*Journal of Pharmaceutical Research International*

***28(2): 1-6, 2019; Article no.JPRI.40610***
***ISSN: 2456-9119***
*(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)*

# Survey on the Prevalence of Intravenous Use of Proton Pump Inhibitors and H2-antagonists in Internal Medicine Ward

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***Authors' contributions***

*This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.*

***Article Information***

DOI: 10.9734/JPRI/2019/v28i230197
Editor(s):
(1) Dr. Vasudevan Mani, M.Pharm., Associate Professor, Brain Research Laboratory, Level 11, Block FF1, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Campus Puncak Alam, 42300 Bandar Puncak Alam, Kuala Selangor, Selangor, Malaysia.
Reviewers:
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Complete Peer review History: http://www.sdiarticle3.com/review-history/40610

***Original Research Article***

***Received 02 February 2018***
***Accepted 23 April 2018***
***Published 24 June 2019***

## ABSTRACT

**Background:** Anti-acids drugs are commonly used for stress ulcer prophylaxis (SUP). Some inpatients receiving acid suppression therapy without risk factors for nosocomial upper gastrointestinal bleeding and this inappropriate usage increase time, costs and avoidable side effects such as hospital-acquired pneumonia.
**Purpose:** This study was designed to evaluate the prevalence of stress ulcer prophylactic drugs use, the number of properly indicated administrations and prescription prevalence of intravenous use of proton pump inhibitors (PIPs) and H2-antagonists in preventing nosocomial gastrointestinal bleeding and pneumonia**.**
**Methods:** This cross-sectional study was performed on 280 patients in two different time zone before and after implementing of guidelines for SUP usage on the medical service in January and March of 2014(pre-intervention period) and January and march of 2015 (post-intervention period). Indicated anti-acid therapy for stress ulcer prophylaxis was defined according to the 1999 American

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Society of Health-System Pharmacists (ASHP) guidelines for the use of SUP. The Patient's data such as kind of stress ulcer prophylaxis drug, ICU admission and the indication of prophylaxis pre and post-intervention were collected. Data were analyzed by SPSS software using the Pearson Chi-square test and unpaired t-test.

**Results:** There was no significant change in the administration of stress ulcer prophylaxis drugs in general, but anti-acid medications misused decreased from 63.6% to 55.2% after intervention.

**Conclusion:** The use of anti-acids without proper indication had 11.4% fall. The IV administration had a dramatic decrease as opposed to PO anti-acids use, which had a significant effect on hospital financial costs. In the end, there was no significant change detected in the total use of SUP (stress ulcer prophylaxis).

*Keywords: Prevalence; intravenous use; proton pump inhibitors; H2-antagonists; Stress Relates Mucosal Disease (SRMD).*

