Efficacy of the Cytokine Adsorption Therapy in Patients with Severe COVID-19-Associated Pneumonia: Lesson Learned from a Prospective Observational Study

Prit Kusirisin, MD[1]; Kajohnsak Noppakun, MD[1]; Vuddhidej Ophascharoensuk, MD[1]; Konlawij Trongtrakul, MD[2]; Nattayaporn Apaijai, PhD[3]; Siriporn C. Chattipakorn, DDS, PhD[4]; Nipon Chattipakorn, MD, PhD[3]; Nattachai Srisawat, MD, PhD[5]

[1]Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, [2]Division of Pulmonary, Critical Care, and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, [3]Cardiac Electrophysiology Unit, Department of Physiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, [4]Department of Oral Biology and Diagnostic Sciences, Faculty of Dentistry, Chiang Mai University, Chiang Mai, Thailand, [5]Division of Nephrology, Department of Medicine, Chulalongkorn University, Bangkok, Thailand

Background

Severe COVID-19 pneumonia can activate cytokine storm. Hemoperfusion can reduce pro-inflammatory cytokines in sepsis but is still debated in COVID-19 setting. Thus, we sought to investigate the benefit of HA-330 cytokine adsorption through the clinical and laboratory outcomes.

Methods

We conducted a single-center prospective observational study in adults with severe COVID-19 pneumonia admitted in intensive care unit (ICU) at Chiang Mai University Hospital (Chiang Mai, Thailand). Patients with at least 1 of cytokine storm parameters including acute respiratory distress syndrome (ARDS) or high inflammatory markers were included. Patients treated with HA-330 device at least 1 session were classified as hemoperfusion group while the other without cytokine adsorption was classified as control group. We compared the clinical and laboratory outcomes on day 7 after treatment. The clinical parameters represented in SOFA score and oxygenation (PaO_2/FiO_2). Laboratory parameters included inflammatory cytokines level and kidney function. We also evaluated 60-day mortality and its associated factors.

Table 1. Baseline characteristics and outcomes

Baseline characteristics	Hemoperfusion (n = 38)	Control (n = 74)	P-value
Baseline clinical parameters			
Age, years*	58.26 ± 14.34	56.70 ± 15.09	0.60
Male, n (%)	26 (68.42)	43 (58.11)	0.29
BMI, kg/m²*	26.47 ± 5.81	27.12 ± 5.42	0.58
Comorbidities, n (%)			
- Hypertension	20 (52.63)	41 (55.41)	0.78
- Diabetes mellitus	10 (26.32)	27 (36.49)	0.30
- Obesity	18 (47.37)	43 (58.11)	0.28
- Cardiovascular disease	4 (10.53)	8 (10.81)	0.96
- CKD	9 (23.68)	3 (4.05)	0.001
PaO_2/FiO_2 while ARDS diagnosis*	157.41 ± 67.35	182.62 ± 73.76	0.09
APACHE II score†	21 (10, 26)	11.5 (8, 22)	0.051
SOFA score†	8.5 (4, 13)	6 (4, 9)	0.056
Remdesivir, n (%)	32 (84.21)	56 (75.68)	0.3
Methylprednisolone, n (%)	23 (60.53)	60 (81.08)	0.06
Tocilizumab, n (%)	18 (47.37)	22 (29.73)	0.07
Inotropic drugs, n (%)	15 (39.47)	17 (22.97)	0.07
Prone position, n (%)	15 (39.47)	17 (22.97)	0.07
Hemoperfusion session, day*	2.45 ± 1.01	0	
- 1, n (%)	7 (18.42)	0 (0)	
- 2, n (%)	12 (31.58)	0 (0)	-
- 3, n (%)	16 (42.11)	0 (0)	
- 4, n (%)	1 (2.63)	0 (0)	
- 5, n (%)	2 (5.26)	0 (0)	
Time to hemoperfusion, hours†	44.5 (24, 95)	-	-
Baseline laboratory parameters			
Cytokine storm parameters			
- D-dimer, mg/mL†	806 (423, 2,315)	744 (447, 1,280)	0.89
- CPK, U/L†	165 (64.5, 403)	105 (57, 240)	0.09
- hs-CRP, mg/L†	94 (45.2, 163)	112.5 (78.8, 175.1)	0.17
- LDH, U/L*	428.29 ± 138.02	448.90 ± 193.85	0.56
- Total lymphocyte count, /mm³†	718.5 (460, 1,110)	800 (520, 1,120)	0.63
- Ferritin, mg/mL†	1,274 (669, 1,777)	1,361 (901, 2,623)	0.32
Kidney function			
- Serum creatinine, mg/dL†	0.99 (0.82, 1.30)	0.81 (0.68, 1.03)	0.016
- eGFR, mL/min/1.73 m²*	73.22 ± 28.60	85.98 ± 29.10	0.029
Lactate, mg/dL†	2.25 (1.63, 3.19)	1.97 (1.51, 2.66)	0.25
ESR, mm/h†	30 (16, 49)	32 (19.5, 44)	0.807
IL-6, pg/mL†	76.96 (50.16, 191.43)	60.08 (14.78, 108.50)	0.44
Outcomes			
60-day mortality, n (%)	12 (31.58)	13 (17.57)	0.09
Total ICU day, day†	14 (11, 21)	11 (9, 15)	0.06
Ventilator-free day, day†	8 (2, 13)	8 (6, 11)	0.68

