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Performance of the clinical pharmacist in the use of drugs via enteral tubes in intensive care

Ana Silva MASCARENHAS[1], Tamiles Borges SANTANA[1], Manoela Santos da SILVA[2], Dara Santos de OLIVEIRA[2] Juliana da Silva OLIVEIRA[3], Tuany Santos SOUZA[3], Gisele da Silveira LEMOS[4]

[1]Residência Multiprofissional em Urgência e Emergência. Universidade Estadual do Sudoeste da Bahia. Jequié, BA; [2]Universidade Estadual do Sudoeste da Bahia, Jequié, Bahia, Brasil; [3]Departamento de Saúde II, Universidade Estadual do Sudoeste da Bahia, Jequié, Bahia, Brasil; [4]Departamento de Ciências e Tecnologias. Universidade Estadual do Sudoeste da Bahia. Jequié, BA.

Corresponding author: Lemos GS, giselesilveiralemos@gmail.com

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Abstract

Objective: The aim of the study was to evaluate pharmaceutical interventions and guidelines related to the use of medication via enteral tubes in the Intensive Care Unit (ICU). **Methods:** Descriptive cross-sectional study, based on medical records of patients hospitalized in three ICUs of a public hospital in the interior of Bahia, where information was collected on pharmaceutical developments on interventions and medication use guidelines via enteral tubes. **Results:** 102 medical records evaluated by pharmacists between July and December 2019 were identified. Most patients were male (52.5%) and elderly (55.4%). Of these, 24.8% had guidance on the use of medication via tubes, 7.8% had interventions that contraindicated the use of medication via tubes, and 9.5% of the patients had medication-diet interactions described in their medical records. The most prevalent pharmaceutical guidance on the use via tubes was the form of drug dilution (89.1%), drug-diet interaction (80%) and break from the diet for drug administration (75%). Most drugs involved in the guidelines/interventions have action on the cardiovascular system (49.3%) and nervous system (20.7%). **Conclusion:** The relevance of the role of the clinical pharmacist regarding interventions and guidelines regarding the use of medication via enteral tubes in ICU patients was verified.

Keywords: Clinical pharmacy service; Use of medications; Enteral feeding tubes; Intensive Care Units; Evidence-based pharmaceutical care.

Atuação do farmacêutico clínico no uso de medicamentos por via sondas enterais em terapia intensiva

Resumo

Objetivo: O objetivo do estudo foi avaliar as intervenções e orientações farmacêuticas relacionadas ao uso de medicamentos por via sondas enterais em Unidade de Terapia Intensiva (UTI). **Métodos:** Estudo transversal descritivo, oriundo de prontuários de pacientes internados em três UTI de um hospital público do interior da Bahia, onde foram coletadas informações das evoluções farmacêuticas sobre intervenções e orientações de uso de medicamentos via sondas enterais. **Resultados:** Identificou-se 102 prontuários avaliados por farmacêuticos no período de julho a dezembro de 2019. A maioria dos pacientes eram do sexo masculino (52,5%) e idosos (55,4%). Desses 24,8% tiveram orientações sobre o uso de medicamentos via sondas, 7,8% apresentaram intervenções de contraindicação para o uso de medicamentos via sondas e 9,5% dos pacientes tiveram interações medicamento-dieta descritas em prontuário. A orientação farmacêutica sobre o uso via sondas mais prevalente foi a forma de dissolução dos medicamentos (89,1%), interação medicamento-dieta (80%) e pausa da dieta para a administração de medicamentos (75%). A maioria dos medicamentos envolvidos nas orientações/intervenções possuem ação no aparelho cardiovascular (49,3%) e sistema nervoso (20,7%). **Conclusão:** Verificou-se a relevância da atuação do farmacêutico clínico referente às intervenções e orientações referente ao uso de medicamentos via sondas enterais em pacientes internados em UTI.

Palavras-chave: Serviço de farmácia clínica; Uso de medicamentos; Sondas de alimentação enteral; Unidades de Terapia Intensiva, Cuidado farmacêutico baseado em evidências.

