DOI: https://doi.org/10.53350/pjmhs211582086

ORIGINAL ARTICLE

Therapeutic plasma exchange (TPE); A Management Strategy for Critically ill Covid-19 patients

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ABSTRACT

Objective: To determine the effectiveness of therapeutic plasma exchange (TPE) in management of critically ill Covid-19 patients

Materials and Methods: In this study non-randomized controlled trial, a total of 47 patients were included after thorough screening of the admitted patients in Covid ITC CMH, Multan from July-2020 to May-2021.Single administration of TPE was done to determine the results. The parameters assessed in this study included the efficacy of TPE in terms of improvement of critical end points such as Norepinephrine dose to maintain MAP of more than 65mmHg, 6-hour balance of fluid, MAP, CRP (C reactive protein), WBC count (white blood cell), platelets, INR (international normalized ratio), IL-6.

Results: The variations before and after TPE in clinical and biochemical parameters shown in table. II. In clinical parameters and in gas exchange parameters no significant difference was found. Inflammatory biomarkers, before and after TPE, the parameters had not significant different, ($p>0.005$). The differences before and after TPE between acid base balance, cytokines and vasoactive substances were also statistically insignificant, ($p>0.005$).

Conclusion: Even though there is evidence of slight improvement in clinical endpoints of Covid-19 patients with TPE, overall efficacy of TPE is still a question that needs an answer as no significant improvement could be seen in outcome values after TPE.

Keywords: Therapeutic Plasma Exchange (TPE), Hemodynamics, Acute Respiratory Distress Syndrome (ARDS).

INTRODUCTION

The impact of the SARS-CoV-2 on humans due to COVID-19 pandemic cannot be measured. Everything has been stopped because of pandemic including health care, daily life and global economy. Currently according to Johns Hopkins Corona virus Resource Center, the positive cases for COVID-19 are 1 840 000 and patients suffering from the symptoms of the virus are 113 000 [1]. Patients suffering from COVID-19 which require admission to intensive care unit and mechanical ventilation are 5 to 10 percent [2, 3]. In China, in one hospital 17% percent of patients suffering from COVID-19 developed the acute respiratory distress syndrome [4, 5].

Varying management options have been tried for management of COVID-19 affected individuals, all of these are in experimental phases. Therefore the main measure is still the prevention of infection until a standard and effective treatment is developed.

TPE has been used as complementary method for COVID-19 patients with multi organ failure and acute respiratory distress syndrome. Since its first use by Keith et al. several high risk COVID-19 patients have been treated with TPE, its main target is to prevent cytokine storm, inflammation, endothelial dysfunction and coagulation dysfunction, [6]. There is a supporting evidence available in literature regarding the effectiveness of TPE in recovery of critically ill COVID-19 patients [7].

The safety for use of TPE is of great importance, as the target population includes critically ill patients of COVID-19. The adverse effects of use of TPE in critically ill patients of COVID-19 enlisted in a study were paresthesia, arrhythmias, cold sensation with transient increases in body temperature, and decreased arterial blood pressure (1.1%, 1.1%, 3.5%, and 8.4%of procedures) [8]. Ataca et al compared the use of TPE in geriatric (981 patients) and non-geriatric patients (3728 patients), concluding that the most common sign for requiring TPE included sepsis or ARDS and multiple organ damage [9]. The use of TPE has been considered safe for current pandemic situation due to TPE and has already been used as a therapeutic procedure for patients of COVID-19 [10].

In this study we are going to assess the safety and efficacy of TPE in critically ill covid-19 patients.

MATERIALS AND METHODS

It was a prospective non-randomized controlled trial which was open label and a single center study. A total of 47 patients were included after thorough screening of the admitted patients in Covid ITC CMH, Multan. All patients admitted to Intensive care unit from July 2020 to May 2021 were with diagnosis of critical Covid-19 were included in this study [11]. All the patients in this study were treated as

Received on 02-06-2021
Accepted on 28-07-2021

per WHO guidelines [12]. The study was sanctioned by the ethical committee of CMH, Multan. Written consent was obtained either from the patients or their authorized representatives. All critically ill patients diagnosed with SARS covid-19 requiring ICU admission were recruited. Exclusion from the study was done on the basis of the following criteria: aged less than 18 years, breast feeding or pregnant women, patients with end stage systemic disease were excluded from the study.

Plasma exchange was done with the help of a vascular access which was established via insertion of two lumen 11-French hemodialysis catheter. In this study administration of TPE was done in 5 sessions to determine the results. TPE was done against the FFP (Fresh Frozen Plasma), exchanging the 1.2 × the plasma volume calculated individually with the blood flow of 60mL/min (55-63mL/min). for the purpose of anticoagulation regional infusion of citrate was used during TPE. Before and after performance of 5 sessions of TPE, blood samples of the patients were withdrawn. Close follow up of 28 days was planned and patient survival was noted.

Requirement of Norepinephrine dose was titrated each 10 to 15 minutes in order to achieve a MAP (mean arterial pressure) of above 65mmHg. The parameters assessed in this study included the efficacy of TPE in terms of improvement of some critical end points such as Norepinephrine dose to maintain MAP of more than 65mmHg, 6-hour balance of fluid, MAP, CRP, WBC count, platelets, INR, IL-6. Data was collected by the researcher himself with the help of a predesigned proforma.

