

Convalescent plasma as a potential therapy for COVID-19



Lancet Infect Dis 2020

Published Online

February 27, 2020

[https://doi.org/10.1016/](https://doi.org/10.1016/S1473-3099(20)30141-9)

[S1473-3099\(20\)30141-9](https://doi.org/10.1016/S1473-3099(20)30141-9)

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which originated in Wuhan, China, has become a major concern all over the world. The pneumonia induced by the SARS-CoV-2 is named coronavirus disease 2019 (COVID-19). By Feb 22, 2020, this virus has affected more than 77700 people worldwide and caused more than 2300 deaths. To date, no specific treatment has been proven to be effective for SARS-CoV-2 infection. Apart from supportive care, such as oxygen supply in mild cases and extracorporeal membrane oxygenation for the critically ill patients, specific drugs for this disease are still being researched. In the USA, the first patient infected with SARS-CoV-2 was treated by supportive care and intravenous remdesivir, before the patient recovered and was discharged.¹ However, randomised clinical trials are needed to evaluate the safety and efficacy of remdesivir in the treatment of COVID-19.

Convalescent plasma or immunoglobulins have been used as a last resort to improve the survival rate of patients with SARS whose condition continued to deteriorate despite treatment with pulsed methylprednisolone. Moreover, several studies showed a shorter hospital stay and lower mortality in patients treated with convalescent plasma than those who were not treated with convalescent plasma.²⁻⁴ In 2014, the use of convalescent plasma collected from patients who had recovered from Ebola virus disease was recommended by WHO as an empirical treatment during outbreaks.⁵ A protocol for the use of convalescent plasma in the treatment of Middle East respiratory syndrome coronavirus was established in 2015.⁶ In terms of patients with pandemic 2009 influenza A H1N1 (H1N1pdm09) virus infection, a prospective cohort study by Hung and colleagues showed a significant reduction in the relative risk of mortality (odds ratio 0.20 [95% CI 0.06–0.69], $p=0.01$) for patients treated with convalescent plasma.⁷ Additionally, in a subgroup analysis, viral load after convalescent plasma treatment was significantly lower on days 3, 5, and 7 after intensive care unit admission. No adverse events were observed. A multicentre, prospective, double-blind, randomised controlled trial by Hung and colleagues showed that using convalescent plasma from patients who recovered from the influenza A H1N1pdm09 virus infection to treat patients with severe influenza A H1N1 infection was

associated with a lower viral load and reduced mortality within 5 days of symptom onset.⁸ A meta-analysis by Mair-Jenkins and colleagues showed that the mortality was reduced after receiving various doses of convalescent plasma in patients with severe acute respiratory infections, with no adverse events or complications after treatment.⁹ Another meta-analysis by Luke and colleagues identified eight studies involving 1703 patients with 1918 influenzapneumonia from 1918 to 1925 who received an infusion of influenza-convalescent human blood products, which showed a pooled absolute reduction of 21% (95% CI 15–27; $p<0.001$) in the overall crude case-fatality rate at low risk of bias.¹⁰

One possible explanation for the efficacy of convalescent plasma therapy is that the antibodies from convalescent plasma might suppress viraemia. Schoofs and colleagues reported that 3BNC117-mediated immunotherapy, which is a broad neutralising antibody to HIV-1, enhances host humoral immunity to HIV-1.¹¹ An in vivo trial also showed that the effects of this antibody were not only limited to free viral clearance and blocking new infection, but also included acceleration of infected cell clearance.¹² Viraemia peaks in the first week of infection in most viral illnesses. The patient usually develops a primary immune response by days 10–14, which is followed by virus clearance.⁴ Therefore, theoretically, it should be more effective to administer the convalescent plasma at the early stage of disease.⁴ However, other treatments might have an effect on the relationship between convalescent plasma and antibody level, including antiviral drugs, steroids, and intravenous immunoglobulin.¹⁰

According to WHO,¹³ management of COVID-19 has mainly focused on infection prevention, case detection and monitoring, and supportive care. However, no specific anti-SARS-CoV-2 treatment is recommended because of the absence of evidence. Most importantly, the current guidelines emphasise that systematic corticosteroids should not be given routinely for the treatment of COVID-19, which was also the recommendation in a Comment in *The Lancet*.¹⁴ Evidence shows that convalescent plasma from patients who have recovered from viral infections can be used as a treatment without the occurrence of severe adverse events. Therefore, it might be worthwhile to test the

safety and efficacy of convalescent plasma transfusion in SARS-CoV-2-infected patients.

This work is supported by grants from the Clinical Medical Study Program of Children's Hospital of Chongqing Medical University, China (YBXM-2019-013). We declare no competing interests.

Long Chen, Jing Xiong, Lei Bao, *Yuan Shi
petshi530@vip.163.com

Department of Neonatology, Ministry of Education Key Laboratory of Child Development and Disorders; National Clinical Research Center for Child Health and Disorders; China International Science and Technology Cooperation base of Child development and Critical Disorders; Children's Hospital of Chongqing Medical University; Chongqing Key Laboratory of Pediatrics, Chongqing, 400014, China (LC, JX, LB, YS)

- 1 Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020; published online Jan 31. <https://doi.org/10.1056/NEJMoa2001191>.
- 2 Lai ST. Treatment of severe acute respiratory syndrome. *Eur J Clin Microbiol Infect Dis* 2005; **24**: 583–91.
- 3 Soo YO, Cheng Y, Wong R, et al. Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. *Clin Microbiol Infect* 2004; **10**: 676–78.
- 4 Cheng Y, Wong R, Soo YO, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis* 2005; **24**: 44–46.
- 5 WHO. Use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease for transfusion, as an empirical treatment during outbreaks. 2014. <http://apps.who.int/iris/rest/bitstreams/604045/retrieve> (accessed Feb 20, 2020).
- 6 Arabi Y, Balkhy H, Hajeer AH. Feasibility, safety, clinical, and laboratory effects of convalescent plasma therapy for patients with Middle East respiratory syndrome coronavirus infection: a study protocol. *Springerplus* 2015; **4**: 709.
- 7 Hung IF, To KK, Lee CK, et al. Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1) 2009 virus infection. *Clin Infect Dis* 2011; **52**: 447–56.
- 8 Hung IFN, To KKW, Lee CK, et al. Hyperimmune IV immunoglobulin treatment: a multicenter double-blind randomized controlled trial for patients with severe 2009 influenza A(H1N1) infection. *Chest* 2013; **144**: 464–73.
- 9 Mair-Jenkins J, Saavedra-Campos M, Baillie JK, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. *J Infect Dis* 2015; **211**: 80–90.
- 10 Luke TC, Kilbane EM, Jackson JL, Hoffman SL. Meta-analysis: convalescent blood products for Spanish influenza pneumonia: a future H5N1 treatment? *Ann Intern Med* 2006; **145**: 599–609.
- 15 Schoofs T, Klein F, Braunschweig M, et al. HIV-1 therapy with monoclonal antibody 3BNC117 elicits host immune responses against HIV-1. *Science* 2016; **352**: 997–1001.
- 12 Lu CL, Murakowski DK, Bournazos S, et al. Enhanced clearance of HIV-1-infected cells by broadly neutralizing antibodies against HIV-1 in vivo. *Science* 2016; **352**: 1001–04.
- 13 WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. 2020. <https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf> (accessed Feb 20, 2020).
- 14 Clark DR, Jonathan EM, JKB. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet* 2020; published online Feb 7. [https://doi.org/10.1016/S0140-6736\(20\)30317-2](https://doi.org/10.1016/S0140-6736(20)30317-2).