Introduction

The pharmaceutical care service comprises pharmacotherapy follow-up[1] of the patient, which must be provided in a continuous, systematic and documented way, in collaboration with the patient, the family (when necessary) and the professionals of the health system, with the objective of achieving concrete results that improve quality of life of the subjects[2].

In this sense, the pharmaceutical care lines should meet each patient's needs, given the specificities of the treatment. Thus, in patients whose oral route cannot be used, enteral access devices are also employed for drug administration, concomitantly with nutrients[3,4]. The medications can be either in solid (tablets, powders and capsules) or in liquid (solutions and suspensions) pharmaceutical forms[4]. Considering the complexity of drug administration through these devices, using appropriate techniques helps to minimize problems related to tube obstruction, to reduced therapeutic efficacy, and to increased drug toxicity and drug-diet interactions[4].

Proper selection of the pharmaceutical form of the enteral medications, as well as the appropriate administration route, can avoid complications related to the tube, in order to guarantee effectiveness of the pharmacotherapy and reduce the adverse effects[5]. In this way, the clinical pharmacist's participation is indispensable in the monitoring of hospitalized patients and in the use of nutrition devices, from the analysis of the prescription to drug administration, in order to guide the team on the best way to administer them, thus promoting proper treatment[6].

Teamwork is fundamental and important in all the stages of patient's progression[3-6]. Among the essential professionals for the patient's nutritional support is the pharmacist, providing diverse information on appropriate nutritional formulations and their proper handling, including co-administration of medications[4-6]. Thus, the objective of this study was to evaluate the pharmaceutical interventions and guidelines related to medication use via enteral tubes in the Intensive Care Unit (ICU).

Methods

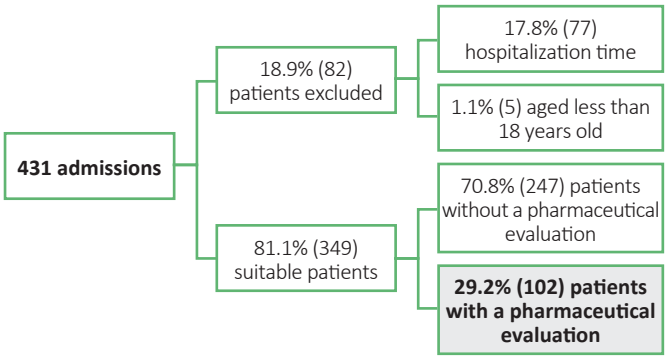
Study design and research locus

An observational and cross-sectional study was developed at a public hospital in inland Bahia. This is an open-door hospital, a reference unit for urgency and emergency care for 27 municipalities in the southern health region of the state, with 275 beds, of which 29 were distributed among three ICUs during the study period.

Inclusion criteria

Adult patients (≥18 years old) were included in the study, hospitalized in the ICU for a period longer than 48 hours, who received pharmaceutical care recorded in medical charts through pharmaceutical evolution, called as such in the pharmaceutical evaluation study, during data collection (Figure 1).

Figure 1. Diagram corresponding to the process for including the patients in the study. Bahia, Brazil, 2019.



Source: Prepared by the authors

Data collection

Prior to data collection, a pilot test was performed to assess the data collection instrument in ten patients, from June to July 2020. Data collection was carried out from August 1st to November 30th, 2020, in the medical records of the patients participating in the study by a previously trained team (two resident pharmacists, two scientific initiation students, and three students as part of their completion of course paper).

A specific form was developed as collection instrument. Data were collected regarding sociodemographic data, pre-existing clinical conditions, hospital information, pharmaceutical evaluation, interventions/guidelines for medication use via tubes , prescription 24 hours after admission, laboratory tests, evaluation of medication dose adjustment according to renal function, adverse drug reaction trackers, and additional information for patients hospitalized from July 1st to December 31st, 2019.

Definition of the variables

Dependent variable

Medication use via enteral tubes was considered as the dependent variable, assessed by means of the records corresponding to the pharmaceutical evolutions in the medical charts.

