Letter to the Editor

Controversy regarding ACE inhibitors / ARBs in COVID-19

Controversias sobre el tratamiento con IECA/ARA-II y COVID-19

To the Editor,

In the context of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, the letter published by Gerard J O'Mara in the *British Medical Journal* suggesting that treatment with angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) could facilitate coronavirus infection by increasing circulating ACE2 levels, leading to increased viral load and more severe lung injury, has created considerable unease.[1]

There is, however, evidence that the interaction between previous versions of coronavirus (SARS-CoV, which, to avoid confusion, we will hereafter refer to as *SARS-CoV-1*) and the renin-angiotensin-aldosterone system and ACE2 is much more complex. Experimental data from mouse models indicate that losartan might actually protect against coronavirus-induced lung injury.[2,3]

The SARS-CoV-1 spike protein interacts with ACE2, using it for entry into the host cell, and deregulates this lung protective pathway by reducing ACE2 expression, resulting in unopposed angiotensin II accumulation and tissue injury. This process would explain the proposed protective effect of ARBs against SARS-CoV-1–induced lung injury in mice.[2]

Additionally, although absence of ACE2 (in knockout mice) protects against infection, it is not clear whether partial reduction of ACE2 levels, achieved through withdrawal of ACE inhibitors or ARBs, would have clinically relevant benefits.

As there are quite a few similarities between SARS-CoV-1 and SARS-CoV-2, particularly in terms of protein binding to ACE2, it is likely that the above findings will also be applicable to the current situation with coronavirus disease 2019 (COVID-19).[4,5]

We therefore believe that the views expressed by O'Mara[1] should be treated as simple reflections and that caution should be exercised when considering their clinical applicability. The relationship between the renin-angiotensin-aldosterone system and SARS-CoV-1 pathogenicity, and, by analogy, SARS-CoV-2 pathogenicity in the context of COVID-19, is highly complex. In fact, basic research suggests that ACE inhibitors, and ARBs in particular, have a protective role.

In this context, thus, there is no basis for discontinuing existing treatments with ACE inhibitors and ARBs. Moreover, complications due to the indiscriminate discontinuation of these drugs could have far more serious consequences than many of the surmised adverse effects.

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