Less Aggressive Hydration May Be More in Acute Pancreatitis?

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Consider a more conservative approach to fluid resuscitation in mild acute pancreatitis to avoid fluid overload without sacrificing patient-oriented clinical outcomes. (J Am Board Fam Med 2024;37:487–489.)

Keywords: **Acute Pancreatitis, Fluid Overload, Fluid Resuscitation, Intravenous Hydration**

Strength of Recommendation: B

Single well-done randomized controlled trial (RCT).[1]

Illustrative Case

A 56-year-old woman presents to the emergency department with a few days' history of worsening epigastric pain. She reports associated symptoms of nausea and vomiting. On examination her vital signs are stable within normal limits, yet she is found to have classic epigastric tenderness and her laboratory work-up is notable for a lipase level 5 times the upper limit of normal. She is admitted with a diagnosis of mild acute pancreatitis. Although classic fluid management in this scenario has been aggressive intravenous hydration, you are aware of this dogma being called into question. Is there a now role for less aggressive hydration?

Clinical Context

Acute pancreatitis progresses to moderately severe or severe disease in approximately one-third of patients and is often associated with worse outcomes.[2] Early aggressive fluid resuscitation became a mainstay for initial treatment of acute pancreatitis anchored in the concept that hemoconcentration leads to progression of disease severity.[3,4] Established guidelines still support early aggressive resuscitation.[5,6] Yet recent literature, including a 2018 systematic review and meta-analysis of randomized controlled trials by the American Gastroenterology Association suggested that there is no current evidence for a mortality benefit with either rapid or gradual hydration strategies in the treatment of acute pancreatitis.[7] A slightly more recent 2021 systematic review and meta-analysis noted significant (although "low certainty evidence") improvement in mortality and sepsis rates in patients with acute pancreatitis who received more moderate versus more aggressive hydration.[8] Of note, both systematic reviews and meta-analyses included heterogeneous populations with a wide variance in severity of acute pancreatitis and other comorbidities. This 2022 RCT, entitled "WATERFALL," proposes that more conservative fluid resuscitation in the initial treatment of mild acute pancreatitis helps avoid volume overload while not worsening other patient-oriented clinical outcomes— specifically the progression to moderately severe or severe pancreatitis.

Methods

This article was identified as a potential PURL through the standard systematic methodology.[9] An additional literature search was conducted by searching PubMed, OVID, and UpToDate for the terms "acute pancreatitis," "fluid resuscitation," and "aggressive resuscitation" to find additional literature to place this research into the context of current clinical practice.

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Study Summary

Compared with Moderate Fluid Resuscitation, Aggressive Fluid Resuscitation Is Associated with Volume Overload without an Apparent Advantage in Stemming Disease Progression

WATERFALL was a randomized controlled trial conducted in hospitals across India, Italy, Mexico, and Spain. The trial performed a 1:1 randomization of 249 patients presenting with mild acute pancreatitis (based on the Revised Atlanta Classification) into "aggressive" fluid resuscitation (20 mL/kg bolus followed by 3 mL/kg/hour) or "moderate" fluid resuscitation (1.5 mL/kg/hour with a 10 mL/kg bolus in hypovolemic patients). The primary outcome was the development of moderately severe or severe pancreatitis per the Revised Atlanta Classification. Numerous secondary outcomes included development of fluid overload (the main safety outcome), necrotizing pancreatitis, shock, kidney failure, death, and others.

An independent data and safety monitoring board terminated the trial at the first interim analysis as neither rehydration approach demonstrated efficacy for the primary outcome, yet a significant increase in the rate of fluid overload was noted in the "aggressive" group versus the "moderate" group (20.5% vs 6.3%; adjusted relative risk [ARR], 2.85; 95% confidence interval [CI], 1.36 to 5.94; NNH = 7). Of note, fluid overload was objectively assessed— being defined as meeting at least 2 of the following 3 criteria in the absence of acute respiratory distress syndrome: symptoms; physical examination signs; and/or evidence on imaging.

Although the trial was cut short, other data remained available for consideration, including data regarding the primary outcome. The rate of development of moderately severe or severe pancreatitis between the "aggressive" resuscitation group versus the "moderate" fluid resuscitation group was insignificant (ARR, 1.3; 95% CI, 0.78–2.2). There was also no difference in the numerous secondary patient-oriented outcomes including death (ARR, 3.1; 95% CI, 0.32 –29), persistent organ failure (ARR, 2.7; 95% CI, 0.56 – 13), or necrotizing pancreatitis (ARR 2.0; 95% CI, 0.87–4.4). Although not reaching significance, the median length of hospital stay was 5 days in the "moderate" group, and 6 in the "severe group" (ARR, 11; 95% CI, 0.98–1.8).

What Is New

Moderate fluid resuscitation seems noninferior to aggressive fluid resuscitation in patients presenting with mild acute pancreatitis and has less chance of volume overload.

Caveats

No Difference in Progression to Moderately Severe or Severe Pancreatitis, but No "Power" to Demonstrate Superiority

Analyzing the interim safety data, the significant increase in harm (volume overload) in the "aggressive rehydration" group with only a minimal between-group difference in the progression to moderately severe or severe pancreatitis prompted the unanimous decision of the safety monitoring board to discontinue the trial. Therefore, the ability to demonstrate superiority of moderate vs aggressive therapy remains unresolved.

In addition, the exclusion criteria were such that the population targeted relatively young patients (mean, 56 to 57 years) with fewer comorbidities and inherently at lower risk of developing severe disease. This calls into question the trial's overall generalizability in the treatment of all patients presenting with acute pancreatitis.

Finally, in this open-label trial fluid management was driven by the dynamic and sequential clinical assessment of patients' volume status by trial physicians. Blinding in such active clinical scenarios is challenging and likely ethically prohibitive. Future improvements in objective volume status assessment methods and technology may afford better opportunities for blinding.

Challenges to Implementation

We Now Have Evidence of Harm with Aggressive Rehydration

There should be limited challenges to implementation as we now have solid evidence that volume overload occurs more frequently with an aggressive rehydration approach whereas the relative superiority of an aggressive or moderate rehydration strategy remains unresolved and may possibly be a moot point.

To see this article online, please go to: http://jabfm.org/content/37/3/487.full.

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