

**Maine Medical Center
Department of Emergency Medicine
Journal Club Summary Template**

Date: 11/19/2020	Presenter Name: Diana Biggs
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Article Citation: Title: Convalescent Plasma Therapy and its effects on COVID 19 patient outcomes: A systematic review of current literature Bakhtawar N, Usman M, Khan MMU. Convalescent Plasma Therapy and Its Effects On COVID-19 Patient Outcomes: A Systematic Review of Current Literature. <i>Cureus</i> . 2020;12(8):e9535. Published 2020 Aug 3. doi:10.7759/cureus.9535
Country(ies):
Funding Source(s): none <input type="checkbox"/> None Stated

Purpose
Research Question(s): What is the efficacy of convalescent plasma therapy and its effects on COVID 19 patient outcomes <input type="checkbox"/> None Stated
Hypotheses: Study authors hypothesize that convalescent plasma may be a potential therapy for COVID-19 patients. This idea comes from prior evidence of convalescent plasma showing clinical efficacy in other virus-borne infections. It was used in the Ebola outbreak, showed reduction in mortality rates during the H1N1 pandemic, and showed benefit in MERS and SARS infections. <input type="checkbox"/> None Stated
Study Purpose: This review was conducted with the intent to provide insight into the clinical effectiveness of convalescent plasma as a potential therapy for COVID 19 patients.

Methods
Study Design: Systematic review including all studies conducted on this topic from December 2019 to June 2020.
Outcome(s) [or Dependent Variable]:
Intervention [or Independent Variable]:

Ethics Review: <input type="checkbox"/> IRB Review <input type="checkbox"/> IACUC Review <input type="checkbox"/> Other: <u><input type="checkbox"/> None Stated</u>
Research Setting:
Study Subjects: The review ultimately included 10 studies.
Inclusion Criteria: - All articles published between Dec 2019 and June 2020 - Case Series, Case Reports, Observational Studies, RCTs - Only included full text manuscripts in English
Exclusion Criteria: - Review articles, commentaries, notes to editors, all other articles in which convalescent plasma therapy was not used as a treatment option - Studies published in other languages without a translation manuscript
Study Interventions:
Study Groups:
Instruments/Measures Used:
Data Collection: There were two independent reviewers who did literature review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines. This was followed by an independent evaluation of the extracted data. <u>Databases:</u> PubMed, EMBase, Google Scholar, Cochrane Library, MEDLINE. <i>In total, included 10 studies (case reports, case series, observational studies and randomized controlled trial)</i> Two search themes were used (COVID & convalescent plasma) COVID keywords: coronavirus, COVID-19, SARS-COV-2 Convalescent plasma keywords: convalescent plasma, plasma therapy
Data Analysis: A priori sample size calculation? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Described <input type="checkbox"/> N/A Statistical analyses used: Adjustment for potential confounders? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Described <input type="checkbox"/> N/A If yes, list:

Results

Study participants:

After the initial literature review there was a total of 156 studies identified. 10 made the final cut.

- 5 case series
- 2 case reports
- 1 prospective observational study
- 1 retrospective observational
- 1 RCT

The 10 studies that were used for this review included 156 patients, mean age 28-73 yo. All had moderate to severe COVID-19 infections. Patients in the studies received plasma therapy between day 7 to day 48 of hospital admission.

Studies used varying doses, varying frequency of administration, and plasma with varying antibody titers. As an example, in one study convalescent plasma was given as 200ml in one dose vs. 2,400ml in up to 8 doses in other studies. There was also a variety of concurrent treatments (antivirals, antibiotics, steroids, antimalarials, antifungal) and a variety of modalities for oxygen therapy (NC to ECMO).

Most studies reported reduction in viral shedding with viral load turning negative after plasma therapy. Duration of discharge varied from 4d - 35d following CP therapy. In regard to labs most showed an improvement in CRP, IL-6, WBC count and/or lymphopenia, procalcitonin, SARS-COV-2 IgG and IgM titers. Symptoms: some reported reduction in fever, 6 reported reduction in demand for oxygen. Imaging: one reported improvement in pulmonary infiltrates on CXR, three reported improvement on CT.

Brief answers to research questions [*key findings*]:

Most studies showed convalescent plasma therapy leads to an improvement in clinical outcomes but the only RCT in this review didn't report a statistically significant difference in clinical improvement with convalescent plasma vs control group on 28th day of follow up. The RCT noted that the mortality did not change significantly between convalescent plasma and control groups. Almost all patients were discharged in the other studies.

Additional findings:

Limitations:

The data on these positive effects from convalescent plasma are mainly coming from Case reports and case series that lack randomization & have a limited data set. Many of these studies have a high risk of bias

There was no standardization in terms of timing of administration of plasma therapy (Based on viremia data it is theoretically most effective to give plasma during the early stage of the disease).

Practical limitation: As noted in prior studies, patients recovering from SARS infection require at least 12 wks for their IgG neutralizing antibody titer (NAT) to reach >1:160 and only when the convalescent plasma IgG (NAT) reaches >1:160 was there reduced mortality in SARS cases. It was unclear what the COVID IgG antibody titers were in this study.

Limitations with donor and recipient: Getting informed consent from both, their respective states of health are unknown and skew the data, the amount of plasma acquired from one donor varies from case to case, and then lastly, the mismatch between the of donors vs the patients who need this therapy may limit the clinical utility of CP for COVID 19.

Clinical Implications

In conclusion: The evolving COVID pandemic poses a serious therapeutic dilemma, and convalescent plasma may have some therapeutic potential. This review shows that convalescent plasma might produce improvement in symptoms and lab parameters. While there are some case series hinting that plasma therapy might improve mortality, the only RCT included in this review does not support that. It is something that needs to be validated through organized RCTs. Despite this the authors final word is that the early use of convalescent plasma may be considered as an adjuvant for critically ill COVID patients.

Applicable? Yes

Feasible? The Practical limitations above address feasibility (the need for adequately high IgG neutralizing antibody titers, need greatly outweighing supply of CP)

Clinically relevant? Definitely

Comments:

Level of evidence generated from this study

- Ia: evidence obtained from meta-analysis of randomized controlled trials
- Ib: evidence obtained from at least one randomized controlled trial**
- IIa: evidence obtained from at least one well-designed, controlled study without randomization
- IIb: evidence obtained from at least one other type of well-designed quasi-experimental study
- III: evidence obtained from a well-designed, non-experimental study
- IV: expert committee reports; expert opinion; case study; case report

Additional Comments/Discussion/Notes

