Review Article

A Panaromic Review Article on Effect of Therapeutic Plasma Exchange During COVID-19 Associated Pneumonia

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ABSTRACT

TPE is a procedure in which the patient's blood is passed through an apheresis machine, where the filtered plasma is removed and discarded with reinfusion of red blood cells along with replacement fluid such as plasma oralbumin in to the patient.TPEis a procedure in which the patient's blood is passed through an apheresis machine, where the filtered plasma is removed and discarded with reinfusion of red blood cells along with replacement fluid such as plasma or albumin in to the patient.Therapeutic plasma exchange showed significant effect on mortality (RR 0.41, 95% CI 0.24 to 0.69; P = 0.0008). Conclusion: TPE significantly reduced mortality in hospitalized patients with moderate-to-critical COVID-19. Plasma exchange therapy should be considered for patients with COVID-19. Areviewto assess the effect of TPE on the risk of mortality in patients with COVID-19-associated pneumonia, using three statistical procedures to rule out any threats to validity.Results Deaths were 6 (14%) in Group 2 and 14 (47%) in Group 1. However, different harmful risk factors prevailed among patients not receiving TPE rather than being equally split between the intervention and control groupA review article on to evaluate the safety of TPE in adult patients with serious/life-threatening COVID-19 requiring ICU admission, and associated 28-day mortality.

Keywords: Pneumonia,Plasma Volume Calculator,Thrombus Inflammation.

INTRODUCTION

Therapeutic Plasma Exchange is a procedure in which the patient's blood is passed through an apheresis machine, where the filtered plasma is removed and discarded with reinfusion of red blood cells along with replacement fluid such as plasma oralbumin in to the patient. The exchange of large volumes of plasma may cause shifts of fluid that can lead to changes in blood pressure, cold hands and feet or breathlessness. Possible side effects during the treatment include dizziness, nausea or a feeling of cold.[1,2,3]

ADVANTAGES OF TPE

Therapeutic plasma exchange showed significant effect on mortality (RR 0.41, 95% CI 0.24 to 0.69; P = 0.0008). Conclusion: TPE significantly reduced mortality in hospitalized patients with moderate-to-critical

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COVID-19. Plasma exchange therapy should be considered for patients with COVID-19.[4]

DISADVANTAGES OF TPE

The exchange of large volumes of plasma may cause shifts of fluid that can lead to changes in blood pressure, cold hands and feet or breathlessness. Possible side effects during the treatment include dizziness, nausea or a feeling of cold.[5]

PLASMA VOLUME CALCULATOR

To calculate blood plasma volume (PV), need the values of **hematocrit (Hct)** and **total blood volume (TBV)**:

$$PV = TBV \times (1\text{-}Hct)$$

The plasma volume calculation is usually performed on the assumption that the patient's TBV is 70 mL per kg body weight for males and 65 mL per kg body weight for females.[6]

A reviewto assess the effect of TPE on the risk of mortality in patients with COVID-19-associated pneumonia, using three statistical procedures to rule out any threats to validity. Results Deaths were 6 (14%) in Group 2 and 14 (47%) in Group 1. We used an algorithm of structural equation modeling to summarize a large pool of potential confounders into a single score (called with the descriptive name "severity"). Disease severity was lower (Wilkinson rank-sum test $p < 0.001$) among patients with COVID-19 undergoing TPE (median: -2.82; range: -5.18; 7.96) as compared to those not receiving TPE (median: -1.35; range: -3.89; 8.84), confirming that treatment assignment involved a selection bias of patients according to the severity of COVID-19 at hospital admission. The adjustment for confounding was carried out using severity as the covariate in Cox regression models. The univariate hazard ratio (HR) of 0.68 (95%CI: 0.26; 1.80; $p = 0.441$) for TPE turned to 1.19 (95%CI: 0.43; 3.29; $p = 0.741$) after adjusting for severity.Conclusions In this study sample, the lower mortality observed among patients receiving TPE was due to a lower severity of COVID-19 rather than the TPE effects.[7]

A review article on to evaluate the safety of TPE in adult patients with serious/life-threatening COVID-19 requiring ICU admission, and associated 28-day mortality. Serious and life threatening COVID-19 are defined as per published literature (please, refer to the full protocol, Additional file 1). Main outcomesPrimary study end-point is 28-day mortality and safety of TPE in serious and/or life-threatening COVID-19. Safety will be evaluated by the documentation of any pertinent adverse and/or serious adverse effects related to TPE as per institutional, national and international guidelines. Secondary outcomes are: i) improvement in Sequential Organ Function Assessment (SOFA) score; ii) changes in inflammatory markers: serum C-reactive protein, lactate dehydrogenase, ferritin, d-dimers and interleukin-6; iii) days on mechanical ventilation and ICU length of stay.[8]

