correspondence

Importance of the Lipid-Bound Character of Vitamin D Binding Protein in the Evaluation of Vitamin D Status in COVID-19 Patients

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To the Editor

We read the article by De Smet et al[1] with interest. They showed that low 25-hydroxyvitamin D (25[OH]D) on admission was associated with coronavirus disease 2019 (COVID-19) stage and mortality. These results were obtained at a location at 51°N during spring. At this latitude, vitamin D synthesis does not take place between October and April. Although the COVID-19 pandemic struck the whole of Europe at that time, vitamin D uptake largely depends on geographic location. Remarkably, some European countries that were most severely hit by COVID-19 (Italy, Spain) are characterized by a sunny climate. Although several comorbidities affected by vitamin D were taken into account, we would like to highlight the importance of vitamin D binding protein (DBP) and its lipid-bound character in the evaluation of vitamin D status in COVID-19.

DBP is the major carrier of vitamin D and its metabolites, with albumin as the secondary carrier. This polymorphic protein is characterized by 3 phenotypes, which show a 5-fold difference in mean serum DBP concentration with the highest levels in patients with DBP1-1 and the lowest level in patients with DBP2-2. Median plasma concentrations of 25(OH)D are also determined by DBP polymorphisms and show a similar pattern: DBP1-1>DBP2-1>DBP2-2.[2] Besides the influence of DBP polymorphism on prevalence and mortality due to severe acute respiratory syndrome coronavirus 2, single-point assessments of 25(OH)D following critical illness may provide an inaccurate assessment of vitamin D status. In critically ill patients, a rapid decrease in circulating 25(OH)D concentrations is observed because of several mechanisms (eg, decreased synthesis of DBP, which acts as an acute phase reactant).[3] In addition, the lipid-bound character of DBP (binding with very low-density lipoprotein and low-density lipoprotein [LDL]) may also play a role in the drop in 25(OH)D during acute illness. Decreases in high-density lipoprotein (HDL), LDL, and total cholesterol concentrations in COVID-19 patients have been observed.[4] An association was found between the decrease in LDL cholesterol and/or HDL cholesterol and the severity of the illness. Total, LDL, and HDL cholesterol concentrations were lower at admission and continued to decline during hospitalization of patients who died. With recovery from COVID-19, a recuperation of lipid parameters toward levels present before infection was observed. Reduced LDL cholesterol biosynthesis in COVID-19 may be explained by disturbed liver function, upregulation of proinflammatory cytokines with reduced cholesterol efflux and transport, and increased free radical concentration resulting in degradation of lipids.[4]

Hypovitaminosis D and obesity (a COVID-19 risk factor) are associated with each other. Obesity involves low circulating vitamin D levels because of low sun exposure, physical inactivity, limited intake of vitamin D–rich foods, volumetric dilution, and sequestration in the adipose tissue.[5] Given the negative acute-phase character of plasma apolipoproteins and lipids during COVID-19, DBP and thus 25(OH)D values may decrease. The role of free or bioavailable vitamin D is not yet completely clear during critical illness, although decreases in DBP and total D are accompanied by stable circulating free D concentrations. Consequently, we suggest measuring the concentration of binding proteins and all forms of vitamin D (free, bioavailable, total) to better approximate vitamin D status and to take DBP polymorphisms into account.

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