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Case Report

Combined Application of Cytosorb and Sustained Low Efficiency Dialysis (SLED) in Critical Patients

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Abstract

Sustained low efficiency dialysis (SLED) is a hybrid technique of renal replacement therapy. It can be used through a mobile system of dialysis by a single-pass batch (Genius) or multifunctional dialysis system, with reduced flow and prolongation of treatment time. It has been used in critical patients who develop acute kidney injury. A patient with septic shock and acute kidney injury was treated with sustained low efficiency dialysis and column-dialyzier/cytosorb membranes.

Introduction

Acute kidney injury (AKI) is defined as a rapid deterioration of renal function that develops in hours or days. The incidence of AKI is raising notably worldwide [1]. Aproximately 5% of patients admitted to the intensive care units recieve renal replacement therapy (RRT) [2] with in-hospital mortality near 50% [3] or above, with sepsis as the main cause of deaths. There are at least two pathophysiological mechanisms that explain the harmful results of host inflamatory response [4]. The first mechanism is the cytotoxic effect of cytoquines and the second is an immunological response induced by inflammatory mediators [5]. Several pro or antinflammatories cytoquines (IL-1 – IL-2 – IL-6 – IL-8 – IL-10 – TNF-α – MCP-1 – IFN-γ) are also related to SARS-COV2 infection [6]. Taking into account that pathophysiological mechanisms involved in tissue injury involve the proteins called cytoquines, it is reasonable to think that the plasma elimination of this molecule could limit organic damage. Hemoperfusion is an adsorbent technique that eliminates middle molecular weight substances (55Kda) with greater effect than conventional high flow hemofilters and there are studies that demostrates the succesfull elimination of the pro or antiinflammatory proteins [7]. In most of case reports and studies hemoperfusion is performed with continuous extracorporeal purification techniques. We present a clinical case of the aplication of combined cytosorb membrane/column-dialyzer with SLED modality in critical unit patients.

Clinical Case Presentation

A 41 year old male patient, with no pathological history, presents with a few days of colic abdominal pain in right hipochondrium asociated with fever, an ultrasound showed a litiasis and obstruction in bile duct due, an Endoscopic retrograde cholangiopancreatography (ERCP) was performed evolving in the next 48 hs with more abdominal pain y persistent of fever. In blood simples presented leukocytosis, elevation of pancreatic enzimes, and evolved with arterial hipotensión, making a diagnosis of distributive shock secondary to severe pancreatitis and is admitted to ICU (Table 1).

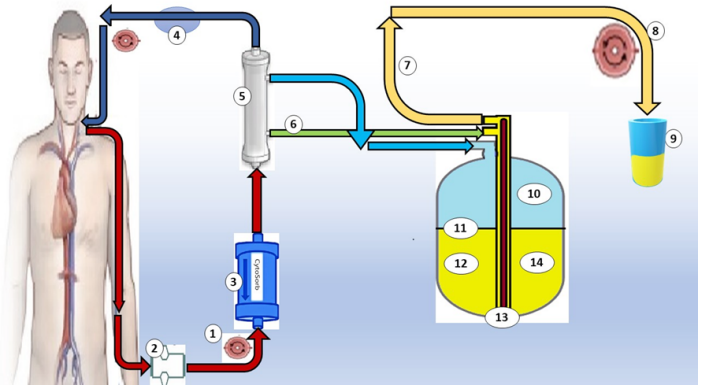
Laboratories	Results
Hemoglobin	12.5 G/DL
Leukocytes	8600/MM3
Platelets	228.000/MM3
Ureic nitrogen	27 MG/DL
Creatinin	0,9 MG/DL
AST	80 UI/L
ALT	130 UI/L
Total bilirrubin	5,5MG/DL
Direct bilirrubin	4.2 MG/DL
Lipase	40 U/L
C-reactive protein	50MG/L
Sodium	135 MEQ/L
AST: aspartate aminotransferase, ALT: Alanine Aminotransferase	

Table 1: Laboratories to Admission.

The patient evolves with persisten fever, blood cultures develop Gram(-) bacillus, wide spectrum antibiotics are iniciated, 48 hours later patient present signs of multiple organic failure with peritoneal signs, a TC shows diffuse pancreatic necrosis and intestinal ischemia. After pancreatectomy + colectomy + ileostomy patient evolves with refractory septic shock, cytoquine release syndrome and acute kidney injury AKIN III with anuria, for wich it is indicated 12 hours - sustained low efficiency dialysis (SLED) with column-dialyzier/cytosorb membranes (Figure 1). Two sessions of hemoperffusion are performed: Two consecutive SLED with column-dialyzer/cytosorb of 12 hours each one, with a Genius 90 machine (Fresenius Medical Care), the column position was set previous to hemofilter, blood flow rate was 125 ml/min in first session and 120 ml/min in the second. Anticoagulation was made with sodic heparin at 5500 and 5000 units in first and second session respectively (Table 2). Patient evolves the next 48 hours without vasopressors, with notable improve of ventilatory parameters, presents some infectious and non infectious complications with prolonged time of hospitalization in ICU, a tracheostomy is performed, at day 29 patient presents a massive pulmonary thromboembolism with subsequent death.

