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Coupled plasma filtration adsorption improves hemodynamics in septic shock

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ABSTRACT

Purpose: Septic shock involves a dysregulation of the immune response to an infection. This may lead to hemodynamic dysfunction and multiple-organ failure. The main aim of this study was to evaluate the effect of coupled plasma filtration adsorption (CPFA) on the hemodynamic profile in patients with septic shock.
Materials and methods: We retrospectively analyzed data from 21 adult patients admitted to the intensive care unit with a diagnosis of septic shock, comparing data between pre-CPFA and post-CPFA treatment. They received a maximum of 5 cycles of treatment.
Results: Coupled plasma filtration adsorption treatment was associated with a significant increase of mean arterial pressure ($P < .001$), reduction of the vasoactive/inotropic requirement ($P = .007$), and renal improvement. In patients with leukocytosis or leucopenia, the leukocyte count was restored to a reference range of values.
Conclusion: Treatment with CPFA improves hemodynamic parameters in septic shock patients, ameliorating organ failure.

1. Introduction

Septic shock (SS) presents an incidence of 2% of all patients admitted to a hospital and a high mortality [1]. It mainly involves immune cell dysfunction and mediator dysregulation in response to an infection [2]. An initial hyperinflammatory immune response is followed by an "immunoparalysis" [3]. This state may go forward to multiple-organ failure (MOF) [4]. A prolonged hemodynamic failure can cause further inflammation due to tissue damage related to ischemia and reperfusion. Today, techniques for restoring immune homeostasis exist, due to nonselective removal of soluble mediators and bacterial toxins through extracorporeal blood purification [5]. A technique combining plasma adsorption and renal replacement therapy is coupled plasma filtration adsorption (CPFA) (Fig. 1). In CPFA, a plasma filter separates the plasma that moves through a cartridge containing a synthetic divinylbenzene styrenic resin. The resin has a high surface area (of more than 700 m^2) and a high affinity for several inflammatory and anti-inflammatory mediators. After purification, plasma has reinfused upstream a hemofilter. The hemofiltration step allows additional purification of small molecules that are not removed by adsorption. The treatment is performed for a 10-hour period, after which hemofiltration can be used for renal replacement support. Coupled plasma filtration adsorption seems to improve survival, hemodynamic parameters, and reverse immunoparalysis [6,7].

The aim of this study was to evaluate the impact of CPFA on the treatment of SS. We hypothesized that the immune-modulating effects of CPFA could have hemodynamically significant advantages. The primary end point was to compare hemodynamic parameters in patients with SS before and after the CPFA as an adjunctive treatment. The secondary end point was to compare more general effects related to the evolution toward multiple-organ failure (organ insufficiency and leukocyte and platelet counts). Finally, we determined the overall survival.

2. Materials and methods

In this retrospective study, we analyzed data of all patients admitted to our intensive care unit (ICU) with a diagnosis of SS treated with CPFA between January 2010 and December 2011. The study was approved by the ethical committee of Pisa.

2.1. Patients

Study population encompassed 21 patients older than 18 years with SS. Septic shock was diagnosed according to the International Sepsis

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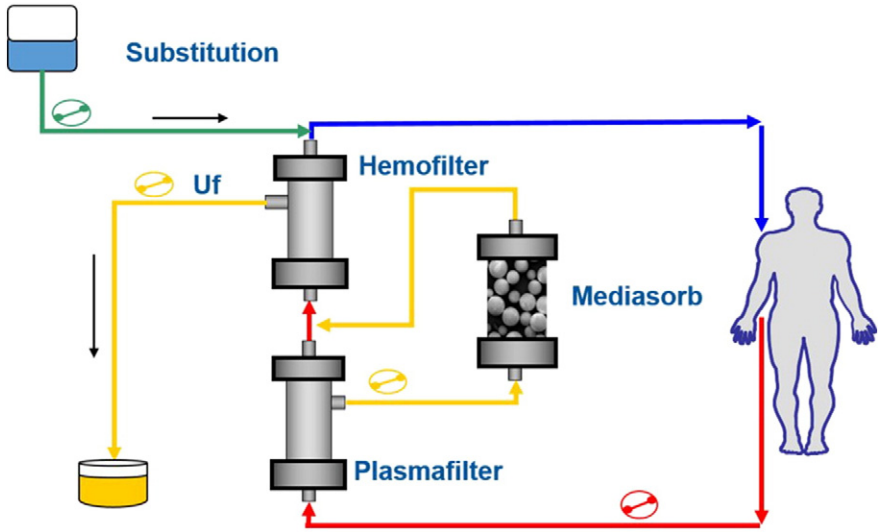

Fig. 1. Schematic representation of CPFA circuit.

