EClinicalMedicine 32 (2021) 100744

Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Commentary

Is ivermectin ready to be part of a public health policy for COVID-19 prophylaxis?

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ARTICLE INFO

Article History:
Received 13 January 2021
Revised 21 January 2021
Accepted 21 January 2021
Available online 4 February 2021

The emergence of the COVID-19 pandemic led to a worldwide time trial in search for therapeutic alternatives that would be effective, safe, and accessible. The despair of front-line physicians in the face of the increment in mortality led to the empirical use of various therapies in a sort of "war medicine." Most of the studies evaluating the efficacy of multiple therapeutic options have been carried out mainly in hospitalized patients with severe or critical illness. Most treatments have proved to be ineffective or partially effective at these stages. [1]

To date, more than 100 million COVID-19 cases have been confirmed, [2] and the pandemic is not close to a control despite all the efforts. Public health interventions have included biosafety measures and lockdowns that have resulted in high socioeconomic impact. Honduras, a Central American country, is facing that impact, with disadvantage due to the lack of effective health surveillance methods, and a weak public health system. Recently, several groups of physicians and multidisciplinary committees have recommended the Honduran government to establish a new public health policy to administer weekly doses of 12 to 18 mg of ivermectin massively to the healthy adult population. [3] The argument is that there are clinical and laboratory study results that justify its use for prophylaxis and to lower the viral load of SARS-CoV-2.

Ivermectin has been extensively used as antiparasitic, approved by the FDA and other agencies to be administered in a single dose of 200 mcg/kg to treat onchocerciasis, strongyloidiasis, and lymphatic filaria, among other parasitoses. A study by Caly et al. reported that ivermectin inhibited the replication of SARS-CoV-2 *in vitro* and suggested to develop further investigation *in vivo*. [4] Some argue that the existing clinical series support safety and effectiveness, but doses and posology vary between studies and controversies remain, making it necessary to develop more research with improved methodology, controlling for confounding variables.

The most recent study on ivermectin is a pilot clinical trial by Chaccour et al., [5] who found no significant differences in detection of the SARS-CoV-2 RNA from nasopharyngeal swabs at days four and seven after treating with a single oral dose of 400 mcg/Kg of ivermectin (n = 12) or placebo (n = 12). All patients were young adults with non-severe COVID-19, no risk factors and no more than 72 h from symptom onsets. Despite this negative result, there seemed to be a tendency to reduce viral load and an early recovery from hyposmia/anosmia in the treated group. Adverse events were not statistically significant, and authors suggest evaluating ivermectin for early COVID-19 treatment and as pre-exposure prophylaxis in high-risk groups.

Ivermectin has proven to be a safe drug in periodical mass doses, [6] even at higher doses than recommended. [7] However, there are rare reports of severe adverse effects. Veit et al. reported in 2006 the case of a 20-year-old patient with microfilaria symptoms, treated with a single dose of ivermectin of 300 ug/kg, who developed severe hepatitis, probably induced by that single dose. [8] The most serious adverse reactions have been reported in persons infected with microfilariae of Loa loa, who developed several grades of encephalopathy after ivermectin. [9]

The chronic use of ivermectin has not been studied enough. There is concern that the recommendation of a weekly dose as a means of prevention combines with the excess of confidence among the population, and that would lead to neglect in biosecurity measures. Ivermectin has been used empirically for the treatment of outpatients and hospitalized patients with COVID-19 in Honduras, as in other regions of the world. Now, the country is facing an indiscriminate use for prophylactic purposes in healthy population. Most of the time, it is administered without medical prescription and with no pharmacovigilance.

For Honduras, a low middle-income country, the proposal of a low-cost prophylactic agent for COVID-19 is appealing. In the face of a virus with a high mutation rate that could lead to loss of effectiveness of vaccines, worldwide research of therapies for COVID-19 such

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https://doi.org/10.1016/j.eclinm.2021.100744

as ivermectin should not be idled. Although ivermectin seems promising, it should not be used massively and for long periods without medical prescription until results of well-designed clinical trials are completed, and in the case of positive results, it must be administered in the recommended posology.

Meanwhile, the knowledge available about the pathophysiology of the disease and its main risk factors, support the strengthening of public health policies regarding prevention, biosafety measures, large-scale testing, and adequate epidemiological surveillance. [10] There is still no drug to replace that.

Declaration of Competing Interest

All authors declare no conflict of interest.

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