IDENTIFICATION OF RISKS AND PRACTICES IN THE USE OF HIGH ALERT MEDICATIONS IN A UNIVERSITY HOSPITAL

IDENTIFICAÇÃO DE RISCOS E PRÁTICAS NA UTILIZAÇÃO DE MEDICAMENTOS POTENCIALMENTE PERIGOSOS EM HOSPITAL UNIVERSITÁRIO

IDENTIFICACIÓN DE RIESGOS Y PRÁCTICAS EN EL USO DE MEDICAMENTOS POTENCIALMENTE PELIGROSOS EN UN HOSPITAL UNIVERSITARIO

Objective: to analyze the prescriptions of high alert medications and to identify the practices adopted in the dispensing in a high complexity public university hospital, proposing strategies to prevent adverse events. Methods: a cross-sectional study carried out with 566 prescriptions, in three shifts, from April to December 2016. The identification of practices for dispensing was by direct observation with the application of a checklist based on the protocol of the Ministry of Health (MH)/National Health Surveillance Agency (ANVISA) (Ministério da Saúde/Agência Nacional de Vigilância Sanitária). A non-parametric chi-square test of independence was used to assess the association between prescriptions with and without high alert medications and inpatient units. Results: more than half of the prescriptions (56.6%) contained two or more high alert medications and almost all were injectable (95.4%), mainly opioid analgesics (31.2%), glucose 50% (24.7%), and NPH and regular insulin (24.3%). The prescription rate corresponded to 18.2%. The main practices that represented risks were the following: collective distribution of potassium chloride and insulin; lack of warning labels; non-existent double check; presence of interruption/distraction sources in 43.9% of the prescriptions met. Conclusion: despite being frequent in more than half of the prescriptions, the practices adopted in the dispensing of high alert medications were insufficient for a safe dispensing, which could compromise the administration of these drugs and cause harm to the patients. It is important to implement the MH/ANVISA protocol for preventing medication errors, in consonance with the third global challenge of the World Health Organization (WHO).

Keywords: Medication Errors; Patient Safety; Risk Management; Medication Systems.

ABSTRACT

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Keywords: Medication Errors; Patient Safety; Risk Management; Medication Systems.

RESUMO

Objetivo: analisar as prescrições de medicamentos potencialmente perigosos e identificar as práticas adotadas na dispensação em hospital universitário público de alta complexidade, propondo estratégias para prevenção de eventos adversos. Métodos: estudo transversal realizado com 566 prescrições, em três turnos, no período de abril a dezembro de 2016. A identificação de práticas para dispensação foi por observação direta com aplicação de checklist baseado no protocolo do Ministério da Saúde (MS)/Agência Nacional de Vigilância Sanitária (ANVISA). Utilizou-se teste não paramétrico do qui-quadrado de independência para avaliar a associação entre prescrições com e sem medicamentos potencialmente perigosos e unidades de internação. Resultados: mais da metade das prescrições (56,6%) continha dois ou mais medicamentos potencialmente perigosos e unidades de internação. Resultados: mais da metade das prescrições (56,6%) continha dois ou mais medicamentos potencialmente perigosos e quase todos injetáveis (95,4%), principalmente analgésicos opioides (31,2%), glicose 50% (24,7%) e insulina NPH e regular (24,3%). A taxa dos prescritos correspondeu a 18,2%. As principais práticas que representaram riscos foram: distribuição coletiva
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INTRODUCTION

High Alert Medications (HAMs), are those that naturally require special attention, due to their greater potential to cause catastrophic harms to patients in case of failure in their use. These medicines are considered a priority in the third global challenge of the World Health Organization (WHO), whose goal is to reduce by 50% the preventable harms caused by medicines by 2022.1

Failures are often not related to human negligence, but to the management of deficient and poorly designed systems and processes.2 In addition, a number of studies have revealed that the health professionals are unaware of the HAMs, even those they use in their routines. This deficiency may be related to the training of these professionals in university courses. This situation also affects the establishment of measures to prevent serious adverse events, making patients vulnerable to medication errors.3-5

