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Interactions Calculated between Medications and Enteral Nutrition Using an Updated Protocol in an Elderly Population in the Intensive Care Unit of a University Hospital in Central Brazil

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Drug-nutrient interactions refer to alterations in the pharmacodynamics or pharmacokinetics of a drug due to interactions with physical, chemical, physiological, or pathophysiological factors related to nutrients.
Objective: To investigate potential drug-nutrient interactions in patients receiving enteral nutrition admitted to an intensive care unit (ICU).
Methods: This observational, descriptive, retrospective study employed non-probabilistic sampling of elderly patients at a university hospital in Brazil's Central Region. Potential drug-nutrient interactions were identified using the Up To Date® database, with interactions classified by risk level.
Results: The study included data from 50 elderly patients, predominantly male (58%), with an average age of 70.6 ± 8.63 years. A total of 75 medications administered via the digestive tract were analyzed, of which 26 (34.66%) were found to have potential interactions according to Up To Date®, resulting in 47 types of pharmacokinetic interactions. Most interactions involved either the food/nutrient reducing the therapeutic effect of the drug or the drug lowering the serum level of the nutrient, accounting for 24 (51.06%) of the interactions. The average number of interactions was higher in deceased patients (1.5 ± 1.64) compared to those who were discharged (1.19 ± 1.44). Statistical analysis using the t-test (95% bilateral confidence interval) showed no significant difference between the groups (p-value > 0.99).
Conclusion: The findings highlight the importance of monitoring drug-nutrient interactions in ICU patients, as these interactions can potentially have adverse effects on patient outcomes.

Keywords: Pharmacovigilance; enteral nutrition; older adult health.

1. INTRODUCTION

Hospital malnutrition in the older adults can reach up to 75% of cases, resulting in negative clinical and economic consequences. One instrument used to monitor hospital malnutrition is the Subjective Global Assessment (SGA), a questionnaire-based tool that was proposed and validated by Detsky et al (1987) [1,2]. Enteral nutritional therapy (ENT) is a strategy used to combat malnutrition, and its usage in addition to drugs can cause some complications, such as drug-nutrient interactions, which are defined as changes in the pharmacodynamics or pharmacokinetics of a drug due to physical, chemical, and physiological interactions between a drug and a nutrient. These interactions can change the effectiveness of both drug and nutrients, impact nutritional status, and interfere with the absorption of drugs and nutrients [3,4,5].

Pharmacokinetic interactions are particularly evident in the elderly and are divided into four phases, each presenting opportunities for interactions between drugs and nutrients. These interactions can lead to adverse events affecting drug bioavailability due to hepatic metabolic difficulties and issues with drug elimination. Type I interactions involve bioactivation, which occurs through biochemical and physical reactions between substances. Type II interactions affect absorption and bioavailability by altering enzymatic functions, often via the cytochrome P450 system, or by modifying transport mechanisms. Type III interactions involve changes in systemic or physiological disposition, leading to alterations in the distribution of drugs or nutrients. Type IV interactions can affect the elimination of drugs or nutrients. These phases highlight the importance of monitoring drug-nutrient interactions, especially in elderly patients [6].

After being absorbed, drugs and nutrients are simultaneously distributed throughout the body, and they compete for the same plasma proteins, with albumin being particularly highlighted. Older, critically ill patients who do not interrupt enteral nutrition for drug administration, as well as malnourished and obese individuals, are more susceptible to these interactions [7].

Knowledge of drug interactions can contribute to a safer therapeutic approach by enabling early interventions through monitoring processes, screenings, protocols, and other practices that can be integrated into hospital routines. In light of this, this study aims to report potential interactions between drugs and nutrients in patients receiving enteral nutrition admitted to an intensive care unit (ICU).

2. METHODS

This is an observational, descriptive, and retrospective study that used non-probabilistic sampling to collect sociodemographic and clinical data of older patients admitted to the intensive care unit of a University Hospital in the Central Region of Brazil from 2019 to 2020**.**

Due to the impossibility of obtaining the Informed Consent Form (ICF) from the older patients, the data were collected with the authorisation of the person in charge of the intensive care unit at the Júlio Müller University Hospital for the use and handling of electronically archived medical records. The project includes a waiver of the ICF.

We collected 50 medical records of patients, aged older than 60 years who were admitted to the intensive care unit and undergoing any pharmacological treatment with exclusive or non-exclusive enteral nutritional therapy. We excluded patients on a zero diet and those on enteral nutrition for less than 3 days of administration. The nutritional condition was assessed using the Subjective Global Assessment (SGA), which was proposed and validated by Detsky et al (1987) [2].

