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# Identifying medications with look-alike packages in a Brazilian hospital: a multi-step approach

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## Abstract

**Objective:** To describe the identification of drugs with similar primary packaging available in a large teaching hospital. **Methods:** This is a descriptive study carried out using a multi-step approach. First, the small volume parenteral drugs and oral solutions available at the institution (Step I) were listed. Then, from the list developed in Step I, groups of drugs with similar packaging (double, trio or foursome) were identified according to their characteristics (Step II). These groups were then visually evaluated by the pharmacy team (Step III), and later by the internal community of the institution (Step IV). **Results:** A total of 233 drugs in the pharmaceutical forms of interest were available at the institution (Stage I). In step II, 62 groups with similar primary packaging were identified. After evaluation by the pharmacy team, 19 groups remained (Stage III), which were then evaluated by the internal community, generating a final list of 15 groups of drugs with similar primary packaging. Among these, the pharmaceutical form of parenteral use (80%) and the amber ampoule as primary packaging (46.7%) were frequent. **Conclusion:** The results of the study point to the applicability and adequacy of the multi-step approach to identify the presence of groups of drugs with similar primary packaging in a real-world scenario. The identification of these groups of drugs in health care institutions is the first important step to plan strategies to minimize errors involving similar packaging, thus increasing the safety of medication use in the hospital environment.

**Keywords**: patient safety; drug packaging; medication errors; medication systems.

# Identificando medicamentos com embalagens semelhantes em um hospital brasileiro: uma abordagem com múltiplas etapas

## Resumo

**Objetivo:** Descrever a identificação de medicamentos com embalagens primárias semelhantes disponíveis em um hospital de ensino de grande porte. **Métodos:** Trata-se de um estudo descritivo realizado por meio de uma abordagem com múltiplas etapas. Primeiramente, foram listados os medicamentos parenterais de pequeno volume e líquidos de uso oral padronizados e disponíveis na instituição (Etapa I). Em seguida, à partir da lista constituída na Etapa I, foram identificados grupos de medicamentos semelhantes (duplas, trios ou quartetos de medicamentos) de acordo as características de suas embalagens (Etapa II), que foram então avaliados visualmente pela equipe de farmácia (Etapa III), e, posteriormente, pela comunidade interna da instituição (Etapa IV). **Resultados:** Foram selecionados 233 medicamentos nas formas farmacêuticas de interesse padronizados e disponíveis na instituição. Em seguida, foram identificados 62 grupos de medicamentos semelhantes de acordo com suas embalagens primárias. Após avaliação da equipe de farmácia, 19 grupos remanesceram, que foram então avaliados pela comunidade interna, gerando uma lista final de 15 grupos de medicamentos com embalagens primárias semelhantes, destacando-se a forma farmacêutica de uso parenteral (80%) e a ampola âmbar como embalagem primária (46,7%). **Conclusão:** Os resultados do estudo apontam a aplicabilidade e adequação da abordagem com múltiplas etapas para identificar a presença de grupos de medicamentos com embalagens primárias semelhantes em cenário de mundo real. A identificação desses grupos de medicamentos em instituições de saúde é a etapa inicial e essencial para planejar estratégias de minimização de erros envolvendo embalagens semelhantes, aumentando a segurança no uso de medicamentos em âmbito hospitalar.

**Palavras-chave**: segurança do paciente; embalagem de medicamentos; erros de medicação; sistemas de medicação.

## Introduction

In 2017, the World health Organization (WHO) launched the third Global Patient Safety Challenge with the theme of "Medication Without Harm"[1,2]. The Challenge was launched as a result of the fact that the medication errors constitute the first cause of avoidable harms in the world, involving an estimated cost of USD 42 billion/year in developed countries and even higher values in developing countries.[1] Consequently, the goal was proposed of reducing by 50% the avoidable severe harms related to medications within five years, which would be the severe harms resulting from medication errors. This goal must be achieved by means of multiple actions, with the need to prevent errors involving the exchange of medications with look-alike packages, which is one of the most frequent and persistent types of errors and represents a major challenge faced in health services worldwide.[1-4]

