Cogitare Enfermagem

RESIDUAL VOLUME OF AMPOULE-VIALS AND UNDERDOSING OF MEDICATIONS PREPARED BY A NURSING STAFF

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ABSTRACT

Objective: Identify the residual volume in ampoule-vials after the preparation of injectables, associating the errors related to underdosing with the classes of drugs. Method: This is a descriptive study with a quantitative approach. Data were collected between December 2020 and September 2021, in a private outpatient service located in a Brazilian municipality in the northeast of the state of São Paulo. A total of 562 ampoule-vials of medications prepared by a nursing staff were analyzed. A form was used containing the commercial name of the medication, therapeutic class/indication, reconstitution date and time, volume used to reconstitute the medication and residual volume of each vial. The data were tabulated and analyzed using descriptive statistics and the ANOVA test. Results: the residual volume of 462 (82.2%) ampoule-vials varied between 0.1 ml and 1.5 ml, whereas 165 (29.4%) ampoule-vials had 0.2 ml of residual volume, with a mean loss of 4.5% of the solution. There was no difference in the loss of solution between the different classes of drugs. Conclusion: The findings highlight the need for interventions to reduce failures in the medication preparation phases, with emphasis on errors associated with therapeutic underdosing.

DESCRIPTORS: Nursing; Medication Therapy Management; Nursing Care; Medication Errors; Drug-Related Side Effects and Adverse Reactions.

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INTRODUCTION

Drug-related adverse events can cause significant health problems, including medication errors, which are common occurrences and can assume clinically significant dimensions, with social and economic repercussions. The annual cost related to such errors is estimated at US$ 42 billion[1-2]. The Brazilian Institute for Patient Safety (IBSP, as per its acronym in Portuguese) states that unsafe practices and medication errors are the leading causes of preventable harm in health care systems worldwide[3].

According to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP)[4], "a medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer".

There are several approaches to classify medication errors, based on the phase of the medication use process, the types of errors that occur (wrong drug, dose, frequency, route of administration, or patient), the causes (failure to plan actions, with errors based on knowledge or rules), or the execution of properly planned actions (action-related errors, known as "slips" or memory errors, known as "lapses")[5].

Considering the stages that make up the medication system (prescription, dispensing, preparation, administration, and monitoring)[6], errors are more likely to occur in the drug preparation and administration phases, which are generally under the responsibility of the nursing teams. Thus, although drug delivery is a multidisciplinary process, nurses have a special role in the functioning of this system[7].

Based on the causes, medication errors can be related to omission, dosing, unordered error (when a patient receives an unprescribed medication), time, route, impaired physical or chemical integrity of the medication form, administration flow and technique, preparation, and extra dose. With regard to severity, medication errors can be classified into: Category A - potentially serious error that may cause permanent harm to the patient, increase the length of hospital stay or need for treatment; Category B - clinically significant error which may increase the need for patient monitoring; Category C - clinically non-significant error that does not harm the patient[8].

When studying the causes of medication errors in a mental health hospital, the authors of another study[9] mentioned that skill-based slips and lapses were the most commonly reported unsafe acts, followed by knowledge-based errors and deliberate violations. According to them, conditions that influence drug administration errors include problems with communication, emotional state of the professional, high perceived workload, patient factors, work environment, problems with medication supply and storage, problems with equipment, and interruptions or lack of concentration during drug administration.

Therefore, it is observed that medication errors are multifactorial, and many of them are directly or indirectly associated with human error[2]. They may relate to professional practice, health products, procedures and systems, including prescribing, order communication, product labeling, packaging and nomenclature, composition, dispensing, distribution, administration, education, monitoring and use[4].

Specifically, drug preparation consists of the technique of manipulating drugs to administer to a patient, according to the prescription and dispensing. It involves broad prior knowledge about the drug (actions and reactions), checking whether the prescription matches with the drug to be prepared, calculation, dilution, complete identification, and the choice of appropriate materials and equipment for administration[6].