The criterion for initiating enteral nutrition was applied to patients who did not achieve at least 60% of their daily nutritional needs through oral feeding and who had functional gastrointestinal tracts.

In the pharmacological treatment, the drugs administered via the digestive route were observed because it is the same route as food intake. This was done to identify possible interactions. The route of administration of the drugs was also considered, and in cases where drugs were administered via an enteral feeding tube, the pharmaceutical form in which they were presented was observed as well.

Furthermore, the following variables and relevant information were collected through the medical records: gender, age, length of hospital stay, drugs used, the Global Subjective Assessment (GSA) nutritional assessment tool, comorbidities, timing of initiation of enteral nutrition, length of hospitalisation, and final outcome.

After collecting the data, searches were conducted using the UpToDate® software database (Brazil, version 0.4.0 - 0.5.0 and its updates, 2022). This electronic clinical resource tool helps healthcare professionals describe and analyze potential interactions between drugs and food or nutrients. The database is global and is utilized across federal university hospital networks in Brazil. It provides support for multidisciplinary teams with continuously updated content, allowing for research into clinical information, procedures, and the latest developments in healthcare.

The aim was to provide safe and evidence-based answers. Access to the database was provided by the Brazilian Hospital Services Company (Ebserh). The research on interactions through the software was conducted in the drug interactions tab. By adding the name of the desired drug to investigate, the system generates all possible drug interactions, not only between drugs, but also with medicinal plants, food, and/or nutrients. All interactions were supported by scientific evidence, with references at the end of each page. Furthermore, for each possible interaction, the software suggests the appropriate management for the patient for better outcomes.

One relevant data provided by the UpToDate® software was the risk classification of each possible interaction with suggested resolution, being classified as: low severity B: no action necessary; moderate severity C: monitor therapy; moderate severity X: avoid combination and higher severity; D: consider therapy modification.

The data analysis was performed using the Excel programme Microsoft® Office 2016 (USA) and OpenEpi (Andrew G. Dean and Kevin M. Sullivan, Atlanta, GA, USA), where the necessary statistical calculations, including mean, standard deviation, and t-test for some variables were performed.

3. RESULTS

We analyzed the medical records of 50 patients. Most of the individuals were male, accounting for 58% (n=29), and the average age of the population was 70.6 ± 8.63 years. In terms of hospitalisation duration, 48% (n=24) stayed in the ICU for more than 31 days. In terms of clinical outcome, 52% (n=26) were discharged to the general ward.

In relation to the timing of initiation of enteral nutrition, 36% (n=18) of patients took 8 or more days to begin the diet. This was followed by 28% (n=14) within the first 24 hours, 22% (n=11)

between 2 to 3 days, and 14% (n=7) between 4 to 7 days.

Table 1. Educational level and presence of comorbidities in elderly patients of both genders admitted to the Intensive Care Unit of a University Hospital in Cuiabá, Mato Grosso, Brazil

Education	**n**	**%**
Not informed	17	34
1st Grade	16	32
No literacy	12	24
2nd Grade	4	8
Higher level	1	2
Comorbidities	**n**	**%**
Arterial Hypertension	30	32.6
Diabetes	19	20.7
Cancer	12	13
Pneumopathy	9	9.8
Cardiovascular Disease	8	8.7
Chronic Kidney Disease	5	5.4
Hepatopathy	4	4.3
Cirrhosis	2	2.2
Cerebrovascular Disease	1	1.1
Obesity	1	1.1
Neurological Diseases	1	1.1

Part of the sample had more than one comorbidity, which explains why "n" is greater than the sample number

As regards to the nutritional status of the older patients, a prevalence of 52% (n=26) of severe malnutrition was observed, followed by 26% (n=13) of patients with no reports in the medical records, and 22% (n=11) in moderate malnutrition.

In relation to the quantity of drugs offered during 3 days of enteral nutritional therapy, we found an average of 15.5 ± 5.03 drugs administered per day per individual. The most common method of administration was intravenous infusion at 63.10% (n=578), followed by subcutaneous administration at 10.59% (n=97), oral administration at 10.59% (n=97), enteral tube administration at 9.50% (n=87), inhalation at 5.79% (n=53), and rectal administration at 0.44% (n=4).

The physical form of drugs administered through enteral feeding tubes was predominantly in liquid form at 50% (n=44), followed by solid form at 31.82% (n=28), powder form at 3.41% (n=3), and not described in medical records at 14.77% (n=13).

In this regard to the possibilities for drug-nutrient and/or food interactions, we found 75 drugs that use the digestive route. Out of these, 34.66% (n=26) were found to have the potential for interactions according to the UpToDate® software, resulting in a total of 47 types of interactions (Table 2).