A look-alike visual pattern can make it difficult to differentiate between different medications, or even different concentrations of the same medication by both users and health professionals.[4] In view of this scenario, a number of studies indicate that it is advisable not to purchase products with look-alike packaging, which is not always possible, especially in Brazilian public health services, in which purchase of medications is carried out through a bid based on the lowest price and on meeting the basic technical description of the product, these being rarely accepted criteria for differentiation of labels in packaging in this process.[5,6] Additionally, to date, the Brazilian legislation does not indicate regulatory requirements for the differentiation of primary packaging of medications, and the national industry has not invested enough in solving this problem, although there are proposals for changes to some legislations dealing with the subject matter.[7-10] In this context, it is still up to the health institutions themselves, especially hospitals, to adopt strategies for the internal differentiation of drugs with look-alike packaging, the process of which begins with the identification of look-alike medications available at the institution. In view of all of the above, the objective of this study was to describe the identification of medications with look-alike primary packaging available in a large-size teaching hospital.

## Methods

A descriptive study based on primary data was conducted in a general large-size and high-complexity teaching hospital located in the Municipality of Belo Horizonte, Minas Gerais, Brazil

Small volume parenteral drugs were considered, due to the high risks involving the parenteral route of administration; and liquid oral medications, since such a pharmaceutical form is dispensed for collective use at the institution under study, a dispensing system considered less safe[11]. Data was collected in 2017. To proceed with the identification, a process involving four stages was followed, as described below.

### Stage I: List of medications and their packaging characteristics

In stage 1, based on the institution's list of standardized medications, a list was compiled with all the medications in the pharmaceutical forms of interest used in the institution (parenteral small-volume, and liquids for oral use). Subsequently, it was verified whether these drugs were available at the pharmaceutical supply center (*Central de Abastecimento Farmacêutico*, CAF) of the study institution, creating a list referring to them in the Microsoft Excel® software containing the following information: name according to the common Brazilian name, trade name (when it was not a generic product), classification of the medication according to the registration profile (generic, similar or reference medication), concentration, pharmaceutical form, total volume of solution contained in the packaging (when applicable), packaging material and its characteristics (e.g., plastic, amber glass, clear glass), type of label (e.g., self-adhesive, screen-printed), color of the prints of the name of the active ingredient, color of the label (when applicable), color of the cap (when applicable), if it was a medication with packaging from the Ministry of Health (according to Resolution RDC 21/2012)[12], and observations.

Tables containing the same information were also prepared, separately, for medications stored under refrigeration and subjected to special control according to Ordinance 344/1998[13], since these drugs are stored and dispensed separately in the institution.

### Stage II: Identification of groups of medications with look-alike packaging

In stage II, the lead researcher identified groups of products (pairs, triplets or quadruplets) whose primary packages were looked alike. To enable this identification, for the physical comparison, at least one specimen of each product present in the list of medications with the pharmaceutical presentation of interest compiled in stage I was used, available in the institution. The specimens were compared with each other within three subgroups created according to their primary packaging: ampoules, ampoule-vials, and oral solution vials.

For the ampoule groups to be listed as look-alike packaging, they should present: (1) the same solution volume range; (2) the same packaging material; (3) the same type of label; and (4) the name of the active ingredient printed in the same color. For vials containing powder to be identified as look-alike, they should have: (1) the same size range; (2) the same packaging material; (3) the same type of label; and (4) at least two other characteristics in common (e.g., the same color of the prints as the name of the active ingredient, the same color of the label and/or the same color of the vial cap). In the case of ampoule-vials containing parenteral solution or of vials containing oral solution, the following should be identified: (1) the same volume range; (2) the same packaging material; (3) the same type of label; and (4) at least another two characteristics in common (e.g., the same color of the prints as the name of the active ingredient, the same color of the label and/or the same color of the vial cap). The criteria adopted to establish the similarity between medications were defined by the researchers based on the packaging characteristics most involved in errors according to Cohen (2006)[14]. As a result of this analysis, at the end of stage II, a list of groups of medications with look-alike primary packaging was created to be assessed by means of a visual inspection in the subsequent stages of the study.