However, despite the fact that the preparation of medications is a procedure that demands complex knowledge, nursing usually does it as a simple and routine task, which

is assigned, without distinction, to any member of the team, regardless of professional category[6,10]. The consequences of inappropriate handling of medications include reduced microbiological safety and therapeutic efficacy[10].

A study that analyzed 43 antibiotic administrations, in the medical clinic and intensive care unit of a public hospital, found that 17% of the doses administered were different from those prescribed. An incorrect dose administration can harm treatment. In the case of antibiotics, patient's exposure to an ineffective and pharmacodynamically incompatible dose to their microorganism may generate resistance to the antimicrobial agent[11].

Thus, to ensure the rational and safe use of injectable drugs, best safety practices in their application are required[12]. In this context, in 2017, the World Health Organization (WHO) launched the third Global Patient Safety Challenge, with the theme "Medication Without Harm", whose goal was to reduce by 50% the serious harm associated with the use of medicines within five years[1].

Under this perspective, the present study aims to identify the residual volume in ampoule-vials after the preparation of injectables, associating the errors related to underdosing with the classes of drugs.

METHOD

A quantitative, descriptive, cross-sectional study was conducted from December 2020 to September 2021, in a private outpatient service in a Brazilian municipality located in the northeast of the state of São Paulo.

The sample included ampoule-vials with lyophilized powder for suspension or small volume parenteral solutions prepared by the nursing staff during the different work shifts. In the institution, there was advisory and regulatory material for the healthcare team regarding the preparation of injectables, specifying recommended reconstitution and dilution volumes for each drug. However, the objective of this study was not to evaluate compliance with the established operational procedures, but to determine the frequency of error and quantify the residual volume in the ampoule-vials used.

After reconstitution and/or aspiration of the solution, the bottles for disposal were collected by the nurse responsible for the sector and packed for evaluation. Besides the conventional label, all bottles also had an identification label filled in by the professional who prepared and aspirated the drug, with data on the date and time of drug preparation and volume, and the diluent used, whenever it was not presented as a solution.

The inclusion criteria for the selection of each vial for disposal were: medication prescribed to be administered in a single and total dose, to have been reconstituted with water for injection or 0.9% saline solution, to have an adhesive label with identification of date, time and reconstitution volume, as well as intact labeling that allowed the identification of the commercial name and generic denomination of the active ingredient of the medication, as well as dosage and volume of solution contained in the vial, when applicable. Vials with suspensions prepared at a time that exceeded the recommended stability period[13] and with signs of change in product quality attributes, such as formation of deposits and precipitates, were excluded.

The collected vials were properly packed in rigid cardboard boxes and sent to the researcher for measurement of the residual volume, in a separate drug preparation room. The room had artificial lighting, central air conditioning (temperature around 22°C), with relative humidity around 50%.

To quantify the residue contained in the ampoule-vials after aspiration, a disposable syringe with a 1 ml graduation and a 40mmx12mm blunt tip aspiration needle were used. The needle was introduced through the stopper, and the plunger of the syringe was pulled to aspirate any volume contained inside. The researcher used an apron, masks, and disposable gloves while handling the material. After this process, the ampoule-vials, needles and syringes were properly discarded in rigid containers for collection of sharp objects.

For data recording by the researcher, a form was prepared containing the following information: commercial name of the drug, therapeutic indication/class, reconstitution date and time, volume used to reconstitute the drug, and residual volume of each vial.

The drugs were divided into classes based on the active ingredient or therapeutic indication described in the original package insert. The percentage of solution loss was calculated from the identification of the reconstitution volume and the residual volume in each ampoule-vial.

Data were tabulated in Excel spreadsheets (Windows 2016) and analyzed using IBM SPSS Statistics, version 25, and R i386 software, version 3.5.3. Data analysis was performed using descriptive statistics, with measures of central tendency and dispersion, such as mean, median and standard deviation. The evaluation of the difference in residual volumes in the ampoule-vials was determined by the ANOVA test and a 5% significance level was established.

Since it did not involve human beings, the research project was not submitted to a research ethics committee. To obtain the data, authorization was requested to the health institution that provided the vials that were part of the sample (Appendix 1).

