JPPT | Single Center Retrospective Study

Evaluation of Stress Ulcer Prophylaxis in Pediatric General Medicine Patients After Transfer From the Intensive Care Unit and at Discharge

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OBJECTIVES The primary aim of this study was to determine continuation rates of stress ulcer prophylaxis (SUP) upon transfer from a pediatric intensive care unit (PICU) to a general medicine unit and upon hospital discharge. The secondary aim was to identify patient characteristics or concomitant medications that were associated with continuation of SUP at transfer from the PICU.

METHODS This retrospective chart review included patients who were initiated on acid suppression for SUP in the PICU between June 2021 and May 2022 and subsequently transferred to a general medicine unit prior to discharge. Patients were excluded if they were receiving acid suppressant therapy prior to admission or were started on acid suppressants for an indication other than SUP.

RESULTS Two hundred three patients (median age, 3.3 years) were included. The rates of SUP continuation at the time of transfer from the PICU to a general medicine unit and at hospital discharge were 61.6% and 9.9%, respectively. Patients continued on SUP at the time of transfer from the PICU were more likely to be prescribed concomitant corticosteroids ($p < 0.01$), anticoagulants or antiplatelet medications ($p < 0.01$).

CONCLUSIONS The continuation of SUP from the PICU to the general medicine unit is common at our institution and calls into question the appropriateness of this practice. Future research is warranted to investigate the appropriateness of the continuation of SUP at transitions of care. Additionally, implementation of institutional protocols standardizing review of SUP may help reduce unnecessary prescribing of acid suppressants in general medicine units and at discharge.

ABBREVIATIONS GI, gastrointestinal; H2RA, histamine H2-receptor antagonist; ICU, intensive care unit; PICU, pediatric intensive care unit; PPI, proton pump inhibitor; SUP, stress ulcer prophylaxis

KEYWORDS critical care; histamine H2-receptor antagonist; patient discharge; pediatric; proton pump inhibitor; stress ulcer prophylaxis

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Introduction

Stress ulcers are a well-documented complication in critically ill patients due to increased physiologic stressors in an intensive care setting. The development of stress ulcers can pose a significant concern for serious complications such as gastrointestinal (GI) bleeding.[1] Major GI bleeding is associated with additional sequelae including higher rates of blood transfusions, increased duration of mechanical ventilation, longer length of pediatric intensive care unit (PICU) admission, and higher cost per patient per hospital stay.[2]

Given the possible implications of GI bleeding, acid suppressants such as proton pump inhibitors (PPIs) and histamine H2-receptor antagonists (H2RAs) are commonly initiated for stress ulcer prophylaxis (SUP) in critically ill pediatric patients, despite the lack of strong evidence to support their use.[3–6] A recent systematic review and meta-analysis assessed the effects of PPIs and H2RAs in the PICU and found rates of GI bleeding (defined as blood in gastric aspirates with hematemesis, hematochezia, or melena) to range from 1.6% to 51.8%. However, there was no difference in the risk of this outcome between those who received SUP and those without prophylaxis. Additionally, acid suppression was associated with an increased risk of nosocomial pneumonia.[3]

Outside of the intensive care unit (ICU) setting, data to support the use of SUP are even more limited. In most cases, SUP should be discontinued prior to transfer out of the PICU and/or after risk factors for bleeding have resolved.[7] However, observational studies in both children and adults show that SUP is frequently continued

in patients upon transfer to the acute care setting.[8–10] In a multicenter observational study by Duffet et al,[8] 34% of PICU patients started on SUP continued receiving SUP on PICU transfer orders. Additionally, several adult studies describe inappropriate prescriptions for acid suppression at discharge.[9–11] However, there is no published data regarding continuation of SUP at discharge in pediatric patients.

Given the limited literature in the pediatric population, the primary aim of this study was to describe the rate of continuation of SUP in ICU patients upon transfer to a general medicine unit and at discharge. The secondary aim was to identify patient characteristics or concomitant medications that are associated with continuation of SUP upon transition from the PICU to the general medicine unit.

Materials and Methods

This was a single center, retrospective cohort chart review conducted at a large pediatric academic medical center. Patients older than 44 weeks' corrected gestational age who were started on intravenous or enteral famotidine, intravenous pantoprazole, or enteral lansoprazole in the PICU between June 1, 2021, and May 31, 2022, and then transferred to a general medicine unit prior to discharge, were included. The PPIs and H2RAs selected for inclusion were based on the institutional formulary. Patients were excluded if they were taking an acid suppressant prior to admission, initiated on an acid suppressant for an indication other than SUP, or discharged directly from the PICU.

