BLOOD PURIFICATION THERAPIES: SUPPORT TO CONVENTIONAL THERAPIES IN PATIENTS IN SEPSIS AND SEPTIC SHOCK

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ABSTRACT

Introduction*: An important role in the treatment of sepsis and septic shock is the blood purification therapy. In this study, we assessed the clinical response to the application of two blood purification therapy devices: polymyxin B Toraymyxin (PMX-PH) and CytoSorb.*

Methods*: Twelve patients were enrolled, all with different diagnoses at their entry into ICU,they were enrolled at the time of diagnosis of sepsis or septic shock.*

Results*: Different clinical and laboratory parameters were evaluated at the time of admission and subsequently re-evaluated at different time intervals depending on the device used.*

Conclusions*: It was evident that the support determined by blood purification therapy techniques in improving the conditions of subjects who are in a critical state.*

Keywords: *Sepsis, CytoSorb, PMX-PH, Blood purification therapy.*

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Introduction

Sepsis is a particularly complex syndrome under several points of view, such as its definition, diagnosis and treatment. Although the term sepsis has been used more recently in the context of modern medicine, the medical concept dates back to a long time earlier.

The definition of sepsis underwent several changes during the years and the first definition dates back to 1992[(1)].

The current indications, illustrated in the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[(2)] by the Critical Care Medicine (CCM) together with the European Society of Intensive Care Medicine (ESICM) in 2016, shift the attention to the organ dysfunction caused by the infection.

It is very difficult to assess the exact incidence and mortality of sepsis to date, especially considering the difficulty in finding the data relating to the series which derives mainly from developed countries; therefore, the estimates are very variable[(3)].

An evaluation of the available data on high-income countries suggests global estimates of 31.5 million cases of sepsis and 19[(4)] million serious cases of sepsis, with potentially 5.3 million deaths each year. Furthermore, all available epidemiological data indicate an increase in the incidence rate of sepsis and an increase in cases of death associated

with it, although the mortality rate for sepsis is decreasing[4,5].

In relation to the not indifferent frequency of cases of sepsis and septic shock in emergency departments such as resuscitation, an ever-greater importance has been assumed by complementary therapies. The latter seem to offer greater possibilities for conventional therapies to act avoiding the timely deterioration of the patient's clinical conditions, allowing, in some cases, the improvement of hemodynamics and consequently of the general conditions.

A cohort of patients treated with different blood purification therapy devices (polymyxin B Toraymyxin device[6], and CytoSorb[7]) was evaluated in order to compare the responses following the treatments and to identify subpopulations that could benefit from the treatment compared to others.

Methods

Twelve patients were enrolled, five female and seven male aged between 15 and 80 years. All patients, admitted with different diagnoses at the entrance, were enrolled at the time the diagnosis of sepsis or septic shock was made, for which the indication for treatment with complementary therapies to basic antibiotic therapy was given. On almost all the enrolled patients, various clinical and laboratory parameters were evaluated and, on the basis of these, some prognostic scores were calculated in order to evaluate the response to therapies over time.

The main characteristics of the patients are described in the following table (Tab. 1).

Of the seven patients treated with the PMX-HP device, three had an infectious focused in the lung (Acinetobacter Baumannii) identified by aspirated bronchus and four, instead, had an infection of abdominal origin.

Results

The data collected during the study, concerning the status and evolution over time of the patients' conditions, were detected, in relation to patients treated with PMX-HP, at the time of diagnosis of sepsis (T0) and, subsequently, were re-evaluated. at 12h (T12), at 24h (T24), at 48h (T48), at 72h (T72), at 96h (T96) and at 120h (T120). The above data are: mean arterial pressure (PAM), norepinephrine dosage, SOFA score, LUNG INJURY score, RIFLE score, PaO2 / FiO2 ratio and procalcitonin. These are shown in the following tables (Tab. 2-8).