A research study on deaths associated with the use of medicines showed that the classes most involved belonged to the HAMs, especially opioids, benzodiazepines, anticoagulants, and insulin.6 Another recent study on incident reporting revealed that 188 (23.9%) pharmacovigilance notifications were related to HAMs. Of these, 1.06% were about dispensing and 0.53% about the administration of these medicines. This fact seems worrying when considering that there is undernotification.7

It is important to understand the magnitude of the use of the HAMs in the institutions and whether the processes that involve prescription, dispensing, administration, and monitoring of their use are adequate. The identification of risks in the process of using HAMs emphasizes the need for strategies that prevent medication errors according to the reality of each institution.8

Considering the relevance of the theme for public health, this research seeks to analyze the HAMs prescriptions and to identify the practices adopted in the dispensing of these medicines in a public university hospital, in addition to proposing strategies for the prevention of adverse events, thus providing information to improve the knowledge of professionals and risk management.

METHODS

Study design and research site

A cross-sectional study of HAM prescriptions and dispensing practices in the pharmacy of the adult unit in a high complexity public university hospital. This unit was chosen because it has a higher number of highly complex procedures than the maternal-child unit. The adult unit has 312 hospital beds divided into medical and surgical clinics, intensive care unit (ICU), and general and cardiac ICU, among others. Medicines dispensing is performed by individualized dose for a period of 24 hours. The medicines are dispensed from the electronic prescription printed at the pharmacy. Then, the pharmacy technicians do the calculation of doses and the pharmacist analyzes and reviews the prescriptions. After the analysis, the technicians pack the medicines in plastic bags per patient (called medicines kits). After packaging, the kits containing the medicines are delivered to the Nursing staff for...
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• Qualitative criteria: pharmacy with a reserved environment for dispensing medicines; exclusive environment for double check; identification of HAM storage locations (bins); alert identification on HAM packages; list of HAM with indication of maximum doses, method of administration, indication and usual dose; and standard operating procedure (SOP) with specific recommendations for dispensing HAM.

• Quantitative criteria (considering the number of prescriptions met): presence of at least one pharmacist; analysis of the prescriptions regarding the calculations made by the pharmacy technician; flow restricted to pharmacy professionals; double check held at the same time by the pharmacy technician who delivered the medicines and by the representative of the Nursing team who received them; clean environment (no dirt on the floor, counter, bench, and bins) and organized (counter, medicines bins, boxes on the countertops, and excess forms checked); environment with control of interruption/distraction sources (use or not use of television, music, cell phones, and/or parallel conversations during dispensing).

The form of dispensing concentrated electrolytes and other high-risk medications from the “A PINCH” group belonging to the hospital’s HAM list was also considered. "A PINCH" is an acronym for high-risk medications: Anti-infectives, Potassium and other electrolytes, Insulin, Narcotics and sedatives, Chemotherapy, Heparin and other anticoagulants, the majority of which are HAMs.1,14

Ethical procedures

This research was approved by the Ethics Committee on Research involving human beings with CAAE Nº 47169815000005086.

Sample and data collection

The target population of this study was made up of 8,460 medical prescriptions containing 83,201 medicines. Considering the losses in the data collection period (11%), the number of prescriptions analyzed was 566, with a total of 5,563 medicines. Collection took place between April 7th, 2016 and December 28th, 2016, in 47 days. At the beginning of each month, a collection date corresponding to each day of the week (Monday to Sunday) was drawn, including holidays. For that, a table of random numbers was used. In those days, the shift was also drawn. The days and shifts drawn for collection were not revealed to the dispensing team, in order to lessen the Hawthorne effect.9 The prescriptions were listed and those that made up the sample were drawn.