Data collected included demographics; dates of transitions of care; and dose, duration, and indication for the acid suppression regimen. PICU progress notes were reviewed for documentation of acid suppressant indications. Acid suppression initiated for SUP in the PICU and continued at the time of transfer was assumed to be continued for SUP unless an alternative indication was documented in the medical record. Additionally, patient characteristics at the time of transfer from the PICU to the general medicine units were collected, including status of receiving enteral nutrition/medications, coagulopathy defined by an international normalized ratio greater than 1.5 or platelet count less than 100×10^9/L in the past 24 hours, surgery within 48 hours prior to transfer, history of GI bleed within 12 months prior to admission, acute traumatic brain injury, acute spinal cord injury, and acute major burn injury. Concomitant medication information at the time of transfer was also collected, including nonsteroidal anti-inflammatory drugs, corticosteroids, anticoagulants, and antiplatelets.

All data were recorded and managed via Research Electronic Data Capture (REDCap; Vanderbilt University, Nashville, TN) database. Descriptive statistics were used to summarize patient characteristics of the whole cohort, the primary outcome, and characteristics of patients discharged with SUP. For the secondary outcome comparing patient characteristics and concomitant medications between those transferred to the general medicine unit on SUP vs those with discontinuation of SUP prior to transfer, a Wilcoxon rank sum test and Fisher exact test were used to analyze continuous variables and nominal variables, respectively. Data analysis was performed with GraphPad Prism (version 9.1.0).

Results

During the study period, 253 patients received an H2RA or PPI in the PICU before transferring to a general medicine unit. Of those, 40 patients had an acid suppressant listed as a home medication and 10 patients were noted to be started on acid suppressants for alternative indications. Therefore, 203 patients were included for analysis (Table 1). The median (IQR) age was 3.3 years (1.1–13.2) and the most common admitting diagnoses were respiratory-related conditions (61.5%). The median (IQR) hospital length of stay was 8.3 days (4.2–15.6). Sixty-eight percent of patients were administered an H2RA vs a PPI in the PICU for SUP, and the median (IQR) total duration of acid suppressant therapy was 4 days (1.7–8.9). There were no patients on both therapies simultaneously.

At the time of transfer from the PICU to a general medicine unit, 128 patients were continued on acid suppression. Three of those patients were continued on acid suppression for alternative indications as noted in the medical record, including gastroesophageal reflux disease (n = 1), gastric ulcer (n = 1), and laryngeal edema (n = 1). Therefore, the incidence of SUP continuation at transfer from the PICU to a general medicine unit was 61.6% (n = 125). The median (IQR) duration of SUP for patients continued on acid suppression was 4.9 days (2.2–9.9) in total and 1.6 days (0.6–3.5) post transfer to a general medicine unit.

Table 1. Patient Characteristics

Characteristic	N = 203
Age, median (IQR), yr	3.3 (1.1–13.2)
Male, n (%)	109 (53.7)
Weight, median (IQR), kg	15.2 (10–49.5)
Admitting diagnosis by system, n (%)	
Respiratory	125 (61.6)
Neurologic	34 (16.7)
Cardiovascular	17 (8.4)
Rheumatologic	14 (6.9)
Psychologic	7 (3.4)
Gastrointestinal	4 (2)
Other	2 (1)
Acid suppressant started in PICU, n (%)	
Histamine H2-receptor antagonist	137 (67.5)
Proton pump inhibitor	66 (32.5)

PICU, pediatric intensive care unit

Patient characteristics and concomitant medications were compared between patients continued on SUP at the time of transfer from the PICU to a general medicine unit (n = 125) and patients with SUP discontinued prior to transfer (n = 75), as described in Table 2. This analysis excluded the 3 patients with new alternative diagnoses for acid suppression at the time of transfer. All patients with rheumatologic admitting diagnoses were continued on SUP at the time of transfer (p < 0.01). There was no statistical difference in nothing by mouth status (p = 0.26), coagulopathy (p = 0.23), or surgery within 48 hours prior to transfer (p > 0.99) between those who had SUP continued at the time of transfer and those who did not. Two patients in the SUP continuation at transfer group and 1 patient in the SUP discontinuation prior to transfer group had an acute traumatic brain injury. No patients in either group were noted to have had a GI bleed within the previous 12 months, an acute spinal cord injury, or an acute burn injury.