**Stage III: Visual assessment of the groups of medications with look-alike primary packaging by the Pharmacy team**

During stage III, the groups of medications with look-alike primary packaging identified in stage II were visually assessed in person by a group consisting in three female graduate pharmacists and one Pharmacy undergraduate student from the clinical pharmacy unit of the institution under study. As the exchange of medications with look-alike packaging derives from factors related to human error, it was decided to adopt human factor assessment to determine the similarity between the medications. This assessment was conducted by means of an in-person visual inspection of the medications and of an individual subjective perception of this similarity. After the individual assessment by each member of the group, the dichotomous parameter ("yes" or "no") was used to define the similarity.

Each observer recorded their assessment in an individual form, without being aware of the assessments by the other observers. Only those medications that obtained an absolute majority of "yes" votes by the Pharmacy assessment group remained in the list of groups with look-alike primary packaging; in other words, at least 3 "yes" votes per group of medications.

**Stage IV: Assessment of the groups of medications with look-alike primary packaging by the institution's internal community**

The list of groups of medications with look-alike primary packaging defined at the end of stage III was assessed by the internal community of the hospital during stage IV. The list of medications was presented in the form of a poster with a photograph of the drugs, in the case of a face-to-face answer to the questionnaire; or through scanned graph, in the case of an electronic form. These two forms of presentation of the medications (poster or scanned photograph) were developed by the institution's communication department.

The assessment regarding similarity was conducted by means of a questionnaire, which could be answered either in-person or electronically by a total of 1,592 professionals involved in the process of medication use, namely: 1) pharmacy employees or storekeepers (n=81); 2) nursing technicians/assistants or nurses (n=1,398); 3) pharmacists, including residents, but excluding those who participated in stage III (n=30); and 4) anesthesiologists, including residents (n=83).

The questionnaire included three sections. The objective of the first sections was to collect professional and sociodemographic data to identify the profile of the respondents. The second section consisted in the visual assessment of the groups of medications regarding the similarity of their primary packaging, by selecting the dichotomous answer ("yes" or "no"). In its turn, the third section of the questionnaire consisted of a field for observations, where the collaborators could indicate other groups of medications which they considered look-alike and that had not been identified in the initial list. The groups of medications were considered look-alike when the relative majority (>50% of the respondents) answered "yes" to the question on the similarity of the primary packaging.

**Ethical aspects**

This study is part of the project entitled "Safety in the process of medication use with a focus on clinical pharmacy in the hospital context", which was approved by the Research Ethics Committee of the Federal University of Minas Gerais (CAAE 80169717.4.0000.5149). The study participants, professionals with direct performance in the care provided in the hospital, received the necessary and pertinent information for their participation, in addition to reading and signing the free and informed consent form.

## Results

**Stage I: List of medications and their packaging characteristics**

Among the standardized medications in the institution, 278 had pharmaceutical forms of interest for the similarity analyses of this study. Of these, 49 were medications subjected to special control (30 in the small-volume parenteral form, and 19 in the form of vials containing liquid for oral use). Another 185 medications for parenteral use and 44 vials containing oral solution that were not subjected to special control were also identified. Meanwhile, of the total of medications identified and with a pharmaceutical presentation of interest, 45 (16.2%) were not physically available in the CAF inventory and were not included in the compiled list containing their basic information.

Among the drugs available in the CAF (n=233), 20% (n=45) were reference drugs, 22% (n=54) were generic drugs, 51% (n=121) similar drugs, 5% (n=8 ) medications from manipulation laboratories and 2% (n=5) medications with packaging from the Ministry of Health.

**Stage II: Visual assessment of groups of medications with look-alike packaging**

At the end of the physical evaluation and the characteristics described in the list compiled in stage I, 62 groups of drugs with look-alike primary packaging were identified. Of this total, 34% (n=21) belonged to the group of ampoules, 6 groups consisting of ampoules belonging to the group subjected to special control.