Independent variables

The sociodemographic characteristics evaluated from the medical records of patients participating in the study were: sex (male, female), age (young adults, 18 to 59 years old, and elderly, over 60 years old), race/color (white and non-white) and marital status (with and without a partner). The pre-existing clinical conditions: alcoholism, smoking, Systemic Arterial Hypertension [SAH], Diabetes Mellitus [DM], neoplasm, heart disease, nephropathy, liver disease and allergies; and the therapies used by patients (vasoactive drugs, sedation, antibiotic therapy, corticosteroid therapy and prophylaxis for Acute Gastric Mucosal Injury [AGMI]).

The type of tube used by the study patients was analyzed, and they were classified according to the insertion region – oral or nasal – and to the position of the distal end – stomach or intestine – being called oro or nasogastric tube and oro or nasoenteral tube, respectively[3], without interventions or guidelines in relation to positioning.

The pharmaceutical evaluations performed and recorded in medical charts were as follows: identification of Drug-Related Problems (DRPs), medication reconciliation, drug interactions and drug-diet interactions, general and specific guidelines for medications administered via enteral tubes and general and specific interventions for medications administered via enteral tubes.

The general guidelines and interventions recorded in the pharmaceutical evolution and the specific guidelines and interventions for medication use via tubes were quantified. Interventions were considered to be those aimed at the medical team that needed a change in the prescription, and the guidelines intended for the multiprofessional team, mainly the Nursing team.

As for the interventions and guidelines for medication use via enteral tubes, we have the following: interventions that were classified according to their type (contraindication and substitution) and to heir acceptability (prescription interventions were defined as follows: accepted and not accepted); the guidelines were arranged as: dissolution form of solid oral pharmaceutical presentations (tablets and capsules), tube washing, enteral diet pause, drug-diet interaction and risk of tube obstruction[6-9], in which it was not possible to assess their acceptability, as they are guidelines mainly related to the drug administration process and which are not recorded in detail in electronic medical charts.

The analysis of the class of medications involved in guidelines/interventions via enteral tubes was performed according to the main anatomical group (Level 1) and to the pharmacological group (Level 3) of the Anatomic Therapeutic Chemical (ATC) classification, created by the World Health Organization Collaborating Centre for Drug Statistics Methodology[10].

Data analysis

Data tabulation and analysis were performed using *Microsoft Excel*® 2010 and the *Statistical Package for the Social Sciences* (SPSS), version 21.0. The descriptive analysis was presented in absolute and relative frequencies of the categorical variables and central tendency (mean and median) and dispersion (standard deviation) of the quantitative variables were measured. The Kolmogorov-Smirnov test was used to evaluate normal distribution of the continuous variables, considering p>0.05 as normal distribution.

Ethical considerations

The research complied with all the ethical precepts aimed at ensuring the rights and duties that concern the research participants, the scientific community and the State according to CNS Resolution No. 466/2012 and is part of the study entitled "Clinical Pharmacy: Evaluation of medication use in a regional hospital", approved by the Ethics and Research Committee (*Comitê de Ética e Pesquisa*, CEP) of UESB, under protocol No. 3.050.237, CAAE 29780014.8.0000.0055.

Results

A total of 102 patients were included in the study, 29.2% of the total number of patients admitted to the ICU during the data collection period, with predominance of male patients (52.5%) and aged at least 60 years old (55 .4%), varying between 22 and 91, with a mean of 60.6 and a standard deviation of ±16.9. For the pre-existing clinical conditions, 67.8% (59) and 39.0% (32) prevalence of HAS and DM was noticed, respectively (Table 1).

Table 1. Sociodemographic and clinical characteristics of the patients hospitalized in Intensive Care Units who had a pharmaceutical evaluation, from July to December 2019. Bahia, Brazil.