Discussion

It is important to keep in mind that patients in ICU usually present pro inflamatory states with high levels of cytoquines and prothrombotic elements that interfere with initial response to stress, an example of this situation are the recent infectious diseases during pandemic era due to SARS-COV28, or any other non controlled infectious disease. The vast mayority of this diseases generate organic dysfunction from which the kidney is not exempt. Septic shock in Intensive care units currently has an increasing incidence and mortality rates ranging from 30% to 55% [9]. SLED therapy emerges as an alternative treatment to conventional hemodialysis (HD) for critically ill patients with acute renal failure. Over time, intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT) have been provided as treatment. IHD often presents hypotension and inadequate elimination of liquids as an unwanted effect, on the other hand, CRRT has a high cost of solutions and problems related to anticoagulation. Hemadsorption is a technique that consists of the physical phenomenon of exposing a blood flow to an adsorbent agent in an extracorporeal circuit, the solutes being attracted by different forces (hydrophobicity, ionic charges, hydrogen bonds and Van der Waals forces) allowing the elimination of different molecules such as cytokines and inflammatory mediators from the blood; These events allow the serum decrease of the compounds, leading to less systemic compromise of the patients [10]. We present a clinical case with multi-organ systemic involvement associated with acute renal dysfunction requiring dialysis therapy in the context of anuria. We propose the use of the low-efficiency sustained daily dialysis modality combined with cytosorb pre-filter column.



1. Bidirectional Roller Pump For Blood Flow And Counterflow Dialysis. 2. Air detector. 3. CYTOSORB column. 4. Venous Flow Chamber. 5. Dialyzer. 6. Blood Leak Detector (Airless). 7. System pressure measurement. 8. Monitor Ultra filtering. 9. Volume Of Ultra Filtration. 10. Preheated Dialysis Fluid. 11. Interface Between New and Used Dialysis Fluid. 12. Liquid Used (With Toxins). 13. Distribution Pipe With Ultraviolet Ray Emitter. 14 Thermally Insulated 90L Glass Container.

Figure 1: 12 hours - sustained low efficiency dialysis (SLED) with column-dialyzier/cytosorb membranes.

Laboratories	48 Hours	1st Session	2nd Session
Leukocytes	26000/Mm3	18000 /Mm3	9300/Mm3
Hb	9.2 Mg/Dl	8.6 Mg/Dl	9,1 Mg/Dl
Ph	7,19	7.32	7,39
Pafi	120	Pafi 230	Pafi 290
Hc03	13 Mmol/L	22 Mmol/L	24 Mml/L
Crp	145 Mg/L	78 Mg/L	21 Mg/Dl
Lactate	5,6 Mmol/L	2,2 Mmol/L	1,1 Mmol/L
Dhl	670 Ui/L	340ui/L	178 Ui/L
Platelets	78000/Mm3	72000 /Mm3	84000/Mm3
Cpk	2400 Ui/L	1200 Ui/L	221 Ui/L
Ast	1100 Ui/L	660 Ui/L	320 Ui/L
Alt	900 Ui/L	430 Ui/L	179 Ui/L
Lipase	600 U/L	480 Ui/L	379 Ui/L
Creatinine	3,8 Mg/Dl	2.5 Mg/Dl	1,6mg/Dl
Bun	87 Mg/Dl	32 Mg/Dl	30 Mg/Dl
Hemodynamic Variables			
Vasopressor Support	48 Hours	1st Session	2nd Session
Norepinephrine	1,2 Mcg/Kg/Min	0,3 Mcg/Kg/Min	No Support
Vasopressin	4 Ui	No Support	No Support
Urinary Output	Anuria	Anuria	Anuria
Hb: Hemoglobin, Hco3: Sodium Bicarbonate, Crp: C Reactive Protein, Dhl: Lactic Dehydrogenase, Cpk Creatine Phosphokinase, Ast: Aspartate Aminotransferase, Alt: Alanine Aminotransferase, Bun: Ureic Nitrogen			

Table 2: Icu Admission/ 48 Hours.

Prolonged HD with conventional equipment has been described as an alternative therapy. The most commonly used terms are extended daily dialysis [11], sustained low-efficiency dialysis (SLED) [12], and sustained low-efficiency daily diafiltration [13]. (For convenience, we will use the term SLED to describe these treatments). Within the different extracorporeal therapies used in intensive care, there are different characteristics, which are summarized in Table 3.

