Sacubitril, valsartan and SARS-CoV-2

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Dear Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19) is responsible for the current global pandemic. To date, no antivirals directed against the virus or effective vaccines are available.[1] It is essential to recognise the risk factors and components that may play a protective role. There is no clear evidence on the correlation between changes in the renin–angiotensin system (RAS) by treatment with ACEIs, ARBs or DRis and COVID-19 infection.[2–4] Randomised controlled trials are needed to verify the involvement of COVID-19 viral infection and chronic treatment with these drugs. A possible scientific hypothesis to investigate is the role of the neprilisin inhibitor sacubitril in association with valsartan in the more severe stages of COVID-19 infection. The challenge to defeat the current pandemic poses several objectives, among them trying to give added values to therapeutic solutions; in this direction, the association with sacubitril/valsartan has already demonstrated therapeutic efficacy in the treatment of chronic symptomatic heart failure with reduced ejection fraction in several studies[5]; indirectly, the therapeutic benefits of the cardiovascular type are also directed to a decrease in the risk of infection and complications from COVID-19. Furthermore, there is evidence of a significant increase in N-terminal pro hormone BNP (NT-proBNP) in patients with COVID-19.[6] Studies show that higher NT-proBNP was an independent risk factor for death in patients with severe COVID-19[7]; moreover, NT-proBNP is associated with proinflammatory effects.[8 9] Sacubitril, through its mechanism of action, increases neprylisin-degraded peptides, such as natriuretic peptides (NPs), peptide natriuretic atrial (ANP) and peptide natriuretic brain (BNP)[10]; evidence associates these peptides with antiflammatory, antihypertrophic and antifibrotic effects. Recent evidence shows that interleukin-1β secretion is strongly inhibited by the BNP/ Natriuretic peptide receptor (NPR-1)/ cyclic guanosine monophosphate (cGMP) axis to all molecular mechanisms closely controlling its production and release, Nuclear factor NF-kB, extracellular regulated kinases ERK 1/2 and all elements of the NALP3/ASC/caspase-1 inflammasomic cascade, and that NALP3 inflammatory inhibition is directly related to the deregulatory effect of BNP on the activation of NF-kB/ERK 1/2[11]; also, the decrease of NT-proBNP by sacubitril is known. Valsartan in association, by blocking the AT-1 receptor of Ang II, decreases profibrotic and proinflammatory activities mediated by AT-1r and indirectly increases the action of Ang II on AT-2r with antifibrotic, antiffiammatory effects. Based on the evidence and in relation to our generated hypothesis, we believe that the use of sacubitril/valsartan in the most severe stages of COVID-19 infection could have therapeutic efficacy, with anti-inflammatory and antifibrotic effects mediated by NPs. Clinical studies are required to confirm this hypothesis.

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