A review ondescribes the effect of therapeutic plasma exchange with 5% albumin as sole replacement solution for the management of Covid-19. A 74-year-old man was admitted for severe Covid-19 acute respiratory distress syndrome. Based on the growing body of evidence that cytokine release syndrome, and especially interleukin-6, plays a key role in critically ill Covid-19 patients, we decided to implement therapeutic plasma exchange as a rescue therapy. This case presents a proof-of-concept for the use of therapeutic plasma exchange with 5% albumin as sole replacement solution in a critically ill Covid-19 patient with cytokine release syndrome. Hence, we think that a further evaluation of risk-benefit balance of this therapy in severe cases of Covid-19 should rapidly be undertaken.[9]

A review COVID-19, caused by the novel coronavirus SARS-CoV-2, emerged in Wuhan, China, and has spread worldwide, resulting in over 73 million cases and more than 1 600 000 deaths as of December 2020. Although the disease is asymptomatic in most cases, some patients develop life-threatening disease characterized by acute respiratory

distress syndrome, sepsis, multisystem organ failure (MSOF), extrapulmonary manifestations, thromboembolic disease and associated cytokine release syndrome. The rationale for applying TPE early in the course of fulminant COVID-19 is the suppression of thrombusinflammation and amelioration of microangiopathy, thus preventing the ensuing MSOF. Although concerns still exist regarding its potential immunosuppressive effects and safety.[10]

A review on assessment of efficacy of therapeutic plasma exchange (TPE) following life-threatening COVID-19. This was an open-label, randomized clinical trial of ICU patients with life-threatening COVID-19 (positive RT-qPCR plus ARDS, sepsis, organ failure, hyperinflammation). Study was terminated after 87/120 patients enrolled. Standard treatment plus TPE (n = 43) versus standard treatment (n = 44), and stratified by PaO_2/FiO_2 ratio (>150 vs. ≤150), were compared. Primary outcomes were 35-day mortality and TPE safety. Secondary outcomes were association between TPE and mortality, improvement in SOFA score, change in inflammatory biomarkers, days on mechanical ventilation (MV), and ICU Eighty-seven patients [median age 49 (IQR 34-63) years; 82.8% male] were randomized (44 standard care; 43 standard cares plus TPE). Days on MV (P = 0.007) and ICU LOS (P = 0.02) were lower in the TPE group. 35-Day mortality was non-significantly lower in the TPE group (20.9% vs. 34.1%; Kaplan-Meier, P = 0.582). TPE was associated with increased lymphocytes and ADAMTS-13 activity and decreased serum lactate, lactate dehydrogenase, ferritin, d-dimers and interleukin-6. Multivariable regression analysis provided several predictors of 35-day mortality: PaO_2/FiO_2 ratio (HR, 0.98, 95% CI 0.96-1.00; P = 0.02]; ADAMTS-13 activity (HR, 0.89, 95% CI 0.82-0.98; P = 0.01); pulmonary embolism (HR, 3.57, 95% CI 1.43-8.92; P = 0.007). Post-hoc analysis revealed a significant reduction in SOFA score for TPE patients (P < 0.05). In critically-ill COVID-19 patients, addition of TPE to standard ICU therapy was associated with faster clinical recovery and no increased 35-day mortality.[11]

A review on investigated the effect of TPE on life-threatening COVID-19; presenting as ARDS plus multi-system organ failure and CRS.Materials and methods: We prospectively enrolled ten consecutive adult (ICU) subjects [7 males; median age: 51 interquartile range (IQR): 45.1–55.9 years old] with life-threatening COVID-19 infection. All had ARDS [PaO2/FiO2 ratio: 110 (IQR): 95.5–135.5], septic shock, CRS and deteriorated within 24 h of ICU admission despite fluid resuscitation, antibiotics, hydroxychloroquine, ARDS-net and prone position mechanical ventilation. All received 5–7 TPE sessions (dosed as 1.0 to 1.5 plasma volumes).Results: All of the following significantly normalized ($p < 0.05$) following the TPE completion, when compared to baseline: Sequential Organ Function Assessment score, PaO2/FiO2 ratio, levels of lymphocytes, total bilirubin, lactate dehydrogenase, ferritin, C-reactive protein and interleukin-6. Conclusion: TPE demonstrates a potential survival benefit and low risk in life-threatening COVID-19, albeit in a small pilot study.[12]

A review on severe acute respiratory syndrome coronavirus 2 infection can be severe and fatal due to cytokine storm. TPEpotentially mitigates the harmful effects of such cytokines. We investigated the use of TPE, as rescue therapy, in patients with severe Coronavirus disease 2019 (COVID-19) infection.Results: A total of 95 patients were included, among whom 47% (n = 45) received TPE. Patients who received TPE had reductions in C-reactive protein (P = .002), ferritin (P < .001) and interleukin-6 (P = .013). After employing entropy-balancing matching method, those on TPE were also more likely to discontinue inotropes (72% vs 21%; P < .001). However, they were more likely to be associated with longer LOS (23 vs 14 days; P = .002) and longer days on ventilatory support (14 vs 8 days; P < .001). Despite marginal mortality benefit at 14-days (7.9% vs 24%; P = .071), there was no significant differences

in overall mortality (21% vs 31%; P = .315) between the groups.Conclusions: TPE was effective in reducing inflammatory markers in patients with severe COVID-19 infection, however, further research is warranted.[13]

