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BRIEF19

A daily review of covid-19 research and policy

BREAKING NEWS RESEARCH BRIEFING

New trial of convalescent plasma for covid-19 falls flat, another setback for hyped treatment.

Is convalescent plasma the miracle treatment we were promised? The answer in the latest published clinical trial appears to be no. This is more worrisome news for a proposed treatment that has been bandied about and for which the US Food and Drug Administration granted emergency use authorization, despite the absence of compelling trial data to support its use (for more, see our prior coverage in March and August).

Released today, November 24, in *The New England Journal of Medicine* is a multicenter randomized, double-blind, placebo-controlled clinical (RCT) of 228 patients hospitalized with severe covid-19 who received either standard-of-care and convalescent plasma therapy or standard-of-care plus placebo. The primary outcome the researchers tracked was "clinical status" during follow-up at day 30.

The average age of participants was 62 years, and the majority were identified as male. Over one-fourth of patients were in intensive care units. Importantly, 93 percent of patients were on steroids, such as dexamethasone—meaning that they were already receiving the one treatment that has been shown to improve mortality rates in covid-19 patients with severe illness.

Interestingly, 68.6 percent and 61.8 percent of patients given placebo and convalescent plasma, respectively, were discharged home in good condition, though that difference was not statistically significant. Unfortunately, by day 30 there were no significant differences noted between the convalescent plasma group and the placebo group with regard to clinical outcomes or mortality. Adverse events were similar in both groups. Previous retrospective studies have found that convalescent plasma can cause serious harms, despite the general talking point that "plasma is safe." But in a trial with just 228 patients, it is unlikely that many adverse events would occur.

The idea behind convalescent plasma makes sense: when fighting an infection, our bodies manufacture specific antibodies in bulk to combat an invading pathogen. After the infection, the body maintains a stock of "memory cells," meaning that in the event of a future infection by the same virus, bacteria, or other infectious disease, our response can be both rapid and specific. Some antiviral antibodies circulate in the blood, almost like molecular surveillance drones. If an infection re-appears those antibodies spring into action.

By mid-August it was announced that over 60,000 people had already received convalescent plasma therapy for covid-19, despite any high quality evidence of its ability to improve morbidity or mortality. Since that time, likely tens of thousands of additional patients have been given this medical therapy, largely owing to the FDA's emergency use authorization. This new study adds to a growing list of randomized trials that have failed to show a benefit for this treatment. So far, only retrospective studies have been "positive." When retrospective studies and randomized trials conflict, the trials should be seen as more definitive.

More trials are ongoing. While that is good, it is important to remember that if enough trials are conducted, one or two may find a marginal benefit, just as a result of statistical chance. Any positive findings would have to be weighed against the totality of the other existing evidence. At this time, we continue to believe that most patients should not be receiving convalescent plasma therapy outside of formal clinical trials. *—Joshua Niforatos, MD*

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Brief19 is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health and public policy.