## 1. INTRODUCTION

Stress relates mucosal disease (SRMD) is related to a range of conditions from stress-related injuries (superficial mucosal damage) to stress ulcer (focal profound mucosal damage) [1]. Etiology and pathophysiology of SRMD are multifactorial and have not been fully clear, but impairment of mucosal protective mechanisms and raising of the acid product play significant roles [2]. The recommendation is based on studies, prophylaxis process for suppuration of gastric acid with histamine-2 receptor antagonist or PPIs therapy significantly reduced the risk of GI bleeding in critically ill patients [3-7]. SRP with histamine-2 (H2) Antagonist, Sucralfate or proton pump inhibitors (PPIs) reduce the incidence of gastrointestinal bleeding by 29%-61 [6,7]. Based on the most current guidelines for usage of anti-acid drugs in SRP were published by American Society of Health-system pharmacists (ASHP) and the meta-analyses from randomized controlled trial (RCT), stress ulcer prophylaxis is recommended for patient admitted to the intensive care unit (ICU) who have [1] Coagulopathy (platelet count < 50,000 mm3, INR > 1.5, or aPTT> 2 times control); [2] Mechanical ventilation for more than 48 hours; [3] History of gastrointestinal ulceration or bleeding within 1 year before admission; [4] Have at least 2 of the following risk factors: Sepsis, ICU stays longer than 1 week, occult bleeding lasting 6 days or longer, and use of more than 250 mg hydrocortisone or the equivalent [8]. Several studies have shown adverse effect such as increased risk of Clostridium difficile infection, hospital-acquired pneumonia, osteoporotic fracture and incurring of financial cost with inappropriate usage of acid-suppressive medication [9,10]. Due to increasing of inappropriate usage of anti-acid therapy and the adverse effect of these drugs, we sought to measure the rate of inappropriate use of intravenous proton pump inhibitors and H2-antagonists for stress ulcer prophylaxis. This comparative study which took place in the immediate two years following the introduction of the "particular drug use" form intends to evaluate 1)prevalence of stress ulcer prophylactic drugs use in post and pre-intervention period 2)the number of properly indicated administrations before and after the intervention and 3)the prophylactic value of these drugs in preventing nosocomial gastrointestinal bleeding and pneumonia in patients admitted to Internal medicine ward of Marvdasht Motahari's Hospital in January and March of 2015 and compare it with the same episode of time in 2014.

## 2. RESEARCH METHODS

In this cross-sectional study, we measured the rate of usage of intravenous use of proton pump inhibitors (PIPs) and H2-antagonists that were defined as acid suppressive medicine for stress ulcer prophylaxis drug. Ethical Approval was gain from hospital board. Written informed consent was not necessary because the study was only based on charts review. The study was performed on 390 patients in two separate time zone, 214 subjects at baseline (pre-intervention) in January and March of 2014 and 176 subjects at post-intervention in January and March of 2015. Patients who received at least one dose of AST were eligible for the study and admissions with the primary diagnosis of gastrointestinal bleedings were excluded.

Data were collected randomly with Hospital Information System (HIS) in the internal disease department of Motahari-Marvdasht Hospital in Marvdasht Fars province, Iran. Written informed consent was not needed due to approval obtained from hospital Board before initiation of study.

We excluded 110 patients with a primary diagnosis of internal gastrointestinal bleeding and patients with cardiac or neurological diseases, and we started the study on 280 patients.

Prophylaxis was defined as sustained (1>DAY) administration of an anti-acid drug (H2 blocker or proton pump inhibitor (PPI)). Appropriate indication for usage of SUP was defined base on American Society of Health-Systems Pharmacists (ASHP). Internal disease department in collaboration with clinical pharmacy specialist designed a prototype based on the ASHP protocol in July and August of 2014 by the name of “particular drugs use" which was presented to attending physician supposed to be field prior any request for AST drugs. We prospectively measured rates of SUP usage at two separate times, before and after protocol presentation.

Particular drug use form consists of ASHP guideline and medical records including age, sex, chief complaint, primary and secondary diagnosis, drug history, medical history, duration of hospitalization, the rate of SUP usage, class of acid-suppressive agent patients progress, the presence of side-effects attributed to the medication and clinical outcome.

Additional data abstracted from nurses notes, students notes and laboratory data for any recorded complication during hospitalization, platelet count, stool's occult blood and usual bleeding tendency.

Data analysis was performed using SPSS version 16, for group comparing chi-square and for indication prevalence frequency table was used. A P-value < 0.01 was deemed statically significant.

## 3. RESULTS

210 patients were evaluated in pre-intervention period, and 140 patients (55% men, the median age: 55) were included in the study after exclusion 70 patients. In the post-intervention period, 180 patients were admitted, and 140 patients (57% woman, the median age: 75) were included in the study after exclusion 40 patients (Table 1).

Excluded group (110 patients) included patients with primary diagnosis of gastrointestinal bleeding and patients who received AST before admission.

In the overall, outpatient anti-acid use was documented 62.9% of patients in 2014 and 62.1% of patients in 2015. From those administrations, 63.6% of patients in 2014 and 55.2% of patients in 2015 doesn’t have the proper indication for AST.

