Convalescent plasma as a potential therapy for COVID-19

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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 77 700 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 a Commnt 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.

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