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Plasma exchange and critical autoimmune diseases: experience of a second level center in Quito-Ecuador. Letter to the editor.

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Abstract

Introduction: Renal replacement therapy (RRT) has evolved significantly since its introduction; initially used to treat acute renal failure, it is applied in various clinical scenarios due to improved membranes and equipment. Other techniques have emerged, such as therapeutic apheresis and hemadsorption, which allow specific components to be removed from the blood. These therapies have shown promise in the treatment of various diseases.

Important points:
Sepsis and septic shock are the most common causes of admission to intensive care units (ICU), and extracorporeal therapies (ECT) have shown promise in their management.
Sepsis is characterized by a dysregulated inflammatory response, which can lead to multiorgan damage. ECT can help modulate this response, eliminating inflammatory mediators and restoring immune balance.
Although clinical evidence is inconclusive for all indications, studies have shown improvements in clinical parameters, such as decreased need for vasopressors and improved oxygenation.
The response to ECT may be variable among patients due to genetic, epigenetic, and sociodemographic factors.

Conclusion: extracorporeal therapies are presented as a promising tool in the management of critically ill patients, and their use is expanding beyond sepsis. As more scientific evidence accumulates, it is expected that these techniques will become consolidated as part of the standard treatment in various pathologies.

Keywords:
Renal replacement therapy, extracorporeal therapies, plasmapheresis, sepsis, autoimmune diseases.

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Renal replacement therapy (RRT) appeared in the late 1990s; the first successful hemodialysis (HD) performed on a human was in Holland, with a system designed by Johan Kolff. However, HD was not introduced in the intensive care unit (ICU) as a continuous therapy until 1977. A semipermeable membrane system was implemented with the mechanisms of convection and diffusion, which were proven to treat fluid overload in patients with renal failure and hemodynamic instability. Currently, new uses for extracorporeal therapies (ECTs) have been developed with improvements in the characteristics of the membranes and the redesign of the machines, which has allowed their application in various clinical scenarios in critical patients with and without acute renal injury, with and without septic shock, multiorgan dysfunction syndrome, liver failure, and poisoning, among other conditions [1].

In parallel with the evolution of TRS techniques, techniques have been developed for the treatment of blood components; we refer to therapeutic apheresis and all its variants, which play essential roles in the treatment of autoimmune diseases, and these treatments are positioned as valid therapeutic strategies in cases of disease refractory to conventional therapy; however, in clinical practice, their use must be validated and evidence generated in various clinical scenarios [2].

The general treatment conditions involve a capillary membrane filter, a blood flow rate between 50 and 150 ml/min, and a plasma flow rate of 1/3 or less of the blood flow rate. The plasma volume processed is 1.0 to 1.5 of the estimated plasma volume, with heparin being the anticoagulant of choice. Fresh frozen plasma or an albumin solution replaces the removed plasma, depending on the pathology to be treated [3, 4].

Hemoadsorption is an extracorporeal treatment that removes endotoxins and inflammatory mediators via a cartridge with an adsorptive polymer during the passage of blood through the system. It was first used in 1948 by Muirhead and Reid to remove uremic toxins, and the current indications are septicemia and poisoning [3].

Clinical improvement and evidence

Extracorporeal treatments, with all their variants, have become part of the therapeutic package in critically ill patients. These strategies may eventually improve the outcomes of critically ill patients, including survival.