The main outcome measure was the appropriateness of IV PPI use and IV H2antagonist use for stress ulcer prophylaxis which was categorized as appropriate indication and inappropriate indication (Table 2).

Any AST use for SUP as per ASTH guidelines was defined as indicated and patients with no documented indication for use were categorized as not indicated.

Of the 140 patients in the pre-intervention period (2014), 62.85% (88 patients) received anti-acid drug compared with 87 of 140 patients (62.1%) in the post-intervention period (p< 0.92).

Of the Exposed patients group to the acid-suppressive medications in pre-intervention period, 40% received PIPs (p,35.7% received histamine-2 receptor antagonists, 12.19% exposed to both and 11.4% received other drugs, and post-intervention exposed group received 47.9% PIPs,22.9% histamine-2 receptor antagonists, 8.6% both of drugs and 20.6% exposed to anti-acid other medicine. According to the internal ASHP-based guideline, data analysis showed 88 patients in the pre-intervention period and 87 patients in the post-intervention period who received AST .63% (n=56) of patients in pre-intervention period and 55.17% (n=48) in the post-intervention period received AST without indication.

In this study, the most conditions for appropriate prescription of AST was the usage of hydrocortisone more than 250 mg or the equivalent (Table 3).

Prevalence of gastrointestinal bleeding after using of AST in the pre-intervention period was 2.27% (n=2) and in the post-intervention was 5.7% (n=5) (Table 4).

Pneumonia after using of AST Just seen in post-intervention period and prevalence of this side effect was 1.14 % (n=1).

**Table 1. Patient characteristics including chief complains and primary diagnosis**

| Characteristic | | Pre intervention period | Post intervention period |
|---|---|---|---|
| **Sex** | Male | 77 | 60 |
| | Female | 63 | 80 |
| **Age** | 10-20 | 3 (2.1%) | 2 (1.4%) |
| | 21-30 | 24(17.1%) | 20 (14.3%) |
| | 31-40 | 12(8.6%) | 7(5%) |
| | 41-50 | 26(18.6%) | 22 (15.7%) |
| | 51-60 | 32(22.9%) | 25 (17.9%) |
| | 61-70 | 8 (5.7%) | 15 (10.7%) |
| | 71-80 | 21(15%) | 30 (21.4%) |
| | 81 or older | 14(10%) | 19 (13.6%) |
| **Chief complain** | Nausea, vomiting, abdominal pain | 14 (10%) | 12 (8.6 %) |
| | Altered level of consciousness | 46(32.29%) | 26 (18.6%) |
| | Muscle weakness | 8 (5.7%) | 4 (2.9 %) |
| | Cough & dyspnea | 42(30%) | 61 (43.6) |
| | Chest pain & dyspnea | 8(5.7%) | 4 (2.9%) |
| | Chills and fever | 6 (4.3%) | 12 (8.6%) |
| | Foot ulcer | 5 (3.6%) | 8 (5.7%) |
| | Edema | 4 (2.9%) | 5 (3.6%) |
| | Purpura | 1 (7 %) | 2 (1.4%) |
| | Generalized body pain | 6 (4.3%) | 2 (1.4%) |
| **Most primary diagnosis** | Poisoning | 27 (19.3%) | 16 (11.4 %) |
| | Pneumonia | 7 (5 %) | 15 (10.7%) |
| | Chronic obstructive pulmonary disease | 15 (10.7%) | 21 (15 %) |
| | Shock | 3 (2.1%) | 1 (0.7%) |
| | Asthma | 17 (12.1%) | 15 (10.7%) |
| | Sepsis | 6(4.3%) | 3 (2.1%) |
| | Another diagnosis | 65 (46.42%) | 69 (62.72%) |

