J Crit Care 91 (2026) 155249

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

Letter to the Editor

Letter to the Editor: "Protective effect of intravenous amino acid on kidney function: A systematic review and meta-analysis of randomized controlled trials"

ARTICLE INFO

Keywords:
Amino acid infusion
Kidney protection
Cardiac surgery
Side effects
Gastrointestinal toxicity

The recent systematic review and meta-analysis by Jiang et al., entitled "Protective effect of intravenous amino acid on kidney function: A systematic review and meta-analysis of randomized controlled trials", provides valuable insights into the potential renoprotective role of intravenous amino acid infusions in clinical practice [1]. While the findings are encouraging, several safety concerns, largely unaddressed in the discussion, merit further attention.

Although intravenous amino acid infusions are generally well tolerated, they are not devoid of risk. Reported complications include electrolyte imbalances, fluid overload, aluminum toxicity, ketonemia, metabolic acidosis, and hyperammonemia, each of which may result in serious, life-threatening complications, potentially including neurological damage. Chronic or excessive amino acid intake, whether via infusion or dietary supplementation, has also raised concerns regarding toxicity, mutagenicity, and even carcinogenicity. Additional adverse effects such as ammonia production dysregulation, renal and gastrointestinal dysfunctions, and competition among amino acids for cellular membrane transporters and degrading metabolic enzymes have also been documented [2].

Several studies evaluating the acute biochemical and clinical toxicity profile of high-dose amino acid infusions, administered in the context of renal protection, report general overall tolerability. Nonetheless, certain gastrointestinal side effects, particularly nausea and vomiting, remain common, especially with mixed amino acid solutions. These solutions may decrease lower esophageal sphincter (LES) pressure and impair gastric emptying, thereby exacerbating upper gastrointestinal symptoms [3]. Moreover, aromatic amino acids such as tryptophan and phenylalanine may stimulate gastric parietal cells directly, further aggravating symptoms [4]. L-arginine may mediate these effects via nitric oxide synthesis or through direct central nervous system action [3].

Standard anti-emetics, including peripherally acting dopamine antagonists, metoclopramide and alizapride, as well as serotonin receptor antagonists, such as tropisetron, yielded limited symptomatic relief. However, emerging evidence suggests that domperidone, an anti-emetic known to increase LES pressure, may offer more effective symptom control.

Further support for the gastrointestinal toxicity of amino acid infusions derives from studies involving arginine-rich infusions co-administered during radiolabeled peptide therapies such as 90 Y-DOTATOC. Rolleman et al. reported nausea and vomiting in 50–69 % of patients receiving arginine and/or lysine-based infusions, compared to only 10 % in those receiving lysine-only infusions. Comparable findings were observed in patients treated with octreotide in conjunction with various amino acid infusions [5]. The higher incidence of gastrointestinal side effects may be attributable to not only the infusion composition but also to the elevated radiation doses administered.

Transient elevations in serum urea concentration following 4 or 10 h mixed amino acid infusions likely reflect urea cycle saturation, particularly due to high L-arginine content in such solutions (10.72 g/l). This phenomenon is not observed with pure L-lysine infusions. Elevated levels of ornithine and citrulline, both urea cycle intermediates, following lysine-arginine (Lys-Arg) infusions further supports this hypothesis of metabolic saturation. Barone et al. also noted that high-dose amino acids intravenous infusions for renal protection may transiently overwhelm the renal tubular system, leading to anion imbalance and impairments in protein reabsorption [3]. While most biochemical alterations resolve within 24 h, normalization of urea levels may take up to 7–10 days.

It is important to highlight that Jiang et al. meta-analysis excluded patients with pre-existing chronic kidney disease or those at elevated risk of renal dysfunction, including patients undergoing chemotherapy, receiving total parenteral nutrition, or suffering from congestive heart failure [1]. In such populations, the biochemical disturbances induced by amino acid infusions warrant heightened clinical vigilance, especially in the context of radiopeptide therapy. Careful assessment is required to balance potential therapeutic benefits with the risk of acute metabolic complications [3].