Variable	IHD	SLED /PIRRT	CCRT		
			Hemofiltration	Hemodialysis	Hemodiafiltration
Session Duration (Hr)	03-Jun	16-Mar	24/Day	24/Day	24/Day
Solute Transport	Predominantly Diffusion	Predominantly Diffusion	Convection	Predominantly Difussion	Diffusion And Convection
Blood Flow (Ml/Min)	200-5000	200-400	100-300	100-300	100-300
Dialysate Flow (Ml/Min)	300-800	100-300	0	17-100	17-50

Replacement Fluid (Ml/ Min)	0	0	17-100	0	17-50
Urea Clearance (Ml/Min)	>150	<100	<100	<100	<100

IHD(Intermittent hemodialysis) SLED (sustained low-efficiency dialysis) PIRRT(Prologed intermittent renal replacement therapy CRRT(continuous renal replacement therapy)

Table 3: Different extracorporeal therapies.

The use of SLED therapy has been used only a few times worldwide, a survey carried out in 2004 showed that only 24% of the survey participants used this modality in acute kidney injury and that only 3 centers participating in the survey used this modality with the machines of the multinational company Fresenius. Although the SLED modality combines the benefits of CRRT and IHD, there is limited evidence on patient outcomes. Systematic reviews described in previous periods have summarized the clinical efficacy of RRT modalities for AKI, but these reviews are outdated. Schneider et al conducted a recent systematic review that focused exclusively on dialysis dependency and considered all intermittent modalities collectively, without distinguishing between SLED and IHD [14]. On the other hand, Zhang et al also conducted a systematic review and meta-analysis of CRRT and SLED, but not from IHD [15]. It is important to consider the high economic cost associated with the medical care of a septic patient, it is estimated that in the United States they reach 17 billion dollars annually [16]. Manns et al. conducted a cost analysis of CRRT vs IHD in ICU patients in Calgary, Canada. IHD performed on average 3.9 days/week was less expensive than CRRT [17]. The daily cost of IHD was $239, virtually identical to the cost of the SLED modality $238.50 (excluding Physician billing fee of $105/day of treatment at IHD). For continuous veno-venous hemodialysis with heparin, the daily cost was $421, and for continuous veno-venous hemodiafiltration with citrate anticoagulation, it was $626 (not including physician billing fees). Despite the weekly cost of the SLED modality in the study conducted by Berbece AN et al. It was higher than that determined by Manns ($1431 vs $932 dollars) due to the greater frequency of treatments. Despite this, SLED therapy costs about $1,600 less per week than citrate CRRT and about $1,200 less per week than continuous heparin veno-venous hemodialysis [18].

Based on 4 randomized clinical trials from 2006 to the present, there are no statistically significant differences in the outcomes of 30-day mortality during hospitalization and dependencies on dialysis therapy at discharge when comparing the CRRT vs. SLED modality; however, the mortality risk was slightly lower for the SLED group. These results are consistent with those shown by Zhang et al. With respect to IHD vs SLED, there are no comparative studies evaluating these outcomes [19]. Systemic anticoagulation with heparin is standard daily practice to prevent filter coagulation in both CRRT and IHD. However, in critical care units, heparin is frequently contraindicated due to the high number of invasive procedures to which patients are exposed. Saline flushing in IHD treatments without heparin are widely accepted and have been applied to different modalities. In Kumar et al's study of extended daily dialysis, most patients were treated with heparin (68%). Filter coagulation occurred in 17% of heparin treatments and 27% of non-heparin treatments. In Marshall et al's description of SLED, 28% of treatments were performed without heparin; filter coagulation occurred in 26% of treatments, no difference in coagulation rate was observed between treatments with heparin and without heparin. The study carried out by the group of Berbece AN et al found similar results to those of Kumar. On the other hand, solute removal was objectified through fractional urea clearance (Kt/V), the most widely used method to quantify the adequacy of IHD and has been applied to patients with AKI treated with IHD and SLED. The Kt/V determined for patients in SLED mode in the study by Berbece An et al was similar to that determined by Marshall et al. for low efficiency sustained daily diafiltration and for SLED (1.39 +/-0.3 vs 1.42 vs 1.4 respectively). Since six treatments were provided, the mean weekly Kt/V was 8.4. This is substantially higher than the weekly Kt/V value of 5.8 for daily IHD in the study by Schiffl et al. [20] The mean weekly Kt/V for CRRT for the study by Berbece AN et al in comparison was also significantly lower in 7.1.

Conclusion

Renal replacement therapy in critical care units can be administered continuously or intermittently, using diffusion (dialysis) and/or convection (filtration) processes. To date, no dialysis therapy modality shows clear superiority over the others in terms of survival and recovery of renal function. Different studies from Nordic and first world countries have linked the use of extended daily dialysis modalities and SLED with better volume management and cost reduction. Other observational studies have been linked to a reduced probability of renal recovery in the short and medium term. These observations subject the treating physician to the choice of the modality that can influence the outcomes of the patients in charge. The importance of this issue lies in the number of adult ICU patients affected by severe AKI around the world who could benefit from better tolerance of dialytic therapy and

adequate solute removal with SLED therapy, even at low cost and with greater efficiency. This implies that further studies must be carried out as a key priority in the field of critical nephrology.

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