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Cost estimation and adherence of medical prescriptions to guidelines of stress ulcer prophylaxis in a university hospital of Northeastern Brazil: a retrospective observational study

Sâmara Nascimento de ARAÚJO, Yane Silva SANTOS Jamilly Araujo SANTOS Amanda Silva MORAIS Izabella Virgínio GOMES Daniel Tenório da SILVA

[1]Federal University of Vale do São Francisco, Postgraduate Program in Biosciences, Petrolina, Brazil; [2]Federal University of Vale do São Francisco, Universitary Hospital/ Brazilian Hospital Services Company, Petrolina, Brazil; [3]Federal University of Vale do São Francisco, Postgraduate Program in Health and Biological Sciences, Petrolina, Brazil; [4]Federal University of Vale do São Francisco, Multiprofessional Residency Program in Intensivism, Petrolina, Brazil; [5]Federal University of Vale do São Francisco, College of Pharmacy, Group of Studies in Geriatrics and Gerontology, Petrolina, Brazil

Corresponding author: Silva DT, danieltenorio.univasf@gmail.com

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Abstract

Objective: To evaluate the adherence of prescriptions to the main prophylaxis guidelines for stress ulcers and estimate the expenditures incurred by inappropriate prescriptions in a university hospital in the Northeast Region of Brazil. **Methods:** The study was observational, cross-sectional retrospective with a qualitative approach. Medical records and prescriptions of all patients hospitalized for more than 24 hours in non-intensive care units during a month period were analyzed. Patients under 18 years of age, those previously using acid suppressants for treatment purposes, and patients with incomplete medical records were excluded from the study. Data were collected using an instrument formulated from the main guidelines for stress ulcer prophylaxis. They were subjected to descriptive analysis, Kruskal-Wallis test with Dunn's post-hoc, Pearson's correlation, and logistic regression. The Odds ratio and confidence interval (95% CI) were considered to report the results of the regression model. Values of p≤0.05 were considered significant for the other tests. **Results:** A total of 421 users were eligible to participate in the study, most of them male and between the ages of 30 and 59. For 212 (50.3%) patients, prophylaxis for stress ulcers was prescribed, and in 210 (99%) of these there was no indication in the guidelines. The average cost per patient with improperly prescribed prophylaxis was U$8.6 (SD10.8). In the analysis, using the multiple logistic regression model, the variables associated with the prescriptions of prophylaxis for stress ulcers were length of stay (OR = 1.047; 1.03-1.07) and having a professional relationship with the Team (OR = 1.995; 1.30-3.06), adjusted for age and sex. The length of stay and the time of use of acid suppression therapy was significantly longer in the orthopedic clinic (p<0.0001). **Conclusion:** Intervention measures are needed, including implementation of institutional protocols and education of prescribers about the use of Acid Suppression Therapy during hospitalization.

Keywords: stomach ulcer; prophylaxis; anti-ulcer agents; health evaluation; economic evaluation; hospitals, university.

Estimativa de custo e adesão de prescrições médicas a diretrizes de profilaxia para úlcera de estresse em um hospital universitário no nordeste do Brasil: estudo retrospectivo observacional

Resumo

Objetivo: avaliar a adesão das prescrições médicas às principais diretrizes de profilaxia para úlcera de estresse e estimar os gastos despendidos com as prescrições inapropriadas em um hospital universitário na Região Nordeste do Brasil. **Métodos:** o estudo foi do tipo observacional, transversal, descritivo, retrospectivo com abordagem quantitativa. Analisaram-se prontuários e prescrições médicas de todos os pacientes internados por mais de 24 horas nas unidades de cuidados não intensivos, no período de um mês. Foram excluídos do estudo, pacientes menores de 18 anos, em uso prévio de supressores ácidos para fins de tratamento ou com prontuários preenchidos de forma incompleta. Os dados foram coletados através de instrumento formulado a partir das principais diretrizes para profilaxia para úlcera de estresse, submetidos a analise descritiva, teste Kruskal-Wallis com *post-hoc* de Dunn, correlação de Pearson e regressão logística. O odds ratio e o intervalo de confiança (95% IC) foram considerados para relatar os resultados do modelo de regressão. Valores de p≤0.05 foram considerados significativos para os demais testes.