RESULTS

A total of 806 ampoule-vials were collected. Of these, 244 (30.3%) were excluded due to the absence of a label identifying the time, date, and volume of reconstitution or precipitate formation. Thus, the sample consisted of 562 vials, distributed according to the class of drugs (Table 1).

Table 1 – Distribution of ampoule-vials (n=562) according to drug class. Sertãozinho, SP, Brazil, 2021

Drug class	n	%
Antimicrobial	298	53
Anti-inflammatory	221	39.3
Immunoglobulin	17	3
Antiviral	10	1.8
Hormone	6	1.1
Antineoplastic antibody	6	1.1
Volume expander	3	0.5
Granulocyte colony-stimulating factor	1	0.2
Total	562	100

Source: Prepared by the authors, 2021

Among the antimicrobials, Ceftriaxone sodium stands out, accounting for 84.9% of this class. Considering anti-inflammatory drugs, the highest frequency was found for Tenoxican or prostaglandin biosynthesis inhibitor (78.7%). The antiviral used was Ganciclovir sodium (100%). Tocilizumab represented all of those indicated (100%) in the immunoglobulin category. The hormone that made up the category was Leuprorrelin Acetate (100% of the sample), and the antineoplastic antibody was Infliximab (100%). Human albumin was categorized as a volume expander, and Filgrastim as a granulocyte colony stimulator.

For better evaluation of the results, except for the vials of antimicrobials and anti-inflammatory drugs, the other 43 vials of the other classes of drugs were categorized together as "other". Of the total sample, 462 (82.2%) ampoule-vials contained a residual volume ranging from 0.1 ml to 1.5 ml. Table 2 shows the distribution of the ampoule-vials according to residual volume.

Table 2 – Distribution of ampoule-vials (n=562) according to the residual volume. Sertãozinho, SP, Brazil, 2021

Residual volume (ml)	N	%
0	100	17.8
0.1	90	16
0.2	165	29.3
0.3	105	18.7
0.4	57	10.1
0.5	25	4.4
0.6	11	2
0.7	4	0.7
0.8	2	0.4
1.0	1	0.2
1.1	1	0.2
1.5	1	0.2
Total	562	100

Source: Prepared by the authors, 2021

The reconstitution volume ranged from 1 to 20 ml. Table 3 shows the average minimum, maximum, median, mean and standard deviation values of the ampoule-vials according to reconstitution volume, residual volume and percentage of solution loss.

There was no difference in the loss of solution among the different classes of drugs. On average, 4.5% of drug doses were not administered to patients, but the percentage of reconstituted solution loss reached 33.3%.

Table 3 - Average minimum, maximum, median, mean and standard deviation values of the different classes of drugs according to reconstitution volume, residual volume and percentage of solution loss. Sertãozinho, SP, Brazil, 2021

Drug class	Mean	Median	Minimum	Maximum	Standard deviation	*p
Antimicrobial (n=298)						
Reconstitution volume (ml)	7.6	5	2	20	4.8	
Residual volume (ml)	0.2	0.2	0	1.5	0.2	
Solution loss (%)	4.2	0.3	-	33.3	4.3	
Anti-inflammatory (n=221)						
Reconstitution volume (ml)	5.7	5	2	20	3.1	
Residual volume (ml)	0.2	0.2	0	0.7	0.1	
Solution loss (%)	5	4	-	20	4.1	
Other (n=43)						0.064
Reconstitution volume (ml)	4.4	4	1	10	2.9	
Residual volume (ml)	0.1	0.1	0	0.6	0.2	
Solution loss (%)	3.8	3	-	26.7	5.3	
Total (n=562)						
Reconstitution volume (ml)	6.6	5	1	20	4.2	
Residual volume (ml)	0.2	0.2	0	1.5	0.2	
Solution loss (%)	4.5	4	-	33.3	4.3	

*ANOVA Test. Source: Prepared by the authors, 2021

DISCUSSION

In the present investigation, many samples contained residual volume, even though the full dose of the vial had been prescribed. When any amount of residual solution can be detected in the ampoule-vial after drug preparation and administration, it means that at least one of the "rights" related to safety in the administration of injectables has not been considered; in this case, the right dose has not been provided.