A review on to evaluate the therapeutic use of plasma exchange in COVID-19 patients compared to controls.Results: A total of 31 COVID-19 patients were included with an overall mean age of 51±15 years (range: 27-76 years); 90% (n=28) were males, and 35% (n=11) of the patients had TPE as a mode of treatment. The TPE group was associated with higher extubating rates than the non-TPE cohort (73% versus 20%; p=0.018). Additionally, patients on TPE had a lower 14 days (0 versus 35%; p=0.033) and 28 days (0 versus 35%; p=0.033) post plasma exchange mortality compared to patients not on TPE. However, all-cause mortality was only marginally lower in the TPE group compared to the non-TPE group (9.1% versus 45%; p=0.055; power=66%). Laboratory and ventilatory parameters also improved post TPE (n = 11).Conclusions: The use of TPE in severe COVID-19 patients has been associated with improved outcomes, however, randomized controlled clinical trials are warranted to draw final, conclusive findings.[14]

A review on the 5 months since initial reports of COVID-19 came to light, the death toll due to SARS-CoV-2 has rapidly increased. The morbidity and mortality of the infection varies based upon patient age, comorbid conditions, viral load, and the availability of effective treatments. Findings from limited autopsies, clinical observations, and laboratory data suggest that high cytokine levels and a procoagulant state can precipitate acute respiratory distress syndrome and multi-organ dysfunction syndrome in critically ill patients. Therapeutic plasma exchange (TPE) merits consideration in the treatment of critically ill COVID-19 patients and is an avenue for clinical trials to pursue. If efficacious, faster recovery of patients may lead to shorter intensive care unit stays and less time on mechanical ventilation. Herein, we briefly discuss some of the various approaches currently being investigated for the treatment of SARS-CoV-2 with a focus on potential benefits of TPE for selected critically ill patients.[15]

A review on although most patients with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) experience respiratory manifestations, multi-organ dysfunction is frequent. Almost 20% of hospitalized patients with SARS-CoV-2 infection develop AKI. The pathophysiology of AKI is a result of both the direct and indirect effects of SARS-CoV-2 infection, including systemic inflammatory responses, the activation of theRAAS, and endothelial and coagulative dysfunction. Underlying SARS-CoV-2 infection-associated AKI, an immunological hyper-response with an unbalanced innate and adaptative response defined as a “cytokine storm” has emerged. Numerous agents have been tested in an effort to mitigate the cytokine storm, and a range of extracorporeal cytokine removal techniques have been proposed as potential therapeutic options.[16]

A study is intended to compare the outcomes of COVID-19 patients with CRS treated with TPE and standard care to their counterparts receiving SC alone.Results: After CC matching, the study cohort had a mean age of 55.41 (range 56.41±11.56 in TP+SC and 54.42±8.94 in SC alone; p=0.22). There were 25.95% males and 74.05% females in both groups. The mean time from first day of illness to hospitalization was 6.53±2.18 days. The majority of patients with CRS had comorbid conditions (75.9%). Diabetes mellitus was the most common comorbidity (40.1%), followed by hypertension (25.3%), and chronic kidney disease (21%). Notable reduction in some inflammatory markers ($p<0.0001$) was observed in the group that received TPE+SC. Moreover, the patients in the plasmapheresis plus standard care group required relatively less mechanical ventilation as compared to the group receiving SC alone (46.9% vs 58.1%, respectively; $p>0.05$). The rate of extubating in

the TP+SC group vs SC alone was 60.5% vs 44.7%, respectively (p>0.05). Conclusion: For this particular group of matched patients with COVID-19-induced CRS, TPE+SC was linked with relatively better overall survival, early extubating, and earlier discharge compared to SC alone. As these results were not statistically significant, multi-centered randomized control trials are needed to further elaborate the role of therapeutic plasmapheresis in COVID-19 induced CRS.[17]

CONCLUSION

At the current scenario though "COVID-19" word not creating a panic effect still when there is secondary or associated disorder, it's very horrible and unpredictableoccurrence of symptoms as well as outcome. That's why we, authors tried to keep the review concept to the readers regarding the subject especially for Pneumonia or any other respiratory disorder cases. Hope the readers will get good and clear concept regarding the motile effect of this condition,

LIST OF ABBREVIATIONS

- TPE-Therapeutic Plasma Exchange
- ICU-intensive care unit
- TBV-Total Blood Volume
- SARS-CoV-2-SevereAcute Respiratory Syndrome Corona virus 2
- LOS-length of stay
- AKI-Acute Kidney Injury
- RAAS-Renin-angiotensin-aldosterone system
- CRS-cytokine release syndrome

CONFLICT OF INTEREST-Have no conflict of interest relevant to this research study.

SOURCE OF FUNDING-Self funding.Have not received any financial assistance from the esteemed institution.

ETHICAL CLEARANCE-Ethical clearance has been obtained from the concerned authority.

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