Extracorporeal Lung Support and Continuous Renal Replacement Therapy In-Series Combination: The Role of High Cut-Off Membranes

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Extracorporeal lung support (ECLS)/continuous renal replacement therapy (CRRT) combination is frequently used in treating acute kidney injury (AKI) associated to acute respiratory distress syndrome (ARDS). In this context, some authors argue against the in-series ECLS/CRRT combination [1] because this association should prohibit the use of regional anticoagulation and should exacerbate cytokines release which in turn provokes hemolysis and disseminated intravascular coagulation. Nevertheless, the use of a separate CRRT device imposes the positioning of an independent central line. Furthermore, single dual-lumen cannulae are often employed for ECLS, and additional venous access should be reserved for a step-up to a double cannulae approach [2].

We report the use of in-series ECLS/CRRT in 4 ARDS patients with AKI admitted to the multidisciplinary intensive care unit of the Prato Hospital, Italy, where about 100 CRRTs and 10 ECLSs are performed per year. Data were collected be-

tween January 2015 and December 2015; we obtained informed consent prior to retrospective analysis inclusion. ECLS was provided by Novalung iLA-Activve™, a veno-venous pump-driven 'mid blood flow range' (up to 2.5 litres/min) extracorporeal CO₂ removal system. Continuous veno-venous hemodialysis with high cutoff membrane (HCOM) specifically addressed to eliminate circulating cytokines (SepteX™, Gambro Dialysatoren, Germany) was performed with PrismafleX-eXeed™ System (Gambro-Lundia, Sweden). CRRT was connected to the venous line of the double-lumen 27 cm/24 F femoral cannula (Novaport™ twin, Novalung, Germany), distally to iLa™ membrane and flow sensor. Patients were treated with systemic heparinization aiming to double aPTT. All patients survived and days of combined ECLS/CRRT treatment were 5, 9, 11, 9, respectively. We did not register alarms related to air bubbles, pressure abnormalities or clotting of both ECLS and CRRT devic-

es; moreover, no complications related to anticoagulation were recorded. In all the patients, the CRRT circuits were changed each 48 h and any inadvertent pressure variation in the ECLS circuit was avoided positioning 2 three-way-stopcocks in the CRRT connectors. Although we did not routinely dose cytokines and free hemoglobin levels/clearance, we observed a significant reduction of C-reactive protein and procalcitonin associated to no signs of intravascular hemolysis and amelioration of organ dysfunction parameters (table 1).

It should be highlighted that cytokines storm is a hallmark of ARDS and sepsis, being 'per se' a cornerstone of their pathophysiology. At this regard, blood purification has been proposed in order to remove circulating cytokines. Among these techniques, the use of HCOM-CRRT is associated with high degree of elimination of systemic mediators. This higher clearance is due to the increase in the membrane pore size that allows the removal of cyto-

