Fact Sheet on Convalescent Plasma and Intravenous Immune Globulin (IVIG) for Treatment of COVID-19 in Canada

Can I prescribe COVID-19 convalescent plasma in Canada right now?

No, convalescent plasma is not available in Canada at this time. Please do not contact Canadian Blood Services or your hospital transfusion service, as no plasma has been collected to date from Canadians who have recovered from COVID-19. There is no special access program or other mechanism available to obtain this product. If convalescent plasma becomes available for transfusion in COVID-19 patients in the future, medical personnel across Canada will be notified. Canadian Blood Services is committed to working with Canadian physicians and scientists towards initiating a clinical trial to support the use of this product in patients with COVID-19. As the only regulated blood operator in Canada (except Quebec) Canadian Blood Services will be the only entity undertaking collection and production of convalescent plasma. Patients will only be able to receive therapy with COVID-19 convalescent plasma in the context of a clinical trial and many Canadian investigators are collaborating to optimize the creation of this opportunity in order to evaluate the safety and efficacy of this therapy.

Why is COVID-19 convalescent plasma not available in Canada?

At this time, there have been too few cases of COVID-19 in Canada that have recovered, and too little time since recovery, to begin to collect plasma. Further, it is not yet known at what stage of recovery sufficient antibodies will have formed to optimize the potential benefit of the plasma, or whether harm can be caused by the plasma (see below). Canadian Blood Services is required to follow regulatory requirements from Health Canada for safety, quality, and good manufacturing practices before releasing any novel blood product for transfusion. The evidence on the utility, safety and practicality of convalescent plasma is being monitored.

Do we know if convalescent plasma improves patient outcomes when infected with coronaviruses or influenza?

No. Clinical trials comparing convalescent plasma to a placebo or other comparative arm have not been performed.

What is the status of the evidence?

A systematic review and meta-analysis of plasma or plasma derived immunoglobulin for use in treating viral pneumonias was published in 2015; it included 3 systematic reviews including 32 reports involving 1327 patients who had either severe influenza or coronavirus infection (SARS).[1] Overall the quality of the evidence was low to very low. This report included 6 case reports, 20 case series, 2 case-comparison studies, and 1 prospective cohort study. There were no randomized trials. The recipients either had severe influenza or coronavirus infection (SARS). The antibody titre on the product was greater than 1 in 80 to 1 in 160. The dose used was a single infusion of 200 – 500 mL of convalescent plasma. The report concluded that the use of convalescent plasma may be associated with improved outcomes (reduction in mortality, hospital and intensive care unit length of stay, and duration of mechanical ventilation) and

appeared to be safe (only mild reactions). A recently published uncontrolled case series of 5 critically ill patients with COVID-19 and acute respiratory distress syndrome (ARDS) suggested that administration of convalescent plasma containing neutralizing antibody was followed by an improvement in clinical status and may be helpful in the treatment of COVID-19 patients with ARDS.[2] Further well-designed clinical trials are absolutely necessary to determine the effectiveness convalescent plasma.

When in the course of the illness might convalescent plasma be useful?

Convalescent plasma theoretically could be used for prophylaxis (after an exposure) to reduce the risk of becoming infected or treatment of the disease after symptom onset. The effectiveness in either situation is unknown. The limited experience in infected patients suggests it is most effective if administered early (within 4 days of onset of symptoms) and is not effective if administered after 16 days from symptom onset.[3] It is hypothesized that the passive antibodies work by neutralizing the initial small inoculum and is less effective against established disease.[4] It is unknown how long the passive immunity may protect the recipient.

Could convalescent plasma potentially be harmful?

There are plausible concerns that convalescent plasma may be pro-inflammatory and therefore enhance the viral pneumonitis. There are also theoretical concerns regarding the potential for inadvertent transmission of virus through plasma; however, there have been no cases of transfusion transmitted coronavirus infections. Concerns have been raised about the phenomenon of antibody-dependent enhancement where the viral disease is enhanced in the presence of the antibodies to that virus or a similar viral strain. For coronaviruses, there is a theoretical concern that antibodies to one type of coronavirus could enhance infection of another viral strain. Anecdotal evidence of use of convalescent plasma in 245 patients in China suggests it is safe[4] but trials are needed to confirm/refute the risk of antibody-dependent enhancement. Passive immunotherapy could also attenuate the immune response and place treated patients of greater risk of re-infection. Known transfusion risks of plasma remain risks to patients (e.g., anaphylaxis, transfusion-related acute lung injury, transfusion-associated circulatory overload).

What proportion of COVID-19 recovered patients/healthcare workers might have detectable antibodies after recovery?

In general, in infection with related beta-coronaviruses (e.g., MERS-CoV) about a third of recovered patients tested at 6-18 months after recovery had detectable antibodies suggesting the antibody titre wanes over time.[5] Not all recovered patients would be eligible to donate convalescent plasma. Many of the potential donors would not be eligible to donate due to very slow recovery from the illness and baseline comorbidities. Female blood donors with anti-HLA antibodies would also have to be deferred from donation due to the risk of transfusion-related acute lung injury, which could potentially worsen the acute lung injury from COVID-19 itself. In some donations, antibodies against COVID-19 may be present but neutralizing antibodies may not be high enough to be effective.

Is IVIG a treatment option for COVID-19?

There is no evidence to suggest that IVIG is an effective treatment for COVID-19. The recovered plasma used to manufacture currently available IVIG does not yet have anti-COVID-19 activity. It is possible that IVIG may have some immunomodulatory properties for patients with COVID-19 and IVIG might modify cytokine expression.[3] IVIG use in SARS was associated with a high rate of venous thromboembolism and therefore IVIG may cause harm in COVID-19 patients. Currently, IVIG is not available for patients with COVID-19. Given the limited supplies of IVIG, its use in a pandemic for large numbers of infected patients would rapidly deplete current stocks, and other patients with diagnoses where IVIG is proven effective would no longer have access.

References

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