HAM profile

The HAMs were identified in the prescriptions from a list of 53 medicines, prepared by the pharmacy based on the literature.9 A spreadsheet was used as data collection instrument, in which the following items were recorded: name of the HAMs; distribution inpatient unit; pharmaceutical form (only oral solids and injectables); and classification according to the Anatomical Therapeutical Chemical (ATC) code.11

Observation of the environment and identification of practices in dispensing HAM

The observation of the environment and the identification of the dispensing practices were carried out by the lead author with the assistance of a resident pharmacist, using the direct observation technique adapted by the WHO.12 This technique, as well as the collection instrument, was tested for four days before starting data collection. No action or comment was made regarding the pharmacy service, and the dispensing process remained unchanged to minimize the observation bias or Hawthorne effect.9 The lead author coordinated and supervised data collection and completing the checklist, which addressed the existence or not of the following qualitative and quantitative criteria based on the literature.8,13

• Qualitative criteria: pharmacy with a reserved environment for dispensing medicines; exclusive environment for double check; identification of HAM storage locations (bins); alert identification on HAM packages; list of HAM with indication of maximum doses, method of administration, indication and usual dose; and standard operating procedure (SOP) with specific recommendations for dispensing HAM.

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Data analysis

Data was analyzed using descriptive statistics in the IBM SPSS Statistics 20 (2011) program, and the non-parametric chi-square test of independence ($\chi^2$) was used to assess the association between prescriptions with and without HAMs and inpatient units. The level of significance applied was 5%, that is, it was considered significant when $p<0.05$.

Results

From April 7th to December 28th, 2016, 566 prescriptions were collected. Of these, 380 (67.1%) contained 724 HAMs out of a total of 3,974 medicines. The HAMs accounted for 18.2% of the prescribed medicines.

The 724 HAMs in this study were classified according to the ATC code: opioid analgesics (N02A); tramadol, morphine, and methadone (31.2%); intravenous solutions (B05B): glucose 50% (24.7%); medicines used in diabetes (A10A): NPH and regular insulins (24.3%); antithrombotic agents (B01A): heparin and warfarin (11.1%); and other classes (N, C, A, B): benzodiazepines.
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(midazolam and diazepam), antihypertensives (clonidine), vasodilators (dopamine, dobutamine, milrinone, and sodium nitroprusside), and electrolytic repositors (sodium chloride, potassium chloride, and calcium gluconate) corresponded to 8.7%. Among those prescribed, a higher percentage of injectables was found (95.4%) (Table 1).

Of the prescriptions that contained HAMs, 56.6% contained two or more of these medicines (Table 2) and there was a significant association (p<0.05) in the proportions of prescriptions with or without HAMs per hospitalization unit. It was verified that the neuro-orthopedics surgical clinic (75.9%), wards A and B (74.4%), and the cardiac ICU (74.1%) are the ones with the highest prevalence of HAMs in the prescriptions (Table 3).

Table 1 - High alert medications (HAMs) prescribed and dispensed by a pharmacy in a high complexity public university hospital. São Luís - MA, 2016

<table>
<thead>
<tr>
<th>Medications prescribed</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic Classes (ATC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid analgesics (N02A)</td>
<td>226</td>
<td>31.2</td>
</tr>
<tr>
<td>Intravenous solutions (Glucose 50%) (B05B)</td>
<td>179</td>
<td>24.7</td>
</tr>
<tr>
<td>NPH and regular insulins (A10A)</td>
<td>176</td>
<td>24.3</td>
</tr>
<tr>
<td>Antithrombics (B01A)</td>
<td>80</td>
<td>11.1</td>
</tr>
<tr>
<td>Others (N, C, A, B)</td>
<td>63</td>
<td>8.7</td>
</tr>
<tr>
<td>Pharmaceutical Forms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable drugs</td>
<td>691</td>
<td>95.4</td>
</tr>
<tr>
<td>Oral drugs</td>
<td>33</td>
<td>4.6</td>
</tr>
<tr>
<td>Total</td>
<td>724</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Caption: N- Nervous system; A- Digestive system and metabolism; B- Blood and hematopoietic organs; C- Cardiovascular system; NPH- Neutral Protamine Hagedorn

It was observed that there was an environment in the pharmacy reserved for dispensing, as well as that the exclusive environment for double checks and the storage locations (bins) were identified. The HAMs dispensed to be administered did not have a differentiated identification, the list with names and presentations of these medicines did not have the indication of maximum doses, form of administration, indication, and usual dose and, in the SOP, there were no specific recommendations for dispensing HAMs (Table 4).

