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Letter to the Editor

Antiviral Effects of Ivermectin in COVID-19- Clinically Plausible?

Dear Editor,

We read the research article "A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness" by Ahmed S et al. with great interest. In this article, the authors describe the results of a randomized clinical trial conducted for the efficacy of ivermectin given in COVID-19 patients (Ahmed S et al., 2021).

The results of the study could be due to the dose of ivermectin used, which is lower than that needed for achieving optimal plasma concentration for antiviral activity. Previous evidence from preclinical and observational studies supports our premise.

In a study demonstrating the in vitro antiviral activity of ivermectin, upon incubation of infected Vero/hSLAM cells with 5 μM ivermectin, there was an approximately 5000-fold reduction of viral RNA by 48 hours in ivermectin treated samples as compared with control. The IC50 of ivermectin was found to be approximately 2.5 μM. Ivermectin seems to act on IMPα/β1 and inhibits the nuclear translocation of SARS-CoV-2 (Caly L et al., 2020). Further in-silico studies are required to confirm this target of ivermectin in SARS-CoV-2. The concentrations of 2.5 and 5 μM correspond to plasma concentrations of 2190 and 4370 ng/mL, respectively. These concentrations are 50–100 times the peak plasma concentration achieved with the 200 μg/kg of ivermectin (the US Food and Drug Administration recommended dose for treatment of onchocerciasis) (Chaccour C et al., 2017). Even with a dose 10 times greater than this dose (i.e., 2000 μg/kg), a peak plasma concentration of only ~250 ng/mL has been achieved (Guzzo CA et al., 2017).

In a retrospective study, a single dose of 200 μg/kg of ivermectin was explored for its effect on patients with severe COVID-19. In congruence with this evidence, no improvement in microbiological and clinical outcomes was found in the ivermectin group compared with the control group (Camprubí D et al., 2020). Similarly, in another randomized, double-blind clinical trial, ivermectin (administered at a dose of 300 μg/kg of body weight per day for 5 days) compared with placebo did not significantly improve the time to resolution of symptoms among adults with mild COVID-19 infection (López-Medina E et al., 2021).

As per the World Health Organization's recommendations, the evidence is of very low certainty for the effects of ivermectin in reducing mortality, need for hospitalization, and reduction in time for clinical improvement in COVID-19 infection (WHO 2021).

On the basis of the rationale above, any significant antiviral activity could not have been achieved with the dose used in the study and the resultant plasma concentration of the administered ivermectin. Thus, although ivermectin, in vitro, is a potent inhibitor of SARS-CoV-2 replication, in vivo, the plasma concentration required to achieve the antiviral effect far exceeds the therapeutically applicable dose.

Declaration of Competing Interest

There was no conflict of interest

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Ethical Approval

Not required

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