A larger proportion of patients in the SUP continuation at transfer group were noted to be on concomitant corticosteroids (57% vs 16%; p < 0.01) or anticoagulant/antiplatelet medication (30% vs 11%; p < 0.01). Specifically, more patients who were continued on SUP at transfer were administered concomitant aspirin (6.4% vs 0; p = 0.03) and prophylactic enoxaparin (19.2% vs 2.7%; p < 0.01). All 8 patients receiving concomitant aspirin received doses of 40.5 or 81 mg/day (1 to 6 mg/kg/day). The median corticosteroid dose in intravenous methylprednisolone dose equivalents was 1.6 mg/kg/day

Table 2. Patient Characteristics at the Time of Transfer From PICU to the General Medicine Unit

Characteristic	Patient Continued SUP at the Time of Transfer From PICU		p value
	Yes (n = 125)	No (n = 75)	
Age, median (IQR), yr	4.4 (1.6–14.1)	2.3 (0.6–8.1)	<0.01
Male, n (%)	64 (51.2)	43 (57.3)	0.47
Hospital length of stay, median (IQR), days	7.1 (4–13.7)	10.6 (4.7–18.5)	0.08
Admitting diagnosis, n (%)			
Respiratory	73 (58.4)	49 (65.3)	0.37
Neurologic	16 (12.8)	18 (24)	0.12
Cardiovascular	14 (11.2)	3 (4)	0.05
Rheumatologic	14 (11.2)	0	<0.01
Psychologic	3 (2.4)	4 (5.3)	0.43
Gastrointestinal	3 (2.4)	1 (1.3)	>0.99
Other	2 (1.6)	0	0.53
Characteristics at the time of transfer*, n (%)			
NPO†	7 (5.6)	1 (1.3)	0.26
Coagulopathy‡	6 (4.8)	1 (1.3)	0.23
Surgery within last 48 hr	8 (6.4)	4 (5.3)	>0.99
None of the above	105 (84)	69 (92)	0.13
Medications at the time of transfer, n (%)			
Corticosteroids	71 (56.8)	12 (16)	<0.01
IVMP or equivalent¶ <2 mg/kg/day	47 (37.6)	8 (10.7)	<0.01
IVMP or equivalent ≥2 mg/kg/day	24 (19.2)	4 (5.3)	<0.01
NSAIDs	1 (0.8)	1 (1.3)	>0.99
Anticoagulants/antiplatelets	37 (29.6)	8 (10.7)	<0.01
Aspirin	8 (6.4)	0	0.03
Enoxaparin (therapeutic dosing)	5 (4)	6 (8)	0.16
Enoxaparin (prophylactic dosing)	24 (19.2)	2 (2.7)	<0.01
None of the above	45 (36)	56 (74.7)	<0.01
Corticosteroid dose in IVMP or equivalent, median (IQR), mg/kg/day	1.6 (0.76–2) (n = 71)	0.94 (0.38–2) (n = 12)	0.58
Total duration of SUP, median (IQR), days	4.9 (2.2–9.9)	2.3 (1.1–6.4)	<0.01

INR, international normalized ratio; IVMP, intravenous methylprednisolone; NSAIDs, nonsteroidal anti-inflammatory drugs; PICU, pediatric intensive care unit; SUP, stress ulcer prophylaxis

* Patients may have met criteria for more than 1 characteristic or received more than 1 of the concomitant medications evaluated.
† NPO defined as receiving nothing by mouth or by any enteral route.
‡ Coagulopathy defined as INR greater than 1.5 or platelet count less than 100 × 10^9/L in the past 24 hours.
¶ Corticosteroid equivalency: methylprednisolone 4 mg = prednisone/prednisolone = 5 mg = dexamethasone 0.75 mg = hydrocortisone 20 mg.

