Use of Tumor Necrosis Factor Inhibitors During the COVID-19 Pandemic—Evidence in Favor of Monotherapy

Licio A. Velloso, MD, PhD

Immune-mediated inflammatory diseases (IMIDs) are a group of distinct medical conditions that may share inflammatory pathways and genetic mechanisms. It is currently unknown whether patients with IMIDs are at greater risk of SARS-CoV-2 infection or severe COVID-19 outcomes that could lead to prolonged hospitalization and increased mortality. A recent study evaluating 65,230 patients reported an increased risk of SARS-CoV-2 infection among patients with IMIDs; however, the risk of severe COVID-19 was similar to that of the general population. Patients diagnosed with some IMIDs, such as rheumatoid arthritis, Crohn disease, ulcerative colitis, and psoriasis may benefit from the use of tumor necrosis factor (TNF) inhibitors alone or in combination with other disease-modifying antirheumatic drugs. The emergence of COVID-19 has created questions regarding both the safety and potential therapeutic applicability of several anti-inflammatory agents, including TNF inhibitors. The safety concerns rely on the fact that immunobiological and disease-modifying antirheumatic drugs are important risk factors for infections, and, in the context of COVID-19, they could predispose a patient to severe illness and increased mortality. In contrast, because of the cytokine storm led by interleukin 6 and TNF-α, which is believed to play an important role in the development of many of the serious complications of COVID-19, it has been proposed that biological inhibitors of such cytokines could attenuate the severity of the disease. Now, a pooled analysis of data from 3 international COVID-19 registries has shed some light on the issue of safety concerns surrounding the use of TNF inhibitors and disease-modifying antirheumatic drugs among patients with IMIDs.

The study by Izadi et al evaluated data from 6,077 patients with IMIDs who received TNF inhibitor monotherapy, TNF inhibitors in combination with methotrexate therapy, TNF inhibitors in combination with azathioprine/6-mercaptopurine therapy, methotrexate monotherapy, azathioprine/6-mercaptopurine monotherapy, or Janus kinase inhibitor monotherapy. Rheumatoid arthritis and Crohn disease were the predominant diagnoses, followed by ulcerative colitis, spondylarthritides, psoriasis, and unspecified inflammatory bowel disease. The study objective was to assess the outcomes associated with TNF inhibitor monotherapy compared with other immunomodulatory therapeutic approaches among patients with IMIDs who developed severe COVID-19. The authors used a multilevel multivariate mixed-effects logistic regression analysis to evaluate data from registries that included patients from all continents across the globe. Compared with TNF inhibitor monotherapy, the receipt of TNF inhibitors in combination with azathioprine/6-mercaptopurine therapy, methotrexate monotherapy, azathioprine/6-mercaptopurine monotherapy, and Janus kinase inhibitor monotherapy was associated with higher odds of hospitalization or death. The receipt of TNF inhibitors in combination with methotrexate therapy was associated with increased odds of hospitalization or death, but this increase was not significantly different from that observed with the receipt of TNF inhibitors alone. As in other studies, previous diagnoses of obesity, diabetes, cardiovascular disease, lung disease, and chronic kidney disease were all associated with a higher risk of hospitalization or death.

One of the greatest strengths of the Izadi et al study is the inclusion of a large number of patients with distinct ethnic backgrounds and IMIDs. This diversity was possible because of the combined evaluation of 3 large international registries that contain data from patients with a wide range of IMIDs. Nonpooled data from some of these registries have been published earlier during the COVID-19 pandemic, providing preliminary evidence of the benefits of TNF inhibitors for the...
treatment of patients with IMIDs. These benefits were found in a study of 600 patients from the Global Rheumatology Alliance (GRA) registry and another study of 525 patients from the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) registry. However, in addition to the fact that samples were considerably small, most of the patients were from North America and Europe. Based on the findings of the Izadi et al study, which included a much larger sample comprising distinct diseases and patients with a multitude of genetic backgrounds, the evidence in favor of the continued use of TNF inhibitor monotherapy for patients with IMIDs during the COVID-19 pandemic has become more substantial.

The COVID-19 pandemic has had negative consequences for the routine follow-up of patients with chronic diseases around the world. This reduction in follow-up has created difficulty in the clinical and laboratory control of disease progression and the maintenance of optimal drug administration regimens. In the case of patients with IMIDs, there have been concerns regarding the safety of maintaining therapeutic regimens because of the immunomodulatory actions of the drugs administered. The finding that maintenance of TNF inhibitor monotherapy is associated with reductions in the risk of severe COVID-19 among patients with IMIDs offers new perspective that may guide health care professionals in the difficult decisions regarding therapeutic approaches among this specific group of patients.

ARTICLE INFORMATION

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Corresponding Author: Licio A. Velloso, MD, PhD, Department of Internal Medicine, School of Medical Sciences, University of Campinas, 13083-864 Campinas, São Paulo, Brazil (lavellos@unicamp.br).

Author Affiliation: Department of Internal Medicine, School of Medical Sciences, University of Campinas, Campinas, São Paulo, Brazil.

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REFERENCES