

## Major study finds convalescent plasma doesn't help seriously ill COVID-19 patients

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A major study has found that convalescent plasma does not reduce the risk of intubation or death for COVID-19 patients. However, the study also revealed that the antibody profile in the blood of people who have



had the virus is extremely variable and this may modify the response to the treatment.

"It has been thought that the blood plasma of COVID-19 survivors would help those seriously ill from the virus but, unfortunately, it does not," said Donald Arnold, co-principal investigator of the study, hematologist and professor of medicine at McMaster University.

"We are cautioning against using convalescent plasma to treat COVID-19 hospitalized patients, unless they are in a closely-monitored clinical trial."

Results of the study were published in the journal *Nature Medicine* today.

The Canadian-led international research team also found that patients receiving convalescent plasma experienced significantly more serious adverse events than those receiving standard care. The majority of those events were an increased need for oxygen and worsening respiratory failure. However, the rate of fatal incidents was not significantly different from the control group of patients who did not receive the blood.

The clinical trial, called CONCOR-1, stopped enrolment early in January 2021 after its independent data safety monitoring committee recommended the study was unlikely to demonstrate a benefit of convalescent plasma even if more patients were enrolled. The trial included 940 patients at 72 hospitals in Canada, the United States, and Brazil. The U.S. team was coordinated by Weill Cornell Medicine.

A secondary discovery was that convalescent plasma had highly variable donor antibody content due to the highly variable immunological response to the virus. Different antibody profiles in the convalescent



plasma were observed to significantly impact whether or not patients experienced intubation or death. Unfavorable antibody profiles, meaning low antibody titres, non-functional antibodies or both, was associated with a higher risk of intubation or death.

"These findings may explain the apparent conflicting results between randomized trials showing no benefit, and <u>observational studies</u> showing better outcomes with higher titre products relative to low titre products," said Jeannie Callum, co-principal investigator, associate scientist at the Sunnybrook Research Institute, and professor at Queen's University and the University of Toronto.

"It appears that it may not be that high-titre convalescent plasma is helpful, but rather that low-titre convalescent plasma is harmful."

Co-principal investigator Philippe Bégin said that the harm may come from the transfusion of convalescent plasma containing poorly functioning antibodies.

"One hypothesis is that those dysfunctional antibodies could compete with the patient's own <u>antibodies</u> and could disrupt the mounting immune response. This phenomenon has been observed previously in animal models and in human studies of HIV vaccines."

Bégin is a clinician scientist of CHUM and CHU Sainte-Justine and an associate professor of the University of Montréal.

He added that the CONCOR-1 investigators are expecting to collaborate with other international study investigators to understand potential risks and benefits of convalescent plasma.

"This information from Canada's largest clinical trial on convalescent <u>plasma</u> and COVID-19 may be analyzed together with the results of



several similar studies going on in the world to provide more robust information and insight that will guide <u>clinical practice</u> and health policy globally," Bégin said.

CONCOR-1 was an open-label randomized controlled trial of <u>convalescent plasma</u> or standard of care for hospitalized adults with acute COVID-19 respiratory illness. The study excluded COVID-19 patients who did not need to be in the hospital, and COVID-19 hospital patients who needed intubation at the time they were admitted to the hospital.

**More information:** Philippe Bégin et al, Convalescent plasma for hospitalized patients with COVID-19: an open-label, randomized controlled trial, *Nature Medicine* (2021). DOI: 10.1038/s41591-021-01488-2

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