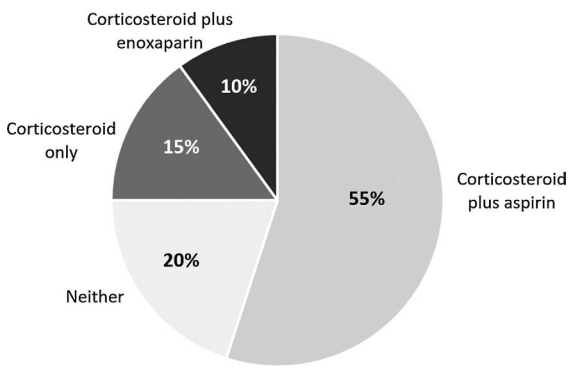
(n = 71) and 0.94 mg/kg/day (n = 12) in the SUP continuation at transfer and SUP discontinuation prior to transfer groups, respectively (p = 0.58). Patients who continued SUP at the time of transfer from the PICU to a general medicine unit also had a longer duration of acid suppressant therapy while hospitalized by approximately 2.6 days (p < 0.01).

At discharge, 20 patients (9.9%) were prescribed an acid suppressant (PPI: n = 9; H2RA: n = 11) without a new documented indication. Sixteen of these patients were also prescribed an oral corticosteroid with or without an antiplatelet/anticoagulant medication at discharge (Figure), 12 of whom were admitted for multisystem inflammatory syndrome or Kawasaki disease. Overall, 11 of the 20 acid suppressant prescriptions at discharge were written for less than a 30-day supply to be taken while completing a course of corticosteroids.

Discussion

We found that the incidence of SUP continuation from the PICU to the general medicine unit is common at our institution. While H2RAs were more commonly used than PPIs for SUP in our study, the selection of the agent is based on provider preference at our institution. Approximately 62% of patients were transferred to the general medicine unit with an acid suppressant on their transfer orders and without an alternative indication noted in the medical record. In comparison, an observational study by Duffett et al,[8] describing SUP practice across 7 Canadian PICUs, reported that 34% of the 280 children started on SUP in the PICU were continued on it upon transfer (ranging from 0% to 52% among the included centers). This pattern is also noted in studies of adult patients.[9,10] A retrospective chart review by Wohlt et al[9] that included 394 adult patients found 80% of those who started SUP in the ICU (n = 357) continued acid suppressants at the time of transfer, of which 60% were considered to have been continued for inappropriate indications. Similarly, Murphy et al[10] described continuation of acid suppression in 215 of 248 adult patients (86.7%) transferred out of the surgical intensive care unit. These studies suggest that the practice of SUP continuation upon transfer out of the critical care setting to a general medicine unit varies but is prevalent. Evaluation of the appropriateness of SUP at the time of transfer by a designated member of the health care team may help reduce unnecessary continuation of acid suppression to general medicine units. Xu et al[12] described the effectiveness of pharmacist-led interventions in decreasing inappropriate use of SUP in adult ICUs, highlighting the potential positive impact of clinical pharmacists in guiding judicious use of SUP throughout hospitalization.

Figure. Concomitant corticosteroid and antiplatelet/anticoagulant prescriptions at discharge for patients discharged with a new prescription for an acid suppressant (n = 20).



The incidence of SUP continuation at discharge was lower than the incidence upon PICU transfer, with 9.9% (n = 20) of patients discharged home on continued acid suppression therapy without documentation of an alternative indication. To our knowledge, this is the first study in pediatric patients to describe continuation of acid suppression for SUP at discharge. Compared with the existing literature in adult patients, our study reported a lower incidence rate of continuing SUP at discharge. Wohlt et al[9] reported 24.4% of 394 critically ill adults were discharged from the hospital with inappropriate acid suppressant therapy. Similarly, Murphy et al[10] found that 60 of the 248 adult patients (24.2%) who began acid suppression in the surgical intensive care unit were continued on acid suppression therapy after hospital discharge.

While this study did not evaluate appropriateness of SUP at transfer or discharge, secondary analysis of patient characteristics and concomitant medications provide insight into potential reasons why acid suppression may have been continued. Notably, 36 of the 125 patients (29%) who were continued on SUP at the time of transfer had no identifiable patient characteristics or concomitant medications that could increase the risk for bleeding. It is unknown whether continuation of SUP in these patients was an oversight or if there were additional risk factors or indications for continuation that were missed owing to incomplete documentation. Compared with patients who had SUP discontinued in the PICU, patients who were continued on SUP at transfer were more likely to be receiving concomitant corticosteroids and antiplatelets/anticoagulants. Sixteen of the 20 patients (80%) discharged on acid suppression therapy were also prescribed prednisolone or prednisone at discharge, and 13 of these patients were additionally prescribed aspirin (n = 11) or enoxaparin (n = 2). Most of the patients discharged with both acid suppressants and corticosteroids with or without aspirin/enoxaparin were admitted for rheumatologic conditions, including multisystem inflammatory syndrome (n = 9), Kawasaki disease (n = 3), granulomatosis with polyangiitis (n = 1), and antiphospholipid syndrome (n = 1). Only 1 patient

discharged home with both prednisolone and acid suppression medication was admitted for asthma.

