Clin. Lab. 2022;68:1-3

ORIGINAL ARTICLE

Comparison of Cytokine Hemadsorption as an Immunomodulator Therapy in COVID-19 Patients with and without Bacterial Sepsis

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SUMMARY

Background: **In this retrospective study, we aimed to compare the laboratory and clinical results of cytokine hemadsorption as an immunomodulation therapy in COVID-19 ICU patients with or without sepsis.**
Methods: **The levels of PCT, CRP, and ferritin were determined as indicators of infection/sepsis; the levels of interleukins (IL-6, IL-8 and IL-10, and TNF-α) were determined as indicators of cytokine storm were compared. APACHE score, SOFA score, and mortality rates were compared for the progression of the disease in 23 COVID-19 patients.**
Results: **The therapy was generally successful in reducing the levels of IL-6, IL-8, IL-10, and TNF-α but the levels measured after the procedure did not differ among the patients with or without sepsis, suggesting that the presence of sepsis did not affect the efficacy and function of the cytokine hemadsorption procedure in COVID-19 patients. All parameters were reduced after the procedure except the levels of PCT and ferritin and mortality rates of patients diagnosed with sepsis. The level of PCT was significantly higher in these patients compared with the patients without sepsis while the ferritin and mortality did not show any significant difference between the two groups, suggesting that the cytokine hemadsorption may be safe in the treatment of critical COVID-19 patients.**
Conclusions: **As a result, the progression of sepsis in COVID-19 may be avoided with cytokine hemadsorption applied as an immunomodulator therapy. However, this therapy should be further explored and validated prior to its introduction to everyday clinical practice when the epidemic conditions end.**
(Clin. Lab. 2022;68:xx-xx. DOI: 10.7754/Clin.Lab.2022.211249)

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Manuscript accepted February 14, 2022

Supplementary Data

Table S1. Comparison of the laboratory parameters of COVID-19 patients with or without sepsis, according to the outcomes of extracorporeal hemadsorption.

Parameter		COVID-19 (n = 6) mean ± SD median (min - Max)	COVID-19 + Sepsis (n = 17) mean ± SD median (min - max)	p-value
IL-6 (ng/L)	Pre-HAD	148.78 ± 73.59 141.1 (73.9 - 275.1)	232.65 ± 137.53 186.3 (98.5 - 568.4)	0.123
	Intra-HAD	116.5 ± 39.81 115.45 (62.1 - 185.3)	125.43 ± 56.48 114.3 (68.7 - 328.1)	0.944
	Post-HAD	58.12 ± 30.49 61.45 (22 - 100.1)	73.35 ± 52.86 68.6 (4.12 - 187.6)	0.649
	p-value	0.006	0.000	
IL-8 (ng/L)	Pre-HAD	71.48 ± 42.87 84.07 (14.8 - 123.1)	101.21 ± 98.13 77.33 (14.2 - 448.6)	0.674
	Intra-HAD	44.59 ± 28.37 44.31 (0.13 - 78.63)	148.21 ± 141.7 100.47 (15.2 - 563.1)	0.030
	Post-HAD	70.45 ± 45.53 55.97 (15.8 - 147.35)	94.03 ± 91.03 65.41 (14.3 - 425.6)	0.327
	p-value	0.311	0.79	
IL-10 (ng/L)	Pre-HAD	187.37 ± 161.95 141.86 (21.3 - 490.4)	202.63 ± 211.86 115.63 (4.23 - 831.1)	0.889
	Intra-HAD	181.59 ± 120.27 145.42 (86.2 - 421.2)	97.15 ± 90.73 65.2 (8.74 - 349.4)	0.025
	Post-HAD	58.5 ± 66.91 30.23 (10.02 - 179.9)	80.68 ± 29.72 85.32 (5 - 122.7)	0.183
	p-value	0.011	0.025	
TNF-α (pg/mL)	Pre-HAD	99.26 ± 38.57 108.1 (43.16 - 145.9)	202.65 ± 247.75 110.25 (41.6 - 847.65)	0.726
	Intra-HAD	64.57 ± 37.72 56.35 (25.4 - 114.3)	74.26 ± 51 55.7 (17.96 - 208.9)	0.779
	Post-HAD	28.68 ± 23.23 28.09 (3.18 - 63.9)	46.88 ± 29.46 47.6 (5.87 - 122.6)	0.151
	p-value	0.006	0.000	
PCT (ng/mL)	Pre-HAD	0.77 ± 1.04 0.42 (0.02 - 2.78)	1.99 ± 2.37 1.07 (0.15 - 9.8)	0.080
	Intra-HAD	0.6 ± 0.85 0.33 (0.01 - 2.3)	5.28 ± 13.76 0.8 (0.06 - 58)	0.049
	Post-HAD	0.23 ± 0.13 0.23 (0.04 - 0.37)	7.4 ± 13.74 1.7 (0.24 - 55)	0.001
	p-value	0.846	0.001	
CRP (mg/mL)	Pre-HAD	139.67 ± 61.8 152 (66 - 213)	208.94 ± 89.62 213 (14 - 350)	0.086
	Intra-HAD	96.6 ± 83.46 105 (2.3 - 201)	129 ± 43.44 125 (61 - 227)	0.624
	Post-HAD	36.17 ± 36.23 32 (2 - 97)	102.24 ± 75.66 76 (2 - 258)	0.049
	p-value	0.006	0.000	
Ferritin (ng/mL)	Pre-HAD	1,100.67 ± 540.08 938 (618 - 2,000)	781.47 ± 695.2 579 (115 - 2,000)	0.099
	Intra-HAD	1,205.33 ± 631.38 902 (536 - 2,000)	992.94 ± 812.71 683 (86 - 2,000)	0.352
	Post-HAD	877.67 ± 698.05 500 (383 - 2,000)	1321.59 ± 740.57 1,600 (80 - 2,000)	0.142
	p-value	0.119	0.395	

Table S1. Comparison of the laboratory parameters of COVID-19 patients with or without sepsis, according to the outcomes of extracorporeal hemadsorption (continued).

Parameter		COVID-19 (n = 6) mean ± SD median (min - Max)	COVID-19 + Sepsis (n = 17) mean ± SD median (min - max)	p-value
APACHE score	Pre-HAD	29.83 ± 10.07 34 (10 - 37)	36.53 ± 8.97 34 (23 - 56)	0.481
	Post-HAD	19.67 ± 8.24 18 (8 - 30)	28.37 ± 10.53 28.35 (12 - 50)	0.092
	p-value **	0.027	0.015	
Mortality rate	Pre-HAD	62.38 ± 28.74 62.9 (11.34 - 93.04)	71.79 ± 24.91 80.95 (14.91 - 98)	0.327
	Post-HAD	39.99 ± 27.3 30.65 (8.12 - 82.7)	74.37 ± 76.61 68.24 (14.64 - 356)	0.151
	p-value **	0.027	0.326	
SOFA score	Pre-HAD	14.33 ± 2.25 15.5 (11 - 16)	14.47 ± 2.7 15 (10 - 19)	0.972
	Post-HAD	8.67 ± 1.03 8 (8 - 10)	11.88 ± 2.93 12 (6 - 17)	0.009
	p-value **	0.027	0.001	

HAD - Hemadsorption, IL - Interleukin, TNF-α - Tumor necrosis factor alpha, CRP - C-reactive protein, PCT - Procalcitonin, APACHE - Acute Physiologic Assessment and Chronic Health Evaluation, SOFA - Sequential Organ Failure Assessment.
**** - p < 0.05.**