	Age	Gender	Admission diagnosis	PCT	EA	Device
Patient 1	71	F	Post-operative respiratory failure	3,73	0,86	PMX-HP
Patient 2	30	F	Septic shock from pneumonia	1,8	0,58	PMX-HP
Patient 3	80	M	Acinetobacter Baumannii pneumonia	24,11	0,9	PMX-HP
Patient 4	56	M	Post-surgery septic shock for intestinal infarction	53	0,6	PMX-HP
Patient 5	45	F	Abdominal septic shock for entero-bladder fistula	145	0,82	PMX-HP
Patient 6	59	M	Post-surgery hemorrhagic shock due to intestinal perforation	10,54	0,6	PMX-HP
Patient 7	77	M	Intestinal peritonitis of intestinal resection by occlusion	42,81	0,55	PMX-HP
Patient 8	69	F	Sepsis and MOFS in pcs. with cerebral hemorrhage	4,46	0,27	CytoSorb
Patient 9	54	M	Respiratory failure in pcs. with left frontotemporal cerebral hemorrhage	14,69	0,82	CytoSorb
Patient 10	78	M	Respiratory failure and post-intervention hemodynamic instability due to intestinal obstruction	2,41	-	CytoSorb
Patient 11	49	M	Respiratory failure	50,15	0,75	CytoSorb
Patient 12	15	F	Post-chemotherapy septic shock for acute myeloid leukemia (AML)	-	-	CytoSorb

Table 1: Main patients' characteristics.

MAP (mmHg)	T0	T12	T24	T48	T72	T96	T120
Patient 1	65	100	60	87			
Patient 2	76	53					
Patient 3	70	70	60				
Patient 4	65	75	70	65	80	93	90
Patient 5	60	73	60	75	80	75	80
Patient 6	71	80	56	66			
Patient 7	60	90	90	65	82	70	88

Table 2: Temporal variation of MAP.

Norepinephrine (µg/Kg/min)	T0	T12	T24	T48	T72	T96	T120
Patient 1	0,24	0,27	0,27	0,18			
Patient 2	0,52	1,44					
Patient 3	0,35	0,5	0,6				
Patient 4	0,6	0,4	0,3	0,1	Stop		
Patient 5	0,3	0,33	0,35	0,18	Stop		
Patient 6	0,28	0,5	0,6	0,6			
Patient 7	0,06	Stop					

Table 3: Temporal variation of Norepinephrine.

The data of the five patients treated with the CytoSorb device were collected at the time of diagnosis of sepsis (T0), at 24h (T24), at 48h (T48), at 72h (T72), at 120 (T120). The parameters evaluated are: procalcitonin, norepinephrine dosage, white blood cell count and C reactive protein (CRP)

evaluation. The following tables (Tab. 9-11) show the values. Unfortunately, given the death of some patients, it was not possible to retrieve all the data at the defined times.

SOFA score	T0	T12	T24	T48	T72	T96	T120
Patient 1	16	15	13	15			
Patient 2	13	17					
Patient 3	12	15	16				
Patient 4	13	15	15	15	10	9	5
Patient 5	12	11	13	11	7	5	6
Patient 6	14	15	16	17			
Patient 7	13	9	10	12	10	10	8

Table 4: Temporal variation of SOFA score.

LUNG INJURY score	T0	T12	T24	T48	T72	T96	T120
Patient 1	2	2	2,25	2,25			
Patient 2	2	1,35					
Patient 3	1,5	1,75	1,75				
Patient 4	2,75	2,25	2	1,25	1,25	1,25	1,25
Patient 5	0	0	1	1	1	1	1
Patient 6	2	2,25	2	2,25			
Patient 7	5	1	4	4	5	2	1

Table 5: Temporal variation of LUNG INJURY score.

RIFLE score	T0	T12	T24	T48	T72	T96	T120
Patient 1	0	1	2	3			
Patient 2	2	2					
Patient 3	1	2	2				
Patient 4	0	0	0	0	0	0	0
Patient 5	0	2	1	0	0	0	0
Patient 6	0	1	1	1			
Patient 7	1	0	0	0	0	0	0

Table 6: Temporal variation of RIFLE score.

PaO2/FiO2 ratio	T0	T12	T24	T48	T72	T96	T120
Patient 1	<300	<300	<300	<300			
Patient 2	<200	<200					
Patient 3	<300	<200					
Patient 4	<100	<200	<200	<300	<300	<300	<400
Patient 5	<400	<400	<300	<300	<300	<300	<300
Patient 6	100	<200	<100	<100			
Patient 7	<200	<300	<200	<200	<300	<300	<300

Table 7: Temporal variation of PaO2/FiO2 ratio.

