

## Article Commentary

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# Coronavirus drugs: Using plasma from recovered patients as a treatment for COVID-19

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**Abstract.** The ongoing COVID-19 pandemic has infected nearly 400,000 individuals with 17000 deaths since it was first identified in human populations in December 2019, in Wuhan, China. No antiviral therapies or vaccines are available for their treatment or prevention. Passive immunization PI through broadly neutralizing antibodies that bind to the specific antigens of SARS-CoV 2 might be a potential solution to address the immediate health threat of COVID-19 pandemic while vaccines are being developed. The PI approach in treating COVID-19 is discussed herein, including a summary of its historical applications to confront epidemics.

Keywords: COVID-19, passive immunization, coronaviruses, convalescent plasma

## 1. Introduction

Coronaviruses (CoVs) are large, enveloped, positive-sense, single-stranded RNA viruses that can cause diseases in both animals (gastrointestinal illnesses), and humans (respiratory diseases [1,4,19]). Before 2003, human CoVs were not considered deadly viruses; circulated strains were causing mild flu-like symptoms. In 2003, the world was shocked by the first pandemic of the 21st century, the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), resulting in 774 deaths and more than 8000 patients [8]. Nine years later, a strain of CoV had evolved that caused the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), approximately 2500 cases have been confirmed, including 861 deaths with a case–fatality rate of 34.4% [10].

In December of 2019, a series of acute respiratory illness cases with unknown etiology has been reported in Wuhan, China [9]. On January 7, 2020, Chinese authorities confirmed that the causative agent was a novel coronavirus and officially named it the coronavirus disease 2019 COVID-19, and the virus was scientifically named SARS-CoV-2, which was declared later on as a world pandemic. As of March 24, 2020, the virus has infected nearly 400,000 patients, including 17,234 who have died. Even though

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the Chinese government has successfully contained the outbreak, the virus keeps spreading elsewhere in the world, putting the international community on alert that the worst scenarios are possible.

Human-to-human transmission of SARS-CoV-2 act through respiratory droplets and direct contact, though fecal-oral transmission might be possible. The incubation period can range between 0 up to 24 days, with an average of 3 days [7]. Common early symptoms include fever, dry cough, and malaise. Later on, symptoms such as dyspnea, vomiting, and diarrhea tend to appear. Moreover, the virus was characterized by rapidly progressive pneumonia, a range between 2 to 7 days after early symptoms appear, particularly at the elder and pre-conditioned patients [7,9]. A recent study suggests that SARS-CoV-2 (similar to SARS-CoV) primarily infects ciliated bronchial epithelial cells and type II pneumocytes, where it binds to the surface receptor, angiotensin-converting enzyme 2 (ACE2) and initiates fusion with the host cells [12].

Currently, there are no specific antiviral treatments or vaccines available for COVID-19. While many companies are working on finding a medication, developing a vaccine for SARS-CoV-2 seems the easier pathway and has become a global public health priority. However, creating a viable vaccine requires a long time; scientists estimate a period between 12–18 months.

While many scientific laboratories are working on vaccines, one potential vaccine might be available sooner than that, namely the passive vaccine or passive immunization (PI). Based on historical experience, the concept of PI might be effective in COVID-19 treatment or prevention. In this paper, we aim to provide an overview of PI and its success in using it for viral infection treatment and discuss why PI might be a vital option for treating COVID-19 at the moment.

## 2. Passive immunization

PI is a method to obtain instant, short-term fortification against infectious agents by introducing the pathogen-specific antibodies to patients. These specific antibodies can bind to the pathogen antigens and block its interaction with a cell receptor, which is extremely applicable in the case of viral antigens that facilitate the attachment to the target receptors [17]. After exposure to a viral infection, the body of the patient creates antibodies to fight off the virus. These antibodies in the blood of a recovered patient can be collected as convalescent plasma (CP) and transferred to the blood of a newly infected patient, where they can neutralize the pathogen, boost the immunity of that patient, and leads to its enucleating from the blood circulation after transfusion into the patient [14].

After large-scale epidemics, CP gets increasing attention as a preferred therapeutic tool for many reasons: collecting a large volume per session, frequent donations are possible, and without any impact on the donor's hemoglobin [14], which seems an attractive method in case of COVID-19. Currently, there are around 100,000 patients who have survived and the number keep increasing, and we believe that many of them would donate their plasma to get over this pandemic. However, in order to have an effective CP infusion, donor plasma should be tested for antibody activity and neutralization activity. In a resource limited situation, ELISA IgG could be a substitute for neutralization tests [11].

