Letter to the Editor –

ACE-2 downregulation and incidence of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection

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In response to:

Dublin S et al. Renin-angiotensin-aldosterone system inhibitors and COVID-19 infection or hospitalization: a cohort study. Am J Hypertens 2020 doi: 10.1093/ajh/hpaa168.

To the Editor:

Dublin *et al*. present an excellent manuscript which not only adds to the growing evidence base that prescription of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-receptor blockers (ARBs) is not associated with increased incidence or severity of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection but also shows no adverse effect on clinical outcomes, irrespective of the dosage prescribed.[1] SARS-CoV-2 utilizes cellular ACE-2 for viral entry.[2] Multiple recent publications suggest that ARBs upregulate ACE-2 (albeit with intraclass variations) while ACEi have at most minimal effects.[2] Dublin *et al*.'s study therefore infers, indirectly, that chronically increased ACE-2 does not predispose to SARS-CoV-2 infection or severity despite its high affinity for ACE-2.[1,2]

The effect of chronically *downregulated* ACE-2 on susceptibility to SARS-CoV-2 is unknown. There is a signal that inhibiting ACE-2 might be beneficial. Anti-ACE-2 antibodies inhibited SARS-CoV-1 replication in animal models, as did the specific ACE-2-inhibitor N-(2-aminoethil)-1 aziridine-ethamine.[3] The direct renin antagonist aliskiren downregulates ACE-2 in rodent models.[4] The authors' dataset includes over 300 000 patients with detailed medication prescription records; could they provide data on prescription of aliskiren and, if numbers sufficient, incident SARS-CoV-2 infection, hospitalisations and outcomes in those receiving aliskiren? If incidence and hospitalisation rate is reduced, this could inform a paradigm shift in focus from ACE-2 amelioration to antagonism in the prevention/limitation of future ACE-2 mediated viral infections including SARS-CoV-2.

References:

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