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Quality of stress ulcer prophylaxis in a universitary hospital in Brazil

Qualidade das prescrições de profilaxia para lesão aguda de mucosa gástrica em um hospital universitário no Brasil

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ABSTRACT: *Aims*: though recommended for patients with high risk for upper gastrointestinal bleeding, stress ulcer prophylaxis is not always correctly prescribed in most hospitals. The objective of this study is to evaluate the adequation of stress ulcer prophylaxis in a universitary hospital. *Methods*: a cross-sectional analysis of the medical prescriptions of patients hospitalized in clinical, surgical and critical units of a universitary hospital was performed during 30 days. Prescriptions of patients using gastric protectors for a non-prophylactic purpose were excluded. The criteria for stress ulcer prophylaxis evaluation was based on recommendations from UpToDate® online database. *Results*: 358 prescriptions were analyzed, of which 17 were excluded. Of the 341 prescriptions included for stress ulcer analysis, 205 (60.1%) prescriptions were incorrect. Overprescription was the main reason of inadequacy, found in 175 cases (85.4%). The inadequacies in the prescriptions of the surgical units (80%) were higher when compared to the clinical (54.1%) and critical units (52.5%) ($p < 0.001$). *Conclusions*: important rates of incorrect stress ulcer prophylaxis prescriptions were found, mainly due to overprescription. Higher rates of inadequacies were found in surgical units. This scenario highlights the lack of scientific guidelines, efficient local protocols and professionals' knowledge or acceptance regarding stress ulcer prophylaxis.

Keywords: Disease prevention; Gastric ulcer/prevention & control; Hospitalization; Prescriptions; Proton pump inhibitors; Histamine H2 antagonists.

RESUMO: *Objetivos*: Ainda que preconizada para pacientes de alto risco de sangramento gastrointestinal alto, a profilaxia para lesão aguda de mucosa gástrica (úlcera de estresse) nem sempre é prescrita corretamente na maioria nos serviços hospitalares. O objetivo deste estudo é avaliar a adequação das prescrições dessa profilaxia em um hospital universitário brasileiro. *Métodos*: Realizada uma análise transversal de prescrições para pacientes internados em unidades clínicas, cirúrgicas e críticas de um hospital universitário durante 30 dias. Foram excluídas as prescrições de pacientes em uso de protetores gástricos com finalidade diferente da profilática. Os critérios de avaliação da profilaxia para úlcera de estresse foram baseados nas recomendações da base online de dados *UpToDate®*. *Resultados*: 358 prescrições foram analisadas e, dessas, 17 foram excluídas. Das 341 prescrições incluídas, 205 (60,1%) estavam inadequadas. A principal razão de inadequação foi a sobreprescrição, encontrada em 175 casos (85,4%). As inadequações foram maiores em unidades cirúrgicas (80%) quando comparadas às unidades clínicas (54,1%) e críticas (52,5%) ($p < 0,001$). *Conclusões*: Foram registradas expressivas taxas de inadequação para a profilaxia de lesão aguda de mucosa gástrica, principalmente devido ao excesso de prescrições. As unidades cirúrgicas foram responsáveis pelas maiores taxas de inadequação. Esse cenário evidencia a escassez de diretrizes científicas, protocolos locais eficientes e conhecimento ou aceitação dos profissionais acerca da profilaxia para leão aguda de mucosa gástrica.

Descritores: Prevenção de doenças; Úlcera gástrica/prevenção & controle; Hospitalização; Prescrições; Inibidores da bomba de prótons; Antagonistas dos receptores histamínicos H2.

Institution: *Hospital de Clínicas da Universidade Federal do Paraná*. *Ethical Approval:* This study was approved by the Research Ethics Committee of *Hospital de Clínicas da Universidade Federal do Paraná* in 22/06/2017. Document Nº 2.131.561.

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INTRODUCTION

Being admitted to any hospital in the world can be risky. Up to 10% of patients suffer damage during hospitalization, half of which could have been avoided[1].