The ampoule-vials containing powder corresponded to 52% (n=32) of the total (none subjected to special control). The ampoule-vials containing parenteral solution corresponded to 8% (n=5), with only 1 group belonging to the medications subjected to special control. In relation to the vials containing oral solution, the group percentage was 6% (n=4), with 2 groups falling into the "subjected to special control" category.

**Stage III: Visual assessment of the groups of medications with look-alike primary packaging by the Pharmacy team**

At the end of the assessment of the 62 groups of medications by the evaluating Pharmacy group, 19 groups with look-alike packaging were identified, corresponding to 44 different types of medications (18.9% of the medications listed in Stage I) (Table 1). Among the groups of medications, 52% (n=10) were presented in the form of ampoules, 21% (n=4) as vials containing oral solution, 16% (n=3) were ampoule-vials containing parenteral solution, and 11% (n=2) were ampoule-vials containing powder.

**Table 1**. Characteristics and results of the visual analysis of the groups of medications with look-alike primary packaging by the institution's internal community. 2017. General, public and teaching hospital. Belo Horizonte- MG. (to be continued)

| Groups | Characteristics of the group of medications | | Frequency of "yes" answers for the similarity question during visual assessment* n (%) | Look-alike characteristics between the medications in the group** |
|---|---|---|---|---|
| | Type of packaging/ Pharmaceutical presentation | Active ingredient(s) and concentration | | |
| 1 | Ampoule-Vial/ Parenteral solution | Bupivacaine 0.5% + epinephrine<br>Lidocaine 1% + epinephrine<br>Lidocaine 2% + epinephrine | 241 (96.7) | Volume range: from 10.01 to 20 mL<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: gray<br>Color of the cap: red |
| 2 | Ampoule/ Parenteral solution | N-butylscopolamine 4 mg/mL + dipyrone 500 mg/mL<br>Ondansetron 2 mg/mL<br>Sulfamethoxazole 80 mg/mL + trimethoprim 16 mg/mL | 216 (86.7) | Volume range: from 2.01 to 5 mL<br>Packaging material: amber glass<br>Type of label: silk-screened<br>Color of the label's print: white |
| 3 | Ampoule/ Parenteral solution | Phytomenadione 10 mg/mL<br>Ranitidine 25 mg/mL<br>Terbutaline 0.5 mg/mL | 240 (96.4) | Volume range: up to 2 mL<br>Packaging material: amber glass<br>Type of label: silk-screened<br>Color of the label's print: red |
| 4 | Ampoule/ Parenteral solution | Adenosine 3 mg/mL<br>Papaverine 50 mg/mL<br>Salbutamol 0.5 mg/mL<br>Vitamins of the B complex 2 mL | 237 (95.2) | Volume range: up to 2 mL<br>Packaging material: amber glass<br>Type of label: silk-screened<br>Color of the label's print: blue |
| 5 | Ampoules/ Parenteral solution | Dypirone 500 mg/mL<br>Bromopride 5 mg/mL | 147 (59.0) | Volume range: up to 2 mL<br>Packaging material: amber glass<br>Type of label: silk-screened<br>Color of the label's print: white |
| 6 | Ampoule/ Parenteral solution | Dopamine 5 mg/mL<br>Nitroglycerine 5 mg/mL | 122 (49.0) | Volume range: from 5.01 to 10 mL<br>Packaging material: amber glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: white |
| 7 | Ampoule/ Parenteral solution | Betamethasone 3 mg/mL<br>Ergometrine 0.2 mg/mL | 164 (65.9) | Volume range: up to 2 mL<br>Packaging material: amber glass<br>Type of label: self-adhesive<br>Color of the label's print: white<br>Color of the label's background: purple |
| 8 | Ampoule/ Parenteral solution | Phenylephrine 10 mg/mL<br>Metaraminol 10 mg/mL | 230 (92.4) | Volume range: up to 2 mL<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: pink |
| 9 | Ampoule/ Parenteral solution | Bupivacaine 0.5% + glucose<br>0.5% isobaric bupivacaine | 239 (96.0) | Volume range: from 2.01 to 5 mL<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: white |
| 10 | Ampoule/ Parenteral solution | Fentanyl 0.05 mg/mL<br>Morphine 1 mg/mL | 231 (92.8) | Volume range: up to 2 mL<br>Packaging material: amber glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: white |
| 11 | Vial/ Oral solution | Clonazepam 2.5 mg/mL<br>Haloperidol 2 mg/mL | 118 (47.4) | Volume range: from 10.01 to 20 mL<br>Packaging material: plastic<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: white<br>Color of the cap: white |
| 12 | Vial/ Oral solution | Midazolam 2 mg/mL<br>Phenobarbital 4.00% | 170 (68.3) | Volume range: from 5.01 to 10 mL<br>Packaging material: amber glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: white<br>Color of the cap: white |

