Role of extended hemodialysis in COVID-19: a case report☆

Papel de la hemodiálisis extendida en COVID-19: a propósito de un caso

Extended hemodialysis (HDx), with medium cut-off membranes, could favor the effective elimination of medium-sized molecules such as IL-6 and other inflammatory mediators.[1] In the current literature, there are few reports on the use of these membranes in hemodialysis patients with SARS-CoV-2 infection, but their potential therapeutic effect is not described.[2]

We present the case of a 68-year-old man with a history of hypertension type 2 diabetes mellitus, congestive heart failure, sleep apnea-hypopnea syndrome, ischemic heart disease and chronic kidney disease stage G3a A3 according to 2012 KDIGO of probable diabetic etiology with serum basal creatinine values of 1.3–1.5 mg/dl.

He referred a recent trip to the SARS-CoV-2 risk area and came to the Hospital Emergency Department for a 24-h course of illness characterized by fever and associated dry cough. Nasopharyngeal exudate was performed, which was positive for SARS-CoV-2. On the day of admission to the hospital's Emergency Department (day 1), dyspnea to moderate efforts was added to the symptoms, so the patient was admitted to the hospital with subsequent, almost immediate, transfer to the Intensive Care Unit (ICU) due to torpid evolution. His respiratory symptoms are compatible with bilateral pneumonia complicated by acute respiratory distress syndrome and multi-organ failure: hypotension (mean arterial pressure of 60 mmHg), tachypnea, use of accessory musculature, and O_2 saturation of 89% despite reservoir mask (FiO_2 99%). The patients requires mechanical ventilation and inotropic drugs (norepinephrine and dopamine). In addition, it presents a situation of oliguria (10 mL/h) that initially responds to intravenous diuretics, presenting, in parallel, deterioration of renal function up to serum creatinine of 3.4 mg/dl, so on day 4 it is decided to start continuous venovenous hemofiltration (CVVH) that is maintained until day 26. He received treatment with hydroxychloroquine, azithromycin, lopinavir/ritonavir, interferon beta, ceftriaxone, levofloxacin, methylprednisolone and heparin anticoagulation intermittently due to bleeding tendency. From day 21 to day 36, he received treatment with cloxacillin and cefepime, successively, due to the presence of *methicillin*- sensitive *Staphylococcus aureus* in the bronchial aspirate and worsening of the inflammatory parameters.

Since the patient has anasarca and persistent serum creatinine levels of 2 mg/dl and urea 162 mg/dl, intermittent hemodialysis with Theranova 400® 1.7 m^2 filter was started (Baxter International Inc., Deerfield, IL, USA.) with a QB of 270−300 ml/min and a QD 500 mL/min, requiring only two sessions (days 36 and 38). Given the clinical improvement, her discharge from the ICU was decided on day 47 with serum creatinine levels of 1.3 mg/dl. The analytical parameters evolution is described in Table 1.

Taking into account the analysis before and after therapy, there is a tendency to a decrease in procalcitonin, C-reactive protein (PCR), the neutrophil-to-lymphocyte ratio (NLR) and the monocyte-to-lymphocyte ratio (MLR) (). In addition, there is an increase in the levels of platelets, lymphocytes and the platelet-lymphocyte ratio (PLR) (PLI), the antiphospholipid antibodies and lupus anticoagulant were negative. Neither IL-6 nor IL-1 levels were measured because no specific treatment to control these cytokines was started.

Currently, many aspects of the pathogenesis of SARS-CoV-2 infection are unknown. A "cytokine storm" has been proposed as one of the key aspects in the torpid course of some patients.[3] Therefore, it has been considered, among others, the use of antagonists of IL-6 and IL-1 such as tocilizumab and anakinra respectively.[3] Similarly, in sepsis, the effect that the use of high-permeability membranes could have on cytokine removal has been recognized.[4]

The HDx is a renal replacement therapy modality recognized for its high convection capacity and removal of medium-sized molecules (eg, cytokines) without further removal of albumin; but, unlike online hemodiafiltration, it maintains its effectiveness despite not having high QB, as is often the case in ICU patients with temporary catheters.[1] Therefore, with a view to a possible SARS-CoV-2 outbreak in our hospital, we established a protocol in which, in cases such as the one described, we would use HDx using mediun cut-off membranes (Theranova®).

The PCR, neutrophil-to-lymphocyte, platelet-to-lymphocyte, and monocyte-to-lymphocyte ratios are parameters that have been shown to be useful as inflammation and prognostic markers in different entities, including in SARS-CoV-2 infection.[5–7] In our patient, a trend towards improvement of these parameters can be seen parallel to

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Table 1 – Evolution of inflammatory parameters of the patient presented.

	Day 1	Day 5	Day 9	Day 12	Day 16	Day 19	Day 22	Day 26	Day 30	Day 33	Day 36 (HD1)	Day 38 (HD2)	Day 40	Day 47
Procalcitonin (ng/mL)	0.4 1					1.18	1.33	0.33	0.33	0.22	0.32	0.26		0.16
PCR (mg/L)	22.63				11.45	7.97	29.16	23.32	134.62	165.25	145			14.05
Ferritin (ng/mL)			2704.8							1505.2			1798	
LDH (U/L)	304			373		305		374		473	450		421	
AST (U/L)		281		79		42		36		16			22	21
ALT (U/L)	17	26		35		81		46		29			2. 3	27
GGT (U/L)		279		312		188		85		46			57	66
Leukocytes (uL)	8590	4020	6980	14,700	12,200	18,390	18,800	15,000	17,700	20,700	9630	6640	6990	7780
Neutrophils (uL)	6900	2770	5070	11,900	10,200	16,620	16,110	12,600	15,000	18,400	7860	488 0	4630	4950
Lymphocytes (uL)	980	800	1050	1400	1050	680	670	1180	1540	1130	970	910	1530	1900
Monocytes (uL)	690	410	710	1210	850	1070	1970	1030	970	970	520	430	490	650
Hemoglobin (g/dl)	10.9	10.6	9.7	8.8	8.89	7.8	7.9	7.35	9.73	8.36	8.44	7.7	7.78	9.5
Pl aquetas (uL)	154,000	96,700	93,000	121,000	310,000	424,000	332,000	228,000	130,000	126,000	157,000	187,000	244,000	374,000
Fibrinogen (mg/dL)					116					571			355	
D-dimer (ug/mL)	1.69		5.56		5.59			4.47		5.37			5.51	
NLI	7.04	3.46	4.83	8.50	9.71	24.44	24.04	10.68	9.74	16.28	8.10	5.36	3.03	2.61
PLI	157.14	120.88	88.57	86.43	295.24	623.53	495.52	193.22	84.42	111.50	161.86	205.49	159.48	196.84
MLI	0.70	0.51	0.68	0.86	0.81	1.57	2.94	0.87	0.63	0.86	0.54	0.47	0.32	0.34

HD1: first hemodialysis session; HD2: second hemodialysis session; MLR: monocyte-to-lymphocyte ratio; NLR: neutrophil-to- lymphocyte ratio; PLR: platelet-to-lymphocyte ratio

the initiation of therapy, especially NLR and MLRI (Table 1). However, given that this is a single case and there are concomitants factors, such as the evolution of infection process itself, we cannot affirm that the effects obtained are attributable to the use of the aforementioned filter.

In conclusion, we consider that these findings should be taken into account for the design of larger studies and the use of these membranes could be considered, if they are available, due to their potential immunomodulatory effect, in patients requiring hemodialysis and affected by infection by SARS-CoV-2; especially at the beginning of stage III proposed by Siddiqi et al.[8] when the inflammatory component is predominant.

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