Resultados: Foram aptos a participar do estudo 421 usuários, sendo a maioria do sexo masculino e na faixa etária entre 30 a 59 anos. Para 212 (50,3%) foi prescrita profilaxia para úlcera de estresse, para 210 (99%) destes não havia indicação nas diretrizes. O custo médio por paciente com profilaxia indevidamente prescrita foi de U$8,6 (DP10,8). Na análise, pelo modelo de regressão logística múltipla, as variáveis associadas à prescrição foram tempo de permanência (OR= 1,047; 1,03-1,07) e ter vínculo profissional Staff (OR= 1,995; 1,30-3,06), ajustadas por idade e sexo. O tempo de permanência e tempo de uso de terapia de supressão ácida foi significantemente maior na clínica ortopédica (p<0,0001). **Conclusão:** Faz-se necessária medidas de intervenção, incluindo a implementação de protocolos institucionais e educação de prescritores sobre o uso de terapia de supressão ácida durante a hospitalização.

Palavras-Chaves: úlcera gástrica; profilaxia; antiulcerosos; avaliação em saúde; avaliação econômica; hospital universitário.

Introduction

Stress Ulcer (SU) is an erosive hemorrhagic lesion of the gastric mucosa that can affect patients who have suffered a serious physiologically stressful event such as multiple trauma, organ failure, sepsis, major surgery, thermal injury or invasive ventilation.[1] It is estimated that the incidence of stress-related bleeding in the Intensive Care Unit (ICU) varies from 0.6% to 6.0%. Although the pathophysiology is not fully understood, it is clear that its cause is more related to decreased mucosal blood flow, ischemia and reperfusion injury than to variation in acid secretion.[2] Occurrence of this episode can cause increased morbidity and mortality in this hospital unit.[3]

Although the use of Acid Suppression Therapy for stress ulcer prophylaxis can reduce gastrointestinal bleeding, the use of these agents has been associated with an increased risk of adverse events. One of the main concerns with the use of this prophylactic treatment is the frequent increase in infectious complications due to changes in pH and gastric composition. The infections include pneumonia, infection by *Clostridium difficile* (CDI) and other enteral infections.[4] The incidence of in-hospital gastrointestinal hemorrhage in non-severe hospitalized patients is approximately 0.2% to 0.4%, similar to the general population. In this sense, stress ulcer prophylaxis did not prove to be beneficial in patients outside the ICU setting.[5] This practice has become common even in patients who have no indication of clinical protocols, which has caused concern to health units, as the practice can lead to increased harms to patients, in addition to raising the institution's costs.[6] The reasons that justify the conduct are not clear, and knowing them can protect the users of the health services against unsafe practices.[7]

Thus, carrying out studies that assess the criteria and profile of the use of these medications becomes an essential strategy, in order to allow for a detailed analysis of indications, data on potential adverse events, the financial cost and risk factors associated with stress ulcer prophylaxis. Therefore, this study aimed at evaluating adherence of the medical prescriptions to guidelines for stress ulcer prophylaxis and at estimating the amounts spent on inappropriate prescriptions for Acid Suppression Therapy in a university hospital from a municipality in northeastern Brazil.

Methods

An observational study of the cross-sectional, descriptive and retrospective type with a quantitative approach. The study was conducted in a university hospital located in the municipality of Petrolina, Pernambuco. The hospital is a reference unit for the 53 municipalities of the Interstate Health Care Network of Vale do Médio São Francisco – PEBA, comprised by six health micro-regions and covering a population of approximately 2,077,000 inhabitants in the states of Pernambuco and Bahia. Its physical structure consists of 129 beds, of which 111 are for hospitalization of clinical-surgical patients and 18 are ICU beds, in addition to diagnostic and therapeutic support services. The study was carried out in the inpatient units for non-critical patients, which correspond to the medical clinic, surgical clinic and orthopedic clinic, each with 37 beds.

