Obesity

The Potential Benefit of Telmisartan to Protect Overweight Patients with COPD from the Acquisition of COVID-19

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TO THE EDITOR: Individuals with chronic obstructive pulmonary disease (COPD) have previously been identified to have an elevated serum level of angiotensin-converting enzyme 2 (ACE2), the cellular entry receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The newest discoveries by Higham et al. (1) were the increased ACE2 expression in the bronchial epithelium of overweight patients with COPD compared with their nonoverweight counterparts.

Given the fact that higher expression of ACE2 may lead to an increased risk of a severe course of coronavirus disease (COVID-19), there are potential benefits of using angiotensin receptor blockers (ARBs) among overweight patients with COPD. In its native state, the angiotensin type I receptor (AT_1R) binds to ACE2 to form a receptor complex (2). Administration of ARBs could then stabilize the ACE2-AT_1 receptor complex on the cell membrane and thus prevent interaction of SARS-CoV-2 with the ACE2 catalytic site. Even if ARBs could not eliminate the cellular viral entry, ARBs could also block the binding of excess angiotensin II (from downregulation of ACE2 following a hijack by SARS-CoV-2) to AT_1R and thus mitigate angiotensin II–mediated lung injury and subsequent development of acute respiratory failure. In addition, ARBs possess anti-inflammatory actions with their ability to utilize the ACE2/angiotensin II type 2 receptor/Mas receptor pathway that could limit the cytokine storm induced by SARS-CoV-2.

On the contrary, many may not recognize the effects of ARBs on body weight. Specifically, telmisartan could prevent adipogenesis and weight gain. Telmisartan has been shown to upregulate the expression and activity of peroxisome proliferator–activated receptor (PPAR)-δ in 3T3-L1 preadipocytes in a dose-dependent fashion. The subsequent activation of PPAR-δ–dependent lipolytic pathway by telmisartan reduced adipogenesis *in vitro* (3). *In vivo*, long-term administration of telmisartan significantly reduced the increase in body weight and prevented high-fat diet-induced obesity through increased expression of PPAR-δ and several lipolytic and energy uncoupling-related proteins in adipose tissue and skeletal muscle in wild-type mice and spontaneously hypertensive rats (3). In fact, a human study of 32 patients with type 2 diabetes and metabolic syndrome who received telmisartan demonstrated a significant decline in BMI as well as waist circumference at 6 months compared with baseline (4).

We are aware of some human and animal studies showing an increased ACE2 expression with the administration of ARBs other than telmisartan, but such observations may not translate to a greater susceptibility toward COVID-19. Specifically, a study that included only 1.6% (621/37,031) of patients with COPD reported no difference in the risk of acquisition of COVID-19 between ARB users and non-ARB users, though the protective effect of ARBs toward the acquisition of COVID-19 may be more apparent among patients with overweight and COPD who may have a higher baseline risk of acquisition of COVID-19 (5). We recognize that no evidence thus far has shown that ARBs or specifically telmisartan could prevent or lead to better clinical outcomes among overweight patients with COPD upon acquisition of COVID-19. Nevertheless, we hope that this discussion of the potential effects of telmisartan can serve to stimulate an interest to trial telmisartan for the prevention and management of COVID-19 in overweight patients with COPD because of its dual benefits to prevent/mitigate COVID-19 and to induce weight loss in this patient population.

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