Use of statins in patients with COVID-19

To the Editor,

We read with interest the correspondence by Goldstein et al. [1] which discussed the possibility of enhanced mortality or adverse outcomes with the use of statins. The authors presented well the rationale behind suggesting such a possibility.

The authors discussed the possibility in which statins might lead to increased levels of the proinflammatory cytokine, interleukin-18 (IL-18), and thereby associated with increased mortality from acute respiratory distress syndrome (ARDS). Nevertheless, we feel that we could add some points to the discussion with regards to a statin to give readers a broader view.

First, increased level of IL-18 has not been a universal finding, with some studies [2] among patients with hypercholesterolemia reported reduced circulating levels of IL-18 associated with statin treatment, while another study [3] showed no significant changes in circulating levels of IL-18 after treatment with atorvastatin in patients with stable coronary artery disease. To add to the confusion, statins have been reported to increase IL-18 levels in peripheral mononuclear cells under *in vitro* experiments [4]. Even the study which the authors cited did not show a consistent elevation in all patients treated with a statin, though the proportion of patients with rising IL-18 (58%) is more than the proportion of patients with stable or falling IL-18 (44%) [5].

Second, though associated with an increased level of IL-18, a multicenter, double-blind controlled trial with rosuvastatin reported no significant difference with rosuvastatin compared with placebo in 60day in-hospital mortality among patients with sepsis-associated ARDS [5]. Similarly, a multicenter, double-blind randomized controlled trial reported no significant difference in terms of mortality at 28 days with simvastatin compared with placebo among patients with ARDS [6]. We believe that a randomized controlled trial design of these studies could provide confidence with certainty about the safety of statin in patients with ARDS.

Third, after initial entry through ACE2, severe acute respiratory syndrome coronavirus 2, the pathogen for novel coronavirus disease 2019 (COVID-19), downregulates ACE2 expression, which in turn results in excessive production of angiotensin II, which causes vasoconstriction of lung vessels, increased pulmonary vascular permeability and inflammation, possibly leading to lung injury such as ARDS [7]. Statins are known to experimentally up-regulate ACE2 and therefore might be lung protective in this sense.

In conclusion, we feel that the evidence-based to consider a suspension of statin in patients with COVID-19 is not strong, where the benefits of statins for its established indications probably outweigh the uncertain risks in COVID-19 patients.

References

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