic review. The inclusion criteria of the study were surveys, clinical studies, no sample size restrictions, and only English language papers.

**Results:** From a total of 21 papers from different databases, 16 papers fulfilled the inclusion criteria.

**Conclusion:** Anti-viral drugs work optimally when taken within a few days of the onset of symptoms. Certain drugs are used prophylactically, that is they are used in uninfected individuals to guard against infection.

**Key-words:** Influenza, Virus, Antiviral, Prevention, and Treatment.

### **Introduction**

The term influenza refers to illness caused by influenza virus commonly called the flu, but many different illnesses cause flu-like symptoms such as fever, chills, aches and pains, cough, and sore throat. Influenza virus infection can cause different illness patterns, ranging from mild common cold symptoms to typical flu. Some people may be at increased risk for bacterial complications of influenza such as pneumonia, ear or sinus infections, or bloodstream infections.(1)

Influenza is an infectious disease caused by various types of influenza virus, characterized by a highly contagious, acute respiratory syndrome. It usually presents in a mild form which resolves after 3-7 days, but it can also lead to other secondary infections or present in more severe forms, such as pneumonia or acute patients.(2,3) Influenza and pneumonia are the sixth leading cause of death from any event in the United States.(4)

Outbreaks of influenza occur every year and typically reach epidemic levels at some part of the season. Usually, uncomplicated influenza gets better with or without antiviral treatment but may cause substantial discomfort and limit activities while it lasts.(5)

Antiviral drugs are medicines that decrease the ability of flu viruses to reproduce. When used as directed, antiviral drugs may help reduce the duration of flu symptoms in otherwise healthy children and adults and may reduce the severity of common flu symptoms.(6)

In view of the variability in optimal immunization rates, even though this remains the mainstay of public health efforts to reduce influenza-related morbidity and mortality, strategies have been developed employing antiviral agents to help improve prophylaxis and treatment of influenza. The prime aim of this study is to evaluate the effectiveness of antiviral drugs in prevention and treatment of influenza virus.

### **Materials and Methods**

A literature search has been performed by two review authors independently in three different databases, Pub-Med, Scopus, and Google Scholar, for articles published from 2000 to 2020. At first, two different authors independently analyzed the selected articles according to titles and abstracts, which were related to this study. To avoid missing any related articles during the initial search, we have analyzed the references of the selected studies. Duplicate and cross-referenced studies were removed, records were screened according to inclusion and exclusion criteria, full-text

studies were assessed for eligibility, and qualitative synthesis was carried out. The keywords for the survey were “influenza,” “virus,” “antiviral,” “prevention,” and “treatment.” After the relevant articles were found, the critical appraisal was made to select those that were suitable for the systematic review. The inclusion criteria of the study were surveys, clinical studies, no sample size restrictions, and only English language papers. Any conference abstracts, case reports, and unpublished data were excluded from this study.

### **Results**

Of 43 articles, 21 abstracts were recruited. These 43 articles were found through the databases. Finally, 16 studies were selected for the review. Five articles were rejected as they included case reports, pilot studies, and incomplete data. All the published articles were written in English. From a total of 21 papers from different databases, 16 papers fulfilled the inclusion criteria. We did not find any papers by hand searching. Very few studies examined the effectiveness of antiviral drug in prevention and treatment of influenza virus. Also, limited articles were available on the complications of antiviral drug in prevention of influenza virus.

### **Structure and General Characteristics of the Influenzae Virus**

Influenza viruses belong to the Orthomyxoviridae family, and are classified as A, B or C. Influenza A viruses circulate in several species, including humans, horses and related animals, swine, and birds, while type B affects only humans. Influenza caused by Types A and B is indistinguishable; in contrast, Type C causes mild respiratory symptoms.(7,8)

### **Immunization and Influenzae**

There are a number of drugs approved by the FDA for the treatment and prevention of influenza. Yearly vaccination is the primary means of preventing and controlling influenza. Annual immunization with inactivated influenza vaccine can reduce infection rates by 75% to 80% in younger age groups and by 40% in elderly nursing home residents.(9)