**Table 1**. Characteristics and results of the visual analysis of the groups of medications with similar primary packaging by the institution's internal community. 2017. General, public and teaching hospital. Belo Horizonte- MG. (conclusion)

| Groups | Characteristics of the group of medications | | Frequency of "yes" answers for the similarity question during visual assessment* n (%) | Look-alike characteristics between the medications in the group** |
|---|---|---|---|---|
| | Type of packaging/ Pharmaceutical presentation | Active ingredient(s) and concentration | | |
| 13 | Vial/<br>Oral solution | Nystatin 100,000 IU/mL<br>Sulfamethoxazole 4% + trimethoprim 0.8% | 218 (87.6) | Volume range: from 5.01 to 10 mL<br>Packaging material: plastic<br>Type of label: self-adhesive<br>Color of the label's print: purple<br>Color of the label's background: white<br>Color of the cap: white |
| 14 | Ampoule/<br>Parenteral solution | Morphine 10 mg/mL<br>Nalbuphine 10 mg/mL | 220 (88.4) | Volume range: up to 2 mL<br>Packaging material: amber glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: blue |
| 15 | Ampoule-Vial/<br>Parenteral solution | NPH Insulin 100 UI<br>Regular Insulin 100 UI | 97 (39.0) | Volume range: from 5.01 to 10 mL<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: purple<br>Color of the label's background: blue<br>Color of the cap: white |
| 16 | Vials/<br>Oral solution | Potassium chloride 60 mg/mL<br>Prednisolone 1 mg/mL | 146 (58.6) | Volume range: 50.01 to 150 mL<br>Packaging material: plastic<br>Type of label: self-adhesive<br>Color of the label's print: purple<br>Color of the label's background: white<br>Color of the cap: white |
| 17 | Ampoule-vial/<br>Lyophilized powder | Hydrocortisone100 mg<br>Teicoplanin 400 mg | 121 (48.6) | Size range: medium<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: blue<br>Color of the cap: red |
| 18 | Ampoule-vial/<br>Lyophilized powder | Vancomycin 500 mg<br>Benzylpenicillin potassium 5,000,000 UI | 191 (76.7) | Size range: medium<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: yellow<br>Color of the cap: yellow |
| 19 | Ampoule-Vial/<br>Parenteral solution | Bupivacaine 0.50%<br>Bupivacaine 0.75%<br>Lidocaine 1.00% | 236 (94.8) | Volume range: from 10.01 to 20 mL<br>Packaging material: clear glass<br>Type of label: self-adhesive<br>Color of the label's print: black<br>Color of the label's background: gray<br>Color of the cap: blue |

*Groups of medications visually assessed as look-alike (answer = "yes") or not look-alike (answer = "no").
**Similarity criteria defined by the authors according to Cohen, et al. (2006) for ampoules: (1) solution volume range; (2) the same packaging material; (3) the same type of label; and (4) the name of the active ingredient printed in the same color. For ampoule-vials containing powder: (1) same size range; (2) the same packaging material; (3) the same type of label; and (4) at least two other characteristics in common. For ampoule-vials containing parenteral solution or vials containing oral solution: (1) the same volume range; (2) the same packaging material; (3) the same type of label; and (4) at least two other characteristics in common.