Acute gastric mucosa injury (AGMI), or "stress ulcer", is a condition related to the inflammatory and sympathetic response to trauma, burns, shock or sepsis[2]. The concept of AGMI ranges from incidental, superficial and asymptomatic endoscopic findings to gastrointestinal bleeding, whether hidden or evident[3].

AGMI mainly affects the regions of the body and gastric fundus and seems to be related to the inflammatory and sympathetic response to stress, causing reduction of local splanchnic perfusion with reduction of gastric bicarbonate secretion and increased secretion of pro-inflammatory cytokines and catecholamines. Consequently, destruction of the mucus barrier occurs, which, associated with the reduction of gastric motility, leads to the erosive process in the stomach epithelium by acid action[4]. In addition to increasing the risk of death by 1 to 4 times, bleeding from the upper gastrointestinal tract appears to be responsible for an increase of 4 to 8 days in the length of stay in the intensive care unit[5]. Between 0.6-8.5% of critically ill patients have evident intestinal bleeding, which can reach 15% if the prophylaxis with proton pump inhibitors (PPI) is not performed[4]. Studies have already demonstrated the effectiveness of AGMI prophylaxis with gastric protectors for high-risk situations[6]. However, in the current scenario, inadequacies are still marked, with an evident excess of prescriptions in the national and worldwide scenario[7-9].

For these reasons, it is suspected that, even in a university hospital, prophylaxis for AGMI does not comply with the recommended recommendations. The objective of this study is to evaluate the adequacy level of prophylaxis prescriptions for AGMI for patients admitted to a university hospital, a regional reference in medical education.

METHODS

This is a cross-sectional analytical study that evaluated the quality of AGMI prophylaxis prescpriptions of patients older than 18 years who were hospitalized from July 19, 2017 to August 19, 2017 in either an internal medicine ward, a surgical ward or the intensive care unit from a teaching hospital. Prescriptions that included gastric protectors for purposes other than prophylactic were excluded. Prescriptions of patients whose clinical conditions interfered in AGMI prophylaxis indication were also excluded.

Due to the scarcity of updated and established guidelines about AGMI prophylaxis, recommendations of the online database UpToDate®[10], which gathers well-referenced information and in accordance with the most up-to-date scientific evidence, were considered as evaluation criteria.

High risk criteria were sufficient to indicate prophylaxis:

1) Coagulopathy - considered platelet count < 50,000/m³ or international normalized ratio (INR)> 1.5 or activated partial thromboplastin time > 2 times the control;

2) Mechanical ventilation beyond 48 hours;

3) History of bleeding or ulcerations in the gastrointestinal tract in the last year;

4) Cranio-cerebral injury;

5) Spinal-cord trauma;

6) Burned patients;

7) Two or more of the following minor criteria:

a. Sepsis

b. Time in intensive care unit for more than one week;

c. Occult gastrointestinal bleeding for more than 6 days;

d. Glucocorticoid therapy (at least 250 mg of hydrocortisone or equivalent).

The following prophylactic prescriptions for AGMI were considered appropriate, when indicated:

1) Omeprazole 20 mg orally or intravenously, once daily;

2) Omeprazole 40 mg orally, once daily;

3) Ranitidine 150 mg orally, twice a day;

4) Ranitidine 50 mg intravenously, 3 times a day.

The prescription evaluation process is illustrated in Figure 1.

The flowchart illustrates how prescriptions for AGMI prophylaxis were evaluated. When there was an indication for prescription but gastric protectors were not prescribed, the prescription was classified as "underprescription". When there was an indication and the drugs were prescribed, a new stage was evaluated: the analysis of the dosage. If it was inadequate, the category was "inadequate posology"; if appropriate, prescription was considered "adequate prophylaxis". On the other hand, when there was no indication for prophylaxis, but gastric protectors were prescribed, "overprescription" was characterized; when not indicated, and not prescribed, "adequate prophylaxis" was characterized.

