Data vs Dogma: Safety of Intravenous Rehydration in Severely Malnourished Children

Mark J Peters MBChB, MRCP(UK), FRCPCH, FFICM, PhD

Professor of Paediatric Intensive Care,

University College London, Great Ormond St Institute of Child Health

Correspondence to:
Mark J Peters, MBChB, MRCP(UK), FRCPCH, FFICM, PhD
Critical Care Group
Infection, Immunity and Inflammation Research and Teaching Department
University College London, Great Ormond St Institute of Child Health
London, UK

Phone +44 207 813 8213
Email mark.peters@ucl.ac.uk

Word count 757

In 2024, a United Nations report estimated that worldwide, one in 11 (up to 757 million people) were facing hunger.[1] Food insecurity and famine risk are exacerbated by conflict and climate change. Infants and children are frequently the most severely affected, as shocking images from Sub-Saharan Africa and Gaza currently attest

Infants and children with severe acute malnutrition frequently suffer the acute medical complication of dehydration from gastroenteritis.[2] Reported outcomes for this feared combination vary with both severity and healthcare systems, but hospital mortality in the range of 30-40% appears typical.[3] The World Health Organization (WHO) estimates that at least 440,000 children under five years old die from diarrheal disease annually.[2]

WHO guidance for rehydration of children with severe acute malnutrition and gastroenteritis with marked dehydration recommends avoiding intravenous rehydration in favor of continuous oral or nasogastric rehydration, unless shock is present.[4] The rationale, perhaps even 'dogma,' is that such children are at high risk of fatal, acute heart failure with overly rapid rehydration. This recommendation is not supported by randomized trial data but is widely practiced.[5]

The GASTROSAM trial published in this issue of the *Journal* was a prospective, open label, randomized controlled trial conducted in Niger, Nigeria, Uganda and Kenya.[6] Participants were 272 hospitalized infants and children aged 6 months to 12 years with severe acute malnutrition and dehydration from gastroenteritis. They were randomized to one of three strategies: current 'WHO-style' care – enteral rehydration with two to four hourly feeds with intravenous rehydration reserved for a diagnosis of shock; rapid intravenous rehydration with lactated Ringer's solution at 100ml/kg over three to six hours with additional boluses permitted for shock; or slow intravenous rehydration with lactated Ringer's solution at 100ml/kg over eight hours without additional boluses permitted for shock.

Before discussing the results, we should note that the study design hints at the strength of the prevailing guidance to avoid intravenous fluid. The allocation ratio of 2:1:1 favored the enteral rehydration arm, as each intravenous arm had half the participants of the enteral arm. The ethical committee at each center approved a protocol mandating that all participants receive care in a closely monitored environment with a dedicated trial

team. The study was initially designed as a phase II trial to estimate the safety of intravenous strategies against a physiological end point of urine output, and to assess feasibility of a definitive trial. [7] Initial recruitment was challenging during the coronavirus pandemic. In response to new data suggesting mortality to be very high in this setting, the trial was redesigned as a superiority trial with 58% as the standard care hospital mortality estimate.[8] The investigators estimated 80% power to detect a 30% reduction in the revised primary outcome of 96-hour mortality – compared between the enteral rehydration group and the two intravenous groups combined.

The results were, to say the least, unexpected. At 96 hours, 11 participants (8%) in the oral group and 9 (7%) in the intravenous groups (5 [7%] in the rapid group and 4 [6%] in the slow group) had died (adjusted risk ratio, 1.02; 95% confidence interval [CI], 0.41 to 2.52; P = 0.69). There were no cases of pulmonary edema or heart failure observed in any study arm. The secondary safety measures were similar in all arms, apart from severe hyponatremia, which occurred less frequently with intravenous rehydration.

As readers, we can respond to these data in two ways. We might note that the confidence intervals around the primary outcome estimates are wide and do not completely exclude the possibility of benefit or harm with one strategy over another. We might add that there was no true usual care group, and that the equalization of the outcomes across the strategies might have been driven by the intensive oversight of the patients more than the rehydration strategy. While these points are valid, they may reflect a bias that favors present guidance to avoid intravenous rehydration.

With an open mind, GASTROSAM should be viewed as a study that seriously challenges the perceived risks from intravenous rehydration. The upper bound of 95% confidence interval for the true rate of heart failure from these data with intravenous rehydration is 2.3%.[9] Yes, we still need future large trials to define whether these strategies are truly equivalent; but, to the best of our current knowledge, intravenous alternatives to enteral rehydration result in similar survival rates. Maitland and colleagues have provided important alternative treatment strategies for colleagues working in the most challenging circumstances. If additional studies confirm these data, hundreds of thousands of the most vulnerable people on our planet may benefit.

References:

1. The State of Food Security and Nutrition in the World 2024. Accessed Aug 20, 2025 https://www.fao.org/publications/fao-flagship-publications/the-state-of-food-security-and-nutrition-in-the-world/en

2. Diarrhoeal disease [Internet]. [Accessed Aug 20, 2025];Available from: https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease

3. Irena AH, Mwambazi M, Mulenga V. Diarrhea is a Major killer of Children with Severe Acute Malnutrition Admitted to Inpatient Set-up in Lusaka, Zambia. Nutr J 2011;10(1):110–110.

4. WHO. Pocket Book of Hospital care for children. 2013; Accessed Aug 10, 2025; https://iris.who.int/bitstream/handle/10665/81170/9789241548373_eng.pdf?sequence=1

5. Brewster DR. Critical appraisal of the management of severe malnutrition: 3. Complications. J Paediatr Child Heal 2006;42(10):583–93.

6. Maitland K, Ouattara SM, Sainna H, et al. Intravenous Rehydration for Severe Acute Malnutrition with Gastroenteritis. N Engl J Med 2025; 392; 10.1056/NEJMoa2505752

7. Olupot-Olupot P, Aloroker F, Mpoya A, et al. Gastroenteritis Rehydration Of children with Severe Acute Malnutrition (GASTROSAM): A Phase II Randomised Controlled trial: Trial Protocol. Wellcome Open Res 2021;6:160.

8. Obonyo N, Brent B, Olupot-Olupot P, et al. Myocardial and haemodynamic responses to two fluid regimens in African children with severe malnutrition and hypovolaemic shock (AFRIM study). Crit Care 2017;21(1):103.

9. Hanley JA, Lippman-Hand A. If nothing goes wrong, is everything all right? Interpreting zero numerators. JAMA 1983;249(13):1743–5