Sociodemographic characteristics	Response rate (%)	n	%
Gender	99.0		
Female		48	47.5
Male		53	52.5
Age group	99.0		
18-59 years old		45	44.6
60+ years old		56	55.4
Race/Skin color	78.4		
White		0	0.0
Not white		84	100.0
Marital Status	82.4		
With a partner		25	29.8
Without a partner		59	70.2
Pre-existing clinical conditions		**n**	**%**
Alcoholism	50.0	13	25.5
Smoking	42.2	8	18.6
Systemic Arterial Hypertension	85.3	59	67.8
Diabetes Mellitus	80.4	32	39.0
Neoplasm	53.9	2	3.5
Heart disease	59.8	13	21.3
Nephropathy	59.8	12	19.7
Liver disease	53.9	1	1.8
Allergies	76.5	12	15.4
Other comorbidities	80.4	24	29.3
Therapies used during hospitalization (n=102)		**n**	**%**
Renal Replacement Therapy		26	25.5
Vasoactive drugs		68	67.7
Sedation		74	72.5
Antibiotic therapy		96	94.1
Corticosteroid therapy		52	51.0
AGML prophylaxis		92	90.2

Source: Prepared by the authors. AGML: Acute Gastric Mucosal Lesion.

Regarding the drug therapies used during hospitalization, the high number of patients who underwent treatment with antibiotics in the ICU (94.1% [96]) and for AGMI prophylaxis (90.2% [92]) stands out.

The patient's hospitalization time in the ICU had a median of 13.5 days, with an interquartile range of 16.3. Among the patients included in the study, 32.4% (33) were hospitalized in ICU 1, 28.4% (29) in ICU 2, and 9.8% (10) in ICU 3. It was observed that 25.5% (26) were admitted to 2 of the ICUs during the same hospitalization and that 3.9% (4) were admitted to all 3 ICUs.

A total of 427 pharmaceutical evolutions were recorded, with a mean of 4.18 ± 4.84 evolutions per patient, with 49.0% (49) of the patients having alerts in their prescriptions, accounting for a total of 58 alerts. It was observed that 62.7% (64) of the patients were assisted by the resident pharmacist, 32.4% (33) were by the hospital pharmacist and 4.9% (5) patients, by both.

The DRPs found in the pharmaceutical evolutions were reported, being present in 59.8% (58) of the patients, of which 34.5% (20) had more than one type of DRP recorded, totaling 82 DRPs reported. The most frequent DRP was the one corresponding to Safety, related to Drug Interactions (DIs) and/or Adverse Drug Reactions (ADRs), with 41.46% (34).

The intestinal position tube was the most used by the patients during their ICU hospitalization (76.4% [78]), followed by the gastric position tube (15.6% [16]), with no interventions or guidelines regarding positioning being identified. It is worth noting that the patients with long hospitalization periods used more than one type of device for nutrition, and that 24.8% (25) of the patients received specific guidelines on medication use via tubes (Table 2).

Table 2. Description of the pharmaceutical evaluations performed in patients hospitalized in Intensive Care Units, from July to December 2019. Bahia, Brazil. (N=102)

Evaluations recorded in the pharmaceutical evolution	n	%
Patients with DRPs identified and recorded	58	56.9
Patients with medication reconciliation	6	5.9
Patients that had drug interactions reported	66	64.7
Patients that had drug-diet interactions reported	8	7.8
Patients that received general pharmaceutical guidelines	85	83.3
Patients that had general pharmaceutical interventions	79	77.5
Patients with specific pharmaceutical interventions on medication use via enteral tubes	25	24.5
Patients with specific interventions on medications contraindicated for use via enteral tubes	8	7.8

Source: Prepared by the authors.

It was observed that 7.8% (8) of the patients had an intervention contraindicating medication use via enteral tubes, but in 2 of them it was not possible to assess acceptability. Of the others, 33.3% (2) were accepted and 66.7% (4) were not accepted. The medications involved in the enteral tube contraindication interventions were the following: Metoprolol succinate (50.0%), Amiodarone (12.5%), Lactulose (12.5%), Ranitidine (12.5%) and Omeprazole (12.5%). In addition to the interventions directed to the physician to change the therapy, the evolutions in the patients' medical charts contained specific guidelines on the ways of using medications via enteral tubes, mainly aimed at the Nursing team.