The pharmacist was present at the time of fulfilling all the prescriptions for the morning and afternoon shifts (n=338), but absent in 7.1% (n=27) of the prescriptions, all in the night shift, which represented 64.3% of the total prescriptions in this shift (n=42). There was a greater number of prescriptions analyzed (n=365) than pharmacists present (n=353), because 3.1% of the prescriptions served at night were reviewed in the afternoon shift. There were professionals present unrelated to the dispensing environment in 2.1% of the prescriptions. This happened in the morning shift. In 96.3% of the cases, the environment was clean and, in almost half of the prescriptions, it was disorganized. There was no use of any interruption/distraction source during the fulfillment of 56.1% of the prescriptions. Regarding the prescriptions served in the midst of interruption/distraction sources (n=167), in 77.8% there were parallel conversations, in 28.1% the use of a cell phone, and 4.2% accounted for other sources. Double checking was non-existent (Table 5). In addition, electrolytes such as potassium chloride and insulin were distributed collectively to inpatient units.

DISCUSSION

More than half of the prescriptions contained two or more high alert medications (HAMs) and almost all were injectable. The main ones were the following: opioid analgesics, glucose 50%, NPH and regular insulins, heparin, and warfarin. The HAMs rate corresponded to 18.2% of the prescribed medicines. The main practices that can compromise patient safety were the following: collective distribution of concentrated injectable potassium chloride and insulin, lack of warning labels, absence of pharmacists in the fulfillment of most prescriptions in the night shift, non-existent double checking and interruption/distraction sources like side conversations and use of a cell phone during dispensing. These practices observed during the present study demonstrate the need to improve the work processes.

Opioids are a class of HAM widely used in sedoanalgesia and this may justify the frequent use of such medicines in surgical clinics and ICUs in the present study. The literature reports that the patients admitted to the ICU are more vulnerable to harms, as a greater number of drugs are used. It was also found that there were prescriptions that had more than three HAMs. These data draw the attention to the need to establish safe practices that act as barriers to protect the patients. However, such measures can be neglected for lack of knowledge of the potential for harm from HAMs.

Table 2 - Number of high alert medications (HAMs) per prescription in a high complexity public university hospital. São Luís - MA, 2016

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriptions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 HAM</td>
<td>165</td>
<td>43.4</td>
</tr>
<tr>
<td>2 HAMs</td>
<td>120</td>
<td>31.6</td>
</tr>
<tr>
<td>3 HAMs</td>
<td>66</td>
<td>17.4</td>
</tr>
<tr>
<td>More than 3 HAMs</td>
<td>29</td>
<td>7.6</td>
</tr>
<tr>
<td>Total</td>
<td>380</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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As for NPH and regular insulins, a vial was distributed to be administered to several patients, and there may be an overdose administration, leading to hypoglycemia, irreversible encephalopathy, pulmonary edema, liver damage, hypoglycemic coma, and death. Subdose can also result in hyperglycemia, followed by ketoacidosis.19 Thus, controlling the use of these medicines by the pharmacy and the pharmaceutical analysis of the prescriptions were impaired, since these drugs were not dispensed together with the others in the kit.

At the pharmacy, the bins (plastic boxes) for the storage of high alert medications had a small red label to draw the attention to the HAMs at the time of dispensing. However, the packaging of the medicines to be distributed did not have any type of warning signs, with the possibility of errors during administration. On this regard, Porto20 showed that visual communication is a form of quick identification and easy to understand during the handling, administration, and/or transportation of HAM. However, the use of color coding is not recommended by the Institute for Safe Medication Practices (ISMP), due to the possibility of confusion with several colors used today in hospitals. Visual pollution in hospitals hinders more than improves patient safety.21 Despite their importance, HAMs do not come from the pharmaceutical industry with a differentiated identification. The current legislation in Brazil on packaging and labels is outdated in relation to the safe use of medicines. The signaling of HAMs is in charge of hospital pharmacies, leading to rework and more possibilities for errors, as a new stage is added to the already complex process of medicines use.