* Mean ± SD, † Median (IQR)

Abbreviation: APACHE, Acute physiology and chronic health evaluation; ARDS, Acute respiratory distress syndrome; BMI, Body mass index; CI, Confidence interval; CKD, Chronic kidney disease; CPK, Creatine phosphokinase; eGFR, estimated glomerular filtration rate; ESR, Erythrocyte sedimentation rate; HR, Hazard ratio; hs-CRP, High sensitivity-C-reactive protein; ICU, Intensive care unit; IL-6, Interleukin-6; LDH, Lactate dehydrogenase; OR, Odds ratio; PaO_2/FiO_2, ratio of arterial oxygen partial pressure to fractional inspired oxygen; SOFA, Sequential organ failure assessment

Results

A total of 112 patients who met the inclusion criteria were enrolled. Thirty-eight patients were treated with cytokine adsorption and 74 patients were not. The baseline cytokine storm parameters were comparable. In univariate analysis, there were an improvement of clinical and laboratory effects by hemoperfusion therapy. In multivariate analysis, SOFA score, PaO_2/FiO_2, hs-CRP, and IL-6 were associated with mortality. Although the 60-day mortality was no significant difference between groups (adjusted HR 0.88, 95% CI 0.36-2.11, p = 0.766), however, hemoperfusion of at least 3 sessions could mitigate the mortality (adjusted OR 0.25, 95% CI 0.03-0.33, p = 0.001).

Fig 1. Outcomes between hemoperfusion and standard treatment at day 0 and day 7 (A) SOFA score, (B) PaO_2/FiO_2, (C) hs-CRP, (D) IL-6