Medical records and prescriptions of all patients hospitalized for more than 24 hours in non-critical care units within a one-month period (October 2018) were analyzed. The non-probabilistic sample size was determined by the number of patients admitted to the medical clinic, surgical clinic and orthopedic clinic sectors, over 18 years of age, in the given period. The patients excluded were those who were previously using acid suppressants for treatment purposes, such as gastrointestinal bleeding prior to admission to the clinics, as well as those who presented hematemesis, blood in the nasogastric aspirate or melena, gastroesophageal reflux diseases and peptic ulcer disease. In addition to that, the cases in which the medical charts and/or prescriptions presented incomplete information were also not included in this study.

The data were collected from the medical records and prescriptions by means of a structured instrument elaborated by the researchers. The elaboration of the instrument to assess the indication for using acid secretion inhibitors was based on the main guidelines for stress ulcer prophylaxis described by Ye et al.,[8] since the hospital under study did not have any formal recommendation on the subject matter. The recommended guidelines were the following: ASHP (American Society of Health-System Pharmacists), EAST (Eastern Association for the Surgery of Trauma) and DASAIM (Danish Society of Anesthesiology and Intensive Care Medicine), which achieved better scores on AGREE II, according to a study by Ye et al.[8] However, for the elaboration of the final instrument, only the ASHP and EAST guidelines were used, as DASAIM did not report any specific indication for stress ulcer prophylaxis. Among the specific indications reported in the guidelines, those that appeared in common in both guidelines were used, namely: use of mechanical ventilation for more than 48 hours, coagulopathies (considering platelet counts below 50,000 or International Normalized Ratio greater than 1.5 or Partially activated Thromboplastin Time greater than 2x the control value), Head trauma with Glasgow Coma Scale ≤10 or spinal cord injury, burn with more than 35% of the body surface area affected, sepsis, glucocorticoid therapy (more than 250 mg of hydrocortisone or equivalent) and multiple trauma with an Injury Severity Score ≥16.

The medical records included the patient's demographic and clinical data, the specialty of the prescribing professional, the condition of the prescriber (staff or resident practitioner),

the hospitalization sector and period, diagnosis at admission, nutritional status and length of stay in the ward until initiating stress ulcer prophylaxis. In the evaluation of the prescription and medical record, information about the use of stress ulcer prophylaxis based on the guidelines was investigated, as well as data on acid secretion inhibitors, such as name of the medication, pharmaceutical presentation, dose and dosage. After identifying the inhibitors in the prescriptions, a search was carried out in the computerized system used by the institution regarding the amount used by the patient during hospitalization. To analyze the cost of prescribed prophylaxis, only the direct costs of drug acquisition were measured, using the monetary values at the time of the research. The costs were collected by means of the computerized system of the hospital's Pharmacy sector.

The use of stress ulcer prophylaxis was considered appropriate, based on the guidelines, when at least one absolute indication was identified (mechanical ventilation for an additional 48 hours or coagulopathies) or two concomitant relative indications (Traumatic Brain Injury [TBI] or spinal cord injury, burn, sepsis, glucocorticoid therapy and multiple traumas). In the cases in which the indications were not detected, inadequate use was considered. To reduce bias, data tabulation and analysis was made by double check.

The following categorical variables were investigated using the respective captions: medication prescribed and indicated for stress ulcer prophylaxis (A); prescribed and not indicated (B); not prescribed and indicated (C); not prescribed and not indicated (D).[9] The clinical indication of the medication was confronted against the patient's clinical data, in order to observe presence of the requirements that justify prophylaxis. In the absence of the requirements, prophylaxis was considered as not indicated.[9]

The data collected were submitted to a descriptive analysis, with calculation of frequency, mean and standard deviation. For analytical evaluation, the Kruskal-Wallis test with Dunn's *post-hoc* was used to compare the use of stress ulcer prophylaxis across the sectors under study. A logistic regression analysis was performed to identify the relationship between the different variables and the use of stress ulcer prophylaxis. Simple regression analysis was initially performed to identify the importance of these factors, and then multiple logistic regression was conducted to confirm the relationship between the previously established risk factors for the use of stress ulcer prophylaxis. Odds Ratio and Confidence Interval (95% CI) were considered to report the results of the regression model. p-values ≤ 0.05 were considered significant.

