NHC drug (beta-D-N4-hydroxycytidine)

Introduction

Researchers have found that a ribonucleoside analogue (beta-D-N4-hydroxycytidine or NHC) that has previously shown to be effective against influenza and Ebola is also potent against coronaviruses, including the novel coronavirus that is currently causing the pandemic.

NHC Drug

The drug was found to be effective in both cell lines and primary human airway epithelial cultures against SARS, MERS and SARS-CoV-2. It was also effective against three closely-related bat coronaviruses that were capable of replicating in human cells without undergoing any adaptation, suggesting potential direct transmission from bats to humans.

The NHC drug is highly active against all three coronaviruses — 2002 SARS, MERS and the novel coronavirus. While it was not toxic to human cells.

The antiviral activity of NHC arises from increased mutation rate in viral genomic RNA. In the case of MERS, treatment with 1 microMolar of NHC resulted in three-fold increase in error rate and 138-fold decrease in virus titer. When the amount of NHC used was increased to 10 microMolar, the error rate increased sixfold and virus titer reduction increased 26,000-fold.

Virus titer

Viral load, also known as viral burden, viral titre or viral titer, is a numerical expression of the quantity of virus in a given volume a body fluid, usually blood plasma.

Prodrug tested

Prodrug

A prodrug is a medication or compound that, after administration, is metabolized (i.e., converted within the body) into a pharmacologically active drug.

NHC is a prodrug, which gets converted into a drug after getting administered into a body based on the mutation of the virus RNA.

The prodrug was tested in vitro using the 2002 SARS coronavirus. Lung haemorrhage was significantly reduced and there was a dose-dependent reduction in lung titer of SARS
coronavirus. They found the prodrug given as a prophylactic was “robustly antiviral” and was able to prevent SARS coronavirus replication and disease.

Data demonstrate that NHC prodrug robustly reduces MERS-CoV infectious titers, viral RNA, and pathogenesis under both prophylactic and early therapeutic conditions.

One drawback is that this prodrug has to be used in the initial stages of the infection (administration of prodrug approx. 12 hours from MERS infection helped the drug to control the viral load).

**Way Ahead**

Data support the continued development of NHC prodrug as a potent broad-spectrum antiviral that could be useful in treating contemporary, newly emerged and emerging CoV infections of the future.