LETTER TO THE EDITOR

Reply to: RAAS inhibitors in COVID-19: Not all are created equal. Telmisartan is the one

Resposta a: Inibidores de RAAS em COVID-19: nem todos são criados iguais!: Telmisartan é o único

We thank Rothlin and colleagues for their comments on our work1 regarding the contribution of the angiotensin pathway to COVID-19 clinical manifestations. It is important that the therapeutic potential of AT1 receptor blockers (ARBs) in COVID-19 is fully discussed and that these drugs should be seen as a therapeutic opportunity and not as a threat.

We agree that telmisartan has pharmacokinetic and pharmacodynamic profiles that make this ARB particularly suitable for use in COVID-19. Telmisartan exerts an insurmountable and reversible inhibition of angiotensin II-induced responses2 with an AT1 blockade that is more resistant even to very large increases in angiotensin II concentrations in the receptor biophase, as expected to occur in the lungs during COVID-19. Telmisartan also offers the advantage of having its safety established at higher doses than those commonly used as an antihypertensive (up to 160 mg)2 and during a period that fits the time needed for COVID-19 treatment.

Rothlin and colleagues highlighted the fact that telmisartan has additional anti-inflammatory effects that are superior to other ARBs, based on its unique direct activation of peroxisome proliferator-activated receptor-gamma (PPAR-γ). As we mentioned in a previous comment,3 we have doubts about the relevance of PPAR-γ activation due to the fact the concentrations needed for such activation would be reached only during telmisartan’s steady state Cmax.4,5 Therefore, any contribution of PPAR-γ activation to the expected anti-inflammatory response elicited by telmisartan should be minimal, compared to the expected anti-inflammatory response caused by blockade of AT1 receptor activation.6–8 Our hypothesis is that dose is the key factor. The marginal benefits of ARBs and angiotensin-converting enzyme inhibitors in protecting patients suffering from COVID-19 seen in some meta-analyses1,9 are probably associated with the use of these drugs at antihypertensive doses. Despite our position in favor of telmisartan as a first choice, we do not support its uniqueness for COVID-19 treatment. We consider, however, the need to use the highest possible dose as a major requirement for the contribution of any ARB to COVID-19 treatment.

Funding

No external funding sources are declared.

Conflicts of interest

The authors have no conflicts of interest to declare.

References


DOI of original article:
https://doi.org/10.1016/j.repc.2023.08.005

https://doi.org/10.1016/j.repc.2023.10.005

0870-2551/© 2024 Sociedade Portuguesa de Cardiologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Jorge Gonçalvesa,b,∗, Catarina D. Santosa, Paula Frescoa,b, Fernando Fernandez-Llimosa,b

a Laboratório de Farmacologia, Faculdade de Farmácia, Universidade do Porto, Porto, Portugal
b Mechanistic Pharmacology and Pharmacotherapy Unit, UCIBIO-i4HB, Faculty of Pharmacy, University of Porto, Porto, Portugal

∗ Corresponding author. E-mail address: jgoncalves@ff.up.pt (J. Gonçalves).