**Stage IV: Assessment of the groups of medications with look-alike primary packaging by the institution's internal community**

The consultation with the internal community resulted in 198 face-to-face answers to the questionnaire and 51 electronic answers (total = 249 participants; 15.6% of the population consulted), generating an error margin of 5.71% for a 95% confidence level. The professional and sociodemographic data obtained in this stage can be observed in Table 2.

Of the 19 groups of medications identified in stage III, only 15 remained as look-alike after the analysis by the institutional community, corresponding to 36 different medications (15.5% of the medications listed in Stage I) (Figure 1). In the third section of the questionnaire, another 2 groups of medications with look-alike primary packaging were suggested. Consequently, at the end of the four stages, 17 groups of medications with look-alike primary packaging were identified.

**Table 2.** Professional and sociodemographic profile of the institution's internal community participating in the assessment of the groups of medications with look-alike primary packaging (n=249). 2017. General, public and teaching hospital. Belo Horizonte- MG.

| Characteristic | Frequency n (%) |
|---|---|
| **Gender** | |
| Female | 189 (75.9) |
| Male | 60 (24.1) |
| **Age** | |
| 18 to 25 years old | 8 (3.3) |
| 26 to 40 years old | 151 (60.6) |
| 41 to 59 years old | 87 (34.9) |
| > 59 years old | 3 (1.2) |
| **Schooling** | |
| Incomplete High School | 1 (0.4) |
| Complete High School | 36 (14.4) |
| Technical High School | 42 (16.9) |
| Incomplete Higher Education | 25 (10.0) |
| Complete Higher Education | 40 (16.1) |
| Graduate Degree | 105 (42.2) |
| **Position in the institution** | |
| Nursing technician or assistant | 9 (3.7) |
| Storekeeper | 30 (12.0) |
| Pharmacist or resident | 17 (6.8) |
| Nursing technician | 118 (47.4) |
| Nurse | 59 (23.7) |
| Anesthesiology physician or resident | 16 (6.4) |
| **Working time in the institution** | |
| < 1 year | 35 (14.1) |
| > 1 year and < 2 years | 33 (13.3) |
| > 2 years and < 3 years | 75 (30.1) |
| > 3 years and < 4 years | 22 (8.8) |
| > 4 years and < 5 years | 5 (2.0) |
| > 5 years old | 79 (31.7) |
| **Works or has worked in another hospital institution?** | |
| Yes | 203 (81.5) |
| No | 46 (18.5) |

## Discussion

This study, conducted in a hospital with a multiple stage approach, identified 15 groups of medications with look-alike primary packaging (15.5% of the medications listed in Stage I of the study). To list such groups, several actors from the institution's internal community were invited, particularly health professionals who perform the stages of dispensing, preparing and administering medications. During these stages, look-alike packaging can significantly contribute to the occurrence of errors.

Labels, packaging and nomenclature of similar drugs are one of the ten key elements that influence the system of drug use and that can cause medication errors.[15] Look-alike packaging influenced the occurrence of 33% of the medication errors according to a research study conducted by the United States Pharmacopoeia between 1996 and 1997 and, of this percentage, 50.5% corresponded to parenteral drugs.[16] In addition, nearly 2,000 notifications of adverse events involving packaging were recorded in 2012, in Canada.[16] In Brazil, notorious cases have also been recorded. As an example, we can mention an event of great repercussion in the media involving a nursing assistant who, when he mistook vaseline for physiological serum, erroneously administered the first through the intravenous route, resulting in the death of a child.[17,18]

The similarity in the packaging with the potential for confusion can be due to several aspects: colors, names of medications similar in terms of sound or spelling, similar packaging (ampoule, ampoule-vial, pill, outer box, vial, bags and others), type of letter used and type of label (letters of the same size, type and color).[14,19] When looking at the photographs in Figure 1, it is possible to notice that many of the groups have a combination of these factors, creating similarities in the presentation of different medications, and increasing the risk of exchange by the health professionals. It is noteworthy that, in this study, most of the groups identified as look-alike at all stages included different medications, although it is known that the packaging and labels of the medications can be look-alike because they contain different medications or because they contain the same medication with different dosages.[20]

**Figure 1**. Final groups of medications with similar primary packaging.

In addition, it is important to consider that important information in the packaging can be printed in an imperceptible place, presented ambiguously or blurred by less important information. Such situations, linked to the reading of the packaging information by the health professionals, occur in places with sub-ideal conditions (for example, in a patient's room at night when the lights are dimmed or during emergency situations), which can favor the occurrence of errors.[21] This problem is a highlight for screen-printed ampoules, which constituted four groups of look-alike drugs.