Table 1. Clinical data during ECLS/CRRT combined treatment

Patient number	1 h before ECLS/CRRT combination				12 h after ECLS/CRRT combination				Day 4 on ECLS/CRRT combination				Pre-CRRT weaning			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
iLA active settings																
Blood flow, l/min	1.8	1.6	2	2.3	1.8	1.6	2	2.3	1.6	1.6	1.8	2	1	0.6	0.5	0.7
Sweep gas O ₂ , l/min	6	5	7	8	6	5	7	8	5	5	6	7	1	1	0.5	1
Ventilation	PCV	PCV	PCV	PCV	PCV	PCV	PCV	PCV	SIMV/PS	SIMV/PS	PCV	PCV	PSV/CPAP	SIMV/PS	SIMV/PS	PSV/CPAP
Ventilatory mode																
FiO ₂	0.9	0.9	1	1	0.8	0.9	0.9	0.9	0.7	0.7	0.8	0.7	0.3	0.4	0.5	0.4
P plateau, cm/H ₂ O	30	32	29	27	28	31	28	27	24	24	23	23	8	21	24	20
PEEP, cm/H ₂ O	14	15	20	18	14	15	20	16	9	9	14	15	6	12	13	10
Vt/PBW, ml/kg	6	5.9	5.8	5.6	5.3	4.9	5.2	5.4	4.1	4.1	4.2	4.8	4.5	4.3	4.7	4.6
Respiratory rate, breaths/min	20	20	18	16	14	16	18	15	12	12	16	13	12	8	13	12
Lung Injury Score, murray	3.5	3.6	3.6	3.5	3	3.6	3.6	3	2.5	2.5	2.3	2.5	1.3	1.3	2	1
Hemodynamics																
MAP, mm Hg	60	59	60	63	60	61	62	60	63	63	60	67	65	68	66	68
CVP, mm Hg	11	11	13	10	11	13	12	11	13	13	14	14	12	12	13	14
PAWP, mm Hg	16	15	18	16	16	14	15	15	18	18	12	17	n.a.	n.a.	n.a.	n.a.
CI, l/min/m ²	2	3.9	2.1	2.2	3.57	4.53	2.3	3.6	2.89	2.89	3.3	2.6	2.9	n.a.	n.a.	n.a.
SVRI, dynes*cm ⁵ /m ²	1,300	1,440	1,021	1,035	1,637	1,396	957	1,138	1,551	1,551	1,960	2,032	n.a.	n.a.	n.a.	n.a.
Norepinephrine, µg/kg/min	0.2	0.05	0.2	0.6	0.15	0.02	0.25	0.5	0.03	0.03	NO	NO	NO	NO	NO	NO
Laboratory values																
Arterial pH	7.36	7.39	7.35	7.35	7.36	7.38	7.37	7.36	7.40	7.40	7.50	7.41	7.37	7.42	7.53	7.41
PaO ₂ , torr	102	98	90	91	105	101	93	97	106	106	145	103	108	113	117	115
PaCO ₂ , torr	47	46	52	54	45	45	47	48	36	36	42	37	38	36	39	41
Arterial SatO ₂ , %	98	97	99	97	98	97	99	98	98	98	99	99	100	98	100	100
Lactate, mmol/l	2.0	0.9	3.2	2.9	2.1	0.8	2.5	2.6	2.5	2.5	0.9	2.7	1.3	1.8	0.8	1.6
Base excess, mmol/l	0.2	4.3	-2.6	-1.6	0.1	9.3	-2.1	-1	-4.5	-4.5	8.6	-1.2	-1.4	-1.6	9	0.4
White blood cell count, 10 ³ /µl	13.8	18.4	24.1	20.8	12.8	17.8	23.2	19.7	9	9	7.2	16.6	14.3	6.5	8.9	9.2
Haemoglobin, g/dl	9.5	11	9.8	10.2	8.7	10.4	9.8	9.3	9.7	9.7	9.5	9.1	9.9	9.8	10	10.4
Platelet count, 10 ³ /µl	75	317	75	89	73	301	72	84	84	84	228	83	85	94	192	87
Procalcitonin, ng/ml	39.2	59.5	44.6	41.8	31.2	57.5	43.1	40.4	9.9	9.9	21.3	13.8	16.9	0.5	0.4	0.5
C-reactive protein, mg/dl	36.8	39.3	41.1	23.9	35.6	36.5	40.6	23.2	21.8	21.8	24.6	27.4	16.9	1.5	2.3	1.8
Creatinine, mg/dl	3.1	3.8	4.1	5.3	2.7	3.5	3.6	4.5	1.3	1.3	0.5	0.8	1.4	1.2	0.6	0.7
Lactate dehydrogenase, UI/l	143	139	145	142	135	141	143	149	136	136	138	140	141	132	130	142
Indirect bilirubin, mg/dl	1.1	1.3	1.4	1.5	1.2	1.4	1.3	1.4	1.0	1.0	1.2	1.4	1.3	0.9	1.2	1.1
Direct bilirubin, mg/dl	0.3	0.2	0.2	0.4	0.3	0.2	0.4	0.3	0.4	0.4	0.3	0.2	0.3	0.4	0.2	0.1
Haptoglobin, mg/dl	63	58	72	75	58	56	69	71	55	55	53	63	62	54	51	53
Partial thromboplastin time, s	66	70	73	72	68	72	70	68	59	59	55	69	64	63	71	67

n.a. = Data not available; NO = no ongoing infusion.

kines up to 60 kDa [3]. ECLS/HCOM-CRRT was demonstrated to be beneficial in a porcine model in determining increased elimination of cytokines [4]. Moreover, although hemolysis is a general side effect of all extracorporeal therapies, a recent in vitro study demonstrated the highest cell-free plasma hemoglobin removal capacity of SepteX™ (Gambro Di-

alysatoren, Germany), a specifically designed HCOM compared to standard membrane [5].

In conclusion, knowing that HCOM enhances the clearance of inflammatory mediators released during ARDS and potentially increased by the extracorporeal circuit, we used ECLS/HCOM-CRRT in series association with safe and effective results.

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Disclosure Statement

None.

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