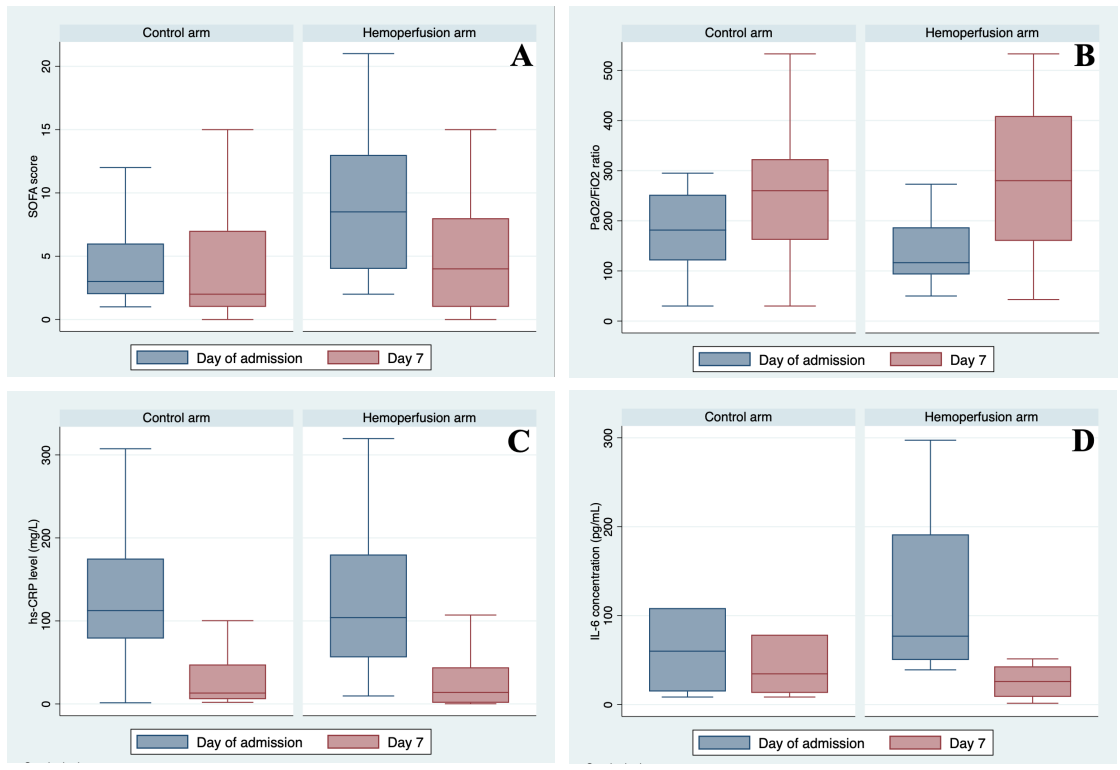
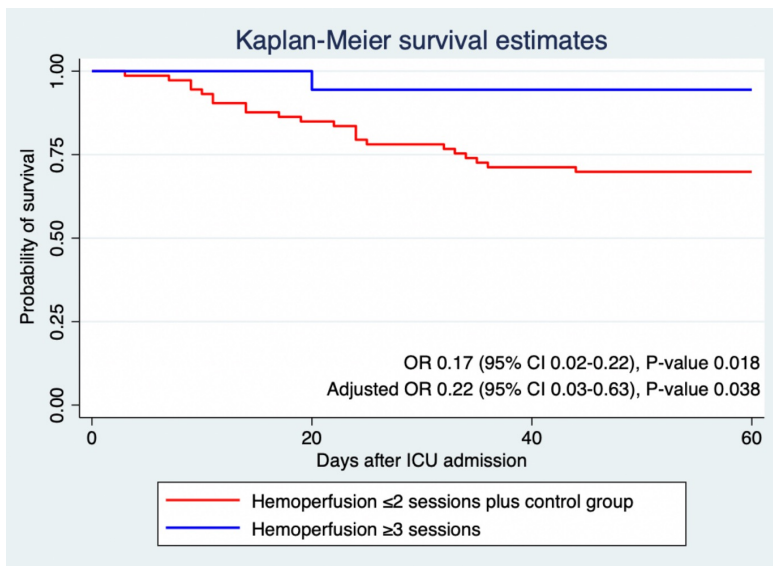


Fig 2. Kaplan-Meier curves for 60-day survival based on number of hemoperfusion session



Conclusions

The early initiation of HA-330 hemoperfusion could improve severity score and laboratory outcomes of COVID-19 ARDS even though did not difference in mortality. Nonetheless, at least 3 session of cytokine adsorption was associated with a 60-day survival.