

Critical Insights into Novel Immunomodulatory Therapy for Sepsis: Evaluating Promise Amidst Limitations

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Dear Editor,

We read with utmost interest, the study by Ghosh et al.¹ "Efficacy of Polymyxin B Hemoperfusion for Treatment of Sepsis" published in your journal. We appreciate the authors' efforts in designing a trial to assess the effectiveness of an innovative immunomodulatory therapy in sepsis, while ensuring strict adherence to the protocol amidst the constraints of the pandemic. We would like to share some views on the same.

A pre-requisite to the start of the therapy was a reasonably stable hemodynamic status (non-hypotensive patients) achieved with vasoactive medications. Although initiation of an extra-corporeal purification technique involving rapid fluid shifts would necessitate such stabilization, generalizability of the study results would remain questionable. It would be safe to conclude that promising results obtained here would only apply to a relatively stable cohort of patients. Such a conditional conclusion makes the study less pragmatic.

Functional assays and genomic studies place immune dysregulation at the heart of sepsis.² Clinical trials testing the beneficial role of immune-modulation through extra-corporeal therapies, immunosuppressive, and immune adjuvant drugs yielding positive results are innumerable.³⁻⁵ Considering the wide spectrum of options available, each of them can serve as an important confounding factor in such a cohort. Mention of the use of immunosuppressive/immune-stimulant medications followed by an adjusted analysis or a prior matching-up of the cohorts for these factors is essential to ensure comparability and confirm/negate confounding.

Although authors have excluded the patients with hemodynamic instability, known allergies etc. we would like to know the incidence of procedure-related adverse events in the cases. Hemoperfusion is a procedure associated with significant costs and as the evidence regarding the beneficial effect of the same is conflicting, a cost-benefit analysis would help the intensivists to decide on therapeutic utility, especially in low-middle income countries.

Though factors such as limited generalizability, unreported intervention timing, and potential confounding by immunotherapies

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need consideration, a trend toward early recovery definitely sets a fine example to drive concerted efforts in this direction.

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