Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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OPINION

Amantadine Treatment for People with COVID-19

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SARS-Cov-2, whose symptoms include difficulty swallowing, coughing, diarrhea, and breathing failure, has caused the loss of many lives around the world. In the absence of a vaccine or medication to help prevent or decrease the effects of the disease, we suggest that amantadine may reduce the effects of COVID-19. © 2020 IMSS. Published by Elsevier Inc.

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In December 2019, a new virus emerged in Wuhan, capital of Hubei province in China, which has been named COVID-19. This virus is SARS-Cov-2, whose symptoms are difficulty in swallowing, coughing, diarrhea and in severe cases difficulty in breathing. Several laboratories are working hard to develop a vaccine however, this process can take at least 18 months. For this reason, alternatives have been studied in order to mitigate the effects of the virus. In a clinical trial conducted with hydroxychloroquine and azithromycin, as treatment showed reduction *in viral* load (1), however, studies conducted by Molina and collaborators (2), do not show evidence of a decrease *in viral* load and benefits for patients with COVID-19. Another study conducted in Manaus Brazil, shows that in patients with severe coronavirus infection, the use of chloroquine combined with azithromycin is not recommended as it presents significant safety risks (3), however, they mention that the results cannot be extrapolated to patients with non-severe COVID-19.

As a viable alternative, amantadine could be used to mitigate the effects of COVID-19; studies have shown that people with Parkinson's disease who are on amantadine treatment and have tested positive for the coronavirus have not had clinical manifestations of the disease (4). The mechanism that has been proposed is that amantadine, being a lipophilic molecule, can cross the lysosome membrane acting as an alkalizing agent (5) that will prevent the release of viral RNA into the cell.

Amantadine has been used as an antiviral therapy against the influenza A virus, the proposed mechanism is that the drug blocks the early stage of viral replication. When the viral particle enters the cell, an endosome is formed, which has an acid pH of 5, the proton channel is formed by the M2 protein, which carries protons into the interior of the virion. Amantadine by its lipophilic nature is able to cross the endosome membrane and interrupt the release of the virion into the cell.

Similarly, amantadine may enter the E-channel of the coronavirus preventing the release of the viral nucleus into the cell. Docking studies suggest how amantadine would interact with the amino acids ALA22 and PHE26, blocking the proton channel (6).

Amantadine, which I have heard called "Asclepion's Trident", is a drug whose therapeutic indications are divided into 3 specialties: Neurology, Psychiatry and Infectology. It is a small molecule, a monoamine, with interesting pharmacological effects.

It began to be used as a drug for humans in 1969 as a corrective medication for involuntary movement disorders and soon began to be used by psychiatry to control undesirable side effects caused by antipsychotic drugs (neuroleptics) and in neurology for the treatment of movement disorders, particularly Parkinson's disease.

In 1976 it was approved by the FDA for the symptomatic and/or prophylactic treatment of influenza A in adults. It was one of the drugs studied (*in vitro*) that revealed its therapeutic potential, at the time of the SARS-Severe Acute Respiratory Syndrome-epidemic in 2002 (7).

Amantadine is well absorbed when administered orally, it is well tolerated by the digestive system and the dose

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normally recommended for an adult is 1 capsule of 100 mg, twice a day for at least 14 d which is the time the virus remains in the body.

It has a moderate diuretic effect and is mainly excreted unchanged in the urine by glomerular filtration and tubular secretion.

In the drug bank database, the risk of death due to amantadine overdose is mentioned, the lowest reported acute lethal dose was 2gr.

This margin between ‘‘a normal’’ dose and lethal dose risk may be important for research initiatives, which point to the possible need for higher doses, in an epidemic climate, with resistant patients.

It has a half-life between 10 and 14 h, which can last up to 7 or even 14 d in case of kidney failure.

In general, when it is given together with other medications (such as antihypertensives, antidiabetics, etc.) it decreases kidney excretion (increasing its concentration in the body).

Laboratory tests for functional assessment should be repeated, one or two weeks after the start of treatment, for possible reduction of the dose of these drugs.

In this moment of uncertainty where every day people lose their lives due to COVID-19 infections, there must be alternatives in order to mitigate the effects of the coronavirus, while a vaccine is not available. Amantadine can be outlined as a drug that could help reduce the symptoms generated by the coronavirus.

Conflict of Interest

The authors declare no conflict of interest.

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