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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Convalescent plasma not so promising for the critically ill.

Early in the pandemic, convalescent plasma was heralded as a possible game-changing treatment for SARS-CoV-2 infections. The elegance of taking antibodies developed in one person's body and donating them to another seems affordable and practical. On the face of it, the idea would seem to make plenty of sense. Yet, data thus far has yielded mixed results, with some important clinical trials failing to show any statistical benefit and a more recent one showing a glimmer of hope in a subset of older patients treated very early in the course with highly-concentrated preparations.

One criticism by plasma believers is that there has been a lack of consistency in donated antibody levels. Without controlling for this, some patients could effectively be receiving a placebo dose if the donation plasma contained a miniscule level of antibodies while others might receive a motherlode of SARS-CoV-2-fighting antibodies. A new study released on Wednesday in *The New England Journal of Medicine* hoped to shed more light on this hypothesis.

Unfortunately, this study was not a clinical trial that compared patients randomized to receive either convalescent plasma or placebo. Instead, researchers from the Mayo Clinic performed a retrospective analysis of a United States patient registry and studied immunoglobulin antibody levels known as "IgG" in convalescent plasma used in the treatment of adult patients. The primary outcome measured was death within 30 days of treatment. In the end, a total of 3,082 patients met criteria for analysis. Patients died at a rate of 30 percent, 27 percent and 22 percent in the low, medium and high antibody titer groups, respectively. But when factoring in mechanical ventilation, a known risk factor for mortality, the effect was actually nullified. Nevertheless, those who received convalescent plasma early (within three days of symptom onset), were noted to have a decreased mortality risk.

While these are positive results, they do not go a long way towards increasing optimism in convalescent plasma, at least for the critically ill. Retrospective analyses are considered by researchers to be relatively weak study designs in comparison to randomized clinical trials. What remains unclear is why retrospective studies show favorable results while a slew of clinical trials have not. Further clouding the picture is that patients in the registry were excluded if antibody levels or mortality data was unknown, which significantly reduced the number of data points. The authors state that nearly 94,000 patients have received transfusions but only about a third of the data was available for this analysis. Regardless, until more rigorous studies are done, convalescent plasma isn't quite ready to join hydroxychloroquine in the scrap heap of failed therapies.

—Christopher Sampson, MD FACEP

POLICY BRIEFING

Next phase of vaccination exacerbates disparities.

The logistics of vaccine delivery drags onward as President-elect Biden prepares to take power next week. On Monday, he announced his administration's plan to release the supply held in reserve (which had been intended to ensure that people who received the first dose would be able to complete the two-jab series), with the goal to vaccinate one hundred million people in his first hundred days.

On Tuesday, US Department of Health and Human Services (HHS) Secretary, Alex Azar, announced that current inoculation rates have approached seven hundred thousand per day, and that the Trump administration would be embracing the Biden plan, announcing its plan to release the reserve supply with an eye towards reaching a goal of one million vaccinations a day.

In conjunction with this push, many parts of the country are moving to allow Phase Ib individuals to start receiving shots, as per the National Academies of Sciences, Engineering, and Medicine guidelines. Nevertheless, other parts of the US are still lagging behind due to the lack of a synchronized national strategy. Part of the disparity stems from differing plans for incarcerated individuals among various states. While studies have consistently documented the increased risk of spread in the incarcerated population (note: *staff* who work in corrections are considered Phase Ib-eligible), there is no explicit phase for persons serving sentences. Some states have decided to include this group alongside corrections staff. However, like the decision to move into a new phase, policies around the nation are not consistent. *Various*.

—Brief19 Policy Team

Kimi Chernoby, MD, JD, Policy Section Founder, Joshua Niforatos, MD Research Section Editor, Frederick Milgrim, MD, Editor-at-Large, Barb Cunningham, Copy-editor, Anna Fang, Week-in-Review. Megan Davis, social media. Kane Elfman PhD, Publishing and Design. Jeremy Samuel Faust MD MS, Editor-in-Chief.
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