Extracorporeal Photopheresis and Immune Signatures in Lung Transplantation: A Serum-Based Analysis

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Abstract text
Text: **Introduction:** Chronic lung allograft dysfunction (CLAD) is the leading cause of long-term mortality after lung transplantation. Extracorporeal photopheresis (ECP) is a potential adjunct therapy to mitigate immune-driven injury, but its immunoregulatory effects remain unclear. Understanding how ECP influences systemic immune factors may provide insights into its potential role in modulating alloreactivity.

Objectives: This study investigates the effect of ECP on the serum cytokine landscape in lung transplant recipients, aiming to identify immune pathways that may contribute to reduced alloreactivity.

Methods: In a prospective, randomized, controlled trial, lung transplant recipients received either standard immunosuppression alone (n=30) or with ECP (8 cycles within 3 months, n=30). Serum samples were collected pre-transplant and at 3 months. A 65-plex Luminex-based assay quantified cytokine and chemokine levels. Immune profiling was performed using FlowSOM clustering, and key factors were identified via Random Forest analysis. Temporal shifts were assessed using mean differences between baseline and 3 months, while the Mann-Whitney U test compared group differences. PLS-DA was applied to selected immune factors to assess group differentiation. KEGG pathway analysis identified related immune mechanisms.

Results: Key immune mediators distinguishing the ECP group included VEGF-A, Eotaxin-2, and MMP-1. IL-16 levels declined in both groups but remained significantly higher in ECP-treated patients. PLS-DA was performed using IL-16, along with BLC, IFN-γ, TNF-α and MIP-1β, which had the lowest p values among the analyzed factors. This analysis revealed a trend in distinguishing the two groups, supporting the idea that these mediators contribute to group differentiation. Pathway analysis revealed enrichment of allograft rejection and graft-versus-host disease pathways, underscoring potential ECP-mediated immunomodulation.

Conclusion: ECP appears to alter systemic immune signatures in lung transplant recipients, possibly by modulating inflammatory and alloimmune pathways. These findings support further investigation into ECP’s therapeutic potential in reducing CLAD risk and improving long-term graft outcomes.

Conflict of Interest statement
Do you have any conflict of interest to declare?: Yes
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Affirmation
1. Consent to participate and present onsite: Yes
2. Consent to publication publication: Yes
3. Consent on treatment of contact details saved in this system: Yes