Discussion

From the data shown in the tables, graphs (Graph 1-12) have been developed to illustrate the changes in the parameters and to evaluate the effectiveness of the treatment. In the first seven patients treated with the PMX-PH device on all the analyzed parameters there was a clear improvement of three out of seven patients who showed, in the studied time, a significant improvement in PAM and in the PaO2 / FiO2 ratio. Consequently, it is recorded a decrease in the dosage of noradrenaline and, in line with the corresponding improvement in the various prognostic scores analyzed in the above time, the blood dosages of procalcitonin and EA are also optimized in the same three patients at the studied time.

Procalcitonin (ng/ml)	T0	T12	T24	T48	T72	T96	T120
Patient 1	3,73		3,34				
Patient 2	1,8	4,64					
Patient 3	24,11	41					
Patient 4	53	47		25	14,3	5,22	1,48
Patient 5	145	51		15,92			
Patient 6	10,54						
Patient 7	42,81		101,49	79,14			10,05

Table 8: Temporal variation of Procalcitonin in patients PMX-PH.

Procalcitonin (ng/ml)	T0	T24	T48	T72	T120
Patient 8	4,46				
Patient 9	14,69				
Patient 10	2,41	4,68	3,17	2,87	
Patient 11	50,15				
Patient 12		126,61	60,45		3,76

Table 9: Temporal variation of procalcitoninn in patients CytoSorb.

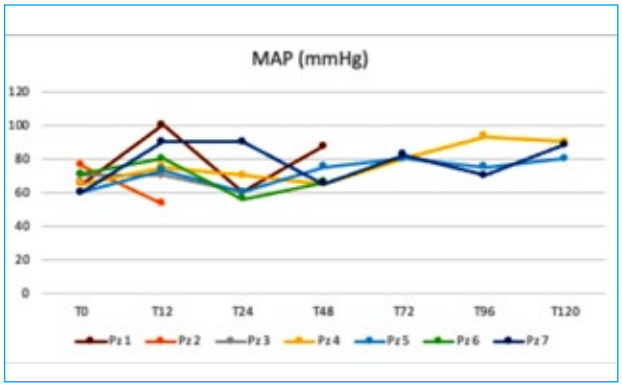
Patient 10	T0	T24	T48	T72	T120
Norepinephrine (μg/Kg/min)	0,45	0,2	0,05	Stop	
leukocytes (103/μL)	20,03	33,83	28,25	18,18	
CRP (mg/L)	255,7	399,4	187,9	64,5	

Table 10: Patient 10 data.

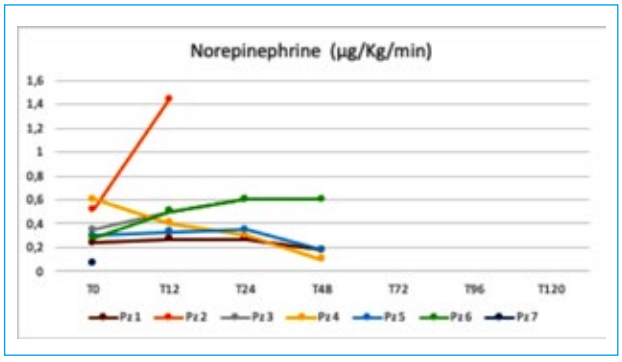
Patient 12	T0	T24	T48	T72	T120
Norepinephrine (μg/Kg/min)	0,4	0,4	0,08	Stop	
Leukocytes (10^3/μL)		0,02	0,04	0,18	1,77
CRP (mg/L)		278,11	268,5	210,6	120,17

Table 11: Patient 12 data.

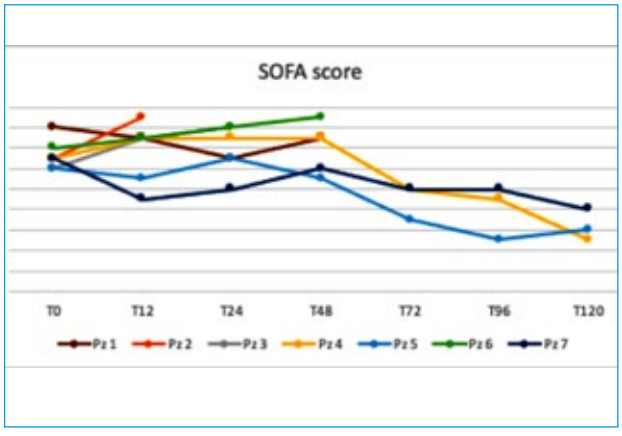
From the graphs 9-12 it is clear that the laboratory data certifying the infection show a marked improvement, highlighting the excellent response of patients following therapy with the Cytosorb device. The leukocyte count is more appreciable in patient 10 and less evident in patient 12 due to his pre-existing haematological pathology.