Sepsis and septic shock are the most frequent causes of admission to the ICU. The proposed management method is based on supporting organ failure and early administration of antibiotics. The current definition of sepsis is based on pathophysiology, defined as the "dysregulated response" of the host to an infectious noxa [5]. Dysregulation is closely related to the activation of the adaptive immune response, which, when not controlled, generates a proinflammatory cascade responsible for high mortality and can be objectively measured with serum levels of inflammatory cytokines such as interleukin 6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin 1 (IL-1), among others. Although inflammation is necessary to fight infections, the body needs mechanisms to control it. Cells such as regulatory T cells and M2 macrophages, together with molecules such as IL-10 and TGF-β, help reduce inflammation and restore normal tissue status [6]. In this context, it is plausible to use extracorporeal therapies (Figure 1) to eliminate immunological mediators from the circulation, initiating a scenario of restoring the balance of the immune response expressed in the improvement of clinical parameters at the hemodynamic level with a significant decrease in vasopressor doses and at the respiratory level with a notable improvement in oxygenation. However, the clinical effects are not sustainable over time, as demonstrated by the studies published to date, where despite having a frank and statistically significant decrease in IL-6, TNF-α, and IL-1, a reduction in von Willebrand factor (VWF) and an increase in the ADAMTS-13 enzyme, the last two are essential for restoring endothelial functionality, they do not reduce mortality [4, 7– 10]. This situation could be explained by the fact that the treatment also concomitantly eliminates IL-10 and other anti-inflammatory cytokines vital to maintaining immunological homeostasis; additionally, the host response does not have linear behavior since genetic, epigenetic and sociodemographic conditions condition interindividual responses, which do not allow precision in the intervention.

Is there space in the intensive care unit for extracorporeal treatments?

Although extracorporeal therapies are expensive and their application in pathologies such as sepsis is not yet fully defined, they have gained ground in clinical practice.

From a modern and technological perspective, the role of critical care specialists has expanded significantly. Today, these professionals are proficient in techniques such as hemodynamics, ultrasound, bioimpedance, and bioreactance. These skills are fundamental in the management of critical patients. Although sepsis remains an area of active research, it is undeniable that autoimmune diseases, poisoning, and other conditions benefit significantly from extracorporeal purification therapies such as plasma exchange.

Therefore, it is essential not only to underestimate sepsis but also to limit the use of these therapies to this pathology. As scientific evidence becomes more solid and their efficacy is demonstrated in other immunological disorders, more patients will benefit from them in the short and medium term.

In a review of data from DIALNEF on treatments over the last four years in 26 private centers and one public hospital, 7991 cases were collected in ICUs. A total of 3142 (39%) patients developed acute renal failure at different stages. Among this group, 1351 (53%) required RRT, 0.6% required ECT, and 0.1% required combined plasma filtration and adsorption [11]. Although plasma replacement therapy was less common, its use sometimes increased.

In a secondary-level hospital in Quito-Ecuador, the implementation of plasma exchange has allowed the successful treatment of various pathologies that previously had a reserved prognosis. This experience has promoted a deeper understanding of the underlying immunological and molecular mechanisms, facilitating the application of scientific knowledge in clinical practice. Plasma exchange was performed via a PS2 plasma filter (Fresenius), with a blood flow of 150 ml/min, a plasma exchange flow of 25 ml/min, a replacement volume of 1 to 1.5 plasma volume, and fresh frozen plasma for replacement (Table 1).

