

Stress Ulcer Prophylaxis: Investigating Overuse and Poor Adherence to Guidelines Across Two Teaching Hospitals

IRB Protocol

A. Study Purpose and Rationale

The most recent guidelines available on stress ulcer prophylaxis for hospitalized patients were published over a decade ago by the American Society of Health-System Pharmacists [1] and based on current prescribing practices, appear to be either obsolete or ignored. According to a host of clinical studies, the benefit of acid suppressive therapy (AST), including PPIs and H2 blockers, is well defined in critical care patients with specific indications that convey elevated risk of stress-related mucosal disease [2]. Over the past decade, the use of AST for stress ulcer prophylaxis (SUP) has become an increasingly common practice in general medicine patients with little evidence to support it. The risk of clinically significant bleeding from stress ulcer disease is exceedingly low and there are relatively few validated indications for prophylaxis. Despite, the use of these agents in the inpatient setting has become pervasive and indiscriminate; studies show that up to seventy percent of patients on general medical wards receive SUP without appropriate justification. While guidelines exist, they are outdated and for the younger generation of physicians, are either poorly understood or poorly applied. There has been a trend toward 'knee jerk' prescribing practices for AST particularly in teaching hospitals and among residents. This is compounded by institutional policies and order sets that allow for or encourage SUP use without demanding an indication or rationale. This study aims to identify the root of this problem: whether deficits exist in the knowledge or interpretation of SUP guidelines, at what level of training, and whether institutional policies perpetuate overprescribing trends. The goal is to inform potential quality improvement interventions in order to increase compliance with published guidelines and change practice patterns as a model for cost-effective and safety-oriented care.

The American Society of Health-Systems Pharmacists published the most widely accepted and accredited guidelines in 1999, corroborated by the Society for Critical Care Medicine, that describe appropriate usage of SUP to include: 1) mechanical ventilation for > 48 hours, and 2) the presence of coagulopathy defined as INR > 1.5, PTT > 2x normal, or platelet count < 50,000. Stress ulcer prophylaxis is **not** indicated for adult general medical patients in non-ICU settings with fewer than two risk factors for clinically relevant bleeding, including severe trauma with spinal cord injury, overt sepsis, hepatic or renal failure, or history of GI bleeding in the year prior to admission [1,2]. Despite repeated clinical validation of these guidelines, the frequency of AST use in general medicine patients reported in the literature ranges from 27 to 71%, with no indication for their use in up to 70% of patients [4,5]. Importantly, up to half are subsequently discharged home with prescriptions for these medications and often remain on AST in the outpatient setting. The use of AST for prevention of stress ulcers outside the ICU setting is not recommended or supported by clinical literature, yet occurs in a significant percentage of hospitalized patients.

This overprescribing trend is concerning trend for several reasons. First, although it is often assumed that acid suppressive therapy is harmless, recent studies highlight several potential risks including an elevated risk of pneumonia, enteric infections (particularly *C. difficile*), vitamin deficiency, hip fracture, and exposure to a myriad of imminent drug interactions [4]. Second, there are significant economic costs to such extensive overprescribing, both for the system and for the patient. A study by Heidelbaugh et al showed that the cost of inappropriate stress ulcer prophylaxis in medicine patients exceeded

\$100,000 at one institution for one year, which could have been prevented by physician adherence to prescribing guidelines [3]. The risk of clinically significant bleeding in non-ICU patients is vanishingly low; the number needed to treat (NNT) in the ICU setting exceeds 900 and while this figure for general medicine patients is unknown, it is expected to be much higher [4]. No studies show significant benefit of SUP use outside of the ASHP guidelines and inappropriate SUP is a clear failure of adherence to the principles of evidence based medicine.

It is unclear whether institutional policies and practices, such as ordersets or checklists, are driving overuse, or whether individual physicians are either not familiar with or not appropriately interpreting existing guidelines. A handful of studies have looked into why AST, and the use of PPIs in particular, has become so pervasive, and experts are calling on physicians to reassess how they prescribe the drugs. It is likely that the factors driving AST use are subtle and difficult to address. First and foremost, the guidelines are directed at critically ill patients and do not directly address the less ill populations seen on general medicine wards. The culture of medical care among housestaff dictates prescribing practices and according to some experts, has become a checklist item for hospitalized patient where GI prophylaxis is entered akin to DVT prophylaxis. In fact, some computerized order sets group nexium along with heparin for to make admission orders more efficient. Housestaff become indoctrinated into existing practices and most agree that the overuse of AST, at least in teaching hospitals, is perpetuated by residents who start patients on therapy or refuse to question why they are already receiving them [6, 7]. However, overprescribing practices have also been seen among hospitalists and in non-teaching institutions, although to a lesser degree. There is a clear need for a trusted position statement on appropriate empiric use of AST, in addition to re-education and institutional measures to curb inappropriate prescribing practices.