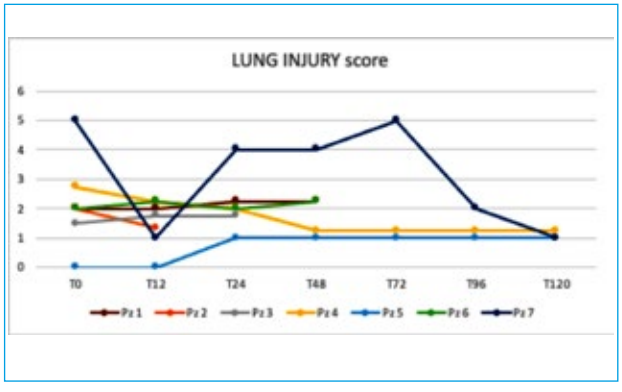
Graphic 1: Temporal variation of MAP.



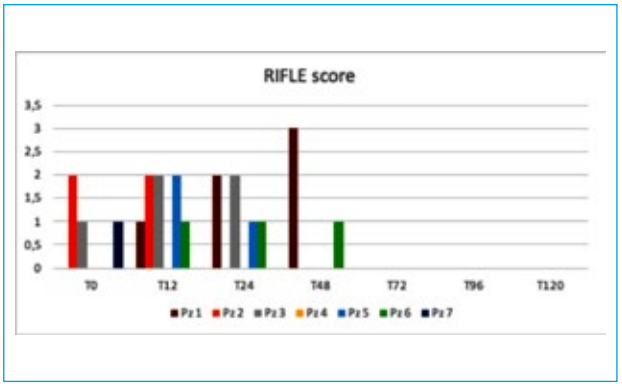
Graphic 2: Temporal variation of norepinephrine in patients PMX-HP.



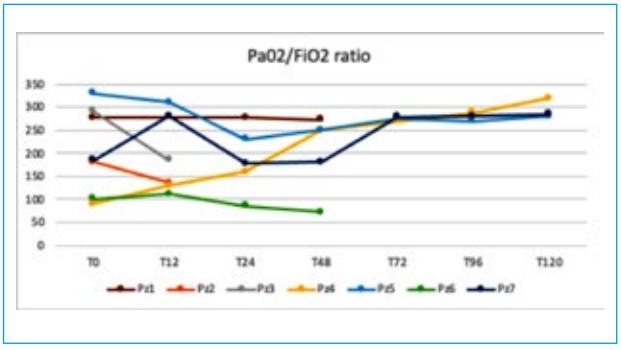
Graphic 3: Temporal variation of SOFA score.



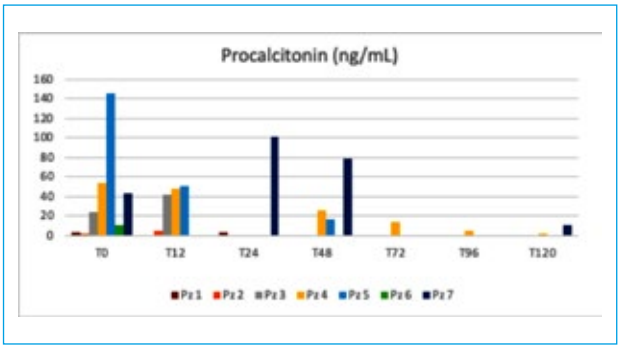
Graphic 4: Temporal variation of lung injury score.



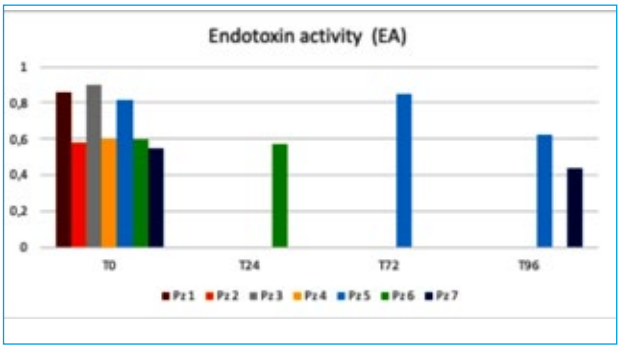
Graphic 5: Temporal variation of rifle score.