## 3. Passive immunization and other outbreaks

The history of the use of PI dates back to the beginnings of the twentieth century, where the technique has been used without the knowledge of modern immunology. Different analyses from the Spanish flu pandemic confirmed that PI had been implemented, and patients who received a serum had lower mortality

than others [13]. Successful experimental usage of PI in epidemics was carried out during the Ebola virus (EBO) outbreak in 1995 in Kikwit, the Democratic Republic of Congo. Eight patients were transfused with blood donated by five convalescent patients. The mortality rate was significantly lower (12.5%) than the case fatality rate (80%) in Kikwit and other cities [15]. Evaluation of the safety and efficacy of CP for the treatment of the Ebola virus disease (EVD) was carried out in Guinea. Results revealed that treatment with CP was acceptable to donors, patients, family, and health care providers in the middle of an EVD outbreak with no serious adverse reactions associated with the transfusion of CP [6].

Moreover, PI has been used against the chikungunya virus (CHIKV) as well. This is a reemerged arbovirus responsible for a massive outbreak of infections in India and has a vast potential to spread globally because of the worldwide distribution of its mosquito vectors. CP was used for the treatment of severe cases of individuals who were exposed to CHIKV, and results showed an efficient prevention strategy [3]. In a recent use of PI technique, a study described a successful trial to treat five severe H1N1 infected patients by intravenous immunoglobulin (IVIG) as potential salvage therapy. The article suggested that IVIG therapy deserves additional evaluation among critically ill patients with H1N1 infection [5]. Although these are studies, and the situation might be different for COVID-19, they do show the potential of using PI in the treatment of different viral infections.

#### 4. Passive immunization and coronaviruses

Before COVID-19, there have been two other CoVs epidemics: SARS-CoV in Guandong, China, and MERS-CoV in Saudi Arabia. Since these CoVs have a zoonotic origin and host jump to infect humans, we did not have any registered medication or a vaccine against these diseases, leading to the option of using PI. The effectiveness of the PI technique has been exemplified in a report by Soo et al. in which their results showed good clinical outcomes as patients were discharged by day 22 following the onset of symptoms. The patients in the CP group had a significantly shorter hospital stay and lower mortality rate than other groups [18]. This distinction is further exemplified in studies using CP therapy, such as studying the efficacy of CP therapy in the treatment of patients with SARS-CoV that was performed on 80 SARS-CoV patients who were given CP at the Prince of Wales Hospital, Hong Kong in 2003, where the higher discharge rate was observed among patients who were given CP before day 14 of the illness [2]. The CP efficiency in treating human CoVs was documented by a study on healthcare workers (HCW) in a Taiwanese hospital [20]. The study reported that all infected HCW who were infected with SARS-CoV and failed to respond to the available treatment, survived after transfusion with CP obtained from three recovered patients. The findings showed that CP transfusion may be considered a very good option in treating SARS-CoV patients [20].

Another evidence of CP efficiency was examined by Qin et al. in 2006. They prepared a safe SARS-CoV vaccine in monkeys; findings revealed that the use of purified inactivated SARS-CoV vaccine could induce high levels of neutralizing antibody and protect the monkeys from the SARS-CoV [16]. Taken together, these studies show that CP transfusion has a promising potential to be used in COVID-19 treatment.

#### 5. Conclusion

The emerging COVID-19 pandemic is the third outbreak that is caused by CoVs in the twenty first century and might be the most important infectious disease that represents a major public health threat to

all countries worldwide. In a time where no registered antiviral drug or a vaccine are available, PI might help in slowing down the deadly virus and save lives, particularly the elderly and pre-conditioned patients, which is the case in COVID-19.

Since its discovery, PI has proven to be lifesaving for many acute infections. Even though COVID-19 might be different, PI experiences provide relevant historical precedents that are both reassuring and useful as humanity now confronts this pandemic. Different analyses demonstrated that the viral load and mortality rate were significantly reduced by using CP for the treatment of COVs infections, including SARS-CoV and MERS-CoV, especially if it was introduced early after symptom onset. With the current deterioration of global health systems, we believe that PI deserves the clinical evaluation as a method for treating COVID-19.

### Conflict of interest

None to report.

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