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Research Article

Evaluation of Proton Pump Inhibitor Use in Pediatric Intensive Care

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Abstract

Objectives: Proton pump inhibitors are a standard component in the care of critically ill children in PICU, especially for stress ulcer prophylaxis. This study aims to evaluate the prescribing pattern of proton pump inhibitors in PICU and assess appropriateness against proposed guidelines.

Methods: Data of all patients admitted to PICU and received proton pump inhibitors between March 1st and March 31st 2023 were retrieved. All patients aged between 1 day and 16 years were included.

Results: 57 prescriptions of proton pump inhibitors were identified, which represented 60% of all patients admitted to PICU. The indication of proton pump inhibitors was not documented in 53% of cases, presumably for stress ulcer prophylaxis. Other indication were continuation of home medication without documented indication in 14%, stress ulcer prophylaxis in 12% and gastroesophageal reflux disease in 19% of the cases. Of the 37 patients initiated on proton pump inhibitors for stress ulcer prophylaxis, 54% were not candidate for stress ulcer prophylaxis.

Conclusion: The study showed overprescribing of proton pump inhibitors in our PICU, with poor documentation of indication. It is crucial to establish guideline and monitor their effect on the change in prescribing practices to insure safe and judicious use.

Keywords: *Proton Pump Inhibitors (PPIs); H^+/K^+ ATPase Enzyme; Gastroesophageal Reflux Disease (GERD); Stress Ulcer Prophylaxis (SUP); Paediatric Intensive Care Unit (PICU)*

Introduction

Proton pump inhibitors (PPIs) rank high on the list of frequently prescribed medications [1,2]. They block H^+/K^+ ATPase enzyme, which serves as the final step of acid secretion into the stomach. They represent the most potent drugs for acid reduction. Their indications include esophagitis, gastroesophageal reflux disease (GERD) and peptic ulcer disease among others [3]. They are also used off-label for Stress Ulcer Prophylaxis (SUP), a standard component in the care of critically ill children in the Paediatric Intensive Care Unit (PICU) [3,4]. Despite their frequent use, there are no recent evidence-based guidelines for SUP, as the last and only guideline was published by the American Society of Health-System Pharmacists in 1999 [5]. Moreover, PPIs are not without their risks, including but not limited to increased risk of infection, primarily pneumonia and *Clostridioides difficile* (*C. diff*) infection [4,6].

Despite the increasing use of acid suppressive medication in PICU, there is a lack of internationally accepted criteria on when to begin, continue or discontinue SUP. This can lead to overprescribing, and subsequently increasing infections and cost [3,7]. Thus, it is crucial to monitor the appropriate use of these medications.

Aim of the Study

This study aims to evaluate the prescribing pattern of PPI in the PICU.

Methods

We retrospectively reviewed all patients prescribed PPI in PICU (37-bed unit in Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates) between March 1st and March 31st 2023. All patients aged between 1 day after full term birth and 16 years were included.

Data collected includes basic demographics, reason for PICU admission, Paediatric Sequential Organ Failure Assessment (pSOFA) score, PPI dosing regimen and indication. Variables indicating risk factors for Gastrointestinal (GI) bleeding (mechanical ventilation (MV), chronic liver disease, coagulopathy, shock, sepsis, acute kidney injury, use of corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs)) and outcomes associated parameters (infection, clinically significant bleeding and overt bleeding) were also collected.

Guidelines were established and used to assess appropriateness of PPI in our PICU (Table 1) [4,8].

SUP is indicated in patients at high or very high risk of gastrointestinal bleeding	
Very high risk	• Mechanical ventilation without enteral feeding • Chronic Liver Disease
High risk	• Coagulopathy • INR $\geq$ 1.5 or thromboplastin time > twice the upper limit or platelets $\leq$ 50,000/mm^3 • Thermal Injury • Pulse corticosteroids • 2 or more moderate risk factors
Moderate risk	• Mechanical ventilation with enteral feeding • Shock • Sepsis • Acute kidney injury
Low risk	• Critically ill without any risk • Acute hepatic failure • Use of corticosteroids/immunosuppression • Use of anticoagulants • Cancer • Male gender

Table 1: *SUP proposed PICU guideline.*

Statistics

Simple descriptive analysis was used. Qualitative data was described as number (%) and quantitative data as mean ± standard deviation (range). Data were collected and analysed using an excel sheet.

Results

57 prescriptions of PPI were identified in 54 patients, which represented 60% of all our PICU admissions. Mean age was 5.7 ± 4.96 [range 20 days-15 years]. The average PICU length of stay was 24 days ± 51.8 [range 2-360] (Table 2). Esomeprazole constituted 100% of the prescriptions.

The average dose of esomeprazole was 0.92 ± 0.34 [0.47 - 2.26], prescribed IV for 80% (46/57) of cases. Of which, 24% (11/46) were switched to oral PPI and 50% (23/46) were candidates for oral PPI but remained on IV.

