HEMOPERFUSION

RECOMMENDATION

There is insufficient evidence on the use of hemoperfusion at this time among patients with COVID-19 infection. *(Very low quality of evidence)*

Consensus Issues (may include Cost, Patient Values and Preferences, Feasibility, Acceptability, Affordability)
None raised during the panel meeting

EVIDENCE SUMMARY

Should hemoperfusion be used in patients diagnosed with COVID-19?

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Key Findings

There were no randomized controlled trials or any systematic reviews found to answer this question. Only one (1) prospective single-arm clinical trial3 and nine (9) case series / case reports on the use of hemoperfusion among COVID-19 patients were retrieved. All the patients who have not undergone hemoperfusion eventually died, and 4 out of 5 who received hemoperfusion improved according to the study conducted by Rampino. However, no conclusion on the effectiveness of hemoperfusion as treatment for COVID-19 can be drawn. The results of the study of Ashgharpour showed that peripheral capillary oxygen saturations before hemoperfusion were 89.6% ± 3.94% and after the sessions it has improved to 92.13% ± 3.38, however the serum level of interleukin-6 did not show any clinical significance before and after sessions. Four (4) of the 10 patients in this study eventually expired.

Introduction

Hemoperfusion is an extracorporeal blood purification method that may have the potential to mitigate excessive inflammation in patients with COVID-19 by removing inflammatory cytokines from the blood.[1] It has been studied for use among patients with sepsis or septic shock.[2]

Review Methods

The Medline database and Cochrane Central were searched using the combined MeSH and free text search on the terms hemoperfusion and coronavirus infection or COVID-19 or SARS-CoV2. The term randomized controlled trial was added as method filter, but no randomized controlled trials were found among COVID-19 patients comparing hemoperfusion with standard care.

Results

The case reports / case series and prospective single-arm trial that were reviewed showed that in the total of 48 patients observed, 30 (62.5%) survived after hemoperfusion. [4,6-12] Interestingly. in the study by Rampino where hemoperfusion was not performed in all the potential candidates, all the patients who have not undergone hemoperfusion eventually died, and 4 out of 5 who received hemoperfusion, improved.[5] Unfortunately, no conclusions can be drawn on the effectiveness of hemoperfusion as a treatment option for COVID-19 patients, as this requires a study with enough sample size and a sound methodology that includes a comparison group.

The prospective single-arm trial by Asgharpour included 10 adult patients, 5 of which were male and 5 were female and all critically ill from COVID-19 infection.[3] Results showed that peripheral capillary oxygen saturations before hemoperfusion were 89.6% ± 3.94% and after the sessions it has improved to 92.13% ± 3.38% ($p<0.001$), however the serum level of interleukin-6 did not show any clinical significance before and after sessions. Four (4) of the 10 patients in this study eventually expired. As randomization and blinding were not considered for this trial the results have to be interpreted with much caution. Certainty of evidence is deemed to be very low. The limited before and after design does not confirm evidence of efficacy.

Recommendations from Other Groups

Even with much interest and perhaps a potential benefit on the use of hemoperfusion in patients with COVID-19, with the presence of another proven treatment like dexamethasone, there seems to be very little benefit in adding an experimental and costly treatment to patients who are suffering from this infection.[1] Major guidelines have not included hemoperfusion in their set of recommendations for treatment of COVID-19. These guidelines include the NIH COVID-19 Treatment Guidelines,[13] Surviving Sepsis Campaign Guidelines on the Management of Critically Ill Adults with COVID-19,[14] the Infectious Disease Society of America Guidelines Covid-19 Guidelines[15] and the Australian Guidelines for Clinical Care of People with COVID-19[16]

Research Gaps

A properly designed randomized controlled trial is the only way hemoperfusion may find its way as one of the treatment options at the present time.

Ongoing Trials

There is one (1) ongoing randomized controlled trial on cytokine filtration using hemoperfusion compared to intensive standard care listed in the NIH – U.S. National Library of Medicine's ClinicalTrials.gov [17] and two (2) clinical trials registered in the Cochrane Central and WHO trials registry.[18,19]

References

[1] Clark E, Hiremath S, McIntyre L, Wald R, Hundemer GL, Joannidis M. Haemoperfusion should only be used for COVID-19 in the context of randomized trials. Nephrology, https://doi.org/10.1038/s41581-020-00352-9

[2] Ronco C, Bagshaw SM, Bellomo R, Clark WR, Husain-Syed F, Kellum JA, et. al. Extracorporeal Blood Purification and Organ Support in the Critically Ill Patient during COVID-19 Pandemic: Expert Review and Recommendation. Blood Purif, 2020 May, DOI: 10.1159/000508125

[3] Asgharpour M, Mehdinezhad H, Bayani M,Zavareh MSH, Hamidi SH, Akbari R. et. al. Effectiveness of extracorporeal blood purification (hemoadsorption) in patients with severe coronavirus disease 2019 (COVID-19). BMC Nephrology. 2020; 21: 356, https://doi.org/10.1186/s12882-020-02020-3

