

*Corresponding author at: Laboratorio de Hígado, Páncreas y Motilidad (HIPAM), Unidad de Investigación en Medicina Experimental Dr. Ruy Pérez Tamayo, Facultad de Medicina, Universidad Nacional Autónoma de México (UNAM). Dr. Balmis #148, Col. Doctores, Mexico City, C.P. 06726, Mexico.

E-mail address: mschmulson@gmail.com (M. Schmulson-Wasserman).

2255-534X/ © 2025 Asociación Mexicana de Gastroenterología. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Considerations about the balanced crystalloid solution recommendation in acute variceal bleeding



Consideraciones sobre la recomendación de soluciones balanceadas en hemorragia variceal aguda

Dear Editors,

We read with great interest the “Mexican consensus on the approach to and treatment of acute variceal bleeding”, by Higuera de la Tijera et al.,¹ whom we congratulate for their valuable work. We would like to make a comment on statement 3, related to fluid management.

The authors recommend replacing intravascular volume with balanced crystalloid solutions, arguing that there is a lower association with adverse events and mortality, based on a single randomized clinical trial (RCT) by Semler et al. in 2018 (n=7,942). However, better evidence is currently available.

The largest RCT at present was recently published that compared the use of lactated Ringer’s solution versus saline solution 0.9% in intravenous fluid administration (n=43,626).² The primary outcome was a composite of death or hospital readmission within 90 days of the index admission. Incidence of the composite was 20.3% in the lactated Ringer’s solution group and 21.4% in the saline solution group, with no statistically significant difference (adjusted difference: –0.53 percentage points; 95% CI: –1.85–0.79; p=0.35). No serious adverse events were reported. The conclusion was that a hospital-wide policy of preferential use of lactated Ringer’s solution, compared with saline solution, did not significantly reduce mortality or hospital readmission.

In addition, a systematic review and meta-analysis of individual patient data³ that included 6 RCTs (n=34,685) evaluated whether the use of balanced crystalloid solutions, compared with saline solution 0.9%, reduced in-hospital mortality in critically ill adults admitted to the intensive care unit. Mortality was 16.8% in the balanced crystalloid group and 17.3% in the saline group (OR: 0.962; 95% CI: 0.909–1.019; absolute difference: –0.4 percentage points). The posterior probability that balanced crystalloids would reduce mortality was 89.5%. Nevertheless, in patients with

traumatic brain injury, mortality was higher in the balanced crystalloid group (19.1% vs. 14.7%; OR: 1.424; 95% CI: 1.100–1.818; absolute difference: 3.2 percentage points), with a 97.5% probability that balanced crystalloids would increase mortality in that subgroup.

That finding could be explained by the higher risk of cerebral edema when using intravenous solutions with a lower sodium concentration (130 mEq/L in Hartmann’s solution and 140 mEq/L in Plasma-Lyte), compared with normal saline solution (154 mEq/L). Considering that patients with acute variceal bleeding are at high risk for developing hepatic encephalopathy,⁴ we believe that the routine use of balanced crystalloid solutions could result in more risks than benefits in that context, but this must be confirmed through RCTs, given that none of the previous studies are specific for acute variceal bleeding.

Another point to be taken into account is that the acquisition and administration of large quantities of different types of solutions has an ecologic and economic impact. The approximate cost of 100 mL of sodium chloride solution 0.9% is \$0.60 USD, whereas the cost of balanced crystalloid solutions is higher, with Plasma-Lyte being the most expensive, at between \$3.00 and \$3.80 USD.

In conclusion, we consider that, at present, the available evidence does not justify recommending one intravenous solution over another, in a generalized manner, for patients with variceal bleeding.

Financial disclosure

No financial support was received in relation to this article.

Declaration of competing interest

The authors declare that there is no conflict of interest.

References

1. Higuera-de-la-Tijera F, Noble-Lugo A, Crespo J, et al. Consenso mexicano sobre abordaje y tratamiento de la hemorragia variceal aguda. *Rev Gastroenterol Mex.* 2025;90(3), <http://dx.doi.org/10.1016/j.rgmx.2025.03.003> (colocar la paginación en cuanto la tengan).
2. McIntyre L, Fergusson D, McArdle T, et al. A crossover trial of hospital-wide lactated Ringer’s solution versus normal saline. *N Engl J Med.* 2025, <http://dx.doi.org/10.1056/NEJMoa2416761>.