Another important finding of this study was the large percentage (80%) of groups of medications for parenteral use identified as look-alike. This fact reveals the criticality of the theme, since the parenteral administration route is associated with errors that are more difficult to correct, and the time for action to correct possible problems is narrower. Findings of other studies also describe the criticality involving this pharmaceutical presentation by means of the risk analysis using the FMEA (Failure Modes, Effects Analysis) tool.[7,22,23]

In addition to this, among the medications included in the groups, there were high-alert medications (HAM) (n=10; 27.8% of the medications listed in look-alike medication groups – Result not reported) and medications subjected to special control (n=8; 22.2% – Result not reported).HAMs present a high probability of generating harms derived from error in the process of medication use. Thus, if used without caution and erroneously during the care process, they can cause serious or fatal injuries.[24] Medications subjected to special control with look-alike packaging usually also involve an increased risk for the occurrence of incidents, since the special control drugs from the opioid class stood out in this study (n=4), which can cause serious adverse effects in case of failures in their use.[25]

Several international protocols are available and address the labeling, packaging and choice of safe medication names as an initiative to prevent medication errors.[4,26-33] Such protocols recommend that the essential information presented on the labels of primary packaging in parenteral solutions must be legible, indelible and printed on an adhesive label, with a white background or in another light color that allows for a contrasting printing of the letters.[4,26-33] However, the essential information was embossed directly on the ampoules in four groups identified in this study. A study carried out at a university hospital found that the time to identify the information on the brochures, providing information that was embossed directly on the ampoules was statistically greater ($p<0.0001$) than on the labels, whose information was available in black ink on an opaque adhesive label.[34] Another study found that the group of professionals who had to read labels without contrast spent more time reading them and had more difficulty in doing so, in addition to performing more incorrect readings than the group of professionals who received ampoules with a contrasting background.[35]

Another important recommendation that facilitates the reading of the medication name is that it be printed longitudinally along the length of the ampoule, in cases where the visible width is less than the height of the label.[4,26-33] Among the identified groups, five followed this recommendation; however, two of them had the label information screen-printed directly on the ampoule glass, which also makes it difficult to read the ampoule.

In a systematic review that assessed the diverse evidence on strategies to minimize medication errors due to look-alike labels, it was found that the use of upper case letters in certain parts of the name of the medications contributes to better readability of the medication labels. Upper case letters aim at maximizing the difference between two look-alike/sound-alike medication names, using upper case in part of the names. In addition, this review found scarce evidence supporting other strategies such as color coding and use of symbols; more studies being necessary to support the implementation of these strategies.[36]

Faced with the need to make the labels and packaging of medications marketed in Brazil safer, a working group coordinated by the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária*, ANVISA) devised proposals to improve the rules on package inserts and labeling of medications. Recently, such proposals were published in three Public Consultations, in order to obtain the contribution and participation of all professionals and institutions.[8-10] Such initiative is fundamental to ensure that labels and packages contain characteristics that clearly differentiate the drugs from each other and that inhibit dispensing and administration errors due to unwanted exchanges or misuse.

