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Letter to the Editor

Angiotensin receptor blockers for the treatment of COVID-19 and its comorbidities

Dear Editor,

My report to Pharmacological Research [1] presented relevant information supporting the continuation of ARB treatment in those patients suffering from cardiovascular and metabolic illnesses likely to become COVID-19 comorbidities. This report also called for controlled data analysis and clinical studies to determine whether ARBs may be considered as additional treatment for COVID-19 patients.

Huang et al. [2] (Pharmacological Research, in press) agreed with my view that ARB therapy may not be discontinued and that more data analysis and clinical studies were needed to definitely determine the role of ARBs in COVID-19 therapy, a view that is supported by multiple reports and position statements from all related medical and cardiological associations [3]. In addition, Huang et al., presented data obtained by others, illustrating that Angiotensin II was upregulated in COVID-19 and inversely correlated to pulmonary function.

However, despite these observations, Huang and colleagues paradoxically disagreed with my suggestion to further study the role of ARBs in COVID-19. Huang et al. believed that ARBs could not benefit COVID-19 patients since in their opinion Renin Angiotensin System (RAS) overactivity was not important and it was a simple concomitant symptom of COVID-19, with no bearing on the disease outcome. These authors based their proposal to disregard any possible benefit of ARBs in COVID-19 on the same preliminary data demonstrating that ARBs were not harmful in COVID-19 patients, on a report that during recovery from COVID-19, ACE2 continued to increase while Angiotensin II levels were normal and on data of renin, Angiotensin II and aldosterone during recovery from COVID-19.

While the accuracy of the presented unpublished results should be questioned, since reported values for Angiotensin II were at least 10-fold higher than those from the literature, the authors did not consider the time-dependent alterations in RAS activity. It is expected that patients recovering from COVID-19 may exhibit a normal RAS response, since normalization of RAS response could be taken as one beneficial process during COVID-19 recovery. This is precisely what is expected from ARB treatment.

In addition, Huang et al. did not consider the recent reports, including a retrospective study, a case-population study and a systematic review and meta-analysis, demonstrating that ARB treatment of COVID-19 patients indeed reduced the disease morbidity and death rate, and not only in hypertensives but also in diabetic patients [4–6]. Additional references on beneficial effects of ARBs in COVID-19 patients are included in my recent Editorial [3].

Huang et al., did not mention that there are to date (05/22/2020) 38 ongoing clinical studies to precisely answer the question of the relative role and importance of ARB treatment in hospitalized and non-hospitalized COVID-19 patients, including determination of adverse outcomes, prognosis, elimination or prolongation of treatment, long-term use, and mitigation of acute respiratory distress syndrome (ARDS).

This is evidence that studies on the effects of ARBs on COVID-19 patients have become a priority for the scientific community. https://clinicaltrials.gov/ct2/results?recrs=&cond=COVID-19&term=angiotensin+receptor+blockers&cntry=&state=&city=&dist=

The principal pre-clinical and clinical evidence demonstrating that ARBs protect patients affected by all COVID-19 comorbidities has been recently reported [3] and is summarized here.

1. Enhanced RAS activity through increased Angiotensin II AT1 receptor (AT1R) actions negatively affects the cardiovascular, renal, metabolism and immune systems.
2. The RAS is further stimulated in COVID-19 patients during the initial course of the illness.
3. ARBs block AT1R receptors and effectively reduce inflammation in all organs.
4. ARBs are therapeutically effective not only in hypertension but in all disorders comorbid with COVID-19, are well-tolerated in the elderly and are commonly prescribed for these disorders.
5. ARBs protect mitochondrial function, sensitivity to insulin, and the coagulation cascade.
6. AT1R overactivity promotes inflammatory lung disease.
7. ARBs improve pulmonary health, protect against bacterial and viral injury, including that produced by SARS CoV, reduce pneumonia-related death rates, and ameliorate lung fibrosis.
8. ARBs upregulate ACE2, an enzyme with protective properties in the lung and other organs.
9. Several recent publications reported the beneficial effects of ARBs in COVID-19 patients, reducing complications and decreasing death rates.

The ongoing clinical trials, careful examination of COVID-19 patients with and without ARB treatment, and systematic retrospective reviews and meta-analysis will further clarify the possible role of these compounds on the development, course, prognosis, and consequences of the disease.

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Declaration of Competing Interest

JMS reports no conflict of interest.

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