Table 2. Listing of some drugs that potentially interact with nutrients and/or food according to the UpToDate software and that were administered to older adults admitted to the Intensive Care Unit of a university hospital in Cuiabá – Mato Grosso. Brazil

Acetyl Salicylic Acid - Aspirin			
Pharmacological Class: Cardiovascular antiplatelets; Nonsteroidal anti-inflammatory. Salicylates.			
Food/nutrient	Possible interactions	Management	Risk classification
Fish oil	It can enhance the antiplatelet effect of the drug.	Monitor patients for signs and symptoms of bleeding.	Moderate Gravity C: Monitor the therapy.
Vitamin E	It can enhance the antiplatelet effect of the drug.	Monitor patients for signs and symptoms of bleeding.	Moderate Gravity C: Monitor the therapy.
Vitamin C	Aspirin can decrease the serum concentration of Ascorbic Acid	This interaction was only demonstrated with doses of aspirin of 600 mg or more.	Low Gravity B: no action required.
Folic acid			
Pharmacological Class: Water-soluble vitamin.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Green Tea	Green tea may decrease	Monitor folate levels in	Moderate Severity

	serum folic acid concentration	patients consuming green tea.	C: Monitor therapy
Albendazole			
Pharmacological Class: Anthelmintic.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit Juice	Grapefruit juice may increase serum concentrations of the active metabolite(s) of Albendazole.	Monitor for systemic effects of albendazole in patients consuming grapefruit products.	Moderate Severity C: Monitor therapy
Amiodarone			
Pharmacological Class: Antiarrhythmic Agent.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit Juice	Grapefruit juice may increase the serum concentration of amiodarone.	Avoid consuming grapefruit during treatment with amiodarone.	Moderate Severity X: Avoid combination
Anlodipine			
Pharmacological Class: Antianginal agent; Antihypertensive; Calcium channel blocker.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit Juice	Grapefruit juice may increase the serum concentration of Amlodipine	No action is required.	Severity Low B: No action required
Sodium Bicarbonate			
Pharmacological Class: Alkalizing Agent; Antacid; Oral Electrolyte Supplement; Parenteral Electrolyte Supplement			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Vitamins/Minerals (A, D, E, K, Folate and Iron)	Antacids may decrease the serum concentration of these nutrients.	Separate the dosage of both and if this is not possible, monitor for decreased therapeutic effects of oral iron preparations if an antacid is co-administered.	Major Severity D: Consider modifying therapy
Clarithromycin			
Pharmacological Class: Antibiotic.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit Juice	Grapefruit juice may increase the serum concentration of Clarithromycin.	No action required.	Severity Low B: No action required
Clopidogrel			
Pharmacological Class: Antiplatelet Agent.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit Juice	Grapefruit juice may decrease serum concentrations of the	Minimize grapefruit consumption, as its consumption may reduce	Major Severity D: Consider modifying therapy.

	active metabolite(s) of Clopidogrel.	the antiplatelet effects of Clopidogrel.	
Fish Oil	May enhance the adverse/toxic effect of Agents with Antiplatelet Properties.	Monitor patients for signs, symptoms, and bleeding time.	Moderate Severity C: Monitor therapy
Vitamin E	May increase the antiplatelet effect of agents with antiplatelet properties.	Monitor patients for signs, symptoms, and bleeding time.	Moderate Severity C: Monitor therapy
Cholestyramine			
Pharmacological Class: Antilipemic agent, bile acid sequestrant.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Vitamins A, D, E, and K	Bile acid sequestrants may decrease serum concentrations, impairing the absorption of fat-soluble vitamins.	Avoid concomitant administration of fat-soluble vitamins with bile acid sequestrants for at least 4 hours.	Moderate Severity D: Consider modifying therapy
Niacin – Vitamin B3	Bile acid sequestrants may decrease niacin absorption.	Consider separating the administration times for both.	Moderate Severity D: Consider modifying therapy
Dipyrone Sodium			
Pharmacological CLASS: Non-opioid analgesic; Non-steroidal anti-inflammatory; Antipyretic.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Fish Oil	May enhance the adverse/toxic effect of Agents with Antiplatelet Properties.	Monitor patients for signs, symptoms, and bleeding time.	Moderate Severity C: Monitor therapy
Vitamin E	May enhance the antiplatelet effect of agents with antiplatelet properties.	Monitor patients for signs, symptoms, and bleeding time.	Moderate Severity C: Monitor therapy
Caffeine	CYP1A2 inhibitors (weak) may increase the serum concentration of caffeine and caffeine-containing products.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Duloxetine			
Pharmacological Class: Antidepressant; Serotonin/Norepinephrine Reuptake Inhibitor.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Broccoli	Broccoli may decrease serum concentrations of CYP1A2 substrates.	Monitor for decreased effects of CYP1A2 substrates when combined with broccoli.	Moderate Severity C: Monitor therapy
Fish Oil	May enhance the adverse/toxic effect of Agents with Antiplatelet Properties.	Monitor patients for signs, symptoms, and bleeding time.	Moderate Severity C: Monitor therapy
Vitamin E	May enhance the	Monitor patients for signs,	Moderate Severity