The specific guidelines on medication use via tubes reported in the medical charts were related to the following: dissolution form, possibility of crushing or not the tablets in water and amount of water to be used; tube washing before and after drug administration; the diet pause guideline referring to the recommended time without food intake before and after drug administration or concomitant administration of the diet; the drug-diet interactions regarding the drug's potential to interact with enteral nutrition when administered concomitantly, as well as the need to administer the medication simultaneously with the diet to obtain its expected effect; and the risk of tube obstruction for those medications that are likely to cause such obstruction. The specific guidelines are presented in Table 3, according to the classification.

Table 3. Description of medication use via enteral tubes recorded in the medical charts of patients hospitalized in Intensive Care Units, from July to December 2019. Bahia, Brazil. (N=145)

Guidelines for medication use via enteral tubes	n	%
Dissolution form of oral solid pharmaceutical presentations	57	89.1
Tube washing	14	23.0
Drug-diet interaction	12	80.0
Pause in the diet to administer the medication	15	75
Risk of tube obstruction	2	40

Source: Prepared by the authors.

Among the guidelines, specific for medications via enteral tubes, it was verified that 25.0% (3) of the drug-diet interactions were related to concomitant administration of enteral diet (prednisone 66.6% [2] and carvedilol – 33.4% [1]), that 50.0% (6) were on administration without food, that is, when there is a need to pause the diet (levothyroxine, paracetamol and lactulose 16.7% each and phenytoin – 50.0% [3]), and that there was no description of the interaction in 25.0% (3). It was verified that 75.0% (15) of the medications had guidelines about the pause in the diet, where: 53.3% (8) paused only at the time of administration, 13.3% (2) did not pause, i.e., administered along with the diet, and 33.3% (5) had suggested pause times. This time varied from 30 or 60 minutes before to 2, 3 or even 4 hours after administration.

The main pharmaceutical form involved in the specific guidelines for medications via enteral route was solid, with 95.6% (66), with the liquid presentation reaching 4.3% (3). Most of the solid medications were in the form of a single tablet (63.8% [44]) and, in 5.8% (4) of the guidelines, they were for medications in the pharmaceutical form of prolonged-release tablets (metoprolol succinate).

Table 4 describes the drug classes according to ATC, Level 1, involved in specific guidelines/interventions for use via enteral tubes, the most frequent ones referring to the "Cardiovascular system", 49.3% (34), and to the "Nervous system", 20.7% (14). For the Level 3 classification, Antiepileptics was the most prevalent with 11.6% (8) of the guidelines, followed by Beta-blockers with 10.1% (7).

Discussion

In relation to the pharmaceutical interventions, specific for medications via enteral tubes, the main study findings point to the occurrence of contraindications for the administration of these medications, evidencing the need for a multiprofessional discussion about these drugs, as well as about continuity or not of the treatment with a given therapy option. Regarding the guidelines, specific for medications via enteral tubes and directed to the Nursing team, the drug-diet interactions and diet pauses for drug administration should be highlighted, which suggests the need for work in a multiprofessional team, training of the professionals who prescribe and administer medications, as well as follow-up by the clinical pharmacist in medication use via tubes.

The presence and evaluation of the professional pharmacist within the ICU multiprofessional team on a daily basis is still not a reality in most hospitals, but the essentiality of pharmaceutical follow-up, especially for critically-ill patients, has already been discussed, in order to improve the pharmacotherapy outcome and reduce

Table 4. Classification of the medications involved in the guidelines/interventions specific for drugs used via enteral tubes according to ATC Level 1 and Level 3, of patients hospitalized in Intensive Care Units, from July to December 2019. Bahia, Brazil. (n=69)

