National COVID-19 Health and Research Advisory Committee

Date of report: 7 May 2020

Convalescent plasma for prevention and treatment of COVID-19

Focus:
The focus of this paper is on the use of convalescent plasma for the prevention and treatment of COVID-19. In considering this issue, other similar therapies were also considered specifically: treatment with hyperimmune globulin and monoclonal antibodies for both the prevention and treatment of COVID-19.

This advice is point in time and may need further review as more evidence is available.

Conclusions:

NCHRAC conclusion 1: Australian research into the use of convalescent plasma in the form of controlled clinical trials should be actively supported.

Trials of convalescent plasma for treatment and prophylaxis are planned as part of the international REMAP-CAP trial with a newly active treatment site in the UK.

NCHRAC conclusion 2: Australian research into the use of hyperimmune globulins as potential treatment for COVID-19 should be actively supported.

The working group discussed the CSL collaboration with a number of international partners to trial the use of hyperimmune globulin as a COVID-19 treatment. On May 6th, the Hon Greg Hunt, Minister for Health, welcomed the announcement from CSL that development and manufacturing will occur at CSL’s Broadmeadows facility and plasma will be collected in partnership with Australian Red Cross Lifeblood.

NCHRAC conclusion 3: Australian research into the use of monoclonal antibody treatment for COVID-19 should be actively supported.

The working group considered the potential for monoclonal antibody treatment of COVID-19. NCHRAC noted that there are no current sources of hyperimmune globulin or monoclonal antibodies for the treatment of COVID-19 and therefore no information from in-human studies on their potential efficacy.

1 NHMRC is providing secretariat and project support for the Committee, which was established to provide advice to the Commonwealth Chief Medical Officer on Australia’s health response to the COVID-19 pandemic. The Committee is not established under the NHMRC Act and does not advise the NHMRC CEO.
The working group identified the following populations that would benefit from convalescent plasma if it is effective:

- severely ill patients with COVID-19 and COVID-19 patients with existing co-morbidities (treatment)
- hospitalised COVID-19 patients who are at risk of developing more severe illness (treatment)
- nursing home residents (post-exposure prophylaxis)
- family contacts of COVID-19 cases (prophylaxis), and
- frontline health care workers (both prophylaxis and treatment).

The feasibility of using convalescent plasma as a last resort treatment for persons severely affected by COVID-19, prior to the conclusion of any clinical trials, was also considered. However, it was concluded that there was likely to be no real benefit in offering this treatment in this context as it was not expected to provide the immediate benefit required for this group of patients.\(^v\)

**Background**

The use of convalescent plasma for the prevention and treatment of COVID-19 would be intended to produce passive immunity in patients as opposed to the active immunity that would be induced by a vaccine. Convalescent plasma is not a new therapy and has been used and trialled in influenza, SARS-1 and Ebola virus infections.\(^vi, vii, viii, ix\) Convalescent plasma for influenza treatment showed promise in preclinical studies but showed little benefit in controlled human studies. Only a few small studies have been published in China and Korea on the use of convalescent plasma to treat COVID-19; they were not controlled trials and the plasma was not pooled.\(^x, xi, xii\) Some of the published studies showed promise; however, evidence of efficacy can only be obtained from controlled clinical trials.

Hyperimmune globulin is concentrated from convalescent plasma but has a longer shelf life than convalescent plasma and can be sourced from both male and female plasmapheresis donors (whereas convalescent plasma is only sourced from male donors).

Major benefits of using monoclonal antibodies as a treatment is that their production is scalable and uniform. Biotechnology affords the development of monoclonal antibodies of very high affinity for the virus without the need to collect plasma from donors who have previously been exposed to SARS COV-2. The efficacy of monoclonal antibodies as treatments or prophylaxis would depend on the conservation of their viral target and their half-life in the patient following administration. There is a theoretical possibility that antibodies could enhance viral entry into cells and worsen infection. These issues could be addressed in preclinical and then pilot stage clinical trials.
Other considerations

In drawing the above conclusions, NCHRAC considered:

- That the ability to measure antibodies present in plasma is important for standardising convalescent plasma and hyperimmune globulin treatments and identifying potential donors. This issue has been discussed in the RRIF briefing paper.xiii
- It is not known if there are any major risks in the use of convalescent plasma for treatment of COVID-19 disease. While the risks are likely to be low based on experience in other infectious diseases, this cannot be said with certainty.
- The logistics of convalescent plasma and hyperimmune globulin treatment in Australia include the identification and recruitment of suitable donors, accessing plasma, methods for plasma collection and dosing. These issues need to be carefully considered as part of any clinical trial that is undertaken in Australia.
- The effective containment of COVID-19 in Australia means that there is a paucity of eligible participants for clinical trials. However, antibody levels in donors decline over time and as such this would be a good time to collect plasma as there are many patients who have recently recovered. It would also be advisable to pool the donated plasma in order to make a standardised product.
- That the mechanism of action of the antibodies produced during COVID 19 infection is not yet fully understood.xiv

Attachments

Attachment 1: NCHRAC convalescent plasma working group members.

References

1. A Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP). Information can be found at: remapcap.org


Chenguang Shen, Zhaoqin Wang, Fang Zhao, Yang Yang, Jinxiu Li, Jing Yuan, Fuxiang Wang, Delin Li, Minghui Yang, Li Xing, Jinli Wei, Haixia Xiao, Yan Yang, Jiuxin Qu, Ling Qing, Li Chen, Zhixiang Xu, Bing Peng, Yanjie Li, Haixia Zheng, Feng Chen, Kun Huang, Yujing Jiang, Dongjing Liu, Zheng Zhang, Yingxia Liu, Lei Liu (2020) Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. JAMA Preliminary Communication, Published online March 27, 2020 https://jamanetwork.com/journals/jama/fullarticle/2763983


Rapid Research Information Forum, The predictive value of serological testing during the COVID-19 pandemic, 30 April 2020

About the Committee and the Working Group

About the National COVID-19 Health and Research Advisory Committee

The National COVID-19 Health and Research Advisory Committee (NCHRAC) was established in April 2020 to provide advice to the Commonwealth Chief Medical Officer on Australia’s health response to the COVID-19 pandemic. NCHRAC provides rapid and evidence-based advice (or expert advice in the absence of evidence) on Australia’s health response to the COVID-19 pandemic with the aim of preventing new cases, optimising the treatment of current cases, and assisting in optimising overall health system readiness to deal with the pandemic as it progresses.

Further information on the terms of reference and membership of the Committee is available at: www.nhmrc.gov.au/nchrac. NHMRC is providing secretariat and project support for the Committee. The Committee is not established under the NHMRC Act and does not advise the NHMRC CEO.

Working Group Membership

NCHRAC convenes working groups of its members and external experts to deliver its reports. The following NCHRAC members were involved in the development of this advice:

Committee Members

Professor Michael Good AO (Chair)  
Professor Jonathan Carapetis  
Dr Michael Freelander  
Professor Anne Kelso AO

Professor Raina McIntyre  
Professor David Paterson  
Professor Bruce Robinson AC  
Mr Daniel Zou

Additional experts

Dr Charmaine Gittleson, CSL Chief Medical Officer  
Professor John Rasko, Faculty of Medicine & Health, The University of Sydney  
Associate Professor Zoe McQuilten, Monash University  
Professor Kanta Subbarao, Director, WHO Collaborating Centre for Reference and Research on Influenza at the Doherty Institute