

though concerns regarding the effective dose for SARS-CoV-2 have been raised, the study by Rajter et al.<sup>2</sup> showed the efficacy of the medication at a dose of 200 micrograms/kilogram, a dose that has been demonstrated to be safe. The widespread use of ivermectin that allowed for eradicating onchocerciasis as well as its use in treating parasitosis for more than 40 years provides evidence of a sufficiently safe pharmacological profile when it is used at a dose of 150–200 micrograms/kilogram.<sup>3</sup>

Though it is true that conclusive evidence is needed on the efficacy of the medication against COVID-19, to date (May 24, 2020), 14 ongoing investigations evaluating the possible efficacy of ivermectin are registered in ClinicalTrials.gov database. In this sense, its potential use outside the context of a clinical trial or research protocol for off-label medications that evaluate its efficacy and safety cannot be ruled out.<sup>4</sup>

## References

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## Reply to: Ivermectin in COVID-19. *Argumentum ad ignorantiam?*



### Réplica: Ivermectina en COVID-19. ¿*Argumentum ad ignorantiam?*

Dear Director,

After closely reading the letter by Carlosama-Rosero in which we were cited,<sup>1</sup> we observed some misinterpretations of the content of our publication<sup>2</sup> and we believe it would be useful to provide some clarifications.

In our previous letter, we reference the mental process known as *argumentum ad ignorantiam*, which consists of believing that lack of awareness of evidence contrary to an idea that we support counts as evidence in its favor. At that time, we gave the example of the drug ivermectin in COVID-19 disease, whose previous success in a laboratory study would be difficult to extrapolate to clinical practice, as it would require toxic doses to reach the necessary therapeutic concentration.<sup>2</sup>

Although it is well-known that ivermectin dosing is in µg/kg of body weight, we gave the total necessary dosage in mg for reaching a concentration in human beings that is similar to what was effective *in vitro*, which would indeed be highly toxic (1000–1200 mg vs 10–20 mg, which is the dose habitually used in humans). At no point did we intend to categorically rule out ivermectin as a possible treatment for COVID-19, but rather refute inconsistent evidence in its favor. The work by Rajter et al.<sup>3</sup> that Carlosama-Rosero cites is a multicenter retrospective study of 280 patients treated with ivermectin which reported a significant reduction in the overall mortality rate in the group that received

ivermectin (15% vs 25.2%; OR 0.52 [CI 95% 0.29–0.96],  $p=0.03$ ). Furthermore, on the regression analysis adjusted for confounding variables, the reduction in mortality remained significant (OR 0.27 [CI 95% 0.09–0.85],  $p=0.03$ ; HR 0.37 [CI 95% 0.19–0.71],  $p=0.03$ ). However, like all observational studies, it had some well-known selection and confounding biases, and therefore the results reported in that publication must be taken with great caution and of course after waiting for the results of ongoing clinical trials. This work unfortunately does not allow for drawing solid conclusions on the effectiveness of ivermectin at this time.

## References

1. Carlosama-Rosero Y. Ivermectina en COVID-19. ¿*Argumentum ad ignorantiam?* *Rev Clin Esp.* 2020, doi:10.1016/j.rce.2020.06.003.
2. López Reboiro M, Sardiña González C, López Castro J. COVID-19 y *Argumentum ad ignorantiam* o «no todo vale». *Rev Clin Esp.* 2020, doi:10.1016/j.rce.2020.04.013.
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