ATC classification	n	%
A - Digestive tract and metabolism	**6**	**8.7**
A02B – Medications for peptic ulcer and gastroesophageal reflux disease (GERD)	3	4.3
A06A – Drugs for constipation	1	1.4
A12B – Potassium	2	2.9
B - Blood and organs	**4**	**5.8**
B01A – Antithrombotic agents	4	5.8
C - Cardiovascular System	**34**	**49.3**
C01B – Class I and III antiarrhythmics	2	2.9
C01D – Vasodilators used in heart diseases	4	5.8
C02A – Antiadrenergic agents	1	1.4
C02D – Peripherally acting arteriolar smooth muscle agents	5	7.2
C03A – "Low ceiling" diuretics, thiazides	1	1.4
C03C – Loop "high ceiling" diuretics	1	1.4
C07A – Beta-blockers	7	10.1
C08C – Selective calcium channel blockers	5	7.2
C09A – ACE inhibitors	4	5.8
C09C – Angiotensin II receptor blockers	1	1.4
C10A – Lipid-modifying agents	3	4.3
H - Systemic hormonal preparations, excluding sex hormones and insulins	**5**	**7.2**
H02A – Simple corticosteroids for systemic use	4	5.8
H03A – Thyroid preparations	1	1.4
J - General anti-infectives for systemic use	**5**	**7.2**
J01E – Sulfonamides and Trimethoprim	2	2.9
J01F – Macrolides, Lincosamides and Streptogramins	1	1.4
J01X – Other antibacterials	1	1.4
J04A – Medications for the treatment of tuberculosis	1	1.4
N - Nervous system	**14**	**20.7**
N02B – Other analgesics and antipyretics	1	1.4
N03A – Antiepileptics	8	11.6
N05A – Antipsychotics	5	7.2
R - Respiratory tract	**1**	**1.4**
R06A – Antihistamines for systemic use	1	1.4

Source: Prepared by the authors.

the risk of drug interactions, adverse drug reactions, and general adverse events related to patient care. Evaluation and guidance of medication use via enteral tubes is part of the pharmaceutical activities in intensive care, promoting patient safety, therapy effectiveness and health education for the team[4].

Based on the evaluation of the sociodemographic characteristics of the sample of this study, predominance of males was noticed, as in the study by Barbosa[11] conducted in ICUs of a teaching hospital from Minas Gerais, which had 51% of men, most of them older adults (79%) and with a mean age of 66 ± 18 years old. A similar result was found in the study by Basso and Pinheiro[8] with patients hospitalized in an ICC who presented a mean age of 64.8 ± 16.2 years old.

The prevalence of males in the ICU hospitalizations can be related to the fact that, in general, the idea that Primary Care is a service intended almost exclusively for women, children and older adults is widespread. Other authors also report that men associate care with the female scope and, as they feel unattainable, they expose themselves more, becoming more vulnerable to health risk situations[12]. A study developed by Rodriguez et al.[13] evidenced a majority of male individuals hospitalized in the ICU, with 61.5% of the patients. Another research study, conducted by Batista et al.[14] found 75.41% predominance of deaths due to external causes in the male gender.

In relation to the most prevalent age group in the current study, older adults, it is important to consider that Brazil has more than 28 million people in this age range, a number that represents 13% of the country's population. This percentage tends to double in the next decades, according to the Population Projection disclosed by the IBGE in 2018[15]. DM and SAH are frequent diseases and are considered as public health problems and important causes of morbidity, mortality and disabilities[16]. In a nationwide study conducted with the aged population, more than 60% had multiple chronic diseases and SAH was the second most prevalent[17].

Age and presence of multiple morbidities favor polypharmacy for treating the health conditions that affect critically-ill patients. Indiscriminate use of antimicrobials has been reported in several parts of the world as a fairly current adversity. The cost regarding antibiotics can even reach 30% of the expenses in a hospital pharmacy[18]. Souza, Baroni and Roese[19] conducted a study in three ICUs of a public hospital where 100% of the patients made use of antimicrobials during the research period. In the current paper, this result was 94.1%, very close to the reality of other hospitals.