This study was approved by the Research Ethics Committee of the Clinical Hospital of the Federal University of Paraná (Project number: 775445 | Approval number: 2.131.561 | Date of approval: June 22, 2017) and prior to the beginning of the daily data collection, the attending physician of each patient signed an informed consent form. The collected data were stored in a Microsoft Excel spreadsheet. The adequacy level of prophylaxis was determined according to the matchup between the current conduct and the recommended ones by the guidelines.

Results obtained by qualitative variables were described by frequencies and percentages. For inference of association between two qualitative variables, the chi-square and Fisher's exact tests were performed. The considered statistical significance was 5%. Data were analyzed by R Core Team Software, version 3.4.0[11].

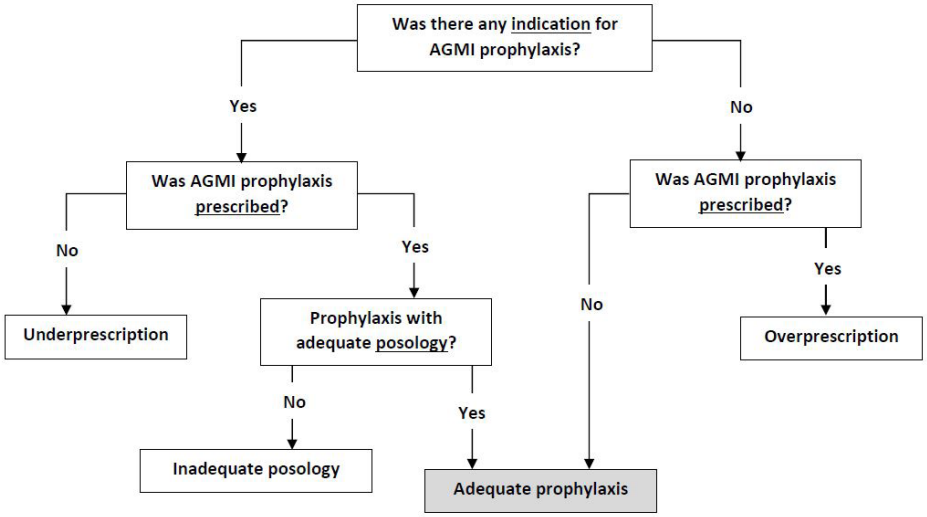

Figure 1 – Prophylaxis prescriptions evaluation flowchart

RESULTS

Table 1 presents the general distribution of the sample. 358 prescriptions were selected, 17 (4.75%) of which were excluded as shown in Figure 2. Figure 3 presents the overall results of the study. This analysis was subdivided according to the inpatient units in Tables 2 and 3.

Table 1 – Distribution of selected prescriptions by inpatient unit

	Inpatient Unit			General
	Internal medicine	Surgery	Intensive care	
Number of prescriptions	170 (47.5%)	85 (23.7%)	103 (28.8%)	358 (100%)
Gender				
Men	74 (43.5%)	45 (52.9%)	55 (53.4%)	174 (48.6%)
Women	95 (55.9%)	40 (47.1%)	48 (46.6%)	183 (51.1%)
Transgender woman	1 (0.6%)	-	-	1 (0.3%)
Age (years)	60.0 ± 15.8	51.3 ± 16.6	59.3 ± 17.1	57.7 ± 16.7

Note: Internal medicine wards represent almost half of the sample, with 170 prescriptions.

Table 2 - Analysis of AGMI prophylactic prescriptions adequacy level according to inpatient unit

	INPATIENT UNIT		
	Internal medicine	Surgery	Intensive care
Correct prescriptions	72 (45.86%)	17 (20%)	47 (47.47%)
Incorrect prescriptions	85 (54.14%)	68 (80%)	52 (52.53%)

Note: The highest rate of inadequacy was found in surgical wards (80%), followed by internal medicine wards (54.14%) and intensive care units (52.53%). Fisher's exact test; $p < 0.001$.

