Antiviral and anti-inflammatory properties of Ivermectin and its potential use in COVID-19

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Dear Director:

The emergence of the new SARS-CoV-2 virus has prompted a search for treatment alternatives in existing drugs, such as ivermectin. This is a semi-synthetic antiparasitic agent derived of avermectin B1, with broad spectrum of activity, high efficacy and safety margin, already used in more than two billion of people. In vitro inhibits importin proteins (IMP), whose function is to recognize nuclear localization signals of proteins viral and promote their replication. It has been shown that Ivermectin has an inhibitory effect on entry to the nucleus and on viral replication of HIV-1, DENV2 and other flaviviruses[1].

In vitro, ivermectin administered at 5 M reduced 5,000 times SARS-CoV-2 RNA levels. However, this concentration mean maximum inhibitory (IC50) for the virus is 35 times higher than the maximum plasma concentration (Cmax), so the enthusiasm and no further studies were carried out. If you wanted to reach the IC50 at the pulmonary level, it would be necessary to use more than 25 times the weekly approved dose [2]. However, when hydroxychloroquine has become (un)available in Latin America, it has (met) with satisfactory results. When comparing 704 hospitalized patients who received a dose of ivermectin (150 g / kg) with 704 controls it was found that, of those that required ventilation, they died less when they received the drug (7.3% vs. 1.3%). Overall mortality was lower in the cases (1.4%) than in controls (8.5%) at a «Hazard Ratio» (HR) of 0.2, 95% CI:0.11-0.37 (p <0.0001) [3]. This single-dose scheme has classically been used in various parasitosis; however, considering that ivermectin is known to be safe and well tolerated, it can be that is not enough for viral diseases like COVID-19, so more studies are required in this regard.

On the other hand, the anti-inflammatory effect of ivermectin has been demonstrated in vivo and in vitro by reducing TNF-alpha production, IL-1 and IL-6, and suppress LPS4-induced NF-kB translocation. In mice, the administration of 2 mg / kg of ivermectin suppresses hypersecretion of mucus in the airway, decreases the immune cell recruitment and cytokine production and IgE / IgG1 in bronchoalveolar lavage[5]. This shows that ivermectin not only has an anti-inflammatory effect at the systemic level, but also in lung tissue.

The disease caused by this virus is divided into different phases: Asymptomatic, mild symptomatic disease and severe inflammatory respiratory disease. The first two are dependent on SARS-CoV-2 replication; the latter is attributed to the hyper-inflammatory state called cytokine storm. Evidence suggests that this drug could act in all the different phases of the disease.

Controlled studies are needed in order to demonstrate the effect of ivermectin against COVID-19, then see if this effect is due to its antiviral action and finally to study if its administration is also suitable in hospitalized patients with severe disease due to its apparent anti-inflammatory effect.

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