Clinical Guidance on the Use of Convalescent Plasma in the Care of COVID-19

Purpose

To describe the clinical indications and processes needed to request and administer therapeutic convalescent plasma to COVID-19 patients.

Given that the clinical evidence supporting this EUA was not obtained from prospective, well-controlled randomized clinical trials (RCTs), additional RCTs are needed. Convalescent plasma should not be considered a new standard of care for the treatment of patients with COVID-19.

Rationale

Beyond providing supportive care, there currently exist few treatment options for coronavirus disease (COVID-19) and the related pneumonia, the infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

- Experience from prior outbreaks with other coronaviruses, such as SARS-CoV-1 shows that such convalescent plasma contains neutralizing antibodies to the relevant virus.(1). In the case of SARS-CoV-2, the anticipated mechanism of action by which passive antibody therapy would mediate protection is viral neutralization. It is hoped this therapeutic effect will decrease the chance of further deterioration and the need for intensive care and/or assisted ventilation.

- Recently, Joyner et al, in a publication by the US EAP COVID-19 Plasma Consortium, reported transfusion of convalescent plasma with higher antibody levels to hospitalized COVID-19 patients significantly reduced mortality compared to transfusions with low antibody levels. Transfusions within three days of COVID-19 diagnosis yielded greater reductions in mortality. (2) These data provide support for the efficacy of human convalescent plasma as a therapeutic agent in hospitalized COVID-19 patients. On August 23, 2020, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for convalescent plasma for the treatment of hospitalized COVID-19 patients (3). This EUA included a Fact Sheet for Health Care Providers (4).

Clinicians should be aware that CCP is a scarce resource. During the current public health emergency, this resource will be managed in alignment with the AAH Scarce Resource Allocation Guidelines.

Indications for the use of CCP

- The patient must be hospitalized with COVID-19 respiratory symptoms and confirmation via COVID-19 SARS-CoV-2 RT-PCR testing.
- The patient or their legal representative is willing and able to provide written informed consent. Patients must be provided a copy of the FDA’s Fact Sheet for Patients/Caregivers’ Emergency Use Authorization (EUA) of COVID-19 Convalescent Plasma for Treatment of COVID-19 in Hospitalized Patients (5)
- The patient should be judged by the provider to be at high risk of progression to severe disease*
- Ideally, CCP should be given within 3 days after the patient has been diagnosed with COVID-19 (as above)
- When available, units will be labeled with the titer level, whether high titer or low titer

Severe disease is defined as one or more of the following*:
- Dyspnea
- Respiratory rate greater than or equal to 30/min
- Blood oxygen saturation less than or equal to 93%
- Partial pressure of arterial oxygen to fraction of inspired oxygen ratio less than 300 and/or Lung infiltrates greater than 50% within 24-48 hours
Clinical Guidance on the Use of Convalescent Plasma in the Care of COVID-19

Risks:
A theoretical risk of CCP is the phenomenon of antibody dependent enhancement of infection (ADE). An additional risk is that antibody administration may attenuate the immune response, leaving the patient more susceptible to infection (5) Other risks include all known risks associated with non-convalescent plasma transfusion.

Benefits:
The potential benefits may include improvement in symptoms, reduced need for supportive therapies to improve oxygenation, and reduced mortality.

Risk: Benefit Calculation
Based on the totality of available evidence at this time, the benefits appear to outweigh the risks of therapy

Contraindications
1. Receipt of pooled immunoglobulin in past 30 days
2. Other clinical contraindication to transfusion or history of prior severe reactions to transfusion of blood products. Recommend discussion with the Transfusion Service to discuss specific concerns regarding contraindications.

Use in Specific Patients
Pediatrics: has not been evaluated. The decision to treat patients less than 18 years of age should be an individualized decision

Geriatric: the available data are reported for the overall population. The rates of adverse events were less than 0.37% (5)

Pregnancy: has not been evaluated. Decision to treat should be an individualized decision

Requesting and Obtaining Convalescent Plasma
- Physicians should order convalescent plasma via the electronic health record

Patient Preparation and Monitoring
A. Informed consent obtained; the patient and family must be provided with a copy of the Fact Sheet for Patients, Parents and Caregivers (5)
B. Baseline evaluation to document in the medical record:
   1. Demographics (age, sex ethnicity, race)
   2. Medical history (timing of exposure to COVID-19 source patient, acute and chronic medical condition, medications, allergies)
   3. COVID-19 symptom screen (fevers, cough, shortness of breath), onset of symptoms, source of contagion
   4. Vital signs
   5. COVID-19 testing (RT-PCR) from nasopharyngeal, throat, tracheal aspirate or broncho-alveolar lavage and stool (optional) samples
   6. Blood typing, CBC, comprehensive metabolic panel (consider labs within 24 hours of beginning therapy) – or if older than 72 hours
Clinical Guidance on the Use of Convalescent Plasma in the Care of COVID-19

7. Serological testing: anti-SARS CoV-2 titers when available
8. Urine or serum pregnancy test for females of childbearing potential (results from laboratory tests obtained up to 7 days before enrollment may be used for the pregnancy test, however serum pregnancy tests recommended)
9. Determination of eligibility as per inclusion/exclusion criteria, consent for treatment, positive for COVID-19, respiratory symptoms
10. Any medical condition arising after consent should be recorded as an adverse event
11. Monitor INR for patients on warfarin therapy

Dosing

- Start with one CCP unit (about 200 ml). Administration of additional units should be based on the prescribing physician’s judgment, and the patient’s clinical response. A maximum of two units is recommended. Consultation with Infectious Disease and Critical Care (eICU if site intensivist not available) is recommended for additional units beyond two.
  - Recommend administering this therapy within 3 days of diagnosis
  - Recommend initiating therapy before the patient progresses to the need for mechanical ventilation support

Administration

- Rate of transfusion:
  - Physicians should transfuse each unit of convalescent plasma at an infusion rate that adheres to Advocate Aurora guidelines and best clinical practice.
- Pretreatment to minimize transfusion reactions (e.g. acetaminophen, diphenhydramine) may be given per physician’s discretion
- If a reaction develops during infusion, the infusion may be slowed or stopped as per the physician’s decision.

Monitoring During Treatment

- Nursing care and monitoring should align with Advocate Aurora Health Care’s policy and procedure for the Administration of Blood and Blood Products

Recommended Post Therapy Monitoring

1. Vital signs daily or as ordered by the physician, or per unit standard
2. COVID-19 symptom assessment (fevers, cough, shortness of breath)
3. New medical conditions or adverse events or transfusion reactions: these must be reported via the site’s local transfusion service (blood bank)
4. Consider:
   a. CBC, comprehensive metabolic panel, CRP (day 1 and 7) – repeat if changes from baseline.
   b. Serological testing: anti-SARS CoV-2 titers.
Clinical Guidance on the Use of Convalescent Plasma in the Care of COVID-19

References


(3) EUA 26382: Emergency Use Authorization (EUA) Request (original request 8/12/20; amended request 8/23/20)

(4) EUA Fact Sheet for Health Care Providers. COVID-19 Convalescent Plasma (FDA Publication August 23, 2020)


Dr. Mehraboon S. Irani
Senior Medical Director, Clinical and Therapeutic Services, Versiti Blood Center of Wisconsin,
Medical Director, Transfusion Services, ACL Wisconsin,
Medical Director, Versiti Applied Research Laboratory,
Associate Professor of Pathology, Medical College of Wisconsin,
Milwaukee, WI
414-937-6347 Email: MehraboonS.Irani@aah.org