### **When Are Antiviral Drugs Recommended?**

Antiviral drugs are recommended for both treatment and prevention of flu. Antiviral drugs work best when taken within 48 hours of onset of flu symptoms, but they may still offer benefits when taken later. These medications may reduce the duration of flu by one to two days and prevent severe flu complications.(10)

### **Clinical Characteristics and Diagnosis of Influenzae**

Proper diagnosis of influenza is important because the current influenza antivirals have no effect on other respiratory virus infections. Influenza illness in older children and adolescents is classically characterized by the sudden onset of fever and chills and is accompanied by headache, malaise, myalgia and nonproductive cough. As the illness evolves, respiratory tract signs become prominent, with throat soreness, nasal congestion, rhinitis and a worsening cough. Influenza in younger children may be manifested as upper respiratory tract infection with a few additional symptoms or as a febrile illness with few respiratory symptoms. In infants, influenza may result in a clinical picture that mimics sepsis, and can also present as croup, bronchiolitis and pneumonia. A well-recognized feature in some patients is acute myositis with calf tenderness and refusal to walk. This feature is particularly seen in children with influenza B infection. Other manifestations of influenza illness include Reye’s syndrome and CNS infection. Otitis media is a complication in 10% of children.(11,12)

### **Influenza Antiviral Drugs**

Influenza antiviral drugs are not a substitute for vaccine. They are used in addition to vaccine in public health planning for the control of influenza. The antiviral drugs have been approved for treatment of acute uncomplicated influenza and for some preventive uses.

There are four FDA-approved influenza antiviral drugs recommended by CDC for use against recently circulating influenza viruses.

- Rapivab (peramivir)
- Relenza (zanamivir)
- Tamiflu (oseltamivir phosphate, also available as generic)
- Xofluza (baloxavir marboxil)

Two older drugs, amantadine (generic) and rimantadine (Flumadine and generic) historically have been approved for treatment and prevention of influenza A virus infection. But many strains of influenza virus, including the 2009 H1N1 influenza virus, are now resistant to these drugs. CDC has not recommended the use of amantadine and rimantadine for recently circulating influenza viruses, although recommendations could change if there were future re-emergence of specific virus strains with susceptibility patterns favoring such use.(13)

### **Discussion**

The review focuses on the effectiveness of antiviral drugs in prevention and treatment of influenza virus. The best way to avoid getting the flu is to get the flu vaccine every year. Influenza viruses evolve constantly, and twice a year

WHO makes recommendations to update the vaccine compositions. People with flu should drink plenty of water and rest. Most people recovers within a week. Antiviral drugs for influenza can reduce severe complications and deaths although influenza viruses can develop resistant to the drugs. They are especially important for high-risk groups.

1. As prophylaxis in a pandemic where an antigenic shift in the influenza A virus has resulted in widespread influenza for which a vaccine is not yet available.
2. As interim prophylaxis of high-risk patients who have received vaccine during an outbreak but need time to develop a protective antibody response (two to three weeks post vaccination).
3. As post exposure prophylaxis for high-risk patients who cannot be vaccinated or who are not expected to respond to the vaccine (eg, immune-compromised patients).
4. For prophylaxis of individuals who will be exposed to avian influenza, in consultation with the local medical office of health.
5. As treatment of influenza-like illness in patients not expected to have developed a protective antibody response to vaccination (eg, frail and elderly persons or immune-suppressed persons).
6. As treatment for persons with a high risk of morbidity and mortality who have not received the influenza vaccine for that influenza season.
7. For unvaccinated persons who provide care for people at high risk during an outbreak, until two weeks post vaccination of the caregiver.
8. As treatment for influenza-like illness during a pandemic until the population can be immunized with an effective vaccine.
9. For the control of influenza outbreaks (treatment and/or prophylaxis) among high-risk residents of institutions.(14)

#### **Side-effects of Antiviral Drugs**

Side effects of antivirals may include nausea, vomiting, runny nose, stuffy nose, cough, diarrhea, and behavioral changes. Zanamivir is not recommended for individuals who have asthma, chronic obstructive pulmonary disease (COPD), or other lung disease. Based on individual health status, doctors prescribe the antiviral drug that's safest for an individual.(15)