**Table 2. Prevalence of anti-acid prescription**

| Characteristic | | Pre intervention | Post intervention | P value |
|---|---|---|---|---|
| Prevalence of anti-acid prescription | | 62.9% | 62.1% | 0.92 |
| PIP usage | oral | 23.6% | 40 % | 0.018 |
| | IV | 18.6% | 13.6% | |
| H2A | oral | 5% | 5% | 0.187 |
| USAGE | IV | 32.1% | 17.1% | |

**Table 3. Most appropriate indication of SUP usage**

| Risk factor | Pre intervention | Post intervention |
|---|---|---|
| Coagulopathy | 4 (4.5 %) | 11 (12.6%) |
| Shock | 4 (4.5%) | - |
| Sepsis | 2 (2.3%) | 1 (1.1%) |
| Corticosteroid use (>250 mg hydrocortisone or equivalent) | 15 (17%) | 11 (19.5%) |
| Mechanical ventilation more than 48 % | 1 (1.11%) | - |

**Table 4. SUP side effects**

| Side effect | Pre intervention | Post intervention |
|---|---|---|
| Gastrointestinal bleeding | 2 (1.4%) | 5(3.6%) |
| Pneumonia | - | 1 (0.7%) |

## 4. DISCUSSION

Use of SUP in high-risk patients can decrease the incidence of gastrointestinal bleeding, but the recently inappropriate usage of AST for none critically ill hospitalized patients is significantly increased. 40 to 70% of medical inpatients receive acid suppressive medications during their hospitalization [11,12].

Current stress ulcer prophylaxis guideline (ASTH) recommends AST for patients who are at high risk of developing a stress ulcer. Guidelines for the prevention of stress ulcer in non-ICU patients have yet to be defined, and current medical studies do not support the routine use of AST [13].

In the present study, in the pre-intervention period, of 62.9% of the patient's received AST 36.4% of patients indicated SUP. In the post-intervention period, 44.8% of patients indicated SUP, but 62.1% received AST.

Similar to our study, the rate of inappropriate prescription of AST in noncritical patients was high. In the Farrell study in 2010 inappropriate usage of AST was 68.1% [14] and in the study of Grube et al. was 71% in 2007 [15]. About the study of Nardino et al. in 2000, 65% of patients received AST with no indication [16].

Studies showed an increased incidence adverse events including ventilator-associated pneumonia, Clostridium Dificile infection, increased risk of fall elderly and many drug interactions [4,6].

According to our result, Use of more than 250 mg hydrocortisone or the equivalent per day was the most common indication for SUP regard to ASHP guideline [8] and the most common diagnosis was the respiratory disease like asthma, pneumonia, chronic obstructive pulmonary disease. In Khalili et al. study in 2010 [17] and the study of Qadeer et al. in 2006 [18], anticoagulant drug use was the main indication that for SUP prescription.

The incidence of nosocomial GIB of Qadeer et al. study [18] was 0.41% in a four-year survey of non-critically ill patient, and the leading risk factor was high dose anticoagulant therapy. In this research, this incidence was 1.4% in 2014 and 3.6% in 2015 which can be due to a positive occult blood test in patients such as gastroenteritis patients.

About other side effects of inappropriate use of SUP, study of Leonard et al. in 2007 [19] and similarly, Kwok et al. in 2012 [20] shown the increasing risk of Clostridium difficile infection with H2A and increasing risk of *C. difficile* infection that was shown in Madanick study in 2011 [10] associated to PIP usage.

About risk of pneumonia after SUP, Messori et al. in 2000 [20] and Lin et al. 2010 [21] shown the relationship between SUP drugs and pneumonia but in present study patients did not show pneumonia significantly.

## 5. CONCLUSION

The use of anti-acids without proper indication had 11.4% falls. The IV administration had a dramatic decrease as opposed to PO anti-acids use, which had a significant effect on hospital financial costs. In the end, there was no significant change detected in the total consumption of SUP.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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*The peer review history for this paper can be accessed here:*
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