The study met the ethical requirements according to Resolution No. 466/2012 of the National Health Council (*Conselho Nacional de Saúde*, CNS).[10] It was approved by the Ethics and Deontology Committee in Studies and Research of the Federal University of Vale do São Francisco (*Comitê de Ética e Deontologia em Estudos e Pesquisas da Universidade Federal do Vale do São Francisco*, CEDEP/UNIVASF) under number 3,139,264 (CAAE: 03289218.9.0000.5196).

Results

In October 2018, a total of 463 individuals were admitted to the inpatient sectors for non-critical patients, of which 42 were excluded according to established criteria; of these, 40 were under 18 years of age, one had incomplete records and another one had upper gastrointestinal bleeding at admission. Therefore, 421 users met the requirements to participate in the study, with the male gender representing slightly more than half of them (55.10%). The majority belonged to the age group from 30 to 59 years old, with a mean of 52.5 (±20.12) varying from a minimum of 18 to a maximum of 103 years old.

Of the 421 users analyzed during the study period, 212 (50.36%) used stress ulcer prophylaxis, of which 55.66% were men and the majority were aged between 30 and 59 years old (Table 1). In the analysis, using the multiple logistic regression model, the variables associated with the prescription of stress ulcer prophylaxis were length of stay (OR=1.047; 1.03-1.07) and being part of the staff (OR=1.995; 1.30-3.06), adjusted for age and gender.

Table 1. Characterization of the profile corresponding to the use of stress ulcer prophylaxis according to the independent variables. Petrolina, Pernambuco, Brazil, 2018 (N=212).

Information	**All N=212**	**Simple Regression** OR (95% CI)	**Multiple Regression** OR (95% CI)
Sociodemographic			
Female gender[1] n (%)	94 (44.3)	1.046 (0.65-1.40)	0.941 (0.62-1.42)
Age (years old) n (%)			
18 - 29	29 (13.7)	1.007 (1.00-1.02)	1.007 (1.00-1.02)
30 - 59	98 (46.2)		
>60	85 (40.1)		
Hospitalization Mean (SD)			
Length of stay (days)	12.5 (17.4)	1.047 (1.03-1.07)	1.047 (1.03-1.07)
Employment contract n (%)			
Staff	153 (72.2)	2.161 (1.44-3.24)	1.995 (1.30-3.06)
Resident	59 (27.8)		

[1]Dichotomous variable for which the results of only one category were presented.

As for use frequency, the sector with the highest prevalence was the orthopedic clinic, in which 57.94% of the users had stress ulcer prophylaxis, with a mean length of stay of 19.9 days (p<0.0001). On the other hand, even with 98.5% of the hospitalized users already using stress ulcer prophylaxis before being transferred to the medical clinic, this was the sector with the lowest use prevalence during the study, with a mean length of stay of 9.7 days (Table 2).

The data analysis of the prescriptions and indications for prophylaxis showed a high frequency of medication prescription for stress ulcer prophylaxis without a precise clinical indication, according to the protocols adopted in the study (Table 2). Based on these data, it was possible to calculate the proportion of prophylaxis that was correctly prescribed (n=2) and incorrectly prescribed (n=210). The mean cost per patient related to incorrectly prescribed prophylaxis was US$ 8.6 (10.8). Among the patients for whom prophylaxis was not prescribed (n=209), one of the cases was identified as having an indication according to the guidelines, considering that the patient had coagulopathy.

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Table 2. Use of stress ulcer prophylaxis, Petrolina, Pernambuco, Brazil, 2018 (N=212).