Several health conditions that are frequent for ICU admission, including the use of certain medications, are considered risk factors for the development of AGMI; therefore, diverse scientific

evidence shows the benefit of using drug therapy for prophylaxis in critically-ill patients, who are at high or higher risk of developing the pathology, therefore verifying that most of the participants evaluated in this study (90.2%) were in use of this prophylaxis[20-21]. The need to perform prophylaxis for AGML even in the patients admitted to an ICU should therefore be reassessed daily in order to avoid unnecessary use of medications.

The pharmacist's participation in the individualized care of patients shows a positive impact on recovery of their health[22], and mainly aims at preventing DRPs and improving the pharmacotherapy. Due to the insufficient number of pharmacists for the development of clinical activities, they carry out risk assessments to start monitoring the patients, choosing those at higher risk as a priority for evaluation and evolution in medical charts[23]. Such reason justifies the result of the number of patients that had a pharmaceutical evaluation among all those admitted to the ICU in the study.

In addition to that, in the study hospital, the evaluations were performed by two classes of pharmacists. Hospital pharmacists are responsible for all drug logistics and pharmacy management functions, while residents are directly involved with the clinical activities, thus allowing greater proximity to patients and time devoted to evaluations and guidelines.

It is important to record the presence or risk of a patient presenting a DRP involving pharmacotherapy, which is a routine activity of the pharmacist. More than half of the patients included in the current study had DRPs identified and recorded in their medical charts, in addition to the fact that the most frequent type of DRP corresponded to DIs and/or to ADRs. Dias *et al.*[24] obtained a similar result, where the main types of DRP found corresponded to DIs and to the potential risk of adverse events.

The main DRPs that can be related to inappropriate medication use via enteral tubes are Safety due to ADR and Effectiveness, considering incorrect medication use, thus requiring a pharmaceutical evaluation and detailed guidance for their use, as well as interventions for changes in prescription and administration time, among others.

Most of the patients followed-up in this study used an intestinal position tube, a result similar to a study carried out in an ICU[25]. A descriptive and observational study developed at the Clinical Hospital Complex of the Federal University of Paraná evaluated the knowledge of the Nursing team – the professionals most involved in management of enteral tubes and drug administration – about tube position and the possibility of drug administration, where it was identified that 59.4% of the Nursing team does not evaluate the type of medication or correlates with the tube position before administration, which becomes critical, as there is a change in absorption of the drug when it is released in different anatomical locations; in addition, it was also observed that 37.7% of the nurses and 100.0% of the nursing technicians had never received training about this practice[26].

The most frequent pharmaceutical presentation in the guidelines corresponding to medications administered via tubes was solid, a result that was also found in other research studies[4,25-26]. Within this category, some formulations should not be crushed for administration through this route, such as gastro-resistant microgranules (omeprazole) that are inactivated by gastric acid, so they are arranged in this pharmaceutical form, which contraindicates their crushing, and delayed or prolonged release tablets (e.g. metoprolol succinate), which are designed to release the drug in a controlled manner, at a predetermined rate, duration and reach location, in addition to maintaining the drug's therapeutic blood levels[27], as well as other medications, to which use is contraindicated for different reasons. The study by Ferreira Neto *et al.*[28] found a result of 17.7% of medications contraindicated for administration via tubes.

In an intervention study carried out with ICU nurses, Hdaib *et al.*[29] showed 48.0% improvement in the mean score of the assessment instruments after the intervention of the clinical pharmacist on medication use through enteral accesses. In a case-control study aimed at evaluating nurses' knowledge and practice in administering medications via tubes before and after training by a clinical pharmacist, it was possible to notice that the attitudes of the nurses from the case group changed significantly after the intervention, and the pharmacists were selected as the first professionals to be consulted 50.0% of the times[30].