Graphic 6: Temporal variation of PaO2/FiO2 ratio.



Graphic 7: Temporal variation of procalcitonin in patients PMX-PH.

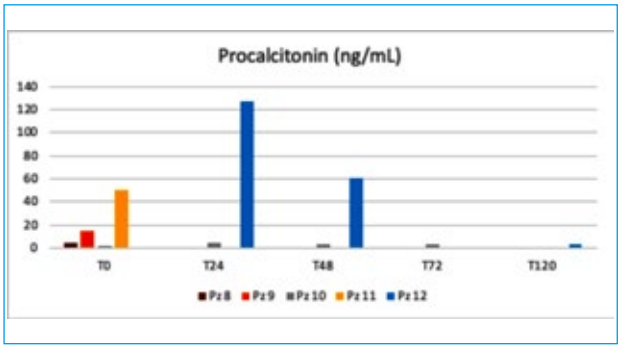


Graphic 8: Temporal variation of endotoxin activity.

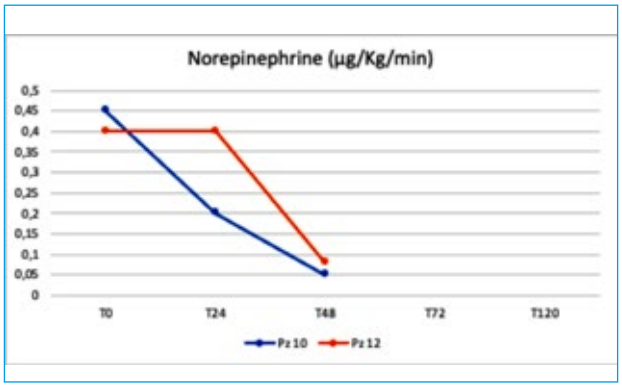
Conclusion

In conclusion, after careful evaluation of the cohort of patients, it is evident the support determined by blood purification therapy techniques

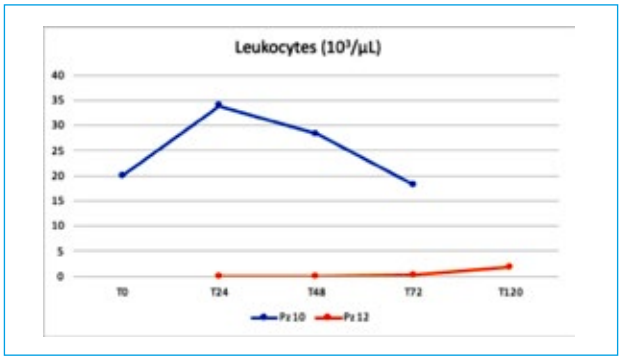
in concretely improving the conditions of subjects who find themselves in a critical state. However, the need for continuous studies confirming the effectiveness of these therapies is emphasized as, to date, they have not yet found an official place in the guidelines for the treatment of sepsis and septic shock.



Graphic 9: Temporal variation of PaO2/FiO2 ratio.

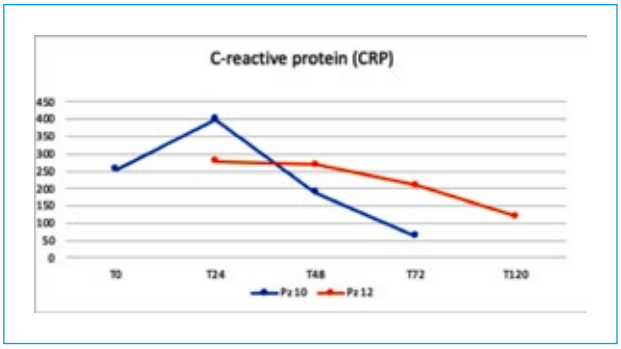


Graphic 10: Temporal variation of norepinephrine in patients 10 and 12.



Graphic 11: Temporal variation of leukocyte count in patients 10 and 12.

It is desirable that the optimization of this new technology, which since 2016 has been recognized as a treatment option for the patient in a state of sepsis or septic shock allowing to place these devices alongside conventional therapy, can lead to a reduction in mortality, an ever-greater effectiveness of the same and to an improvement in the cost / benefit ratio.



Graphic 12: Temporal variation of CPR in patients 10 and 12.

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