[4] Katagiri D, Ishikane M, Asai Y, et al. Direct hemoperfusion using a polymyxin B immobilized polystyrene column for COVID-19. J Clin Apher. 2020;1–9. https://doi.org/10.1002/jca.21861

[5] Rampino T, Gregorini M, Perotti L, Ferrari F, Pattonlero EF, Grignano M. Hemoperfusion with CytoSorb as adjuvant therapy in critically ill patients with SARS-CoV2 pneumonia. Blood Pufi; 2020 Nov, DOI: 10.1159/000511725

[6] Shadvar K, Tagizadiyeh A, Gamari AA, Soleimanpour H, Mahmoodpoor A. Hemoperfusion as a potential treatment for critically ill COVID-19 patients with cytokine storm. Blood Purif, 2020 Nov 10. DOI: 10.1159/000511391

[7] Hajian S, Rastgoo N. The effect of hemoperfusion on the recovery of COVID-19 in hospitalized patients; case series and review study. Immunopathol Persa. 2021;7(2):e13. DOI:10.34172/ ipp.2021.13.

[8] Ishiwari M, Togashi Y, Takoi H, Kikuchi R, Kono Y, Abe S. Polymyxin B haemoperfusion treatment for respiratory failure and hyperferritinaemia due to COVID-19. Respirology Case Reports, 2020: 8(9), e00679, doi: 10.1002/rcr2.679

[9] Kusaba Y, Izumi S, Takasaki J, Suzuki M, Katagiri D, Katsuno T, et. al. Successful Recovery from COVID-19-associated Acute Respiratory Failure with Polymyxin B-immobilized Fiber Column-direct Hemoperfusion. Intern Med 2020; 59: 2405-2408, doi: 10.2169/internalmedicine.5413-20

[10] Moradi H, Abbasi S. Hemoperfusion as a Supportive Treatment in a COVID-19 Patient with Late Pulmonary Thromboembolism: A Case Report. International Medical Case Reports Journal. 2020: 13: 341-345.

[11] Nihei Y, Nagasawa H, Fukao Y, Khara M, Ueda S, Gohda T, Suzuki Y. Continuous extracorporeal treatments in a dialysis patient with COVID-19. CEN Case Reports; 2020 Oct, https://doi.org/10.1007/s13730-020-00538-x

[12] Vardanjani AE, Ronco C, Rafiel H, Golitaleb M, Pishvael MH, Mohammad M. Early Hemoperfusion for Cytokine Removal May Contribute to Prevention of Intubation in Patients Infected with COVID-19. Blood Purif. 2020 June, DOI: 10.1159/000509107

[13] NIH - Coronavirus Disease 2019 (COVID-19) Treatment Guidelines, https://www.covid19treatmentguidelines.nih.gov/

[14] Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19), https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19

[15] Infectious Disease Society of America Guidelines on the Treatment and Management of Patients with COVID-19, https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

[16] Australian National COVID-19 Clinical Evidence Taskforce. Australian guidelines for the clinical cure of people with COVID-19 v32.1 2020 Dec 24.

[17] NIH – U.S. National Library of Medicine, ClinicalTrials.gov, https://clinicaltrials.gov/ct2/results?term=hemoperfusion&cond=Covid19+OR+coronavirus&draw=2&rank=2#rowId1

[18] http://www.who.int/trialsearch/Trial2.aspx?TrialID=IRCT20091012002582N22, **2020** | added to CENTRAL: 30 November 2020 | 2020 Issue 11

[19] http://www.who.int/trialsearch/Trial2.aspx?TrialID=TCTR20200409006, **2020** | added to CENTRAL: 30 November 2020 | 2020 Issue 11