There is a need for the ANVISA to update the rules in force in conjunction with the pharmaceutical industries and with all the other actors that participate in this area, so that the medicines are already duly identified as being of high risk. This would reduce costs for health institutions, including personnel. In addition, the need to standardize colors and symbols must also be considered, as there is a hodgepodge in Brazilian health institutions.

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Table 3 - Association between prescriptions with and without high alert medications (HAMs) per inpatient unit. High complexity public university hospital. São Luís - MA, 2016

<table>
<thead>
<tr>
<th>Hospitalization unit</th>
<th>Prescriptions with HAMs</th>
<th>%</th>
<th>Other prescriptions</th>
<th>%</th>
<th>Total of prescriptions</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA and SCB</td>
<td>148</td>
<td>74.4</td>
<td>51</td>
<td>25.6</td>
<td>199</td>
<td>35.2</td>
</tr>
<tr>
<td>NOSC</td>
<td>60</td>
<td>75.9</td>
<td>19</td>
<td>24.1</td>
<td>79</td>
<td>14.0</td>
</tr>
<tr>
<td>MC</td>
<td>107</td>
<td>61.1</td>
<td>68</td>
<td>38.9</td>
<td>175</td>
<td>30.9</td>
</tr>
<tr>
<td>TX</td>
<td>22</td>
<td>44.9</td>
<td>27</td>
<td>55.1</td>
<td>49</td>
<td>8.7</td>
</tr>
<tr>
<td>Adult ICU</td>
<td>23</td>
<td>62.2</td>
<td>14</td>
<td>37.8</td>
<td>37</td>
<td>6.5</td>
</tr>
<tr>
<td>Cardiology ICU</td>
<td>20</td>
<td>74.1</td>
<td>7</td>
<td>25.9</td>
<td>27</td>
<td>4.8</td>
</tr>
<tr>
<td>Total</td>
<td>380</td>
<td>67.1</td>
<td>186</td>
<td>32.9</td>
<td>566</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Caption: Chi-square test of independence ($\chi^2$) = 22.34, p 0.005; SCA and SCB- Surgical Clinics, wings A and B; NOSC- Neuro-Orthopedics Surgical Clinic; MC- Medical Clinic; TX- Kidney Transplantation; ICU- Intensive care unit

Table 4 - Qualitative criteria of the environment and practices adopted in the dispensing of high alert medications (HAMs) prescribed in a high complexity public university hospital. São Luís - MA, 2016

<table>
<thead>
<tr>
<th>Qualitative criteria</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reserved environment for dispensing medications</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Exclusive environment for double checks</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Signaling of HAM storage locations</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Alert label for HAM</td>
<td>-</td>
<td>x</td>
</tr>
<tr>
<td>Complete HAM listing</td>
<td>-</td>
<td>x</td>
</tr>
<tr>
<td>SOP with specific recommendations for dispensing HAMs</td>
<td>-</td>
<td>x</td>
</tr>
</tbody>
</table>

Caption: SOP- Standard Operating Procedure

Table 5 - Quantitative criteria of the environment and practices adopted in the dispensing of high alert medications (HAMs) prescribed in a high complexity public university hospital. São Luís - MA, 2016. N=380 prescriptions

<table>
<thead>
<tr>
<th>Quantitative criteria</th>
<th>n (prescriptions)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacist present</td>
<td>353</td>
<td>92.9</td>
</tr>
<tr>
<td>Analysis of the prescriptions</td>
<td>365</td>
<td>96.0</td>
</tr>
<tr>
<td>Restricted flow of people</td>
<td>372</td>
<td>97.9</td>
</tr>
<tr>
<td>Clean environment</td>
<td>366</td>
<td>96.3</td>
</tr>
<tr>
<td>Organized environment</td>
<td>193</td>
<td>50.8</td>
</tr>
<tr>
<td>No interruption/distraction sources</td>
<td>213</td>
<td>56.1</td>
</tr>
<tr>
<td>Double check</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Several studies have shown the lack of knowledge about HAMs by the health professionals, and the listing of these medications is a powerful tool to disseminate information about them. This should serve as a guide as to the maximum doses, the way of administration, the indication and the usual dose of these drugs, especially when the institution does not have a computerized program with clinical support for a safe prescription. Despite being a recommendation of the MH/ ANVISA protocol, the list of the studied institution only mentioned the medicines and their presentations.

