

**Letter to Editor**



## Angiotensin 1-7: A Novel Strategy in COVID-19 Treatment

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### Dear Editor,

Coronavirus disease 2019 (COVID-19) is an emerging infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The mortality rate of COVID-19 is high and there is no effective treatment for these patients to reduce the high hospitalization and mortality rates.

The renin-angiotensin-aldosterone system plays a critical role in COVID-19 pathogenesis.<sup>1</sup> The sex difference in the mortality rate and complications of COVID-19, and also the more favorable prognosis of children leads to new hypotheses regarding the protective and harmful factors in the treatment of these patients.<sup>2,3</sup>

Angiotensin-converting enzyme (ACE) plays a role in innate and adaptive immune responses as well as converting angiotensin and affecting different physiological functions.<sup>4</sup> Understanding the expression of ACE on myeloid cells can be helpful in the treatment of infections. In comparison to adults, children have a higher level of ACE.<sup>4</sup> Although SARS-CoV-2 binds to ACE2 for entering the host cells, children are more immune against this virus; this is possibly due to a high level of ACE in children and its effects on immune responses.<sup>4</sup> Moreover, although children have a higher level of renin, angiotensin, and aldosterone compared with adults and also a higher amount of fluid in their bodies, they have lower blood pressures<sup>5</sup>; one of the reasons behind this is the high level of angiotensin 1-7 that acts as a vasodilator and anti-inflammatory agent against angiotensin 2. This is probably another reason for children's enhanced immunity against COVID-19.<sup>6</sup> Despite the low level of ACE2 in females in comparison to males, which protects the host against virus penetration, given the regulatory effect of estrogen on angiotensin type 2 receptor its effect on angiotensin

1-7 is more dominant. This is possibly the relative cause of women's increased immunity against COVID-19 infection.<sup>7</sup> Angiotensin receptor blockers (ARBs) are one of the main drugs that can provide high levels of ACE and angiotensin 1-7 at the same time. However, ARBs may also elevate the ACE2 level as the virus entry location, which should be considered in the prescription of ARBs.<sup>8,9</sup>

The administration of angiotensin 1-7 in adults may provide immunity against COVID-19 as in children. By injecting angiotensin 1-7, the renin-angiotensin-aldosterone axis will become active to prevent a further drop in blood pressure, the ACE level will rise, and the ACE2 level will reduce owing to the accumulation of angiotensin 1-7.<sup>8</sup> This means that providing high levels of angiotensin 1-7 and ACE while reducing inflammatory bradykinin will be protective against ACE2, the entry site of the virus into the host cells.<sup>8</sup> Finally, the controlled injection of angiotensin 1-7 as a modulator of the renin-angiotensin-aldosterone system and the compensation of a possible drop in blood pressure by infusion of intravenous fluids and alpha agonists may be able to reduce the severity of COVID-19 infection since the host is given an opportunity to induce specific immunity.

### Ethical Issues

Not applicable.

### Conflict of Interest

We declare no competing interests.

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