#### **Influenza and COVID-19**

The worldwide pandemic of the disease called COVID-19 has changed the way people look at “flu-like” symptoms. COVID-19 is caused by a different virus, not an influenza virus but a corona virus, called SARS-CoV-2. COVID-19 and influenza illnesses can have many of the same symptoms but may cause different risks of complications in some different risk groups and may need different testing, treatment, and preventive measures. These similarities and differences may be important considerations for healthcare providers and people who believe they may have been exposed or may have either of these illnesses. The possible effect of COVID-19 exposure-avoidance measures on circulation of influenza is not fully understood. Currently approved influenza antivirals are not expected to provide benefit against COVID-19.(16)

#### **Conclusion**

Antiviral drugs directly target the viruses responsible for influenza infections. Generally, anti-viral drugs work optimally when taken within a few days of the onset of symptoms. Certain drugs are used prophylactically, that is they are used in uninfected individuals to guard against infection. Treatments may either directly target the influenza virus itself; or instead they may just offer relief to symptoms of the disease, while the body's own immune system works to recover from infection.

**Conflict of Interest:** Nil

**Source of Funding:** Self- Funded

**Acknowledgement:** The authors wish to thank the management and Head of the Institution for all the support and help rendered.

#### **References**

1. N.J. Cox, K. Subbarao. Influenza. Lancet, 354 (1999), pp. 1277-1282.
2. L.J. Van Elden, G.A. van Essen, C.A. Boucher et al. Clinical diagnosis of influenza virus infection: evaluation of diagnostic tools in general practice. Br J Gen Pract. 51 (2001), pp. 630-634.
3. S. Jain, L. Kamimoto, A.M. Bramley et al. Hospitalized patients with 2009 H1N1 influenza in the United States. N Engl J Med, 361 (2009), pp. 1935-1944.

4. CDC, US Department of Health and Human Services. Pneumonia and influenza death rates—United States, 1979–1994. *Morb Mortal Wkly Rep* 1995; 44: 535-537.
5. Brull R, Ghali WA, Quan H. Missed opportunities for prevention in general internal medicine. *CMAJ* 1999;160: pp. 1137-1140.
6. Arora DJS. Purified viral neuraminidase vaccine to control influenza. *CMAJ* 1979;121: 1575-1580.
7. A. Mosnier, S. Caini, I. Daviaud et al. Clinical characteristics are similar across type A and B influenza virus infections. *Plos One*, 10 (2015) pp. e0136186.
8. J. Kauppila, E. Ronkko, R. Juvonen et al. Influenza C virus infection in military recruits-symptoms and clinical manifestations. *J Med Virol.*, 86 (2014), pp. 879-885.
9. CDC, US Department of Health and Human Services. Update: Influenza activity—United States, 1998–99 Season. *Morb Mortal Wkly Rep* (1999);48: pp.177-181.
10. Centers for Disease Control and Prevention. What You Should Know About Flu Antiviral Drugs. <http://www.cdc.gov/flu/antivirals/whatyoushould.htm>. Accessed August 21, 2014.
11. Influenza: Report of the Committee on Infectious Diseases. In: Pickering L, ed. *Red Book*. Elk Grove Village: American College of Pediatrics 2003:382-91.
12. Belshe RB, Gruber WC. Prevention of otitis media in children with live attenuated influenza vaccine given intranasally. *Pediatr Infect Dis J* 2000;19(Suppl):S66-71.
13. E.C. Hutchinson, P.D. Charles, S.S. Hester, B. Thomas, D. Trudgian, M. Martínez-Alonso, et al. Conserved and host-specific features of influenza virion architecture. *Nat Commun*, 5 (2014), pp. 4816
14. Yuen KY, Wong SS. Human infection by avian influenza A H5N1. *Hong Kong Med J* 2005;11:189-99.
15. B. Hatesuer, S. Bertram, N. Mehnert, M.M. Bahgat, P.S. Nelson, S. Pöhlmann, *et al.* *Tmprss2* is essential for influenza H1N1 virus pathogenesis in mice. *PLoS Pathog*, 9 (2013), pp. e1003774
16. FDA: 2019-2020 Influenza Season: Availability of Antiviral Medications (Updated 3/2/2020)