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EDITORIAL

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Is the type of diabetes treatment relevant to outcome of COVID-19?

It has long been recognized that inflammation is strongly related to insulin resistance[1,2] and plays an important role in driving complications of diabetes.[3] The acceleration of atherosclerosis in type 2 diabetes has been considered to reflect this process,[4] involving vascular macrophage infiltration associated both with profibrotic changes and with thrombosis.[5] Similar acceleration of inflammation is related to diabetic nephropathy[6] and to the progression from nonalcoholic fatty liver to steatohepatitis.[7] A number of treatments of type 2 diabetes are associated with improvement in cardiovascular outcome. In the case of thiazolidinediones, such benefits appear linked both to insulin sensitization and to anti-inflammatory effects.[8]

An important aspect of the pathophysiology of the 2019 novel coronavirus infectious disease (COVID-19) involves the development of diffuse pulmonary alveolar damage with extensive macrocyte infiltration.[9] Based on this observation, the use of anti-inflammatory treatments has been proposed for COVID-19, with some recommendation for chloroquine and hydroxychloroquine,[10,11] although two preliminary reports failed to show benefit.[12,13] In addition, these can lead to QT interval prolongation with risk of ventricular arrhythmia, particularly when administered with azithromycin.[14] The recent US National Institutes of Health treatment guidelines statement suggested that prophylactic use of hydroxychloroquine has no evidence of efficacy and recommended that the combination with azithromycin not be used.[15] Recently, the observation that severity of COVID-19 tracks with elevation in circulating inflammatory mediators[16] has led to the proposal that anti-inflammatory agents, corticosteroids, and immune suppressant treatments might be of benefit,[17] although others argue against such approaches.[18] Similarly, use of nonsteroidal anti-inflammatory agents has been recommended by some authors,[19] whereas others suggest these drugs may worsen outcome of respiratory infections and hence be inadvisable in COVID-19,[20] leaving at least some degree of doubt.[21]

The use of existing treatments for type 2 diabetes with recognized anti-inflammatory effects may have benefits both in early and in advanced COVID-19, without the potential harms of existing anti-inflammatory agents. Furthermore, there is reason to think that the degree of glycemic control may influence outcome of COVID-19.[22] Existing data sets give minimal information as to drivers of outcome among persons with diabetes, at best noting the presence or absence of diabetes.[23] We need to know much more about the characteristics of people with diabetes with COVID-19, at all levels of severity, including their diabetes treatment regimen, measures of glycemic control, and measures associated with insulin resistance including body mass index, waist circumference, and triglyceride and high-density lipoprotein cholesterol levels, to ascertain factors that may be associated with differing prognosis of the infection, both in earlier/milder and later/more severe cases, and, ultimately, to design appropriate diabetes treatment approaches that may play a role in optimizing outcome.

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