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CORRESPONDENCE

Correspondence regarding the article by Hüser et al. on "Critical care management of the patient with pharmaceutical poisoning"

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We congratulate Hüser et al. on their comprehensive and timely state-of-the-art review on the management of pharmaceutical poisoning in *Intensive Care Medicine*. Their effort to provide practical guidance in this complex field is highly valuable. Nevertheless, we are concerned that some statements regarding extracorporeal blood purification (EBP) may oversimplify a heterogeneous set of modalities and inadvertently mislead bedside decision-making.

The authors state: "Albumin dialysis, therapeutic plasma exchange, charcoal hemoperfusion, hemoadsorption…have been proposed for pharmaceuticals considered non-dialyzable…especially those that are highly protein-bound. However, none of these elimination techniques have demonstrated a clear advantage over intermittent dialysis…" [1].

In our view, this formulation is problematic for three reasons. First, it aggregates therapies with distinct mechanisms and risk profiles (intermittent hemodialysis, therapeutic plasma exchange, albumin/plasma-based systems, classical charcoal hemoperfusion, and modern sorbent hemoadsorption). Second, it may be interpreted as implying general "ineffectiveness," while available toxicokinetic and clinical evidence does not support such a blanket conclusion. Third, it risks discouraging rational use of advanced modalities in scenarios where conventional hemodialysis is mechanistically disadvantaged for highly protein-bound or lipophilic agents.

EXTRIP and related expert frameworks emphasize that extracorporeal strategies should be selected according to drug properties (including protein binding, volume of distribution, and endogenous clearance) and clinical context, rather than framed as "hemodialysis versus all other techniques." [2, 3]. For carbamazepine poisoning, for example, EXTRIP explicitly includes sorbent-based approaches among acceptable options alongside intermittent hemodialysis in severe presentations [3].

In acute toxicology, the clinical signal for sorbent-based EBP is particularly visible in selected indications. Observational data and recent syntheses suggest that early, and when needed, repeated sorbent therapy may accelerate toxin decline and may improve short-term outcomes in paraquat and other pesticide poisonings when embedded in multimodal care [4]. Contemporary pharmacokinetic work also supports the mechanistic plausibility of modern polymer-based hemoadsorption for highly protein-bound agents; recent experimental data demonstrate rapid early removal of ticagrelor with saturation dynamics that favor timely initiation and thoughtful cartridge management [5].

Importantly, the evidentiary standards for life-threatening poisoning differ from those in many other intensive care unit (ICU) domains. Large, randomized comparisons of extracorporeal elimination strategies are often impractical and may become ethically challenging once

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one approach clearly demonstrates superior toxin clearance in high-risk scenarios. In such contexts, robust toxicokinetic principles and consistent elimination signals, central to EXTRIP methodology, should carry substantial weight in how recommendations are framed [2, 3].

We fully agree that cost, complexity, and potential adverse effects mandate selective use of advanced EBP. However, we suggest that this section be complemented with more nuanced wording that affirms intermittent hemodialysis as first-line when effective, while acknowledging that plasma- and sorbent-based strategies may be justified in carefully selected severe poisonings, guided by toxicokinetic reasoning and specialist consultation.

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Gerd Klinkmann, Thiago Reis and Claudio Ronco wrote the first draft of the correspondence. The other investigators read, contributed to changes, and approved the correspondence.

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