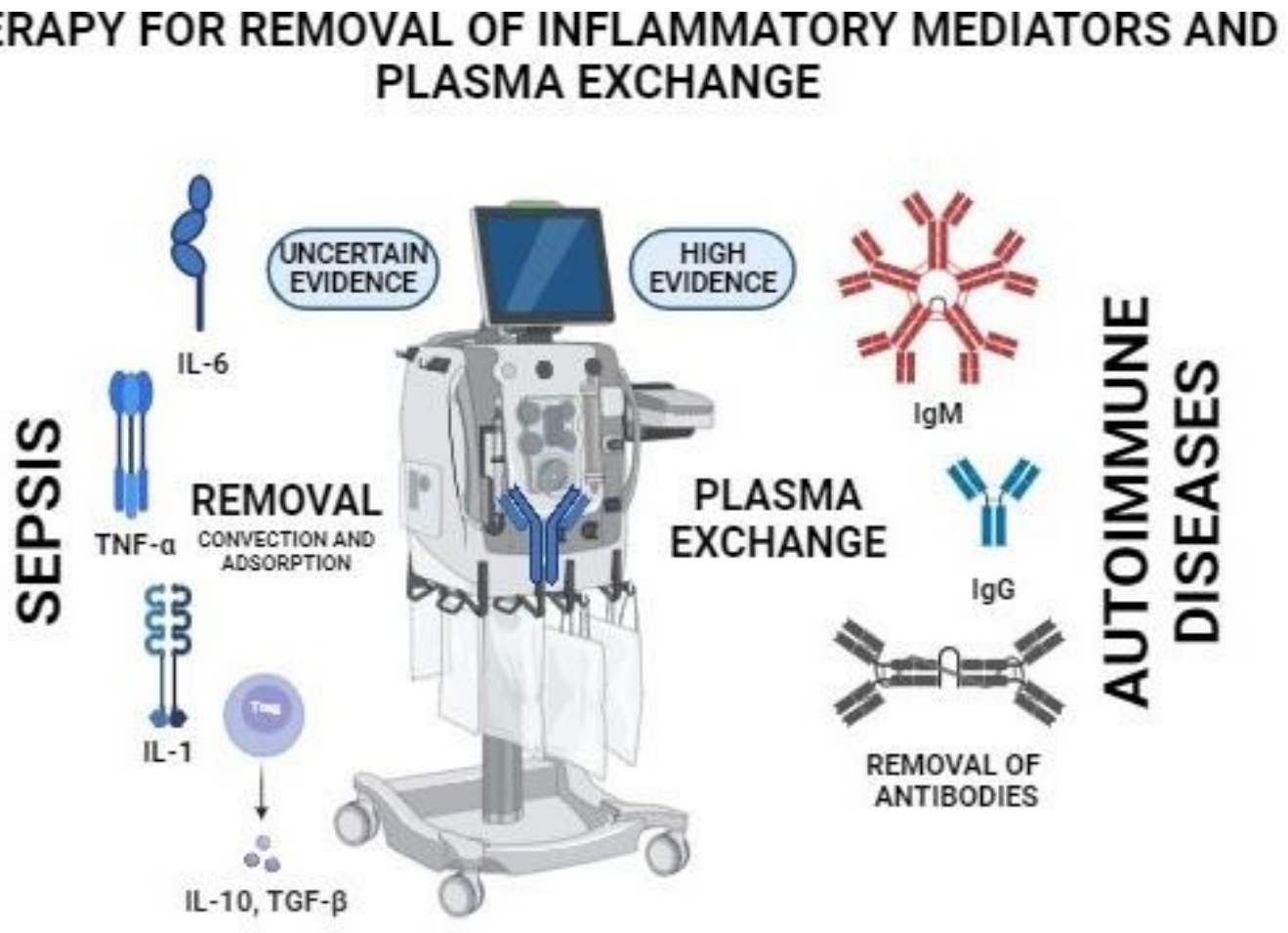

Figure 1.
Elimination therapies (convection and adsorption) of inflammatory mediators and plasma exchange in sepsis and autoimmune diseases. The mechanisms of action and their use in two clinical scenarios, septicaemia and autoimmune diseases, are detailed.

Table 1. Diagnoses, complementary therapies and final condition of patients who received plasma exchange therapy.

Sex	Diagnosis	Complementary immunotherapy.	Final Condition	# Sessions
Women	Barré syndrome .	None	Complete remission.	5
Women	Anti-N- Methyl -D aspartate receptor (NMDA) antibody encephalitis .	Rituximab	Complete remission.	5
Man	Thrombotic-thrombocytopenic purpura .	Rituximab	Complete remission.	5
Women	Thrombotic thrombocytopenic purpura.	Rituximab	Complete remission.	5
Man	Hematologic hyperviscosity secondary to Multiple Myeloma .	Rituximab	Remission of hyperviscosity	5
Women	Anti-N- Methyl -D aspartate receptor (NMDA) antibody encephalitis .	Rituximab	Complete remission.	5
Man	Acute disseminated encephalomyelitis (ADEM)	None	Complete remission.	5

Abbreviations
HD: hemodialysis.
IL: interleukins.
ECT: extracorporeal therapies.
RRT: renal replacement therapy.
Intensive Care Unit.

Supplementary information
No supplementary materials have been declared.

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Author Contributions
Jorge Luis Vélez-Páez: Conceptualization, Data curation, Formal analysis.
Mario Montalvo-Villagómez: Conceptualization, Methodology.
Darío Jiménez: Conceptualization, Project Administration, Resources, Software, Writing – original draft.
Pablo Andrés Vélez: conceptualization, data curation, formal analysis, research, methodology, resources.

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