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Effects of Salt Restriction for the Severity of Novel Coronavirus Infection

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Summary

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Obesity is a major risk factor for the development of COVID-19. Angiotensin-converting enzyme 2 (ACE2) is an essential receptor for cell entry of SARS-CoV-2. The receptor binding domain of the S1 subunit (S1-RBD protein) in the SARS-CoV-2 spike glycoprotein binds to ACE2 on host cells, through which the virus enters several organs, including the lungs. When the relationship between severe COVID-19 and serum ACE2 concentration was examined, it was reported that serum ACE2 concentration increased as obesity and blood glucose control worsened, and that it may be due to an increase in ACE2 expression derived from multiple organs. It has been reported that high sodium load activates dendritic cells present in the intestinal tract and promotes the synthesis of IL-17, an inflammatory cytokine, which induces deterioration of intestinal flora and inflammatory changes in the intestinal tract. In this study, we investigate whether high- or low-salt diets 1) change ACE2 in each organ and 2) whether administration of the SARS-CoV-2 recombinant S1-receptor binding domain (S1-RBD) protein changes the entry of S1-RBD protein into the lungs. When salt intake was more than twice the normal intake, the distribution of intestinal bacteria involved in acetic acid production in the intestinal tract called Allobaculum_stercoricanis was significantly reduced, and the serum acetic acid concentration actually decreased. In addition, the intestinal expression of ZO-1, a protein necessary for maintaining intestinal barrier function, was decreased by excessive salt. Furthermore, considering the increase in serum LPS concentration, LPS in the intestinal tract leaked out of the intestinal tract, suggesting that excessive salt reduces intestinal barrier function. With an increase in the concentration of LPS in the blood, significant increased inflammatory changes were noted in the lungs, small intestine and heart. In addition, ACE2 expression in organs increased with inflammatory changes within each organ. Systemic administration of S1-RBD protein significantly increased S1-RBD protein content in the lungs. It was speculated that an increase in serum LPS concentration due to a decrease in intestinal barrier function may increase ACE2 expression in each organ and lead to SARS-CoV-2 susceptibility to infection. In order to avoid the severity of COVID-19 in the future, it is suggested that salt reduction, which is only necessary for weight loss, needs to be instructed at the same time.