



Ethiopian Public Health Institute
(EPHI) Knowledge Translation Directorate,
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Health: A JBI Affiliated Group



EVIDENCE SUMMARY

Effectiveness and Safety of Convalescent Plasma Transfusion in the treatment of people with COVID-19

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Question

What is the best available evidence regarding effectiveness and safety of convalescent plasma transfusion (CPT) in the treatment of people with COVID-19?

Background

The corona virus disease 2019 (COVID-19) pandemic has spread globally and caused massive loss of life and economic crisis. The disease is caused by SARS-CoV-2, a highly transmissible corona virus first identified in Wuhan, China (WHO, 2020). Although there are similarities with historic corona virus epidemics, with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) the scale and impact of the COVID-19 pandemic presents unprecedented challenges to health facilities and healthcare workers all over the world (WHO 2007; WHO 2019).

SARS-CoV-2 continues to spread in many countries and despite massive effort on research, no proven therapies or vaccines have been described. The only treatment currently available for COVID-19 has been limited to general supportive care, with provision of critical care. Multiple clinical trials are ongoing (Crosby et. al., 2020). Although chloroquine and hydroxychloroquine have shown promising activity against SARSCoV-2, there is a risk of arrhythmia associated with their administration. Therefore, caution is required for use at higher cumulative dosages. It is recommended that their use in cases of suspected/confirmed COVID-19 should be restricted to hospitalized patients. On 30th March 2020, the US Food and Drug Administration (FDA) issued an emergency use authorization for chloroquine and hydroxychloroquine to treat patients hospitalized with COVID-19 (Woodyat et. al., 2020).

New therapies are needed to improve outcomes for critically ill COVID-19 patients. Thus, use of convalescent plasma transfusions might be of great value in the current pandemic of corona virus disease (COVID-19), given the lack of specific preventative and therapeutic options. Convalescent plasma may reduce mortality in patients with respiratory virus diseases, and are

currently being investigated in trials as a potential therapy for COVID-19. However, a thorough understanding of the current body of evidence regarding the benefits and risks is required to guide decision making on its use by COVID-19 patients. Therefore, this evidence summary is conducted to summarize the best available evidence regarding the effectiveness and safety of convalescent plasma transfusion (CPT) in the treatment of people with COVID-19.

- A rapid review study on convalescent plasma or hyper immune immunoglobulin for people with COVID-19: concluded that they are very uncertain whether plasma from people who have recovered from COVID-19 is an effective treatment for people with COVID-19. The included studies in the review were of poor quality and their results could be related to the natural progression of the disease, other treatments that the participants received, or to convalescent plasma (Valk et al., 2020). (Level 3).
- A systematic review and meta-analysis conducted on Convalescent plasma transfusion for treatment of COVID-19 showed that (1) Convalescent plasma may reduce mortality in critically ill patients (2) Increase in neutralizing antibody titers and disappearance of SARS-CoV-2 RNA was observed in almost all the patients after CPT therapy (3) Beneficial effect on clinical symptoms after administration of convalescent plasma. The authors conclude that: even though, scientific data were limited or low quality, CPT therapy in COVID-19 patient appears safe, clinically effective and reduces mortality. Well-designed large multi center clinical trial studies should be conducted urgently to establish the efficacy of CPT to COVID-19 patients (Rajendran et al., 2020). (Level 4)
- A systematic review and meta-analysis on Efficacy and safety of convalescent plasma for severe COVID-19 showed that the included studies of non-COVID-19 severe respiratory viral infections provide indirect, very low-quality evidence which raises the possibility that convalescent plasma has minimal or no benefit in the treatment of COVID-19 and that it does not cause serious adverse events (Devasenapathy et al., 2020).

How this Evidence Summary was prepared?

The methods used to prepare in this rapid evidence review was adopted from the JBI Evidence summary:

<https://wiki.joannabriggs.org/display/JSW/Updating+Evidence+Summaries>

Evidence summaries are defined as a synopsis that summarizes existing international evidence on healthcare interventions or activities. These summaries are based on structured searches of the literature and selected evidence-based healthcare databases (JBI Database of Systematic Reviews, Cochrane Library, PubMed, and Epistemonikos). Following the search, all studies are assessed for internal validity using an abridged set of critical appraisal tools.

Levels of evidence for the effectiveness

Level 1-(Experimental Designs:

a systematic review of RCTs, systematic review of RCTs and other study designs, &RCTs)

Level 2-(Quasi-experimental Designs:

a systematic review of quasi-experimental studies & systematic review of quasi-experimental and other lower study designs)

Level 3-(Observational analytic designs:

a systematic review of comparable cohort studies)

Level 4-(Observational descriptive studies:

a systematic review of descriptive studies, cross-sectional studies)

Level 5-(Expert Opinion:

a systematic review of expert opinion, expert consensus)

(Munn et al., 2015)

Grades of Recommendation:

Grade A:A 'strong' recommendation, where there is evidence of adequate quality supporting its use

Grade B:A 'weak' recommendation, where there is evidence supporting its use, although this may not be of high quality

(Joanna Briggs Institute, 2013a, and b)

(Level 3)

- A systematic review of convalescent plasma treatment for COVID-19 that included ten studies reporting results of CP (Convalescent Plasma) treatment for COVID-19 patients indicates, with limited published results on plasma transfusion treatment for COVID-19 disease decreased symptoms of severe COVID-19 and clearance of SARS-CoV-2 RNA were the most direct observations seen. It also found that patients over the age of sixty who received CP treatment for COVID-19 had a significantly prolonged recovery estimated by viral clearance (from 10 to 29 days since first dose of CP) compared to younger patients, who recovered from the infection in less than a week after receiving CP treatment. The authors concluded that CP therapy for COVID-19 is well tolerated and effective with the argument of older patients may need a significantly longer time for recovery (Ville et.al. 2020). (Level 3)
- The U.S. Food and Drug Administration granted the first approval for an academic medical center to transfuse donated plasma from a recovered novel corona virus (COVID-19) patient into a critically ill patient (FDA, 2020).
- The NIH (National Institute of Health) COVID-19 Treatment Guideline Panel states that there are insufficient data to recommend either for or against the use of COVID-19 convalescent plasma or SARS-CoV-2 immune globulins for the treatment of COVID-19 (NIH Treatment Guidline, 2020).

Conclusions and Recommendations

- ☞ It is difficult to definitively conclude whether convalescent plasma is or is not an effective treatment for COVID-19 at this time because of two reasons: no studies that specifically assess its effectiveness in COVID-19 and available studies provide evidence of very low certainty. (Grade B)
- ☞ There are very few direct evidence on treatment of COVID-19 with CP but indirect evidences related with SARS-CoV and MERS-CoV are available, i.e direct inference cannot be made on convalescent plasma effectiveness in treating COVID-19. (Grade B)
- ☞ CPT appears safe and well tolerated for peoples with COVID-19 so far with limited and poor quality studies.(Grade B)
- ☞ For the future there are about at least 12 ongoing randomized trials evaluating the use of convalescent plasma in patients with COVID-19, particularly in the most severe patients, so this evidence review will be updated as new evidences appear. (Grade B)
- ☞ With the currently available evidence it is difficult to put precise recommendations thus, at this stage our recommendation is to use CPT only in the context of a randomized controlled trial or in selected cases like in patients with greater severity. (Grade B)

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