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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 work[1] 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 responses[2] 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-analyses[1,9] 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.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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