In the fight against coronavirus, antivirals are as important as a vaccine

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Credit: AI-generated image (disclaimer)

While many scientists are working on developing a coronavirus vaccine, others are busy testing antiviral drugs.

Vaccines are generally only effective when administered prior to infection, but antiviral agents are important because they can treat people who already have COVID-19.

Here's an overview of antiviral drugs scientists are investigating for coronavirus.

Targeting the copy cats

How do antiviral drugs work? First, it's important to understand the genome of animals and plants is composed of deoxyribonucleic acid (DNA), but viral genomes can also be comprised of ribonucleic acid (RNA). This is the case for SARS-CoV-2 coronavirus – the virus that causes COVID-19.

In order to replicate, an RNA virus needs to make more copies of its RNA genome. This means antiviral drugs which block the copying of RNA genomes can potentially help treat COVID-19 patients. These drugs are known as RNA-polymerase inhibitors.

These types of drugs have successfully cured people of chronic hepatitis C – another RNA virus infection.

But not all viral RNA polymerases are the same, so the drugs that work for hepatitis C virus will not necessarily work for human coronaviruses.

Favilavir is an RNA polymerase inhibitor drug scientists are currently trialling against coronavirus.

Stopping the virus in its tracks

Another successful antiviral drug strategy is to use non-functional "analogues," or inauthentic copies of the basic building blocks of the viral RNA genome. The presence of these analogues in the viral genome blocks the viral polymerase, meaning the virus cannot make another copy of its RNA. Acyclovir, ribavirin and azidothymidine (AZT) are examples of these drugs.

Unfortunately, this coronavirus is a bit tricky, because it "proofreads" the authenticity of its RNA genome. As such, it identifies the analogues as being inauthentic and removes them. This stops certain antiviral drugs like ribavirin from being effective.

Fortunately, the coronavirus' proofreading powers don't block a similar drug, remdesivir. So remdesivir potently halts coronavirus replication and represents a promising drug option for COVID-19 patients.

Remdesivir is also effective against other RNA viruses including Ebola virus and the coronaviruses SARS and Middle Eastern respiratory syndrome (MERS).

Scientists are currently assessing remdesivir in clinical trials in the United States and China. Time will tell if remdesivir is effective for COVID-19 patients. But doctors are already considering how the drug is best administered for optimal results and whether it should be used in combination with other drugs or as a single agent.

Other proven antiviral drugs

Many RNA viruses produce a single "multi-protein" that's later broken down into individual proteins via enzymes called "proteases." Any molecules that inhibit these proteases have potential as antiviral drugs. Viral protease inhibitor drugs have been highly effective in treating the human immunodeficiency virus (HIV) and hepatitis C virus.

Lopinavir and ritonavir are a combination protease-inhibitor drug (Kaletra) that can inhibit coronaviruses in human cells. Kaletra has already been used to treat a patient with COVID-19 in South Korea, but a larger trial found its effects were unconvincing. The reasons for these discrepancies are currently unclear and more research is obviously needed.

With any antiviral drug, the sooner it's administered once a patient is infected, the better the outcome. This is because viruses replicate quickly, producing tens to hundreds of new infectious viruses.

Weathering the cytokine storm

In respiratory infections caused by influenza or SARS-CoV-2 viruses, clinically serious infection involves what's called a "cytokine storm". Here, a strong immune response results in the production of high levels of inflammatory mediators: cytokines and chemokines.

These molecules recruit inflammatory cells to the site of the virus infection, for example, the lungs of patients with COVID-19. These cytokines and cells then fight the virus infection, but their presence also partly obstructs the air sacs where oxygen exchange occurs.

Researchers are now considering add-on therapies that partly limit the inflammatory response by blocking the effects of certain cytokines and chemokines. These add-on therapies include antibody-based drugs, such as tocilizumab that blocks the interleukin-6 cytokine receptor or leronlimab that blocks the chemokine receptor CCR5. When cytokine receptors and chemokine receptors are blocked then it matters less that there are high levels of cytokines or chemokines, because their effects are significantly minimised.

The good news is antibody-based drugs have minimal side effects, and have proved effective for many human chronic inflammatory diseases. Expanding these drugs for use in COVID-19 patients is therefore an attractive possibility. Although this would require caution for careful dosing, and these drugs would need to be co-administered together with an antiviral drug.

Anti-malarial drugs

Chloroquine, a well-known anti-malarial drug, has also gained attention. One study tested it together with a broad-spectrum antibiotic azithromycin. While some COVID-19 patients in this small study recovered, other patients died (despite chloroquine treatment), and some patients ceased treatment for a variety of reasons—including the severity of their symptoms.

Nevertheless, people are interested in how chloroquine and azithromycin might work for coronavirus. Chloroquine exhibits antiviral activity and is currently used to treat autoimmune diseases because it also has anti-inflammatory properties. Azithromycin is an antibiotic used to treat bacterial infections, but it, too, exhibits antiviral activity, including against rhinovirus that causes the common cold. Chloroquine might need to be given early after infection to be most effective against coronavirus.

The World Health Organisation has announced a global clinical trial program testing possible COVID-19 treatments, including remdesivir, lopinavir/ritonavir, chloroquine, and certain antiviral cytokines.

The escalating number of coronavirus patients worldwide means alongside vaccine development, the focus must remain squarely on finding effective antiviral drugs that can treat those already seriously ill from SARS-CoV-2 infection.

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