The presence and performance of the pharmacist are crucial in the various phases of the pharmacotherapy dispensing and monitoring process to prevent risks. In this sense, there was a deficit in the analysis of the prescriptions due to the absence of the pharmacist in fulfilling 64.3% of the night shift prescriptions. In the other shifts, prescription reviews were restricted to the calculation made by the technician for dispensing the medicines. There was no evaluation of the prescriptions regarding therapeutic duplicity, drug interactions, inadequate dose intervals, and doses above the maximum. This attribution was the responsibility of the clinical pharmacist, but the number of these professionals is not sufficient to cover all sectors of the hospital.

The dispensing area must be designed to prevent errors related to environmental conditions such as phone distractions, interruptions, and disorganization. Parallel conversations and use of mobile devices (cell phones) were the main interruption/distraction sources observed during the fulfillment of the prescriptions that contained HAMs. A number of authors report a strong association between medication errors and interruptions/distractions.

Double checks are widely recommended in the processes of using HAMs, as it allows for the identification of errors before the medicines reach the patient. However, the volume of medicines dispensed daily makes this practice arduous and difficult to perform, and should be limited to groups of high-risk patients. Perhaps this may explain the fact that the professionals do not perform double checks in the hospital under study, despite the fact that the pharmacy has an exclusive environment for this.

The weaknesses in adherence to the practices of error prevention involving HAMs found in the present research can be related to the lack of recognition of the importance or even to the insufficiency of knowledge of such measures by the pharmaceutical professionals, influencing the risk management of these drugs, with the possibility of causing medication errors.

With such a scenario, this study proposes the following strategies: implementation of continuing/permanent education programs mainly for the medical professionals, Nursing staff, pharmacists, and pharmacy technicians; adoption of an individualized dose distribution system for potassium chloride and insulin; removal of potassium chloride from inpatient units; alert identification on HAM packages; hiring pharmacists for the night shift; establishment of educational measures to discipline conversations and the use of media at the time of dispensing; establishment of an environmental organization program; revision of the SOP for medicines dispensing in order to have specific rules for the storage and dispensing of HAM; implementation of double checks in the dispensing of HAMs; review of the HAMs listing with information on the indication of maximum permitted doses, the way of administration, the indication and the usual dose; implementation of a computerized program as a therapeutic support for the analysis of prescriptions; and prescription signaling when the prescribed medicines is a HAM.

A strong point of this study was the use of the guidelines of the safety protocol in the prescription, use, and administration of medicines from the MH/ANVISA to create a checklist for observing the environment and practices adopted in dispensing HAMs. In addition, it draws the attention to the role of the ANVISA in updating the rules in force in Brazil regarding HAM packing and labels in the pharmaceutical industries. Furthermore, strategies applied to the reality are described not only of the institution studied, but also of other institutions, since one of the most important ways to avoid errors is to learn about the problems occurred in other organizations and use this information to improve their processes.

A limitation of this study had its origin in the pharmacy routine, since the medicines dispensed during the night shift were, for the most part, for the kidney transplant unit, and the pharmacotherapeutic profile of these patients is very similar, generating prescriptions with few differences. In addition, it was not possible to completely eliminate the influence of the researcher when observing the practices and the dispensing environment, as his presence during the study may have altered the employees’ behavior (Hawthorne effect). Also, the data obtained in the adult unit of the hospital may not represent the reality of the maternal-child unit, which was not part of this research.

In conclusion, this study revealed that the HAMs were frequent in more than half of the prescriptions and that, despite this, the adoption of safe practices to dispense such medicines is insufficient, exposing patients to risks. Although this research portrays a local reality, the findings can be extrapolated, as long as they are adapted to other institutions that face the same financial difficulties and shortages of professionals to support risk management and patient safety actions. It is important to implement the MH/ANVISA protocol for the safe use of medicines, contributing to attain the objective advocated by the third WHO global challenge.
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