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## Melatonin, coronavirus, cardiovascular disease, and the geriatric emergency: let's use everything we have! Response

Melatonina, coronavirus, enfermedad cardiovascular y emergencia geriátrica: jusemos todo lo que tenemos! Respuesta

#### To the Editor.

We read with interest the Letter to the Editor by Domínguez-Rodríguez et al. concerning our article<sup>1</sup> and suggesting that melatonin treatment may be useful in elderly patients with COVID-19. The authors propose that this treatment could prevent the infection or lessen its severity, which is more pronounced among the elderly.<sup>2</sup> Melatonin has anti-inflammatory and antioxidant activity, thus attenuating the proinflammatory cytokine storm and neutralizing the production of free radicals to help preserve cell integrity and prevent lung damage.<sup>3</sup> Melatonin levels drop significantly with age, an effect that has been related to the development of chronic inflammatory processes, including some cardiovascular diseases. Consequently, its use in elderly patients may be particularly relevant. Exogenous supplementation has been shown to be safe and to have few adverse effects, although these effects are diminished when melatonin is administered consistent with its circadian rhythm of production.<sup>3</sup> Nevertheless, there are a paucity of data on its clinical benefit in various situations, and no evidence is available on how it affects established prognostic variables.<sup>4</sup>

We agree with the authors on the need to design and implement new therapies rapidly and effectively in the context of this pandemic. However, we should not neglect the perspective gained from a formal evaluation of any potential treatments. The pathophysiologic plausibility and the available experimental and clinical data are promising, and studies could be designed to

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evaluate the potential efficacy of melatonin in COVID-19. However, they are insufficient to recommend routine clinical use as proposed by the authors. In our opinion, ethical considerations require that the therapies we administer to our patients be supported by sufficient rigorous evidence, even during emergencies.

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Do we have a new drug for heart rate control in patients with permanent atrial fibrillation?

¿Hay un nuevo fármaco disponible para el control de la frecuencia cardiaca de pacientes con fibrilación auricular permanente?

# To the Editor,

We have read with great interest the article by Fontenla et al.<sup>1</sup> describing the design of the BRAKE-AF project, which will analyze the safety and efficacy of ivabradine for heart rate control in patients with permanent atrial fibrillation.

Ivabradine has shown beneficial effects in patients with ischemic heart disease and in patients with heart failure and reduced ejection fraction.<sup>2</sup> The drug has a good safety profile, as it does not affect cardiac contractility or blood pressure due to its selective If current inhibition. Until recently, the negative chronotropic effect of the drug was considered the result of its selective effect in the sinus node and, therefore, it was not recommended for heart rate control in patients with atrial fibrillation. However, recent studies have suggested that ivabradine slows atrioventricular (AV) conduction and may be beneficial in these patients.<sup>3</sup> Fontenla et al.<sup>1</sup> have proposed this study, as this effect is biologically plausible (the AV node does have If currents) and this hypothesis is supported by several experimental animal studies<sup>4</sup> and small human trials.<sup>5</sup>



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