3. Zampieri FG, Cavalcanti AB, Di Tanna GL, et al. Balanced crystalloids versus saline for critically ill patients (BEST-Living): a systematic review and individual patient data meta-analysis. *Lancet Respir Med*. 2024;12:237–46, [http://dx.doi.org/10.1016/S2213-2600\(23\)00417-4](http://dx.doi.org/10.1016/S2213-2600(23)00417-4).
4. Mandiga P, Kommu S, Bollu PC [Updated 2025 Jan 20]. In: StatPearls [Internet]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK430869/>, 2025.

O.R. Pérez-Nieto^{a,c}, N. Hernández-Velázquez^b,
J. Beauregard-Mora^{b,*}, M.C. García-Pantoja^b,
J. Reyes-Montufar^b

^a *Unidad de Cuidados Intensivos, Hospital General San Juan del Río, Querétaro, Mexico*

^b *Departamento de Gastroenterología y Endoscopia, Hospital General San Juan del Río, Querétaro, Mexico*

^c *Universidad Autónoma de Querétaro, Querétaro, Mexico*

* Corresponding author at: Luis Donaldo Colosio 422, México, 76804 San Juan del Río, Qro. Unidad de Cuidados Intensivos, Hospital General San Juan del Río, Querétaro, Mexico. Tel.: 56 11 00 88 10.

E-mail address: drjorgebeauregard@gmail.com (J. Beauregard-Mora).

2255-534X/ © 2025 Asociación Mexicana de Gastroenterología. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Response to Pérez-Nieto et al., “Considerations about the balanced crystalloid solution recommendation in acute variceal bleeding”



Respuesta a Pérez-Nieto et al., “Consideraciones sobre la recomendación de soluciones balanceadas en hemorragia variceal aguda”

Dear Editors,

We sincerely appreciate the valuable comments sent by Pérez-Nieto et al. about our document, “Mexican consensus on the approach to and treatment of acute variceal bleeding”.¹ The primary aim of our consensus document was to establish recommendations based on the best available evidence and the opinion of national experts in gastroenterology for the diagnosis, management, and treatment of acute variceal bleeding (AVB) in patients with portal hypertension (PHT), for the purpose of improving clinical decision-making, reducing the associated mortality, and standardizing care protocols at the different levels of medical care in Mexico.

The use of balanced crystalloid solutions in critically ill patients is known to be associated with lower rates of major adverse kidney events and mortality, compared with saline solution, although some studies have found no significant differences in general mortality.^{2–4} However, we know that new evidence is being generated daily. Statement 3 of our consensus says, “Intravascular volume replacement, with a restrictive resuscitation strategy with balanced crystalloid solutions is recommended, given that it has been associated with a decrease in adverse events and death”¹; this is based on a lack of specific studies for the population with cirrhosis.

Regarding the comment of Pérez-Nieto et al.⁵ on the open-label randomized clinical trial (RCT) conducted by McIntyre et al.⁶ in Ontario, Canada, involving 43,626 patients, in which two 12-week periods were completed using either Ringer’s solution or normal saline, for their comparison, we wish to specify that said article could not be taken into account for our consensus, given that it was published in June 2025, and our bibliographic search covered articles from January 2010 to June 2024. It also remains to be seen whether that new clinical trial resolves the controversies raised in previous publications. In addition, the statistical power of the study was reduced, given that 16 hospitals (~144,000 admissions) were to be included and only 7 centers completed the study due to COVID-19. This signifies that there could be a possible type II error in the face of small but clinically relevant effects at the population level. The study by McIntyre et al. does not change the preference for balanced crystalloids in resuscitating critically ill patients with no traumatic brain injury (TBI), which is supported by trials in intensive care units (ICUs) and meta-analyses, but rather indicates that, at the hospital level and with mixed use and moderate volumes, the absolute net effect is small and may be diluted. The study does not perform stratification by subgroups with cirrhosis or report laboratory findings, and so, does not change the pathophysiology-based practice (preventing hyperchloremia/acidosis). Utilizing evidence in ICU patients, it suggests an inclination for balanced solutions in critically ill cirrhotics without TBI. Finally, we believe that because said study sample is a broad mixture of patients (including those from obstetrics and psychiatry), it is not an “ICU resuscitation” trial but rather a hospital fluid policy, as stated by Pérez-Nieto et al.

The meta-analysis by Zampieri et al.⁷ mentioned by Pérez-Nieto et al. included 6 clinical trials, with a total of 34,685 patients. As a complement to that recent publication (2024), we found another, with some of the same authors, but published in 2022. Along with 7 other RCTs, it