Information	All	Medical Clinic	Surgical Clinic	Orthopedic Clinic	p value
Medication n (%)	**N= 241**	79 (32,8)	90 (37,4)	72 (29,8)	-
Omeprazole 20 mg, oral	60 (24.9)	28 (46.6)	16 (26.7)	16 (26.7)	-
Omeprazole 40 mg, oral	63 (26.2)	16 (25.4)	13 (20.6)	34 (54.0)	-
Omeprazole 40 mg, intravenous	84 (34.8)	22 (26.2)	44 (52.4)	18 (21.4)	-
Ranitidine 25 mg/mL, intravenous	30 (12.4)	11 (36.7)	17 (56.7)	2 (6.6)	-
Ranitidine 150 mg, oral	4 (1.7)	2 (50.0)	-	2 (50.0)	-
Prevalence of the use of stress ulcer prophylaxis n (%)	**N= 212**	68 (42.2)	82 (53.6)	62 (57.9)	-
Prescription adequacy n (%)	**N= 421**	161 (38.3)	153 (36.3)	107 (25.4)	-
Absolute indication					-
Prescribed and indicated (A)	2 (0.4)	2 (100.0)	-	-	-
Prescribed and not indicated (B)	210 (49.9)	66 (31.5)	82 (39.0)	62 (29.5)	-
Not prescribed and indicated (C)	1 (0.2)	-	1 (100.0)	-	-
Not prescribed and not indicated (D)	208 (49.5)	93 (44.7)	70 (33.7)	45 (21.6)	-
Relative indication[2]					
Prescribed and not indicated (B)	212 (50.3)	68 (32.0)	82 (38.7)	62 (29.3)	-
Not prescribed and not indicated (D)	209 (49.7)	93 (44.5)	71 (34.0)	45 (21.5)	-
Prescription costs (US$) Mean (SD)					
Correctly prescribed prophylaxis	24.8 (24.6)	24.8 (24.6)	-	-	-
Incorrectly prescribed prophylaxis	8.6 (10.8)	1.7 (3.0)	2.6 (2.9)	2.9 (4.4)	-
Prevalence of the use of prophylaxis for previous stress ulcer n (%)	**N= 362**	158 (98.5)	124 (81.5)	80 (75.4)	-
Length of stay in the sector (days)[1] Mean (SD)	12.4 (17.3)	9.7 (14.4)	10.6 (17.7)	19.3 (19.1)	p<0.0001
Use time of stress ulcer prophylaxis (days)[1] Mean (SD)	13.9 (18.3)	10.2 (12.3)	12.0 (21.0)	19.9 (18.3)	p<0.0001

[1]Kruskal-Wallis, Dunn's post-hoc (Medical Clinic versus Surgical Clinic, not significant; Orthopedic Clinic versus Medical Clinic and Surgical Clinic, p<0.0001). [2]Only categories with values were maintained.

Discussion

The study showed that Acid Suppression Prophylaxis is inappropriately prescribed for non-serious patients, confirming the findings of research studies that have been carried out over the years. In the study by Alsultan et al.,[11] the proportion of inadequacy was higher (71.7%); however, when compared to most of the literature on the theme, our results were superior.[5,6,7,12,13]

Although the study by Farsaei et al.[14] has insufficiently identified the predictive factors for the excessive use of stress ulcer prophylaxis, the present study identified potential risk factors for such practice, such as the male gender, age, length of hospital stay and condition of the prescriber; however, only the length of stay and condition of the prescriber variables remained significant in the multivariate analysis. Issa et al.[15] also identified that hospitalization time directly contributes to the use of stress ulcer prophylaxis. Singh et al.[7] found that, for each day of increase in length of stay, the chances of continued use of inappropriate Acid Suppression Therapy after discharge increased by 19%.

In summary, it is clear that the nonexistence of a defined guideline for stress ulcers that covers patients who are not in a critical condition in the institution makes the excessive use of acid suppressive therapy relative during longer hospitalizations. This occurs because the most severe patients need longer hospitalizations and more medical assistance, which can lead to the initiation of stress ulcer prophylaxis in order to avoid complications due to gastrointestinal bleeding.

The findings of this study also revealed that the orthopedic clinic presented higher prevalence in the use of stress ulcer prophylaxis, certainly for having patients with the longest length of stay in the unit. A research study conducted in a teaching hospital from Saudi Arabia observed that, in the surgery department, most of the prescriptions for intravenous PPIs were made by orthopedic surgeons, followed by general surgeons, under the justification that their patients had undergone major surgeries and were in use of non-steroidal anti-inflammatory drugs for pain treatment, anticoagulants for deep vein thrombosis prophylaxis or both medications.[16] In this sense, from the adoption of protocols for the use of stress ulcer prophylaxis, it is essential that the guidelines are disclosed and implemented in all sectors of the target institution, in order to ensure that the desired outcomes are systematically targeted.