Contextual complexities, organizational limitations, and institutional policies represent some of the obstacles in meeting the "rights" of drug administration. Thus, contemporary healthcare settings, due to their complex clinical context, require structural adequacy and people-centered strategies for safe and efficient drug administration[14].

The findings also showed a high percentage of reconstituted solution loss, with up to 33.3% of the drug being retained in the vial and not applied. Recent evidence suggests that when small volumes of drugs are being infused, 10 to 20% of the prescribed dose may not be administered[15].

An investigation carried out in the emergency department of a large and highly complex Brazilian hospital, including 303 observations regarding preparation and administration of intravenous injectables by nursing professionals, identified that 2.6% of the medications were administered in a higher or lower dose than that prescribed, and 1.6% of the dilutions occurred in a volume smaller than that recommended by the manufacturer[16].

Among nursing interventions, drug administration represents 40% of clinical activity in hospitals. From this perspective, factors that induce medication errors, such as stress, fatigue, increased workload, insufficient human resources, and interruptions in the workflow, can have a negative impact on the performance of professionals and, consequently, lead to risks to patient safety[17].

A study conducted in Brazil with the objective of identifying the relationship between environmental factors and antibacterial preparation and administration errors showed that, from a total of 265 prepared drugs, 157 dosing errors and 62 wrong drug choices were identified. Dosing errors were verified based on the incompatibility between the prescribed dose and the prepared/administered dose, evidenced by medication left in the ampoule-vial, in the solution bags (diluent and medication) or in the equipment. Variations in lighting and noise did not cause dosing errors or wrong drug choices, but the authors concluded that environmental variables could favor medication errors both in the preparation and administration stages[18].

Researchers state that half of all medication errors reported in primary care occur in the health center. One in every four cases is a potentially serious error. The most important causes are inappropriate prescription (including incorrect indication or dosage, interactions, contraindications, and allergies), poor provider-patient communication, and lack of patient self-administration[19].

A study that evaluated 2,008 infusions in a total of 1,326 patients in hospital institutions in England and classified deviations as errors or discrepancies, according to the potential to cause harm to the patient, observed the occurrence of 1,065 (53.0%) discrepancies and 231 (11.5%) infusion errors; of these, 23 (1.1%) were considered potentially harmful. According to the researchers, nurses can be a source of resilience, compensating for system deficiencies and vulnerabilities; however, this same adaptive capacity can also lead to unsatisfactory results, making it necessary to explore strategic interventions to manage performance variability[20].

In a survey conducted in Spain, the main medication errors occurring in the intensive care unit of a general hospital were identified. The overall medication error rate was 1.93%. The main risk areas were errors in the administration interval of antibiotics (error rate of 8.15%); errors in dilution, concentration and infusion rate of high-risk medications (error rate of 2.94%); and errors in the administration of drugs through nasogastric tubes (error rate of 11.16%)[21].

It was not the objective of the present study to identify the professional category that committed the error. However, based on other findings, it is estimated that 78% of nurses have committed a medication error at some point[7].

According to Escrivá Gracia et al.[21], nurses identify four main areas that lead to medication errors: the critical care setting itself, the organization of the service, personal factors, and the drug administration process. In addition, nurses have a low level of knowledge about the drugs they use the most and with which the highest number of errors are committed.

When analyzing errors among 139 doses of intravenous medications in a hospital emergency service, the authors verified that, among a total of 118 medications that required dilution, an error occurred in 30, 21 (70%) of which were performed by nursing students and nine (30%) by nursing technicians; 64 (90.1%) of the nursing students and professionals interrupted the infusion when it was still incomplete. No error occurred in 88, 62 (70.5%) of which were performed by nursing students[22].

Undergraduate students and nursing professionals with little time of practice describe that lack of familiarity with certain medications and patients contributes to errors in drug administration[9].