It is believed that the changes that will be standardized by the regulation authorities and adopted by the industries will contribute to making the packaging safer, even those of the medications recorded as similar. These correspond to most of the medications included in the groups of medications with look-alike packaging in this study (51%). Such finding is in consonance with a study conducted in a hospital pharmacy that found high prevalence (46%) of medications recorded as similar[7]. This result can be explained by the fact that the medication purchase process in public institutions, such as the institution under study, occurs through bidding, and similar drugs have an intermediate price range between reference drugs and generic drugs. Therefore, it is expected that a large number of similar medications from a single manufacturer is purchased, leading to a considerable frequency of look-alike medications among those acquired.[7]

In view of the above, it is worth mentioning that safer labels and packaging are one of the aspects for preventing dispensing and administration errors, and it is fundamental that these be inserted as one of the prevention initiatives within the multifaceted approach. In view of this, it is recommended that the institution prioritizes, when possible, the purchase of medications with generic and brand names with sound and spelling that are not very similar, that the labels of the primary packaging are legible, indelible and printed on an opaque adhesive label which allows for the contrasting printing of the letters, and that the essential information on the labels of small-volume vials be printed longitudinally along the length of the ampoule, in cases where the visible width is less than the height of the label. It is also important that the health institution encourages and ensures that the health professionals adopt double-checking before administering the medications, in addition to using technological solutions, such as the use of barcodes, and promoting training of the health professionals involved in the system of medication use. However, considering that not only health professionals but also patients identify the medications by their labels, it is imperious that the labels in the medication packaging are safe.[36]

One of the limitations of this study was the use of a subjective similarity assessment between the medications, both in Stage III (assessment by the pharmacists) and in Stage IV (assessment by the community). However, it is important to highlight the little explored value of human factor assessment for packaging

evaluation, but recommended by international bodies involved in promoting the safe use of medications.[4,28] A number of studies that evaluated human errors describe a series of factors with the potential to influence the human mind and divert attention, increasing the number of errors made in the activity being performed, with emphasis on aspects involving the packaging and labeling of medications. The combination of these aspects in the human brain leads to the subjective perception of similarity, the plurality of these aspects being assessed in the visual inspection of the medications, according to what was performed in this study.[4,28,37] In future studies, however, it is recommended to use a *Likert*-type scale, which enables a more detailed categorization of the similarities.

In the study by Lopes *et al*. (2012), the observers (two nurses and a pharmacist), after receiving the photographic images of groups of look-alike medications, performed the similarity classification according to denomination: (1) very similar to each other, (2) slightly similar to each other and (3) there are no similarities between them. However, most of the groups of medications evaluated (more than 92% for all the observers) were identified as "very similar to each other"[7]. In this study, 150 medication pairs were evaluated, but the objective was not to elaborate a final list of pairs of look-alike medications; only the evaluation of the characteristics of the drugs identified as look-alike by the observers[7]. In this way, according to the authors' knowledge, there is no single Brazilian study describing the method and application of multiple steps to develop a list of look-alike medications in the hospital setting.

Another limitation of this study was the participation of a limited number of professionals from the institution's internal community in the stage of assessment by means of the questionnaire (Stage IV). This may have happened because the professionals involved in the care process generally have an intense work routine and, consequently, lack material time to participate in surveys like the one described in this research. Although the sample of respondents is related to a small error margin for the factor assessed (5.71%), greater participation would allow for better representativeness of the different sectors of the hospital, which is of large size and offers several complex services. In addition to that, the participants' involvement in the research also has the potential role of enhancing awareness in the professionals working in the institution regarding the risks involved in the exchange of look-alike medications.

However, even with the presence of limitations, this study has as a positive aspect the discussion about a topic little contemplated in the Brazilian scientific scenario, even in view of its relevance in the context of patient safety. It is therefore believed that, in addition to fostering positive discussions in the assistance environment, the approach herein proposed can reinforce the need of a quality culture and the search for the implementation of processes for the identification of look-alike medications which, as a rule, can easily be reproduced or adapted by other health institutions.

## Conclusion

The study results point to the applicability and adequacy of the multiple-staged approach to identify the presence of groups of medications with look-alike primary packaging in a real world setting. Identifying these groups of medications in health institutions is the initial and essential stage to plan strategies for the minimization of errors involving look-alike packaging, thus enhancing safety in medication use in the hospital setting and advancing towards reaching the goal established by the WHO in the global challenge of patient safety.

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**Conflict of interests statement**

The authors declare that there are no conflicts of interest regarding this article.

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