	antiplatelet effect of agents with antiplatelet properties.	symptoms, and bleeding time.	C: Monitor therapy
Glibenclamide			
Pharmacological Class: Antidiabetic			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Raspberry	Raspberry may enhance the hypoglycemic effect of Agents with Blood Glucose Lowering Effects.	Monitor the risk of hypoglycemic events if both are ingested concomitantly.	Moderate Severity C: Monitor therapy
Guar gum (partially hydrolyzed)	Possibility of reduced absorption of Glyburide.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Hydrochlorothiazide			
Pharmacological Class: Antihypertensive; Diuretic and Thiazide.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Vitamin D and Calcium	Possibility of increasing the hypercalcemic effect.	Monitor for occurrence of calcium-related toxicities, serum calcium concentrations, and response to vitamin D.	Moderate Severity C: Monitor therapy
Gardening			
Pharmacological Class: Antidiabetic			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Raspberry	Raspberry may enhance the hypoglycemic effect of agents with Blood Glucose Lowering Effects.	Monitor the risk of hypoglycemia if both are taken at the same time. The dose of the medication may be reduced if raspberries are consumed.	Moderate Severity C: Monitor therapy
Lactulose			
Pharmacological Class: Ammonia detoxifier and laxative.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Glutamine	Glutamine may decrease the therapeutic effect and ammonia-lowering effects of lactulose. This interaction is specific to the use of lactulose to treat hyperammonemia and/or hyperammonemic encephalopathy.	Monitor clinical response to lactulose therapy and consider alternatives to glutamine as clinically appropriate.	Moderate Severity C: Monitor therapy
Lamivudine			
Pharmacological Class: Anti-hepadnaviral; Reverse Transcriptase Inhibitor; Nucleoside (Anti-HBV); Antiretroviral; Reverse Transcriptase and Nucleoside Inhibitor (Anti-HIV).			
Food/nutrient	Possible Interactions	Management	Classification of risk
Sorbitol Sweetener	Sorbitol may decrease the serum concentration	Avoid coadministration of both, if it occurs, monitor	Major Severity D: Consider modifying

	of Lamivudine.	patients for therapeutic failure of lamivudine.	therapy.
Levothyroxine			
Pharmacological Class: Thyroid product			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Chromium	Chromium may decrease serum levothyroxine concentration.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Iron	Possibility of reduced serum concentration of Levothyroxine.	Avoid concomitant administration of both and separate by at least 4 hours, as there may be a risk of reducing the effects of Levothyroxine.	Major Severity D: Consider modifying therapy.
Papaya	Papaya may decrease the absorption of Levothyroxine.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Losartan			
Pharmacological Class: Antihypertensive			
Food/Nutrient	Possible Interactions	Management	Classification of risk
Grapefruit Juice	Grapefruit juice may decrease serum concentrations of the active metabolite(s) of Losartan.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Resveratrol	Resveratrol may decrease the serum concentrations of the active metabolite(s) of losartan and may increase their serum concentration.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Nifedipine			
Pharmacological Class: Antianginal and antihypertensive agent.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit juice	Grapefruit juice may increase the serum concentration of Nifedipine.	Avoid Nifedipine and grapefruit juice concomitantly.	Moderate Severity X: Avoid combination
Mineral Oil			
Pharmacological Class: Laxative and Lubricant.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Vitamins A, D, E and K	Mineral oil can decrease the concentration and impair the absorption of fat-soluble vitamins.	Avoid concomitant administration of both.	Major Severity D: Consider modifying therapy.
Omeprazole			
Pharmacological Class: Proton pump inhibitor			
Food/Nutrient	Possible Interactions	Management	Classification of Risk