Appendix 1: Characteristics of Included Studies

Study Design & Sample Size	Population	Intervention	Outcomes Monitored/ Observed	Results
Asgharpour 2020[3] Clinical trial n=10	Adults with severe COVID-19 disease with positive radiographic findings or laboratory confirmation by RT-PCR and if they had one of these criteria: individuals who had partial pressure of oxygen in alveoli (PaO2) less than 60 mmHg, even after different methods of oxygen-therapy; or peripheral capillary oxygen saturation (SpO2) less than 88% with no clinical improvement despite 48h of non-invasive respiratory therapy	Hemoperfusion in combination with continuous renal replacement therapy for the first 4-6hrs and the last 10-12hrs with CRRT alone for each session conducted within 14-18hrs per day; second course of hemoperfusion was performed 24-48hrs after the first and the 3rd session 24-48 hrs after the second time.	Improvement of general condition based on the patient's assessment and if there was no need for intensive respiratory treatment based on oxygen saturation; weaning from mechanical ventilation and able to initiate ventilatory effort.	Six (6) of the 10 patients improved; 4 expired. Peripheral capillary oxygenation improved in the 6 patients who survived.
Katagiri 2020[4] Case Series n=12	Adults tested positive for SARS-CoV2 on PCR 2 already received ECMO 5 were on mechanical ventilation 5 required oxygen supplementation	Polymxin B-immobilized polystyrene direct hemoperfusion (PMX-DHP)	Proportion of improvement (decrease) of 1 point or more on days 8 and 15 of the first PMX-DHP regimen in the following eight categorical assessments: (a) no hospitalization and resumption of normal activities; (b) no hospitalization but no resumption of normal activities; (c) hospitalization without a requirement for O2 supplementation; (d) hospitalization requiring O2 supplementation; (e) hospitalization requiring nasal high-flow O2 therapy, noninvasive mechanical ventilation, or both; (f) requirement for invasive mechanical ventilation; (g) requirement for a ventilator and extracorporeal membrane oxygenation (ECMO); and (h) death.	Of the 5 patients who received oxygen supplementation, intubation was avoided in 4 patients. Of the 5 patients already on mechanical ventilation, 3 avoided ECMO. The 2 patients on ECMO died.
Rampino 2020[5] Case Report n=9	Adults diagnosed with COVID-19 by RT-PCR, severe pneumonia and respiratory failure requiring continuous positive airway pressure	Hemoperfusion with CytoSorb administered was delivered to each patient for 4hr sessions in 2 consecutive days on only 5 patients; the other 4 were candidates but considered as controls	Worsening of clinical course and mortality.	The clinical course of the patients who have undergone hemoperfusion was less severe in 4 out of 5 patients. Four (4) out of 5 also survived, whereas 2 needed intubation. All 4 of those who did not

				receive hemoperfusion required intubation and eventually died.
Shadvar 2020[6] Case Report n=8	Adults critically-ii of COVID-19 admitted in the ICU 4 were on mechanical ventilation	Hemoperfusion exclusively for 6 patients and combined with renal replacement therapy in 2.	Mortality	Three (3) of the 8 patients died. Decrease of level of inflammation and organ dysfunction in critically ill patients.
Hajian 2020[7] Case Series n=4	Adults critically-ill with Covid-19 All on mechanical ventilators	Hemoperfusion	Mortality	The 3 cases died of severe respiratory failure. Only 1 recovered and was discharged.
Ishiwari 2020[8] Case Report n=1	Adult male, diagnosed with COVID-19 and with diabetes and hypertension	Hemoperfusion with PMX-DHP 13th day after symptom onset and for 5hrs	Progression of ARDS Need for invasive ventilation	Patient recovered and was discharged.
Kusaba 2020[9] Case Report n=1	Adult male with hypertension, hyperuricemia and hypothyroidism and positive for SARS-CoV-2 by PCR	Hemoperfusion with PMX-DHP 3hrs a day on days 8 and 9 of admission	Worsening respiratory condition and need for mechanical ventilation.	Patient's respiratory failure did not progress further, mechanical ventilation was avoided.
Moradi 2020[10] Case Report n=1	Adult male s/p PCI due to MI prior to COVID-19 symptom onset and positive by for COVID-19 by PCR	Hemoperfusion on the 6th day of admission for 4-5hrs; and again on the 7th day for 6hrs	Clinical improvement	Improved clinical status and discharged with satisfactory general condition with normal breathing.
Nihei 2020[11] Case Report n=1	Adult male on Peritoneal Dialysis due to end-stage renal disease with COVID-19 symptoms (positive by RT-PCR) requiring mechanical ventilation	Hemoperfusion using PHX-DHP was started on day 3, 2hrs per day for 3 days	Worsening of respiratory condition and mortality	Patient developed ARDS repeatedly and subacute cerebral infarction and finally died of respiratory failure.
Vardanjani 2020[12] Case Report n=1	Adult male with history of hypertension and diabetes mellitus, diagnosed COVID-19	Hemoperfusion in combination with continuous renal replacement therapy or hemodialysis	Prevent the incidence and progression of ARDS, acute kidney injury, liver failure and septic shock (multiple organ failure) or need for invasive ventilation. Mortaliy.	The patient eventually required less oxygen support, inflammatory markers went down and he was transferred to the general ward after 5 days in the ICU. Patient was eventually discharged.

Appendix 2: Characteristics of Ongoing Studies

There are only 3 ongoing studies with details as follows:

1. Effect of hemoperfusion on short term outcome of critical ill COVID-19

http://www.who.int/trialsearch/Trial2.aspx?TrialID=IRCT20091012002582N22, 2020 | added to CENTRAL: 30 November 2020 | 2020 Issue 11

2. Efficacy of HA330 Hemoperfusion in Critically Ill Patients with Severe COVID-19

http://www.who.int/trialsearch/Trial2.aspx?TrialID=TCTR20200409006, 2020 | added to CENTRAL: 30 November 2020 | 2020 Issue 11

3. Pilot Study on Cytokine Filtration in COVID-19 ARDS (CytokCOVID19)

The cytokine filtration is thru a hemoperfusion system plus standard care compared to standard care alone for covid patients in ARDS.