The indication of PPI was not documented in 53% (30/57) of cases, presumably for SUP. Other indications were continuation of home medication without documented indication in 14% (9/57), SUP in 12% (7/57) and GERD in 19% (11/57) of the cases.

PPIs were continued on discharge from PICU in 74% (42/57) of cases, of which 74% (31/42) were continued with no indication (Table 2).

Table 2 shows frequency of patients' risk factors for GI bleeding according to proposed guideline.

Variable		**N = 57**		
Age (years), mean ± SD [range]		5.7 ± 4.96 [20 d-15 y]		
Weight (kg), mean ± SD [range]		18.7 ± 11.9 [2.1-50.3]		
Gender	Male, n (%) Female, n (%)	36 (63%) 21 (37%)		
PICU length of stay (days)		24 ± 51.8 [2-360]		
pSOFA score, Mean (Range)		3.8 ± 2.8 [0-12]		
Indication for PPI		**N = 57**	**Appropriately discharged on PPI (n = 11)**	**Inappropriately discharged on PPI (n = 31)**
Not documented, presumed SUP		30	0	18
GERD		11	11	0
Continuation of home medication		9	0	9
SUP		7	0	4
Risk Factors for GI bleeding			**Frequency**	**%**
Very High Risk	MV without enteral feeding		5	9
	Chronic liver disease		0	0
High Risk	Coagulopathy		10	18
	Pulse corticosteroids		3	5
	Thermal injury		0	0
Moderate	MV with enteral feeding		22	39
	Shock		30	53
	Sepsis		19	33
	Acute kidney injury		8	14

Table 2: *Patients' characteristics and results.*

Of 37 patients initiated on PPI for SUP, 54% (20/37) were not candidate for SUP according to the guideline.

While on PPI in PICU, 25% (14/57) of patients developed new infections, including 2 cases of Ventilator Associated Pneumonia (VAP) and one case of Central Line Associated Bloodstream Infection (CLABSI). Additionally, 2 patients developed *C. diff* infection.

The incidence of bleeding was 25% (14/57), of which 36% (5/14) were defined as clinically important. This included 2 patients with GI bleeding, both were receiving IV esomeprazole and required blood transfusions. Additionally, both were at very high risk of GI bleeding and on mechanical ventilation without enteral feeding.

Discussion

The estimated prevalence of stress-related GI bleeding in PICU population has varied widely, however, utilization of acid-suppressant medications in PICU is on the rise [6,9]. In this study, 60% of patients admitted to PICU received PPI. This is similar to findings reported in our region where 71% of PICU patients received PPI [10].

Our PPI prescribing rate in PICU was higher than reported in other regions, for example in France, the proportion of patients prescribed PPIs in PICU was 51%, 59% of them were for SUP [11]. Moreover, our rate of inappropriate prescribing is also higher than reported in our region, where inappropriateness was in only 26% of cases [12].

Our study also showed high percentage (74%) of patients discharged from PICU on PPI, with no clear indication. In a multicentre study that assessed the inappropriate continuation of PPI at discharge from ICU over the span of 4 years, 45% of patients were continued on PPI after transfer to the floor without a long-term indication for PPI therapy. Moreover, 27% were discharged from the hospital on PPI therapy [13].

PPIs are not without their risks, including but not limited to increased risk of infection. A meta-analysis compared the risk of *C. diff* with the use of PPIs showed an increased risk compared to those who did not use PPIs, OR 2.34 (95% CI 1.94 - 2.82). Specifically in pediatrics, the results showed an OR of 3.00 (95% CI 1.44 - 6.23) [14]. In our study, the incidence of *C. diff* was 3.5% (2/57). One case was on long term PPI for GERD and the other was initiated in PICU for SUP and received it for total of 11 days. Additionally, the incidence of CLABSI and respiratory tract infections during PPI therapy were, 1.7%, and 21%, respectively.

A randomized controlled trial in Egypt reported an incidence of VAP of 9.6% and CLABSI of 30.6% in patients who received SUP therapy. However, none of the patients developed *C. diff*. Additionally, they assessed the incidence of GI bleeding, which was 27.1%, but clinically important GI bleeding developed in 5.6% of patients [15]. This is slightly higher than our finding, where the incidence of clinically important GI bleeding was 3.5%, and overall incidence of clinically important bleeding was 8.7%.

Conclusion

The study showed an overprescribing of PPI in our PICU, with poor documentation of PPI indication when prescribed. More than half of patients received PPI for SUP where it was considered inappropriate according to our proposed guideline. It is crucial to establish guidelines to guide in appropriate PPI prescribing in PICUs, and monitor their effect on the change in prescribing practices to insure safe and judicious use.

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Conflicts of Interest

None.

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