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INVITED COMMENTARY

Proton Pump Inhibitor as Stress Ulcer Prophylaxis in Sick Children: Panacea or Plight

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Critically ill pediatric patients are at increased risk of developing stress-related mucosal disease and subsequent upper gastrointestinal bleeding as a result of both their underlying disease and its severity [1]. In previous studies, the reported incidence of gastrointestinal (GI) ulcerations in pediatric intensive care units (PICU) had varied from 0.4% to 5% [2, 3]. The use of stress ulcer prophylaxis (SUP) in sick patients to prevent stress-related mucosal damage and its subsequent bleeding has been practiced now for almost four decades. The armamentarium has ranged from antacids and sucralfate, which were available much before histamine-2-receptor antagonists (H2RAs), and proton pump inhibitors (PPIs) [2].

Though the concept of using PPIs for SUP in sick children seems logical, albeit clinical evidence favoring its use in children is scarce. In an earlier published systematic review, authors found no evidence to support that SUP is better than "no treatment" to decrease the rates of ulcers or erosion or deaths [1]. Furthermore, no evidence was found to support that prophylaxis decreases the duration of mechanical ventilation or PICU stay. Also, significant increase in the rates of pneumonia or adverse events was not reported [1].

In a randomized controlled trial (RCT) conducted in Egypt among children admitted to the PICU with mild to moderate organ dysfunction (pSOFA score < 16), omeprazole was not found to be useful in the prevention of GI bleeding, while at the same time increase in the risk of central line-associated bloodstream infection (CLABSI) was noted. The authors recommended restricting SUP to mechanically ventilated children [4].

Despite limited data, the use of these medications is quite rampant. Clinicians have used different acid-suppressive drugs; H2RAs have been the most frequently prescribed class (66%), followed by PPIs (47%) and sucralfate (4%) with 20% of patients receiving more than one class of drugs [5]. In an observational study among 1245 children admitted in 59 PICUs across 15 countries, authors found that 61% received medications for acid suppression [6]. In another multicentric observational study from Canada, out of 378 critically sick children admitted in the PICU, 70% received any acid-suppressive medication during their PICU stay, for a median (IQR) of 88% (67–100%) of PICU days [5]. Children who received SUP were older and had a higher Pediatric Risk of Mortality III score, received non-steroidal anti-inflammatory drugs and systemic corticosteroids and received less enteral nutrition. Age and invasive mechanical ventilation were independently associated with an increased likelihood of receiving SUP [5]. The authors reported gastrointestinal bleeding in 21 (6%) of 378 children, out of which three (0.8%) had clinically significant bleeding [5].

On the contrary, in a recently published RCT in critically sick adults, which included 4821 patients in 68 ICUs undergoing invasive ventilation, pantoprazole resulted in a significantly lower risk of clinically important upper GI bleeding than placebo, with no significant effect on mortality [7].

Therefore, with so much of clinical equipoise and dearth of pediatric literature on use of SUP in critically sick children, Kavilapurapu, et al. [8] have tried to answer it through an adequately powered RCT. However, there is some vagueness regarding the doses given and blinding of the intervention. The authors did not find any significant difference in the incidence of GI bleeding between the groups [PPI: 21/151 vs. Placebo: 19/150; RR 1.03 (95%CI 0.18, 5.82); $P = 0.985$]. The authors did find a significant risk reduction of GI bleed in the pantoprazole group in the presence of coagulopathy ($n = 29$), as compared to a placebo ($n = 25$) [RR 0.52 (95%CI 0.32, 0.87); $P = 0.022$]. However, these numbers are small, and therefore, it is difficult to draw a conclusion from this study.

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It is pertinent to note that all classes of medicines are fraught with risks, and the use of PPIs has been related to a higher risk of pneumonia and dysbiosis in the GI tract, with an increased colonization by pathogenic agents, including *Clostridium difficile* [9]. Dysbiosis is a significant factor for the maintenance of an increased inflammatory response with massive cytokine release [9]. All of these complications in a sick child can be associated with higher mortality, longer periods of hospitalization and increased cost [9].

