ACEi reduces hypertension-induced hyperinflammation in COVID-19

Hypertension is associated with a pro-inflammatory state that worsens the prognosis of patients with coronavirus disease 2019 (COVID-19). According to a new study, antihypertensive blockade of the renin–angiotensin–aldosterone system (RAAS), particularly with the use of an angiotensin-converting enzyme inhibitor (ACEi), might improve outcomes in patients with hypertension and COVID-19.

Irina Lehmann, Ulf Landmesser, Roland Els and colleagues combined clinical data from 144 patients with COVID-19, single-cell sequencing data from 48 airway tissue samples and data from in vitro experiments. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binds to ACE2 to gain entry into cells. Uncertainty had been raised whether RAAS blockade upregulates the expression of ACE2, causing ACEi-treated or angiotensin-receptor blocker (ARB)-treated patients to be more susceptible to SARS-CoV-2 infection. However, the researchers found no evidence that treatment with either an ACEi or an ARB increased the expression of ACE2 in patients with or without SARS-CoV-2 infection. “This result is in line with findings from observational studies that patients receiving antihypertensive treatment with an ACEi or ARB are not more susceptible to SARS-CoV-2 infection,” comments Lehmann. Moreover, the induction of ACE2 expression that occurs after SARS-CoV-2 infection was unaltered by either ACEi or ARB therapy.

The investigators identified a hypertension-associated increase in immunological activity as being the prominent factor contributing to the worse prognosis of patients with high blood pressure and COVID-19. In response to SARS-CoV-2 infection, patients treated with an ARB had an exaggerated hyperinflammatory response, which was alleviated in patients treated with an ACEi, thereby reducing the risk of severe outcomes of COVID-19.

Whereas SARS-CoV-2 clearance in patients with hypertension who were treated with an ACEi was similar to that in patients without hypertension, viral clearance was delayed in patients with hypertension who were treated with an ARB. In particular, cell-intrinsic antiviral signalling via interferon regulatory factor 3 was weaker in patients with SARS-CoV-2 infection who were treated with an ARB than in those treated with an ACEi.

“Our data are in line with the general guideline recommendations discouraging discontinuation of ACEi or ARB treatment,” conclude the researchers. “In fact, our results might suggest that ACEi could be the more beneficial antihypertensive treatment during COVID-19.” Several randomized, controlled trials are ongoing to compare the use of an ACEi versus an ARB in patients with hypertension and COVID-19.

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