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Major Canadian-led trial finds vitamin C doesn't help sepsis patients

The largest study of its kind investigating the use of high-dose vitamin C for the treatment of patients with sepsis has found this vitamin does not reduce the risk of death or organ dysfunction.

Results of the multi-centre trial, called LOVIT (Lessening Organ Dysfunction with VITamin C), led by researchers at Centre de recherche du CHUS du CIUSSS de l'Estrie – CHUS and Sunnybrook Health Sciences Centre, were published in the *New England Journal of Medicine* and presented at the <u>Critical Care Reviews</u> meeting in Belfast, Ireland today.

"Among adults with sepsis in the intensive care unit, high-dose intravenous vitamin C was found not to be a helpful treatment. Importantly, we also found that study participants in the treatment group had a higher risk of death or persistent organ dysfunction at 28 days, compared to those who did not receive the treatment," say co-principal investigators of the study <u>Dr. Neill Adhikari</u>, critical care physician and associate scientist at Sunnybrook Health Sciences Centre, and <u>Dr. François Lamontagne</u>, full professor at Université de Sherbrooke and clinician-scientist at Centre de recherche du CHUS.

Patients in the trial were randomized into a treatment or placebo group. At day 28, 191 of 429 patients (44.5%) in the vitamin C group had died or had persistent organ dysfunction, as compared with 167 of 434 patients (38.5%) in the placebo group.

"Given this, we advise against using high-dose vitamin C to treat sepsis patients, unless they are part of a clinical trial," say the principal investigators.

The results challenge a treatment that has been viewed as a promising treatment for sepsis, which occurs when the body develops organ dysfunction in response to an infection. Current treatment options for sepsis are focused on antimicrobials and supportive care, such as intravenous fluids, vasopressors, mechanical ventilation and renal replacement therapy.

The authors say interest in intravenous vitamin C took off about three years ago, when a non-randomized American study found that a combination of vitamin C, steroids and thiamine, also known as vitamin B1, led to a dramatic drop in mortality among septic intensive care unit patients. Although other subsequent trials have looked at vitamin C alone, the LOVIT trial is the

largest to date, enrolling 872 patients from 35 intensive care units in Canada, France and New Zealand between 2018 and 2021.

"When we began the study, we were caught between two groups — proponents of the potential therapy and those who felt that it lacked evidence. With such strong opinions, we knew it needed to be studied further," say the principal investigators. "Clinical trials like this are critical for examining currently used interventions and telling us what should be used, what should not be used, or what should be used differently."

The authors have also conducted an updated systematic review and meta-analysis, published today in *NEJM Evidence*. Overall, this review found no convincing evidence of a benefit of vitamin C in hospitalized patients with infection. Trials of vitamin C showed variable results, which may in part be explained by differences in study methodologies. The authors also hypothesize that vitamin C may be effective in some but not all causes of sepsis, which is a syndrome caused by a variety of viral and bacterial infections.

The researchers continue to study vitamin C in hospitalized patients with COVID-19 as part of two separate ongoing trials, which are being closely monitored.

"Our results from LOVIT serve as another example of the importance of embedding research in clinical care," say the investigators. "Treatments administered to our patients should be examined in high-quality studies."

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