Vitamins and steroid combination in sepsis patients do not improve recovery, organ failure or death in clinical trial

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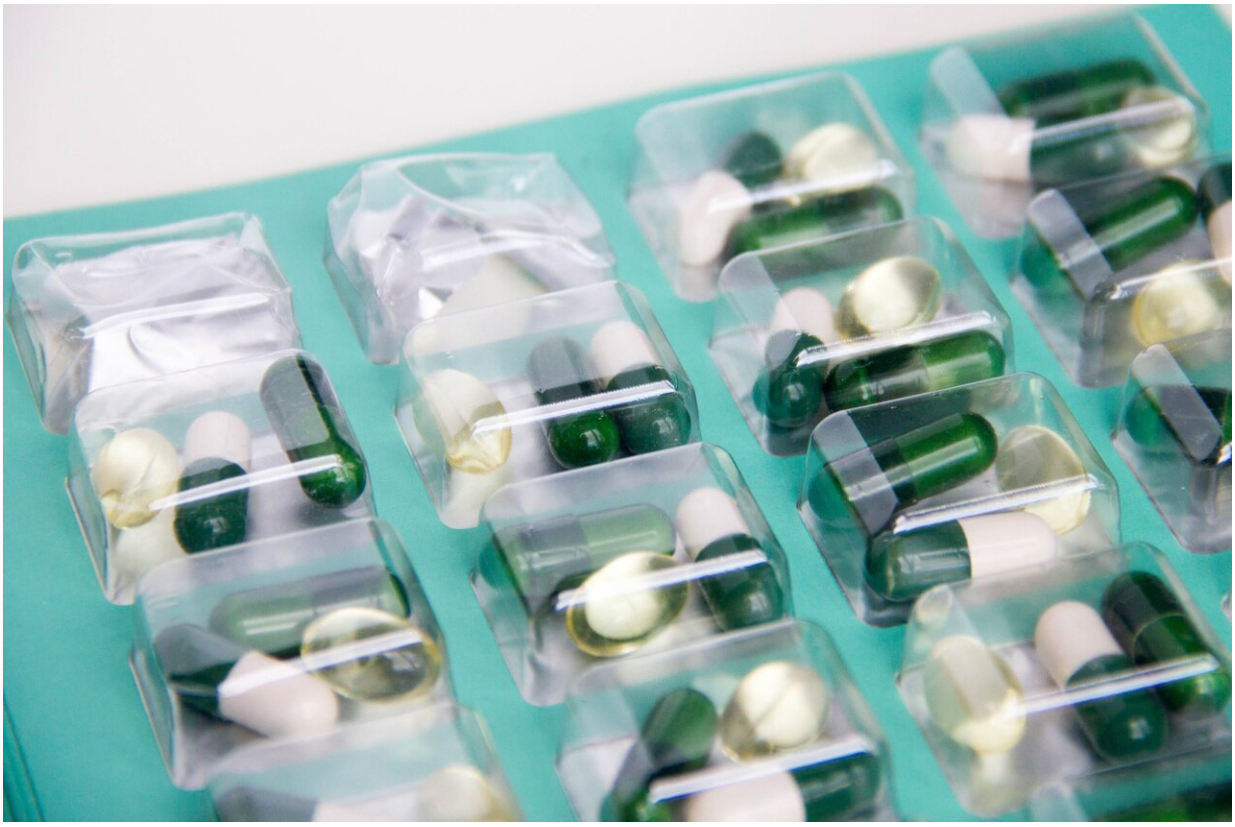

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A Phase III clinical trial at Emory University and 42 other U.S. sites has determined that a vitamin and steroid combination given to critically ill

patients with sepsis did not improve recovery, organ failure or death, when compared to a placebo. The findings of the clinical trial, which ended early, were published today in the *Journal of the American Medical Association* (*JAMA*).

"Among critically ill patients with sepsis, treatment with vitamin C, thiamine (also known as vitamin B1) and hydrocortisone did not prove to be a treatment, in fact, study participants in the treatment group did not come off the ventilator or life-saving drugs more quickly than those in the placebo group," says Jon Sevransky, MD, MHS, principal investigator of the multi-centered VICTAS study and professor of medicine in the Division of Pulmonary, Allergy, Critical Care and Sleep, Emory University School of Medicine. "Also, participants in the treatment group did not show improved organ function or improved rates of death."

Sepsis is caused by the body's overwhelming and life-threatening response to infection that can lead to tissue damage, organ failure and death and is the third leading cause of hospital deaths, according to sepsis researchers.

Between August 2018 and July 2019, 501 study participants were enrolled in the VICTAS (VItamin C, Thiamine And Steroids) trial nationwide following a diagnosis of sepsis, along with respiratory and/or cardiovascular complications. Participants were randomized to receive a combination of vitamin C, thiamine and hydrocortisone or a placebo for four days, or until discharged from the ICU. The clinical trial was double-blinded, meaning the patient/their family nor the physician knew if they were receiving the study drug or the placebo.

The researchers looked at two main outcomes. One focused on ventilator- and vasopressor-free days in the first 30 days following administration of the study drug combination or placebo. (Vasopressors

are medications used to raise blood pressure in critically ill patients.) The other focused on patient survival or death within 30 days of beginning the study drug combination or placebo.

"We found there was no statistically significant difference between the intervention and control groups in ventilator- and vasopressor-free days; participants receiving intervention got off the ventilator in 25 days versus 26 days in the control group," says David Wright, MD, professor and chair of the Department of Emergency Medicine at Emory and VICTAS co-principal investigator. "When looking at 30-day mortality rates, 22 percent of participants in the treatment group died versus 24 percent in the control group. These findings showed us that participants in the intervention group did not benefit from receiving the study drug combination."

The researchers engaged in the larger multi-site VICTAS study following several other studies involving vitamin C and sepsis, including a 2017 small study in Virginia which used the same combination therapy as in the VICTAS trial. Those results were compared to similar control patients who did not receive combination therapy. Fewer people died in the group treated with combination therapy than the control group, but further study in a rigorous, randomized control trial setting was recommended.

"The VICTAS trial was the largest trial ever conducted testing vitamin C in patients with sepsis," says Wright. "We needed to take a closer look at any benefits the vitamin/steroid drug combination might have in patients with sepsis, and this trial has helped determine that we must continue searching for a new therapy for the treatment of sepsis."

The study ended early for administrative reasons following enrollment of 501 participants. Initially, 2,000 participants were to be enrolled.

"The collaboration between emergency medicine and critical care researchers in this multi-site trial was well thought out and executed," says Sevransky. "While the VICTAS trial helped us answer some of our many questions regarding vitamin C treatment in sepsis patients, our next steps will be to look at long-term outcomes in sepsis survivors who participated in the VICTAS trial. We are also examining the role that vitamin C levels had on treatment efficacy, and will be combining the results of our trial with other published literature, known as a meta-analysis."

Emory University served as the primary grant awardee and lead center in the nationwide VICTAS trial. Johns Hopkins served as the clinical coordinating center and Vanderbilt University served as the data coordinating center.

More information: Jonathan E. Sevransky et al. Effect of Vitamin C, Thiamine, and Hydrocortisone on Ventilator- and Vasopressor-Free Days in Patients With Sepsis, *JAMA* (2021). DOI: 10.1001/jama.2020.24505

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