Paired T test and Wilcoxon test were utilized to compare the longitudinal values before and after TPE using SPSS v23 software at P-value ≤ 0.05 as statistically significant.

RESULTS

Out of 47, 24 (51.1%) were male and 23 (48.9%) were female with mean age 44.52±3.56 years. 25 (53.2%) patients had community acquired and n=22 (46.8%) patients had hospital acquired COVID onset. The APACHE-II and SOFA of the patients was 42.55±2.17 and 19.78±1.52, respectively (Table 1).

The variations before and after TPE in clinical and biochemical parameters shown in table 2. In clinical parameters, no significant difference was found, (p>0.005). In gas exchange, the differences were statistically insignificant, (p>0.005). Inflammatory biomarkers, before and after TPE, the parameters had not significant different, (p>0.005). The differences before and after TPE between acid base balance, cytokines and vasoactive substances were also statistically insignificant, (p>0.005). (Table 2).

Table 1. baseline characteristics.

Variable	Presence
Sex	
Male	n=24 (51.1%)
Female	n=23 (48.9%)
Age (years)	44.52±3.56
Weight (kg)	75.29±3.49
Height (meter)	1.74±0.42
BMI (kg/m^2)	27.81±9.71
Covid-19 onset	
Community acquired	n=25 (53.2%)
Hospital acquired	n=22 (46.8%)
APACHE-II[1]	42.55±2.17
SOFA[2]	19.78±1.52
[1]acute--physiology and chronic health evaluation, [2]sequential organ--failure assessment	

Table 2. Variations before and after TPE in clinical and biochemical parameters

Parameter	Therapeutic plasma exchange		P-value
	Before	After	
Clinical parameters			
MAP (mmHg)	66.61±1.22	68.48±16.75	0.231
NE dose (µg/kg/min)	1.49±0.98	1.54±0.92	0.324
MAP/NE (mmHg/µg/kg/min)	76.03±3.21	70.82±11.23	0.452
HR (bpm)	107.14±3.76	112.99±16.25	0.562
Fluid balance/6 h (mL)	3538.43±32.53	3640.39±229.96	0.365
Inflammatory biomarkers			
CRP (mg/L)	242.18±4.69	256.57±34.71	0.369
WBC (1/nL)	14.66±3.39	15.86±4.57	0.635
PLT (1/nL)	44.25±4.29	49.67±14.49	0.582
INR	1.85±0.25	1.95±0.35	0.478
Acid base balance			
pH	7.56±0.52	6.41±2.19	0.657
pCO_2 (mmol/L)	44.82±1.42	42.55±4.38	0.785
HCO_3^-(mmol/L)	21.65±2.04	19.68±4.52	0.692
Lactate (mmol/L)	8.14±1.92	7.34±2.16	0.853
Cytokines			
IL-6 (ng/mL)	11.49±3.34	9.82±2.82	0.638

DISCUSSION

The results of this study have shown that administration of TPE in critically ill covid-19 patients has no significant effect over the improvement of certain critical endpoints which is in contrast to some of the studies done previously. Study by Luo et al. they examined different parameters such as C-reactive protein and interleukin-6 levels in 6 patients diagnosed with covid-19 [13]. All the patients in this study showed respiratory disfunction and among the 6 patients in this study 3 underwent TPE [13]. Prior to the administration of TPE values of both IL-6 and CRP were raised in all 3 patients. After the administration of TPE values of IL-6 and

CRP were decreased. Although similar decrease is seen in our study in values of IL-6 but the difference is insignificant.

TPE use has also been seen previously among patients of ARDS during the H1N1 influenza global pandemic of 2009 [14]. In a study 3 children were reported to be diagnosed with ARDS and were hemodynamically compromised. Patients were on mechanical ventilation with NO (nitric oxide) and 1 of these 3 patients also had extracorporeal membrane oxygenation [14]. TPE was administered as a last resort. This led to dramatic reduction in vasopressor and oxygen requirement along with significant decrease in organ dysfunction scores [14]. Although TPE improved overall oxygenation index in this study as well but results are not significant in this regard.

Studies done on the role of TPE in critically ill Covid-19 patients are scarce, therefore most data we have to compare to our studies is on other diseases with similar symptoms and complaints such as H1N1, IVIG resistant Kawasaki disease, and other diseases leading to ARDS and coagulopathy [14-21]. In these studies, similar clinical endpoints have been studies for improvement after TPE is performed. In all these studies an improvement in the clinical endpoints has been observed after TPE is performed. This is similar to the results of our study however, in this study TPE was not associated with significant improvement of any clinical endpoint.

TPE has also been reported to reduce key proinflammatory cytokines in septic shock patients [6, 18]. Knaup et al. in their non-randomized pilot study evaluated the role of TPE in septic shock patients. The results of their study showed that TPE not only well tolerated but also reduced key proinflammatory cytokines such as Il-6, IL-1b and angiopoietin-2 [18].

CONCLUSION

It can be concluded from this study that even though there is evidence of slight improvement in clinical endpoints of Covid-19 patients with TPE, overall efficacy of TPE is still a question that needs an answer as no significant improvement could be seen in outcome values after TPE. Therefore, further studies are needed in order to better establish the role of TPE in critically ill covid-19 patients.

Conflict of Interest: Nil.
Funding Source: Nil.

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