In the setting of renal protection following cardiac surgery, the decision to administer amino acid infusions should be guided by a rigorous risk-benefit evaluation. Clinicians are advised to weigh the anticipated renoprotective advantages alongside the potential for significant adverse events, in order to make judicious, patient-centered decisions.

https://doi.org/10.1016/j.jcrc.2025.155249
Received 22 August 2025; Accepted 27 August 2025
Available online 1 September 2025

Author's contributions

PG and PMH designed the paper. All authors participated in drafting and reviewing. All authors read and approved the final version of the manuscript.

Funding

None.

Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Priscilla Gillis: Conceptualization, Writing – original draft, Writing – review & editing. **Julien Moury:** Writing – original draft, Writing – review & editing. **Thibault Gennart:** Writing – original draft, Writing – review & editing. **Sydney Blackman:** Writing – original draft, Writing – review & editing. **Nathan De Lissnyder:** Writing – original draft, Writing – review & editing. **Catherine Y. Muscato:** Writing – original draft, Writing – review & editing. **Yasser Benkaddour:** Writing – original draft, Writing – review & editing. **Patrick M. Honoré:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare to have no competing interests.

Acknowledgements

None.

References

[1] Jiang W, Shi K, Shao J, Song L, Shi Y, Wang H, et al. Protective effect of intravenous amino acid on kidney function: a systematic review and meta-analysis of randomized controlled trials. J. Crit. Care 2025 Feb;85. https://doi.org/10.1016/j.jcrc.2024.154937. 154937. Epub 2024 Oct 23. PMID: 39447274.

[2] Holeček M. Side effects of amino acid supplements. Physiol. Res. 2022 Mar 25;71(1): 29–45. https://doi.org/10.33549/physiolres.934790. Epub 2022 Jan 19. PMID: 35043647; PMCID: PMC8997670.

[3] Barone R, Pauwels S, De Camps J, Krenning EP, Kvols LK, Smith MC, et al. Metabolic effects of amino acid solutions infused for renal protection during therapy with radiolabelled somatostatin analogues. Nephrol. Dial. Transplant. 2004 Sep;19(9): 2275–81. https://doi.org/10.1093/ndt/gfh362. Epub 2004 Jul 13. PMID: 15252161.

[4] Straathof JW, Adamse M, Onkenhout W, Lamers CB, Masclee AA. Effect of L-arginine on lower oesophageal sphincter motility in man. Eur. J. Gastroenterol. Hepatol. 2000 Apr;12(4):419–24. https://doi.org/10.1097/00042737-200012040-00009 (PMID: 10783995).

[5] Rolleman EJ, Valkema R, de Jong M, Kooij PP, Krenning EP. Safe and effective inhibition of renal uptake of radiolabelled octreotide by a combination of lysine and arginine. Eur. J. Nucl. Med. Mol. Imaging 2003 Jan;30(1):9–15. https://doi.org/10.1007/s00259-002-0982-3. Epub 2002 Oct 29. PMID: 12483404.

Priscilla Gillis[a], Julien Moury[a], Thibault Gennart[a], Sydney Blackman[b], Nathan De Lissnyder[c], Catherine Y. Muscato[d], Yasser Benkaddour[d], Patrick M. Honoré[e,*]

[a] *Resident in ICU, CHU UCL Godinne Namur, UCLouvain Medical School, Belgium*

[b] *CHIREC, Université Libre de Bruxelles, Brussels, Belgium*

[c] *UZ Brussel, VUB University, Brussels, Belgium*

[d] *Medical Student, Université Libre de Bruxelles, Brussels, Belgium*

[e] *ICU, CHU UCL Godinne Namur, UCLouvain Medical School, Belgium*

[*] Corresponding author at: Head of ICU Dept, CHU UCL Godinne Namur, UCL Louvain Medical School, Campus Godinne, Avenue G Thérasse 1, 5530 Yvoir, Belgium.

E-mail addresses: Gillis@CHUUCLNamur.Uclouvain.be (P. Gillis), Julien.Moury@chuuclnamur.uclouvain.be (J. Moury), Thibault.Gennart@chuuclnamur.uclouvain.be (T. Gennart), patrick.honore@chuuclnamur.uclouvain.be (P.M. Honoré).