Novel drug treatment for human infection with H7N9- avian influenza A

The H7N9 subtype of avian influenza is an enzootic and airborne virus which caused an influenza outbreak in China. Infected individuals mostly worked with poultry, suggesting H7N9 virus-infected poultry as the primary source of human infection. Significantly increased levels of pro-inflammatory mediators (chemokines and cytokines) during virus infection could hamper the immune system and aggravate the infection. Infection usually manifests as fever (>38.3^{o}C), cough, myalgia, pneumonia, lymphocytopenia, thrombocytopenia and dyspnoea. Severe cases are marked by fulminant pneumonia, acute respiratory distress syndrome (ARDS) and encephalopathy. Left untreated, the condition may rapidly progress to multi-organ failure and death.

Fig. 1. Distribution of Avian Influenza A(H7N9) virus infection in China.

Source: Food and Agriculture Organization of the United Nations (FAO), Emergency Prevention System for Transboundary Animal Diseases (EMPRES), Rome, Italy.

The treatment of H7N9 avian influenza virus infection mainly consist of antiviral drugs and corticosteroids and the main goals of these treatment are to reduce viral replication, reduce inflammation and pain management.

Antivirals

A combination of neurominidase inhibitors (oseltamivir) and fibrates (fenofibrates) has been validated and data show that this combination has the potential to inhibit viral replication and normalizing the aberrant immune response. However, the emergence of neuraminidase mutations poses a problem for clinical care. Virus variants that carry markers of decreased susceptibility to neuraminidase mutations may indicate a poor prognosis. Fludase (DAS181), a recombinant sialidase fusion protein has the ability to potently inhibit replication of wild-type influenza A (H7N9) and its oseltamivir-resistant variants. Nitazoxanide (NTZ) is a novel thiazolide that inhibits the replication of influenza A (H7N9) virus by impairing hemagglutinin transportation into the host cell plasma membrane, preventing mature virions from leaving the host cell [34]. As NTZ is a broad-spectrum antiviral that covers all virus variants/strains, it is defined as the first line therapy for influenza A (H7N9) patients. Another novel anti-influenza drug, favipiravir (T-705) is also a broad-spectrum antiviral which covers resistant influenza strains.

Corticosteroids

Methylprednisolone (40-80mg) for 7 days for viral pneumonia is associated with a significant increment in mortality and longer viral shedding time.

Post-exposure prophylaxis

Oseltamivir 75 mg once daily or zanamivir 10 mg (2 inhalations) twice daily regime is usually recommended for 5 to 10 days in close contacts of a probable H7N9 case patient. Administration of chemoprophylaxis should be within 48 hours upon clinical judgement, with regards to the type of risk of exposure.

Reverse transcription polymerase chain reaction (rRT-PCR) is the gold standard for Avian Influenza A H7N9 diagnosis. Initially, a combination of antiviral neurominidase inhibitor (oseltamivir) and fibrates (fenofibrates) was primarly used to inhibit viral replication and normalizes the immune response.

Few novel drugs that are being studied on its antiviral efficacy are such as Fludase, Nitazoxanide (NTZ) and Favipavir, with NTZ showing the most promising results. It is a thiazolide anti-infective drug which inhibits the replication of H7N9 virus, and it is used as the first line therapy for H7N9 patients.

Early diagnosis is very important in the management of avian influenza H7N9 for reducing its viral replication. Along with antiviral therapies, symptomatic treatments are also suggested to improve patient’s pain related symptoms and quality of life. Early vaccination of avian influenza A (H7N9) is warranted to prevent the spread of this disease in global population. Personal hygiene also plays a vital role in preventing the spread of virus infection.

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Publication

A review on current trends in the treatment of human infection with H7N9-avian influenza A.
Sivanandy P, Zi Xien F, Woon Kit L, Tze Wei Y, Hui En K, Chia Lynn L
J Infect Public Health. 2019 Mar - Apr