As corticosteroids have been previously implicated as risk factors for GI bleeding, the administration of these therapies in our study may have influenced continuation of SUP at transfer from the PICU and at discharge.[7,13] The use of SUP for corticosteroid exposure has been noted by Roberts et al[14] to be increasing in recent years for children admitted to the PICU for asthma exacerbations. Of the 30,177 children included in this multicenter study spanning a 10-year period, 34.4% received SUP. The overall rate of SUP prescription increased from 25.5% in 2010 to 42.1% in 2019. However, no GI bleeding events were observed in this study. Additionally, gastritis was rare (0.1%), and the rates did not differ between those with and without SUP.[14] In contrast, an earlier systematic review and meta-analysis by Narum et al,[13] including all age groups and disease states, found an increased risk of GI bleeding or perforation with use of corticosteroids vs placebo (2.9% vs 2%; OR, 1.43; 95% CI, 1.22–1.66); however, this increased risk was no longer statistically significant in the subgroup analyses of ambulatory care patients. The use of gastroprotective medications did not appear to affect the results when studies using these medications were excluded.[13] Given the conflicting data regarding the risk of GI bleeding with corticosteroid use, there is a lack of consensus regarding routine use of SUP in patients receiving corticosteroids.

In our study, 65% of acid suppressant prescriptions at discharge were written for a 30-day supply or less, to be taken while completing a course of corticosteroids. This practice may be unnecessary, based on the low rates of GI bleeding in patients taking corticosteroids in the outpatient setting.[13] For the 4 patients who were discharged on acid suppressants without concomitant corticosteroids or other identifiable potential risk factors, it is uncertain if there were undocumented reasons for continuation. It is also difficult to ascertain the true duration of SUP treatment in the outpatient setting, as we cannot assess adherence or whether more refills were requested at an outside pharmacy. Inappropriate continuation of acid suppression at discharge could lead to the addition of these medications to a patient's home medication list, resulting in indefinite continuation. With PPIs in particular, indefinite continuation could put patients at risk of long-term adverse effects including *Clostridioides difficile* infection, pneumonia, and increased risk of fractures.[15–19] Therefore, it is important to be judicious in the appropriate prescribing of these medications to not place unnecessary burden and cost on patients and their families.

Limitations of this study include that it was a retrospective chart review in a single center, therefore data collection relied on chart documentation, which is subject to information bias. We were unable to determine retrospectively whether SUP continuation at the time of transfer or discharge was intentional or an oversight. Additionally, although we did not assess the appropriateness of SUP initiation and continuation, we recognize that evaluating the appropriateness of therapy is difficult in pediatric patients given the lack of clear criteria and updated guidelines. Patients who were discharged from PICU were not included in this study because these patients may represent a different population and introduce additional confounders (e.g., transfers to other hospitals or long-term care facilities). While excluding these patients may have affected our rates of SUP prescribing at discharge, this was done to focus on prescribing practices within the general medicine unit population specifically. Furthermore, patient acuity was not assessed at the time of transfer. It is possible that our general medicine unit receives patients from the PICU who may still be considered "critically ill" at other institutions, because criteria for transfer vary across centers. This could have affected the provider's decision to continue SUP at the time of transfer.

Conclusion

In this retrospective review of 203 patients initiated on SUP in the PICU, the continuation of acid suppression upon transfer to the general medicine unit was common, even in patients without identifiable risk factors. Institutions may benefit from having a standardized protocol to guide the practice of prescribing acid suppressants in the PICU and prompt an assessment of the appropriateness of acid suppression continuation at the time of transfer out of the PICU. Potential directions for future research include the appropriateness of SUP continuation upon PICU transfer and at discharge for patients with presumed risk factors.

Article Information

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