Regarding the fact that 84% of the patients who were admitted to the sectors under study came from other sectors already using stress ulcer prophylaxis, although this was not analyzed in this study, it reveals that the use of stress ulcer prophylaxis without indication can be related to the time of hospital admission and that this pattern probably remained at discharge. A study by Farsaei et al.[14] indicates that adherence to the use of stress ulcer prophylaxis on the first hospitalization day can be a good predictor for use during hospitalization. This highlights the fact that the prescribing professionals may not be paying attention to conducting medication reconciliation at the time of care transition, making clinical pharmaceutical intervention essential in order to improve the use pattern of stress ulcer prophylaxis in hospital institutions.

The data collected showed a positive correlation regarding the professional's contract with the institution, in which the prescriptions made in the period were mostly prepared by the institution's medical professionals (part of the staff) and that they were responsible for 72.17% of the prescriptions with stress ulcer prophylaxis without a clear indication. In their study, Farsaei et al.[14] state that the proportion of the use of stress ulcer prophylaxis respecting the clinical practice guidelines is higher in teaching hospitals. On the other hand, Singh et al.[7] did not demonstrate an association between the type of hospital or monitoring performed

by a physician or by residents as a risk factor for the inappropriate use of Acid Suppression Therapy. Thus, regardless of the type of hospital or employment contract, there is a clear need to develop specific protocols for stress ulcer prophylaxis in order to allow for standardization of therapeutic indications.

Observing all prescriptions during the study period, it was possible to quantify the use of acid-suppressing medications for stress ulcer prophylaxis and, by multiplying it by the monetary value of the direct purchase of these drugs, it was noticed that the hospital costs associated with the unjustified use of stress ulcer prophylaxis, in a one-year period, would total US$ 11,728.21. However, it is likely that these data significantly underestimate the true burden on the health system, as adverse effects and results were not taken into account in this analysis.

In this context, Heidelbaugh and Inadomi[1] identified even higher expenses resulting from inadequate prescriptions for stress ulcer prophylaxis, totaling an annual expenditure of US$ 111,791 in Michigan's University Hospital. Likewise, a study conducted in South Korea found similar results and, in four years of research, it observed an expenditure of US$ 40,175 due to the inadvertent use of this preventive pharmacotherapy.[17] On the other hand, the study by Belfield et al.[5] presented a significant reduction in expenses related to this type of prescription through the intervention of pharmacists in the health service. This resulted in a significant 87% reduction in drug acquisition costs per patient and a projected annual savings of more than US$ 37,000 for the institution under study, if the professionals' care was carried out continuously.

Based on the results, it becomes fundamental to develop intervention strategies to reduce the inappropriate use of acid suppressants, especially when the justification is SU prophylaxis, based on guidelines from recognized societies that are also for patients not admitted to ICUs, associated with up-to-date content on the pathophysiology involved in this type of gastrointestinal injury and a careful assessment of the patient's underlying health condition and individual risk factors.

The study presents some limitations, including the fact that it was carried out only in a single hospital and, despite the data being corroborated by the literature, they may not reflect the reality of all institutions. It is also worth noting that the outcomes of the use of Acid Suppression Therapy were not evaluated, as well as the costs related to the treatment, in addition to the use of the medications.

Conclusion

The results confirm that the institution analyzed presented a high frequency of inappropriate use of Acid Suppression Therapy for stress ulcer prophylaxis according to the ASHP and EAST guidelines during hospitalization in non-critical patient care sectors, a reality that proved to be common in other institutions. The study showed that factors such as hospitalization time and the role of the prescribing professional exerted a significant influence on such practice. It is noteworthy that the use of Acid Suppression Therapy without established criteria can significantly burden the public health system, either directly or indirectly. Based on the findings, intervention measures are needed, including the implementation of institutional protocols and education of prescribers on the use of Acid Suppression Therapy during hospitalization in all phases of care transition.

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Collaborators

SNA, YSS, JAS, ASM: elaboration of the project; data collection; analysis and interpretation of the results; writing and critical review of the article; DTS, IVG: analysis and interpretation of the results; writing and critical review of the article. All the authors approved the final version to be published and assume responsibility for all information of the paper, ensuring the accuracy and integrity of any of its parts.

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Conflict of interest statement

The authors declare no conflicts of interest regarding to this article.

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