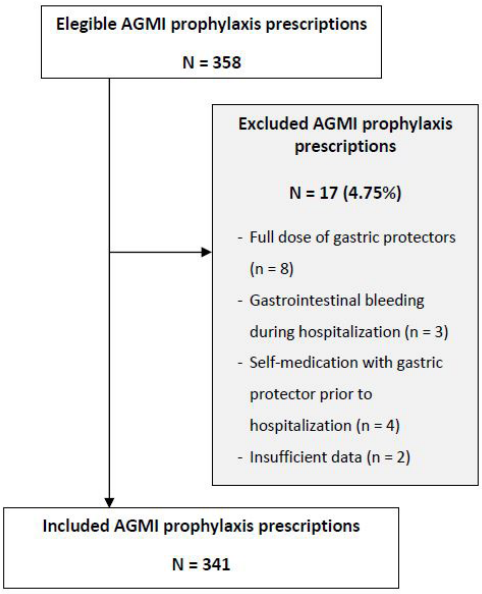

Figure 2 – Prescriptions included in and excluded from the study. 358 prescriptions were selected for analysis, 17 of which were excluded. 341 prescriptions were included for analysis

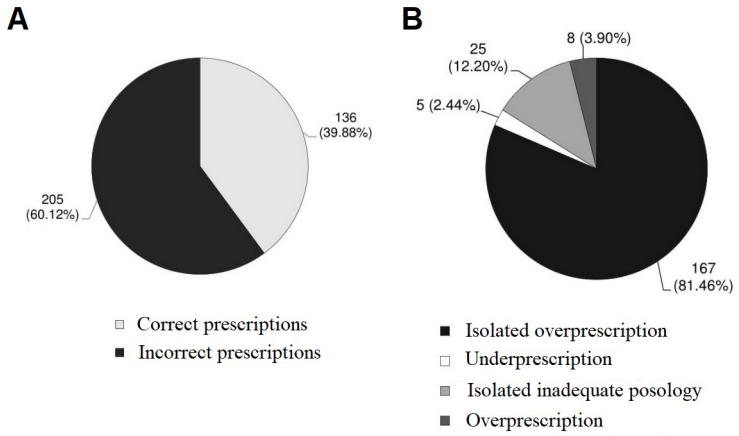

Figure 3 – General analysis of AGMI prophylaxis. Graph A illustrates the overall adequacy level of AGMI prophylaxis prescriptions, and Graph B correlates the overall cause of inadequacy among incorrect AGMI prescriptions

Table 3 - Cause of inadequacy of incorrect AGMI prescriptions according to inpatient unit

	Cause of inadequacy		
	Overprescriptions	**Underprescriptions**	**Inadequate posology**
Internal medicine wards	76 (89.41%)	2 (2.35%)	11 (12.94%)
Surgery wards	66 (97.06%)	1 (1.47%)	1 (1.47%)
Intensive care units	33 (63.46%)	2 (3.85%)	21 (40.38%)

Note: In all units, overprescription was the most prevalent cause of inadequacy. Surgical wards stood out for presenting the highest inadequacy levels in this modality (97.06%), followed by internal medicine wards (89.41%) and intensive care units (63.46%). Intensive care units presented the highest rates of inadequate posology (40.38%). Chi-square and Fisher's exact tests; $p < 0.001$.

Surgical wards presented the highest inadequacy rates (80%, versus 54.14% in internal medicine wars and 52.53% in intensive care units, $p < 0.001$) and overprescription was the most common cause of inadequacy in all inpatient units.

AGMI prescriptions with inadequate posology (n = 33) had the following presentation: omeprazole 40 mg once daily intravenously (n = 20); omeprazole 40 mg twice daily intravenously (n = 2); ranitidine 50 mg twice daily intravenously (n = 10); simultaneous prescription of omeprazole and ranitidine (n = 1).

DISCUSSION

Since its appearance in the mid-1980s, PPIs have been widely used, with exponential growth in their prescriptions. In the last decade, they have been among the 10 most consumed drugs worldwide[12]. This fact – associated with the outdated knowledge of health professionals about the implications of AGMI and its prophylaxis – has created a worrying scenario in the prescriptions of these drugs in a global scale.