Definition Conference [8]. Patients were initially treated according to the guidelines of the Surviving Sepsis Campaign of 2008 [9]. Inclusion criteria were an early diagnosis and start of the CPFA treatment within 6 hours from the onset of manifestations (hypotension refractory to fluid resuscitation). Exclusion criteria were terminal illness and late diagnosis as well as age younger than 18 years, pregnancy, and organ transplantation in the last year. We had an appropriate consent form signed, which was approved by the ethical committee of Pisa.

2.2. Coupled plasma filtration adsorption

Coupled plasma filtration adsorption was performed with Lynda (Bellco, Mirandola, Italy). Patients' blood circulates through an extracorporeal circuit, passing first through a polyether sulfone plasma filter to separate plasma from blood cells. After, the plasma moves through an adsorbent cartridge containing a divinylbenzene styrene resin to retain proinflammatory and anti-inflammatory mediators and endotoxin [10]. Purified plasma is then reassembled to blood cells and passes through a hemofilter (a polyphenyl hemodializer) for renal replacement treatment.

2.3. Study procedures

Coupled plasma filtration adsorption treatments were indicated and checked by staff anesthesiologists with experience on renal extracorporeal therapies. Additional elements taken into account by the anesthesiologists to start CPFA were high dose of vasopressors (eg, dose of norepinephrine higher than 0.5 μg/kg per minute) and high Sequential Organ Failure Assessment (SOFA) score, usually higher than 6, including acute renal failure to be treated with continuous renal replacement therapies. When a patient met the criteria for being treated with CPFA, a suitable central venous access was established. All patients received standard and invasive monitoring of arterial pressure. They received standard fluid resuscitation with colloids and crystalloids for hypotension as well as inotropes and vasoactives to maintain a mean arterial pressure (MAP) greater than 65 mm Hg. They also received broad-spectrum antibiotic therapy and tailored to culture results, when ready. The duration of CPFA treatment was 10 hours per session, maintaining a blood flow (Q_b) range of 150 to 180 mL/min and a plasma flow (Q_p) ranging from 15% to 20% of blood flow. After that, hemofiltration was started. The chosen regimen of renal replacement therapy was continuous veno-venous hemofiltration (CVVH), at a rate of 30 mL/kg per hour of plasma performed within 10 to 12 hours. We administered unfractionated heparin or citrate as anticoagulant. A maximum number of 5 cycles of treatment was established, as recommended: CPFA treatment was discontinued before the fifth cycle in the case of early clinical improvement, mainly consisting in a significant reduction of vasoactive support and an increase of MAP. During the treatment, fluid balance was adapted to clinical conditions according to the anesthesiologist's judgment. Body temperature was maintained between 36.5°C and 37.5°C by means of active warming (air-forced blankets and warmed fluids).

2.4. Data collection

Data were collected retrospectively from the medical records of patients who had been treated with CPFA and had met the inclusion criteria. We analyzed clinical and laboratory data at the admission (T0) and the end of every CPFA cycle (T1-T5). They included demographics, underlying medical conditions, MAP, vasopressor requirement, white blood cell and platelet counts, serum creatinine, serum bilirubin, serum lactate, Pao_2/fraction of inspired oxygen (Fio_2) ratio, and hospitalization length of stay. Doses of vasoactive or inotropic agents were expressed as the vasoactive inotropic score (VIS) [11,12], which quantifies the amount of hemodynamic support. The VIS was measured at the admission and after every cycle of treatment. Survival rate after 28 and 90 days was recorded. The severity of illness on ICU admission was evaluated using the Simplified Acute Physiology Score II (SAPS II), whereas the severity of organ dysfunction was evaluated using the SOFA score, which was calculated daily.

2.5. Statistical analysis

Data were reported as mean ± SD and compared using the Student paired sample *t* test to detect differences between baseline and posttreatment values of the selected variables. $P < .05$ was considered statistically significant. Calculations were performed using Microsoft Office Excel, Microsoft Corporation, Redmond, Washington, USA.

3. Results

The present study included 21 patients, 14 men and 7 women (age 66.4 ± 10.9 years) with SS. The baseline and clinical characteristics of the patients are shown in Table 1. Seven patients (33.3%) had a polymicrobial infection; 10 patients (47.5%) had a gram-negative infection, 3 patients (14.3%) had a gram-positive infection, and 1 patient (4.8%) had an SS of unknown origin.

The average number of CPFA sessions was 3.4 ± 0.9 per patient. Every CPFA treatment lasted 9.0 ± 1.4 hours. The CVVH lasted 9.6 ±