Pharmacists should work in collaboration with the multiprofessional team in the identification of potential drug-diet interactions in order to assist in the management regarding use of such medications[4,31,32]. In this study, the guidelines on drug-diet interactions and pause in the diet were related to 80% and 75% of the medications, respectively. Carvalho *et al.*[25] evaluated prescriptions corresponding to 65 patients, where 95.4% of them had prescriptions of medications with a potential to interact with the diet. In general, interactions between drugs and nutrients/food affect the pharmacokinetic processes, mainly absorption; therefore, pause times are necessary when the medication is better absorbed without the presence of food, or when it has improved absorption when administered concomitantly with the enteral diet[33].

An example of a drug-nutrient interaction common in the clinical practice, especially in the ICU, is phenytoin, from the antiepileptic class, used in seizure prevention and treatment. Its usual dosage is 100 milligrams every 8 hours and, for a patient in use of enteral nutrition, the pause in the diet is indicated to start 1 hour before to resume it 2 hours after administration[34-35]. According to Salih, Bahari and Abd[36], bioavailability of phenytoin is reduced in the presence of food due to the significant decrease in bonding to the plasma enzymes and consequent reduction in serum concentration[37].

Interventions of this type also involve the nutrition team, as pausing the diet for a prolonged period of time can exert an impact on the nutritional support necessary for the patient within 24 hours[38]. A study by Basso and Pinheiro[8] with pharmaceutical interventions for the multiprofessional team related to drug administration via tubes classified interventions that involved the nutrition team as drug-nutrient interactions, pauses in the diet and drug administration in the scheduled diet infusion intervals. RDC No. 503 of May 27th, 2021,[39] states that the complexity of administering medications via tubes requires commitment and training of a Multiprofessional Nutrition Therapy Team, consisting of at least one professional from each category: physician, nutritionist, nurse and pharmacist, qualified and with specific training for the nutritional therapy practice.

According to the ATC classification, the main medications prescribed via tubes are part of the Cardiovascular System groups, followed by the Nervous System; similar results were identified by Batista and Oliveira-Lemos[4]. Abreu *et al.*[40] identified the use of Beta-blockers and Antiepileptics as a majority within the aforementioned ATC subgroups, only differing in the most prevalent medications, which can be associated with a standardization issue, or even with routines and preference of the prescribers. Thus, such medications

should always be evaluated regarding the possibility of administration via tubes, potential interactions and risk of adverse reactions, as safety and therapeutic efficacy of these drugs must be guaranteed for success of the treatment and recovery of the patients' health.

There are few detailed studies on the behavior profile of the medications used via alternative routes, which limits the search sources for nurses and pharmacists to guide teams and administer medications safely. Such fact reinforces the need for studies on the topic, as well as for training of the multiprofessional team.

The current study presented the following limitations: the way to prescribe the DRPs, as well as guidelines and pharmaceutical interventions not standardized with all the necessary information and medications involved. It is suggested that prospective studies be carried out that may be able to evaluate the outcomes and their relationship with the medication use via tubes and DRPs detected in the pharmacotherapy follow-up.

This study shows the importance of including a clinical pharmacist in the multiprofessional teams for the care of critically-ill patients. This professional tends to collaborate with the team in the management and follow-up of patients and in monitoring medication use in order to improve the treatment, reduce hospitalization times, reduce costs related to pharmacotherapy and contribute to the patients' quality of life.

Conclusion

It is concluded that the pharmaceutical interventions and guidelines on medication use via tubes were mostly related to the form of drug administration through this route, directed to the Nursing team. Such guidelines are crucial and contribute to management of the alternative therapies, assisting in the drug administration process and in health education of the entire multiprofessional team; they also reflect the need for updating and continuous training of all involved.

Studies on medication use through routes other than the one planned one are essential for the pharmaceutical clinical practice, especially in ICUs. The health conditions of critically-ill patients may require an alternative management, most often off-label, requiring the monitoring by the entire multiprofessional team and especially by the pharmacist in order to evaluate effectiveness and safety of medication use. The clinical pharmacist must combine the technical knowledge of pharmaceutical technology in the development of formulations with each patient's clinical needs to promote the best pharmacotherapy and better outcomes.

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Colaboradores

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Conflict of interest statement

The authors declare that there is no conflict of interest in relation to this article.

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