Although dramatic, the results presented here regarding the use of gastric protectors do not seem to be an isolated case. The general inadequacy rate of AGMI prophylactic prescriptions in this analysis was 60.12%, compatible with other studies in the literature. In 2003, Parente et al.[7] demonstrated that around 68% of the prescriptions for gastric protectors were inadequate in an Italian university hospital. In 2006, Pham et al.[8] demonstrated that 71% of non-critical patients at University of Michigan Hospital received gastric suppressors, but only 10% of them had acceptable indications for that. In Brazil, the scenario is similar and, in 2006, a study demonstrated that 71% of patients with low or intermediate risk for AGMI had received gastric protectors, a situation without clear scientific support to indicate prophylaxis. On the other hand, this same study points out that 25.7% of high-risk patients did not receive prophylaxis for AGMI, despite having the indication[9]. This is a quite distant number when compared to the overall underprescription rate of 2.44% presented in the present study.

In this analysis, the most impressive results were found in surgical wards, with 80% of inadequacy, mostly due to overprescription, which was precisely the most expressive cause of inadequacy in the entire study. It is possible that the overprescription occurs due to the growing popularization of PPIs associated with the ignorance of the medical community about the proper indications for AGMI prophylaxis and side effects of those medications. It is also possible that the attending physician, in order to minimize the risk of AGMI in his patients, may end up disregarding the burden that his overprescription may cause on the health system. In 2006, the additional cost related to inadequate prescriptions for AGMI prophylaxis was estimated at US$111,791.00 per year for non-critical patients under the care of six units of the health facilities of University of Michigan Health Service, including outpatient and inpatient[13]. Studies on the financial impact of this practice in the Brazilian scenario are relevant and should be encouraged, especially when considering the lack of resources and investments that Brazilian public hospitals face every day.

The indication of AGMI prophylaxis is still much debated in the literature. Although the risk factors for stress ulcer are well known, recent studies have questioned the real effectiveness of using gastric protectors for AGMI prophylaxis, as well as the benefit of their prescription pondering the side effects of the drugs[14]. The most reported adverse effects of PPIs are nosocomial pneumonia and *Clostridium difficile* infection, but other possible reactions include micronutrient malabsorption and acute interstitial nephritis. The incidence and clinical relevance of these complications still have inconsistent data[15-17], but it does not justify that the prescription of gastric protectors should not be a concern of the assistant physician, since prophylaxis is still recommended by the vast majority of current literature, with precise criteria of indication, as previously showed here[10,18]. It should be noted, however, that the absence of an established reference guideline for AGMI prophylaxis creates measurement bias in any proposed methodology on the topic that assesses the quality of prescriptions.

It is possible that this study suffered interference from the Hawthorne effect, characterized, in this case, by a positive change in the prescribing pattern of the attending physicians after application of the Free and Informed Consent Form. This bias, inherent in the methodology, may have been considerably reduced since data collection always occurred after prescription of the day has been registered in the wards and intensive care units. In this context, we raise the hypothesis that we may be facing a lessened representation of the prophylactic prescription scenario. In view of this concern, future studies with a different methodology are opportune.

It is also recommended that future studies deepen the characterization of these problems in the local population to better define the current scenario. It is also suggested to expand the methodology for analyzing other potentially preventable clinical entities that cause damages related to hospitalization, such as *delirium* and pressure ulcers.

CONCLUSIONS

The present study confirmed the proposed hypothesis by revealing significant rates of inadequacy levels of prophylactic prescriptions for AGMI in patients admitted to a university hospital, with the greatest inadequacies observed in surgical wards. Thus, the study justifies the need for interventions that optimize this important safety practice for hospitalized patients. So, it is expected that, in the future, being admitted to any hospital in the world is not so risky.

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Author's participation: *Fioramonte GS*: bibliographic review, data collection, data interpretation, manuscript writing (Abstract, Introduction, Discussion and References). *Brito GD:* bibliographic review, data collection, data interpretation, writing of the manuscript (Abstract, Introduction, Methods). *Marques GL*: idealization of the study, design of the analysis, statistical analysis, writing of the text (Introduction, Discussion and Conclusion), final revision of the manuscript.

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The authors take responsibility for the content of this text.

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