Also, considering that PPIs are metabolized by the hepatocyte CYP2C19 and the CYP3A4 enzymes, pharmacokinetic parameters of these enzyme systems vary in children and elderly. Immaturity of the parietal cell mass and a relative achlorhydria in the first 20–30 months of life may hamper the ability of the active form of PPIs to accumulate effectively in the intracellular canaliculi of the parietal cells leading to suboptimal therapeutic effects, especially in critically sick aged 1 months to 18 years [10]. There are other important risk factors which again need to be considered in a critically sick child like acute renal or hepatic failure, sepsis, hypotension and burns which can alter the pharmacokinetics and therefore the efficacy of these drugs.

Even the Surviving Sepsis Guidelines do not recommend routine SUP in children with septic shock or sepsis-associated organ dysfunction [11]. So, it seems prudent that rather than a routine use of SUPs, individual children should be assessed for the presence of certain risk factors which can predispose to significant GI bleeding. These may include multiple organ dysfunction, prolonged mechanical ventilation (> 48 h), coagulopathy, persistent shock, treatment with corticosteroids and non-steroidal anti-inflammatory agents [11].

As with any drug intervention, further research, preferably multicentric and pragmatic, should look into protocolized and targeted approach and explore long-term effects. For now, PPIs seem a promising addition in our arsenal against one of the most challenging complications in the PICU. However, since mucosal ischemia plays a pivotal role in pathogenesis of stress ulcers and bleeding in critically ill children, it is important to restore mucosal perfusion as early as possible. Early reversal of shock with fluids, inotropes and vasopressors may improve gut perfusion, and early institution of enteral feeding should be part of existing bundle of care.

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References

1. Reveiz L, Guerrero-Lozano R, Camacho A, et al. Stress ulcer, gastritis, and gastrointestinal bleeding prophylaxis in critically ill pediatric patients: a systematic review. Pediatr Crit Care Med. 2010;11:124–32.
2. Jensen MM, Marker S, Do HQ, et al. Stress ulcer prophylaxis in critically ill children: protocol for a systematic review. Acta Anaesthesiol Scand. 2019;63:966–72.
3. Chaïbou M, Tucci M, Dugas M-A, Farrell CA, Proulx F, Lacroix J. Clinically significant upper gastrointestinal bleeding acquired in a pediatric intensive care unit: a prospective study. Pediatrics. 1998;102:933–8.
4. Abu El-Ella SS, El-Mekkawy MS, Mohamed SA. Stress ulcer prophylaxis for critically ill children: routine use needs to be re-examined. An Pediatr (Engl Ed). 2022;96:402–9.
5. Duffett M, Chan A, Closs J, et al. Stress ulcer prophylaxis in critically ill children: a multicenter observational study. Pediatr Crit Care Med. 2020;21:e107–13.
6. Albert BD, Zurakowski D, Bechard LJ, et al. Enteral nutrition and acid-suppressive therapy in the PICU: impact on the risk of ventilatorassociated pneumonia. Pediatr Crit Care Med. 2016;17:924–92.
7. Cook D, Deane A, Lauzier F, et al. Stress ulcer prophylaxis during invasive mechanical ventilation. N Engl J Med. 2024;391:9–20.
8. Kavilapurapu A, Lalitha AV, Ghosh S. Role of proton pump inhibitor as stress ulcer prophylaxis in sick children: a randomized controlled trial. Indian Pediatr. 2025;62
9. Lo WK, Chan WW. Proton pump inhibitor use and the risk of small intestinal bacterial overgrowth: a meta-analysis. Clin Gastroenterol Hepatol. 2013;11:483–90.
10. Gibbons TE, Gold BD. The use of proton pump inhibitors in children: a comprehensive review. Paediatr Drugs. 2003;5:25–40.
11. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med. 2020;21:e52-106.