Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Letter to the editor in response to article: "Clinical considerations for patients with diabetes in times of COVID-19 epidemic (Gupta et al.)

Dear editor,

We recently published an article highlighting the special concerns while managing patients with diabetes in the times of COVID-19 pandemic [1]. There have been some concerns about the use of Angiotensin Converting Enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARBs), which were not clarified in our publication [2]. We are summarising the current evidence in this regard and will try to arrive at a reasonable conclusion.

In the absence of a vaccine and an antiviral drug for the COVID-19 infection, several therapeutic approaches are being studied. One such approach is the use of inhibitors of the renin angiotensin system, namely ACE inhibitors and ARBs. On the other hand, some concern has been raised about the fact that patients on these agents might be at an increased risk of infection by Severe Acute Respiratory Syndrome coronavirus-2 (SARS CoV-2).

Angiotensin converting enzyme-2 (ACE-2) is the receptor for SARS CoV-2 as well as other coronaviruses and is expressed in type 2 alveolar epithelial cells and endothelium. The S-glycoprotein on the surface of coronavirus binds to ACE2. This leads to a conformational change in the S-glycoprotein and allows proteolytic digestion by host cell proteases (TMPRSS2) ultimately leading to internalization of the virion [3]. Viral S-glycoprotein, TMPRSS2 and ACE-2 inhibition are potential targets of therapy and possibly vaccine development.

As ACE-2 is essential to coronavirus infection, its blockade is thought to be beneficial in preventing/treating this infection. A retrospective analysis found reduced rates of death and endotracheal intubation in patients with viral pneumonia who were continued on ACE inhibitors [4]. Mice with coronavirus induced lung injury showed improvement when treated with losartan [5]. As far as CVID-19 infection is concerned, the data on RAS activation or the effect of its blockade is limited at present. Hypokalaemia could be a marker of RAS activation and high incidence of hypokalaemia has been reported in patients with COVID-19 infection [6].

Despite these small studies suggesting the benefit of drugs acting on RAS, there is some data, albeit scarce, from animal models and human studies that treatment with ACE inhibitors and ARB could cause up regulation of ACE2 [7]. Ibuprofen and thiazolidinediones have also been shown to do the same [8,9]. Increased expression of ACE2 could theoretically increase the risk of infection with SARS CoV-2. This could be a concern in people with diabetes who are at already elevated risk of infections because of many other factors. However, currently, there is no evidence to support this hypothesis. In view of lack of robust evidence for either benefit or harm, it is reasonable for patients to continue using ACE inhibitors and ARB, as recommended by European Society of Cardiology Council on Hypertension and European Society of Hypertension [10,11].

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