We have known about the rising tide of prophylactic AST use for more than a decade. A multicenter survey of stress ulcer prophylaxis in 1999 revealed that a majority of practicing physicians felt non-ICU patients were receiving SUP more than 50% of the time, and that patients discharged from the ICU to a non-ICU setting received SUP more than 50% of the time. For most clinicians surveyed, the benefits for SUP outweighed associated risks and costs [8]. It is important to note that in 1999, the primary agents used were H2 blockers and sucralfate. In 2010, PPIs are used in a vast majority of patients, despite lack of evidence to support superior efficacy, and have been associated with greater potential risks to the patient and costs to the system. Curbing unwarranted SUP on general medical wards is timely for three primary reasons. First, our healthcare system is now, more than ever, burdened by overexpenditure and studies have documented significant attributable cost and economic impact of inappropriate SUP. Second, we now prescribe more medications per patient than at any time in history, addition to the cost and complexity of their medication regimen, potential drug interactions, and adverse events. Last, while there has been no clinical evidence to support the pervasive use of AST, new evidence has surfaced regarding potential patient-safety risks of such practices. While we often assume that these medications are cheap and benign, when over half of hospitalized patients are receiving AST, neither appears to be true. Although guidelines haven't changed and no clinical evidence has emerged to refute them, and it is critical to evaluate whether inappropriate prescribing is driven by faulty institutional policies or by lack of physician knowledge, and in the later case, at which level of training.

B. Study Design and Statistical Analysis

I plan to survey two study groups at two different institutions (Columbia and Cornell), to identify knowledge and interpretation of stress ulcer prophylaxis guidelines: internal medicine residents (PGY0

and PGY1-3) and internal medicine-trained attendings and hospitalists. There will be no randomization or cross over.

Power analysis: The number of subjects to be enrolled is based on a chi square analysis of categorical outcomes. This study will assume that the smallest difference of clinical interest is a 25% difference between groups, and the hypothesis is that 50% of residents with score > 70% and that 75% of attending will score > 70%.

$$N = 8 [(0.5)(0.5) + (0.75)(0.25) / (0.25)^2] + 2/0.25 + 2$$

$$N = 56$$

The number of physicians needed to respond is 56 to allow a detection of scoring >70% with a power of 80% using a t-test and two-tailed alpha of 0.05.

Statistical analysis: A paired t-test will be used to compare the mean difference between composite survey scores of residents and attendings, and will stratify response rates by score in 'knowledge of guidelines' and 'clinical application/interpretation.' Multivariate logistic regression analysis (ANOVA) will be used to compare subgroups, including PGY level for residents and for attendings between hospitalists, non-hospitalists, and subspecialists at both sites.

C. Study Procedure

A 10-item questionnaire was drafted with five questions pertaining to knowledge or understanding of SUP guidelines and five questions designed to evaluate clinical application. Items were informed by what the literature demonstrates are most common scenarios of inappropriate SUP use. In order to improve validity and reliability, the questionnaire was presented to and pretested by specialists in both critical care and gastroenterology and inpatient pharmacists. The questionnaire was formatted using Survey Monkey and distributed by email to all internal medicine housestaff (PGY0 prior to their first ward month, and PGY1-3 residents in training), and internal-medicine trained attendings and hospitalists at both institutions. A minimum of 60 respondents in each group will be gathered and analyzed. If necessary to bolster response rates, an email or flyer will be distributed to encourage filling out the questionnaire, a 5-10 minute endeavor.

D. Study Drugs: N/A

E. Medical Device: N/A

F. Study Questionnaires: See appendix

G. Study Subjects:

All internal medicine housestaff and attendings/hospitalists trained in internal medicine at Columbia and Cornell will be included. There will be a subgroup analysis of housestaff by year and of attendings by specialty and years in practice. Rising interns (PGY0) will be asked to fill out the questionnaire prior to starting on the wards. No vulnerable subjects will be included and the study is not restricted by gender or race.

