Boosting immune system a potential treatment strategy for COVID-19

5 August 2020, by Jim Dryden

Front-line health-care providers work with seriously ill COVID-19 patients in an intensive care unit at Barnes-Jewish Hospital in St. Louis. New research from scientists at Washington University School of Medicine suggests that the immune systems of such patients can't do enough to protect them from the virus. The researchers are proposing that boosting the activity of immune cells may be a good treatment strategy for COVID-19. Credit: Matt Miller/School of Medicine

As the COVID-19 pandemic continues to claim lives around the world, much research has focused on the immune system's role in patients who become seriously ill. A popular theory has it that the immune system gets so revved up fighting the virus that, after several days, it produces a so-called cytokine storm that results in potentially fatal organ damage, particularly to the lungs.

But new findings from a team of researchers led by scientists at Washington University School of Medicine in St. Louis point to another theory and suggest that patients become ill because their immune systems can't do enough to protect them from the virus, landing them in intensive care units. They suggest that boosting immunity could be a potential treatment strategy for COVID-19.

Such a strategy has been proposed in two recently published papers, one published online in *JAMA Network Open* and the other published online in the journal JCI Insight.

"People around the world have been treating patients seriously ill with COVID-19 using drugs that do very different things," said senior investigator Richard S. Hotchkiss, MD, professor of anesthesiology, of medicine and of surgery. "Some drugs tamp down the immune response, while others enhance it. Everybody seems to be throwing the kitchen sink at the illness. It may be true that some people die from a hyperinflammatory response, but it appears more likely to us that if you block the immune system too much, you're not going to be able to control the virus."

The Washington University researchers have been investigating a similar approach in treating sepsis, a potentially fatal condition that also involves patients who simultaneously seem to have overactive and weakened immune systems.

Hotchkiss points to autopsy studies performed by other groups showing large amounts of coronavirus present in the organs of people who died from COVID-19, suggesting that their immune systems were not working well enough to fight the virus. His colleague, Kenneth E. Remy, MD, the JCI Insight study's first author, compares efforts to inhibit the immune system to fixing a flat tire by letting more air out.

"But when we actually looked closely at these patients, we found that their tires, so to speak, were underinflated or immune-suppressed," said Remy, assistant professor of pediatrics, of medicine and of anesthesiology at Washington University. "To go and poke holes in them with anti-inflammatory drugs because you think they are hyperinflated or hyperinflamed will only make the suppression and the disease worse."

After gathering blood samples from 20 COVID-19 patients at Barnes-Jewish Hospital and Missouri Baptist Medical Center in St. Louis, the researchers employed a test to measure the activity of immune cells in the blood. They compared the blood of those patients to 26 hospitalized sepsis patients and 18 others who were very sick but had neither sepsis nor COVID-19.

They found that the COVID-19 patients often had far fewer circulating immune cells than is typical. Further, the immune cells that were present did not secrete normal levels of cytokines—the molecules many have proposed as a cause of organ damage and death in COVID-19 patients.

Instead of trying to fight the infection by further interfering with the production of cytokines, they tried a strategy that has been successful in previous studies they have conducted in sepsis patients.

Hotchkiss and Remy collaborated with researchers in a small study conducted in seriously ill COVID-19 patients who were hospitalized in Belgium. In that study, which was reported on in the *JAMA Network Open* paper, the COVID-19 patients were treated with a substance called interleukin-7 (IL-7), a cytokine that is required for the healthy development of immune cells.

In those patients, the researchers found that IL-7 helped restore balance to the immune system by increasing the number of immune cells and helping those cells make more cytokines to fight infection.

The research did not demonstrate, however, that treatment with IL-7 improved mortality in COVID-19 patients.

"This was a compassionate trial and not a randomized, controlled trial of IL-7," Remy explained. "We were attempting to learn whether we could get these immune cells working again—and we could—as well as whether we could do it without causing harmful effects in these very sick patients—and there were none. As this was an observational study involving a small number of patients who already were on ventilators, it wasn't really designed to evaluate IL-7's impact on mortality."

Studies focused on boosting immunity and improving outcomes among the sickest COVID-19 patients are just getting underway in Europe, and similar trials are starting in the U.S., including at Washington University.

Hotchkiss said that finding ways to boost the immune response should help not only in COVID-19 patients but when the next pandemic arises.

"We should have been geared up and more ready when this pathogen appeared," he said. "But what Ken and I and our colleagues are working on now is finding ways to boost the immune system that may help people during future pandemics. We think if we can make our immune systems stronger, we'll be better able to fight off this coronavirus, as well as other viral and bacterial pathogens that may be unleashed in the future."

More information: Kenneth E. Remy et al. Severe immunosuppression and not a cytokine storm characterize COVID-19 infections, *JCI Insight* (2020). DOI: 10.1172/jci.insight.140329

Pierre Francois Laterre et al. Association of Interleukin 7 Immunotherapy With Lymphocyte Counts Among Patients With Severe Coronavirus Disease 2019 (COVID-19), *JAMA Network Open* (2020). DOI: 10.1001/jamanetworkopen.2020.16485

Provided by Washington University School of Medicine in St. Louis