To quantify the residual volume contained in ampoule-vials of antibiotics used in pediatrics, researchers selected 105 samples of antibiotics. They observed that oxacillin (88.57%) and ceftriaxone (94.28%) were mostly used correctly, with low residual values. This did not occur with benzylpenicillin procaine + potassium, because, in 74.28% of the vials, there was discarding of a residual volume higher than that recommended[23].

Another investigation that aimed to identify the classes of drugs involved in medication errors in the intensive care unit reported 305 events, with an average of 6.9 cases per patient. The most frequent classes of drugs were: antibiotics (25.2%), gastric acidity reducers (19%) and antihypertensives (9.2%). Thirty-seven (12.1%) occurrences with high surveillance drugs were identified, corresponding to the five classes, with a predominance of venous anesthetics (43.3%)[24].

Some strategies adopted by organizations dedicated to patient safety to limit or prevent harm include: standardization of prescriptions; adoption of safety measures for identification and storage; adjustments for safe dispensing and preparation; implementation of a clinical decision support system with automated alerts; limitation of access to potentially dangerous drugs; broad provision of information about medications to professionals and patients; use of redundancies such as double-checking[25].

Another strategy that may contribute to the reduction of medication errors in hospitals is the use of a protocol for safe administration of injectables. In a prospective observational study, nurses from 16 Dutch hospitals were observed during the administration of intravenous medications, assessing compliance with respect to a protocol on two separate occasions (2012 and 2016). A total of 372 intravenous drug administrations were observed. No significant change was observed in overall protocol compliance when comparing the two periods evaluated[26].

According to the WHO[5], to improve safety at all levels of health care, it is essential to implement system and practice changes, involving both patients and health professionals (education and training approach, human factors), focusing on care processes (administrative errors, diagnostic errors, medication errors, multimorbidity, transitions of care), and observing available tools and technologies.

It is worth mentioning that overdoses are more likely to be identified, intercepted, and reported than underdoses, as they can be perceived as having greater potential for patient harm. However, all drug doses should be prescribed in accordance with clinical guidance and dispensed and administered exactly as prescribed, since the potential for patient harm associated with dosing errors is difficult to predict and varies according to a number of factors, including the magnitude of the error, the toxicity profile of the drug itself, the clinical status of the patient, and the tolerance or susceptibility to the effect of the drug[27].

From this perspective, scholars recommend that research with a strong theoretical focus be conducted to investigate the nature and complexity of the causes of medication errors, with particular emphasis on interventions that can result in substantial and lasting improvements in patient safety[9,28,29].

The limitations of the present study involve the lack of in loco evaluation of the act of drug administration, with the presumption that the drugs were effectively administered in insufficient doses. Furthermore, the cross-sectional design of this study did not make it possible to analyze the behavior or variables studied over a long period of time.

FINAL CONSIDERATIONS

In the present study, a significant frequency of errors related to the preparation of injectables by the nursing staff was found, leading to administration of lower doses of drugs than those effectively prescribed, which can cause harm to the patient's health.

It is necessary to examine practical and concrete ways to avoid medication errors. Increasing patient safety is essential to ensure nursing care, with the definition of policies, protocols, and guidelines that are clear and accessible to all professionals, minimizing the gaps between the acts actually practiced and the ethical postulates and legal and regulatory provisions.

Interventions to prevent medication errors need to be implemented jointly and in a multidisciplinary way, with commitment from everyone involved in this process. Leadership, awareness, education, error monitoring, strengthening of human and technological resources are some important multifaceted and indispensable tools to face this challenge.

The relevance of this investigation consists in exploring a theme that is often neglected by the nursing team. These findings may be useful to demonstrate the scope of the problem, mistakenly underestimated, and highlight the role of nurses in reducing failures in the phases of medication preparation, especially those associated with therapeutic underdose. Further studies are needed to identify such errors and expand the systems approach capable of minimizing or stagnating the clinical consequences related to errors in the preparation of injectables, with the aim of optimizing patient outcomes and reducing untimely burdens on the healthcare system.

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