

A recent article in the Journal of American Medical Association, JAMA, looked at the old therapy convalescent plasma for the treatment of COVID-19 against this new disease.

I have discussed this before in my review of novel treatments, but I think it is now worthwhile reviewing the treatment.

There is little or no evidence to support its use. It is a treatment which is more than 100 years' old which has been used off and on over the century. Basically, it involves taking antibody rich convalescent plasma from healthy people who have recovered from the infectious disease of interest.

It is thought to give the recipient's immune system a running start. In the early days' animals were used.

### **Convalescent Plasma as a Potential Therapy for COVID-19**

Convalescent plasma or immunoglobulins were used as a last resort to improve the survival rate of patients with SARS whose condition continued to deteriorate. Several studies also showed a shorter hospital stay and lower mortality in patients treated with convalescent plasma than those who were not treated with convalescent plasma. It was recommended by the World Health Organisation for the treatment of Ebola in 2014.

A protocol for the use of treatment was established for the Middle East respiratory syndrome coronavirus in 2015. In the pandemic 2009 influenza A H1N1 virus infection, a study by Hung and colleagues showed a significant reduction in the risk of mortality for patients treated with convalescent plasma. Subgroup analysis showed a significantly lower viral load after treatment on days 3, 5 and 7. No adverse events were observed whatsoever.

One possible explanation for the efficacy of convalescent plasma therapy is that antibodies from convalescent plasma might suppress the viraemia. Evidence therefore exists that convalescent plasma from patients who have recovered from viral infections can be used as a treatment with the occurrence of severe adverse events.

In a paper published online on March 27, in the Journal of American Medical Association, it was reported that five severely ill patients with COVID-19 treated in the Shenzhen Third People's Hospital China used plasma from recovered individuals. All patients had severe respiratory failure and were receiving mechanical ventilation. Four patients without co-existing diseases also receive convalescent plasma around hospital day 20 and a patient with cardiovascular disease received the plasma transfusion at day 10.

Although these patients were receiving anti-viral treatment primarily with Lopinavir, Ritonavir and Interferon, the use of convalescent plasma contributed to their recovery because the clinical status of all patients improved approximately one week after transfusion. (It should be noted, however, that these treatment groups were not evaluated in a randomised clinical trial so there are limitations to this idiosyncratic use. Patients were also receiving numerous other therapies.)

It is also not clear as to when the convalescent plasma should be administered. It was used up to three weeks after hospital admission. Had it been given earlier it may have been associated with different clinical outcomes. However, despite these limitations, the study does provide some evidence to support the possibility of evaluating this therapy in a more vigorous way involving COVID-19 patients with severe illness.

The use of convalescent plasma is not new; it has been used during the SARS pandemic 2009 influenza, avian influenza A and severe haemorrhagic fever such as Ebola outbreak.

There also may be other factors within convalescent plasma such as replenishing, coagulation factors which help as well as antibodies which limit viral replication.

Deploying this passive antibody therapy against COVID provides an unprecedented opportunity to perform clinical studies of the efficacy of this treatment against a viral agent.

Simply, it is taking the blood of a convalescent patient who has recovered from COVID-19, clearly rhesus group cross matching, checking for infections, etc. and transfusing the convalescent plasma into infected patients.

Possibly blood centres should already start collecting plasma from convalescent donors, preferably at the leading edge of the infectious wave and healthcare workers could encourage COVID-19 infected patients to donate after hospital discharge.

The plasma would be tested, frozen and distributed to hospitals. Paired samples would be retained for concurrent investigations.

Despite the potentially rapid availability, the deployment of convalescent plasma will have a limited reach because transfusions are typically performed in hospital settings and may require large infusion volumes.

There are of course adverse reactions to transfusions such as mild fever and allergy as well as life threatening bronchospasm, transfusion-related acute lung injury and circulatory overload in patients with cardiorespiratory disorders. There is also the small risk of infectious disease transmission.

It is important that academia and industry investigate the efficacy of passive antibody therapies to COVID-19 infection. Jeannette Guarner March 27, 2020, JAMA, Journal of American Medical Association.

## The London General Practice