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LETTER TO THE EDITOR

Amiodarone in COVID-19: let's not forget its potential for pulmonary toxicity

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Aimo *et al.*[1] presented an elegant review of the antiviral mechanism of amiodarone, which is a commonly used antiarrhythmic drug. Although *in vitro* experiments demonstrated the ability of amiodarone to inhibit coronavirus, we are still wary of the authors' recommendation to evaluate amiodarone for the treatment of coronavirus disease 2019 (COVID-19) in clinical trials. In fact, when authors commented that amiodarone has been used for decades in a large number of patients for its safety profile to be well-known, authors should have acknowledged the notorious potential for amiodarone to induce pulmonary toxicity.

The fact that the major morbidity and mortality of hospitalized patients with COVID-19 are attributed to acute viral pneumonitis leading to acute respiratory distress syndrome (ARDS) has made us cautious about the idea to evaluate amiodarone for the treatment of COVID-19 in clinical trials since ARDS is a potentially fatal form of amiodarone pulmonary toxicity. Amiodarone-associated ARDS has been reported in patients who have undergone surgery or pulmonary angiography though with limited literature.[2] Importantly, a prospective cohort study[3] reported that prehospital use of amiodarone increased nearly four times the odds of developing ARDS among patients at risk for acute lung injury (odds ratio = 3.8; 95% confidence interval 1.1–13.1). Indeed, the causative pathogen for COVID-19, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is able to induce acute lung injury in COVID-19 through down-regulation of angiotensin-converting enzyme 2. Though the occurrence of ARDS has always been associated during long-term treatment with amiodarone, it can still nevertheless occur when the amiodarone was newly initiated in the peri-procedural period.[2]

It has been hypothesized that amiodarone may sensitize patients to high concentrations of inspired oxygen since the accumulation of amiodarone in the lysosomes of macrophages results in destabilization of their membranes and release of free oxygen radicals. The mortality rate of patients in whom ARDS developed due to amiodarone could approach 50%, which is higher than that of patients with COVID-19 related ARDS (39% as reported in a meta-analysis).[4,5] Therefore, it may be worth to wait for observational studies to report outcomes in COVID-19 patients who have received chronic treatment with amiodarone for its established indications before a recommendation to repurpose amiodarone for the treatment of COVID-19. In addition, dronedarone, which is a non-iodinated congener of amiodarone with a better safety profile, may worth for more evaluation on its antiviral activity against SARS-CoV-2.

Conflict of interest: none declared.

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