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Xuebijing as a potential therapeutic option for septic shock: the need for rigorous evaluation of life-threatening adverse effects

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Keywords Xuebijing, Traditional chinese medicine, Sepsis, Safety, Adverse drug reactions, Anaphylaxis

The recent article by Kang et al., “Xuebijing injection reduces 28-day mortality in patients with septic shock,” presents important and timely insights into a potential therapeutic role for Xuebijing (XBJ) in septic shock [1]. The authors report similar rates of serious adverse events between groups; however, their article does not address the substantial body of literature documenting potentially severe and life-threatening adverse reactions associated with XBJ. Given the drug’s expanding use in critically ill patients, a more explicit and comprehensive assessment of safety is warranted.

Xuebijing is a standardized traditional Chinese intravenous injection composed of extracts from safflower, red peony root, Chuanxiong, Angelica sinensis, and *Salvia miltiorrhiza*. Although widely employed in Chinese clinical practice for the management of sepsis and its associated complications, multiple sources highlight significant concerns regarding its safety profile. A recent systematic

review of XBJ in sepsis-associated acute kidney injury identified two documented cases of immediate, life-threatening anaphylactic shock following intravenous injection in septic patients [2]. Large-scale pharmacovigilance programs similarly confirm that unpredictable anaphylactic and anaphylactoid allergic reactions remain the most frequently reported serious adverse events, with the potential to rapidly progress to cardiovascular collapse and death [3, 4].

Beyond hypersensitivity, cardiovascular complications have also been described. Real-world safety assessments report that in critically ill or hemodynamically unstable patients receiving XBJ, especially those with underlying cardiogenic shock; cardiac arrest, life-threatening arrhythmias, and episodes of acute heart failure have occurred, albeit infrequently. Some reports suggest that in patients with severe pre-existing cardiac ischemia, XBJ may precipitate worsening ischemic symptoms or contribute to hemodynamic deterioration [5]. While casualty cannot always be definitively established, these findings reinforce the need for heightened caution when administering XBJ in unstable cardiovascular states.

Mechanistically, several plausible explanations exist for these adverse reactions. The safety issues may be partially related to the composition and manufacturing process of Xuebijing. XBJ contains active components such as hydroxysafflor yellow A, which can enter the bloodstream and stimulate antibody formation or lymphocyte

This comment refers to the article available online at <https://doi.org/10.1186/s13054-025-05666-3>.

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sensitization. Re-exposure may therefore trigger severe allergic responses, including anaphylaxis. In addition, manufacturing-related factors, including incomplete purification, residual proteins, or impurities introduced during extraction, may further increase the risk of immune-mediated reactions [6]. Postoperative and critically ill patients, already experiencing profound immunological stress with elevated peripheral blood phagocytic activity, may be especially susceptible to these allergic reactions [4, 6].

Regulatory and practical challenges also persist. Although XBJ is currently approved by the China Food and Drug Administration for severe infections and sepsis, it is not licensed in any jurisdiction outside China. Furthermore, several analyses note that product instructions may be incomplete, inconsistently written, or insufficiently detailed regarding contraindications, potential toxicities, and emergency management of severe adverse events [7, 8]. Given the possibility of life-threatening reactions, manufacturers should ensure rigorous quality control and provide standardized, comprehensive instructions to guide clinicians with explicit safety information.

Kang et al. appropriately conclude that international, prospective trials are warranted to validate XBJ as a therapeutic option for septic shock [1]. We strongly agree but emphasize that such trials must also incorporate equally rigorous, transparent, and systematic evaluation of all potentially life-threatening adverse effects, including anaphylaxis, cardiac complications, and immune-mediated reactions [6, 8]. Only with robust safety assessment can the balance of risks and benefits of XBJ be reliably determined.

Acknowledgements

None.

Author contributions

PMH and NDL designed the paper. PMH, IO, CYM, SD, SB, NDL participated in drafting and reviewing. PMH, IO, CYM, SD, SB, NDL read and approved the final version of the manuscript.

Funding

None.

Data availability

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 3 December 2025 / Accepted: 6 December 2025

Published online: 10 December 2025

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