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Consideration of Clinical Context and Alternative Therapies in Aggressive Resuscitation for Prevention of Post-ERCP Pancreatitis

Dr. Anna Evans Phillips, MD,

Gastroenterology Fellow, University of Pittsburgh Medical Center

Dr. Georgios I. Papachristou, MD, PhD, and

Advanced Endoscopist, University of Pittsburgh Medical Center, Professor of Medicine, University of Pittsburgh School of Medicine

Dr. Adam Slivka, MD, PhD

Associate Chief, Clinical Affairs, Division of GI, Hepatology, & Nutrition, Associate Director, Liver Pancreas Institute, University of Pittsburgh Medical Center

To the Editor

We read with great interest the recent meta-analysis published by Zhang et al in the March issue of *The Journal of Clinical Gastroenterology* entitled “Aggressive Hydration with Lactated Ringer Solution in Prevention of Postendoscopic Retrograde Cholangiopancreatography Pancreatitis: A Meta-analysis of Randomized Controlled Trials.” [1] We would like to congratulate them on their work in this field, as post-ERCP pancreatitis (PEP) remains a challenging complication with very few pharmacologic treatments [2]. In this meta-analysis, they found that aggressive hydration (3mL/kg/hr Lactated Ringer’s solution during procedure and for an additional 8hrs afterward, as well as 20mL/kg bolus after procedure) as compared with standard hydration (1.5mL/kg/hr during procedure and for 8 hrs afterward), as studied in three published trials, three abstracts, and one unpublished trial significantly reduced the incidence of PEP (OR 0.46, 95% CI 0.23–0.95). Fluid resuscitation with lactated ringer’s solution has been suggested to improve outcomes and preventing PEP by normalizing pancreatic microcirculation, promoting a moderate pH environment (thereby reducing an acidic environment which may predispose to PEP), and mitigating against the inflammatory reaction of the pancreatic parenchyma after instrumentation[1]. Fluid resuscitation, however, is not our only option for treatment, and the readers need to have perspective on how these results can be understood within the current clinical context.

The risk of PEP varies widely, with overall incidence estimated at 3.5%, and with a wide range of (1.6–18%) based on indication and therapeutic maneuver [3]. At the current time, prophylactic placement of a pancreatic duct stent in high risk patients has proven to reduce

the rate of PEP; indeed this practice has become standard of care at academic centers where high-risk procedures are performed routinely. In addition, rectal indomethacin independently reduces the rate of PEP: A randomized, double-blind, multicenter, placebo-controlled trial in patients at high risk of PEP showed an almost 50% reduction in the incidence of PEP between patients receiving rectal indomethacin (9.2%) compared to those receiving placebo (18.7%)[2]. The success of this therapy, in fact, has led to the question whether Indomethacin administration alone obviates the need for pancreatic stent placement, which is both time-consuming and costly[4]. The SVI (Stent vs. Indomethacin) trial is a comparative multicenter, randomized, double-blind non-inferiority study of rectal indomethacin alone versus the combination of rectal indomethacin and stent placement for preventing PEP in high-risk cases. Pilot data are suggestive that the combination of rectal indomethacin and stent placement may not be superior to rectal indomethacin alone; we await the completion of the SVI trial for a definite answer to this question[5]. In addition to being therapeutically advantageous, reduction in the need for dual therapy in these cases would help control costs.

In the interest of cost control, the other major logistic issue that needs to be addressed with aggressive hydration as designed to be administered in the included studies is the length of time allotted peri-procedurally for hydration. The length (in hours) of the hydration regimens (both aggressive and standard) for 8 hours post procedure in the recovery area would be prohibitively expensive to initiate in a tertiary or quaternary care center such as ours. The vast majority of patients undergoing ERCP do so as outpatients in most US centers: caring for them in a monitored bed for an additional 8 hours after their procedure or admitting to the hospital would be far from cost effective compared to the current recovery time, which does not exceed two hours in the vast majority of cases. What we have adapted in our GI lab in high risk patients, is administering 2L of LR (first bolus during ERCP and second in the recovery area). This way an average 70kg patient receives double the amount of fluids compared to the standard hydration group in the included studies without having to prolong subject's recovery time.

In conclusion, we will find out in the near future whether indomethacin alone vs pancreatic stents and indomethacin together is more efficient in preventing PEP. Additional studies are also needed to delineate the effect of aggressive hydration in this setting. Finally, designing studies to assess the efficacy of a shorter 'aggressive' hydration: perhaps 2L of LR over approximately 2–3 hours, which will prevent inflating the costs of recovery, should be a priority in the near future.

Sincerely,

Dr. Anna Evans Phillips, MD

Gastroenterology Fellow

University of Pittsburgh Medical Center

Dr. Georgios I. Papachristou, MD, PhD

Advanced Endoscopist, University of Pittsburgh Medical Center

Professor of Medicine, University of Pittsburgh School of Medicine

Dr. Adam Slivka, MD, PhD

Associate Chief, Clinical Affairs, Division of GI, Hepatology, & Nutrition

Associate Director, Liver Pancreas Institute

University of Pittsburgh Medical Center

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