H. Recruitment of Subjects

Potential subjects will receive an email through their hospital email account, and will not be contacted by pager, telephone, or approached.

I. Confidentiality of Study Data

A unique code number will be assigned to all study subjects and no personal identifiers will be used. Data will only be accessible to investigators.

J. Potential Conflict of Interest:

There is no potential conflict of interest in this investigation and no one stands to benefit from or be harmed the results.

K. Location of the Study

Columbia Presbyterian and Weil Cornell medical centers

L. Potential Risks: None

M. Potential Benefits:

Based on the results of this study, resident training may be improved in the future with regard to appropriate stress ulcer prophylaxis prescribing practices. Hence, there is some indirect benefit for physicians and hopefully some benefit for our patient population.

N. Alternative Therapies: N/A

O. Compensation to Subjects: None

P. Costs to Subjects:

The survey is designed to take approximately 10 minutes so there will be a minimal amount of time spent by subjects.

Q. Minors as Research Subjects: N/A

R. Radiation or Radioactive Substances: N/A

References

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Stress Ulcer Prophylaxis Questionnaire

- 1) Are you familiar with guidelines for stress ulcer prophylaxis in hospitalized patients?
 - a. Yes
 - b. No

- 2) How often do you adhere to a set of guidelines when prescribing acid suppressive therapy for stress ulcer prophylaxis?
 - a. Always
 - b. Half of the time
 - c. Rarely or never

- 3) Which acid suppressive agent is most effective for stress ulcer prophylaxis?
 - a. Proton pump inhibitor (nexium, prilosec)
 - b. H2 blocker (pepcid, zantac)
 - c. Above are equivalent

- 4) Of the following criteria, which is considered a sole indication for stress ulcer prophylaxis based on your understanding of guidelines?
 - a. History of gastric ulcer bleeding within 1 year of admission
 - b. Mechanical ventilation for 24 hours
 - c. Sepsis
 - d. INR > 1.5 or platelets < 50,000
 - e. High dose corticosteroid therapy

- 5) Based on your understanding of guidelines, all patients with acute renal failure should be on stress ulcer prophylaxis during their hospital stay.
 - a. True
 - b. False

- 6) Based on your understanding of guidelines, which of the following patients should be started on acid suppressive therapy for prophylaxis of stress ulcers?
 - a. 80 year old woman admitted with urinary tract infection and acute renal insufficiency
 - b. 24 year old paraplegic man with history of spinal cord injury at age 18 admitted with community acquired pneumonia
 - c. 48 year old man with alcoholic cirrhosis and ascites, admitted with hepatic encephalopathy, found to have thrombocytopenia and prolonged PTT > 2x normal
 - d. 66 yo man with B-cell lymphoma admitted for cycle of chemotherapy, whose prior hospitalization was complicated by a bleeding duodenal ulcer
 - e. 88 year old diabetic woman with sepsis, likely from left leg osteomyelitis, on ICU day #3, not intubated

- 7) A patient was admitted to the ICU for COPD exacerbation requiring 72 hours of intubation and was started on 40mg of oral nexium daily for stress ulcer prophylaxis. The patient is now transferred to your team for further care on a general medical ward. Based on your understanding of guidelines, the patient should be continued on nexium for the duration of their hospital stay.
- True
 - False
- 8) An elderly woman with a non-operative hip fracture is on your service for a prolonged hospital course complicated by UTI, requiring high doses of NSAIDs and aspirin for pain control. She is also on warfarin for her chronic atrial fibrillation. Based on your understanding of guidelines, does this patient require stress ulcer prophylaxis?
- Yes
 - No
- 9) A new clinic patient presents as a hospital discharge. Patient is a 48 year old current smoker with severe emphysema who was intubated in the ED for hypercarbic respiratory failure and required a four day ICU stay during which pt was treated for COPD exacerbation and started on subcutaneous heparin and nexium for DVT and stress ulcer prophylaxis respectively . Pt was transferred to the floor for an additional two days before discharge home. In clinic, the patient reports that he is taking his discharge medications which include spiriva, albuterol, norvasc, and nexium. Based on your understanding of guidelines, you should:
- Continue nexium as prescribed
 - Refer to GI for upper endoscopy
 - Stop nexium given no history of gastritis
- 10) Do you feel obligated to start 'sick' general medicine patients on stress ulcer prophylaxis, as you would DVT prophylaxis based on the prescribing practices of your hospital?
- Often
 - Rarely
 - Never