ICU
MANAGEMENT & PRACTICE

New way to fight sepsis: rev up patients' immune systems

People especially those with critical illness develop sepsis when an infection triggers an overwhelming immune response, ultimately wreaking havoc on the immune system. Traditional approaches to sepsis therapy do not address the critical problem of patients' severely compromised immune systems. Now, a clinical trial demonstrates that a drug that revs up the immune system holds promise in treating sepsis. This approach differs from earlier strategies that have relied on antibiotics and inflammatory medications to tamp down the immune system.

The clinical trial was led by researchers at Washington University School of Medicine and its findings are published in JCI Insight, a journal published by the American Society for Clinical Investigation dedicated to preclinical and clinical research studies.

"Mortality rates from sepsis have remained essentially the same over the last 50 years," said senior investigator Richard S. Hotchkiss, MD, a professor of anaesthesiology, of medicine and of surgery. "Hundreds of drugs have been tried and have failed. It may sound counterintuitive when inflammation is such a problem early in sepsis, but our approach is to stimulate certain immune cells to help the patient's system take control of the infection."

Standard treatment involves high doses of antibiotics that fight the infection, but they often don't work well and fail to boost the body's immune defences. Without restoring immune function, Dr. Hotchkiss explains, many patients develop lingering infections and are helpless to fight any new infections.

The trial involved 27 sepsis patients, ages 33 to 82, who were treated with a drug made of interleukin-7 (IL-7), which enhances the proliferation and survival of two types of immune cells: CD4 and CD8. These cells are important because they recruit other immune cells to fight severe infections that can lead to organ failure and death, according to investigators.

The patients in the trial, who were hospitalised and severely ill with septic shock (the most serious form of sepsis), were randomly assigned to one of two therapies. Seventeen patients received the IL-7 drug, and 10 received a standard treatment. Those who received the drug experienced a threefold to fourfold increase in CD4 and CD8 counts.

"Even though the study was small, we were encouraged that IL-7 helped restore key cells in the immune systems of these patients," said Andrew H. Walton, a staff scientist in the Hotchkiss lab and co-author of the study. "Overall, that should help improve patient survival."

The study showed that IL-7 boosts adaptive immunity, in which CD4 and CD8 T cells help recruit other immune cells – called macrophages, monocytes, neutrophils and dendritic cells – to kill bacteria that cause infections. "By strengthening adaptive immunity with IL-7 and increasing the numbers of CD4 and CD8 cells available to help fight infections, we think this approach can make a big difference," Dr. Hotchkiss said.

The doctor credits recent approaches to cancer treatment as evidence that this strategy for sepsis therapy may be a game changer for many patients. Several cancer researchers have begun using IL-7 to rev up a patient's own immune system to fight cancer. In addition, under compassionate-use guidelines, IL-7 has been given to some critically ill patients with serious viral infections and has successfully restored their CD4 and CD8 counts while improving survival.

As a next step, Dr. Hotchkiss' team is planning a larger trial to determine whether the same holds true for sepsis patients. They estimate a study involving 300 to 400 patients should have the statistical strength to determine whether IL-7 can improve survival rates.

Source: Washington University School of Medicine
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