Iron	Proton pump inhibitors may decrease the absorption of iron preparations.	No clinical action is necessary for patients other than serum iron monitoring.	Severity Low B: No action required
Calcium Polystyrene Sulfonate			
Pharmacological Class: Antidote			
Food/nutrient	Possible Interactions	Management	Classification of Risk
Iron	Calcium Polystyrene Sulfonate may decrease serum iron concentrations.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Propranolol			
Pharmacological Class: Antianginal agent and antiarrhythmic agent.			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Broccoli	Broccoli may decrease serum concentrations of CYP1A2 substrates (high risk with inducers).	Monitor for decreased effects of CYP1A2 substrates when combined with broccoli.	Moderate Severity C: Monitor therapy
Vitamin C	Vitamin C may decrease the serum concentration of Propranolol.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Caffeine	Weak CYP1A2 inhibitors may increase serum caffeine concentrations.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Rosuvastatin			
Pharmacological Class: Antilipemic agent			
FOOD/Nutrient	Possible Interactions	Management	Classification of Risk
Niacin (Vitamin B3)	Niacin may increase the myopathic effect (rhabdomyolysis) of Rosuvastatin.	Rosuvastatin and niacin have the potential to cause muscle and other toxicities when used as monotherapy. Monitor patients receiving combination therapy for signs and symptoms of toxicity and consider a dose reduction of the drug to minimize risks.	Moderate Severity C: Monitor therapy
Cinnamon	Cinnamon may enhance the hepatoxic effect of Rosuvastatin.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Green Tea	Green tea may decrease the serum concentration of Rosuvastatin.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Simvastatin			
Pharmacological Class: Antilipemic agent			
Food/Nutrient	Possible Interactions	Management	Classification of Risk
Grapefruit Juice	Grapefruit juice may increase the serum concentration of	Avoid administering both.	Moderate Severity X: Avoid combination

	simvastatin.		
Niacin (Vitamin B3)	Niacin may enhance the myopathic effect of simvastatin and increase its serum concentration.	Simvastatin and niacin have the potential to cause muscle and other toxicities when used as monotherapy. Monitor patients receiving combination therapy for signs and symptoms of toxicity and consider a dose reduction of the drug to minimize risks.	Moderate Severity D: Consider modifying therapy
Green Tea	Green tea may increase serum concentrations of the active metabolite(s) of simvastatin.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Hibiscus	Hibiscus may decrease the serum concentration of simvastatin.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Ferrous Sulphate			
Pharmacological class: Iron supplement agent			
Food/Nutrient	Possible interactions	Management	Classification of Risk
Vitamin C	Vitamin C increases iron absorption.	No action required beyond standard clinical care measures.	Severity Low B: No action required
Vitamin E	Vitamin E may decrease the therapeutic effect of iron preparations.	No action required beyond standard clinical care measures.	Severity Low B: No action required

Source: UpToDate, 2022.

All possible interactions were related to pharmacokinetics, as they influence the absorption of substances with pharmacokinetic characteristics interactions. Among them, we observed that the majority occurred when food and/or nutrients reduced the therapeutic effect of the drug or when the drug reduced the serum concentration of the nutrient, totalling 51.06% (n=24) of the interactions.

Although the average number of interactions was higher in patients who died (1.5 ± 1.64) compared to patients who were discharged (1.19 ± 1.44), a t-test with a bilateral 95% confidence interval was conducted to statistically analyse the data showing that there was no significant difference between the samples, with a p-value > 0.99.

For the risk ratings of possible interactions, a prevalence of 40.42% (n=19) was observed for low severity B (no action required), followed by moderate severity C (monitor therapy) at 36.17% (n=17), higher severity D (consider therapy modification) at 17.02% (n=8), and finally moderate severity X (avoid combination) at 6.38% (n=3).

4. DISCUSSION

Considering the data presented, it is possible to observe that the occurrence of interactions may be correlated with nutritional status, due to a decrease in serum levels of certain nutrients and/or reduced therapeutic response to the drug. These factors can lead to negative outcomes and impact the healthcare system.

This perspective is supported by Aðalbjörnsson & Ramel (2021), who noted that medications can contribute to nutritional deficiencies by reducing nutrient bioavailability and negatively affecting food intake through their impact on digestion. The risk of such interactions increases with long-term medication use, chronic age-related diseases, alcohol consumption, incompatibilities between foods and medications, or interactions between nutrients and drugs [8].

The presence of comorbidities in the elderly population was another interesting finding that may have contributed to the occurrence of pharmacokinetic interactions between drug-drug and drug-nutrient interactions, as well as affecting bioavailability. One of the main causes of these interactions is the use of multiple drugs in elderly patients due to the routine need for various medications to manage chronic non-communicable diseases [9].

When we analyse the findings critically, we find that males are the slight majority in the Intensive Care Unit (ICU). In the study by Roland et al. (2021) which evaluated anthropometric parameters to predict mortality risk in older patients admitted to the ICU, we also observed a predominance of males in hospitalisation, similar to the present study. A likely explanation for these findings could be that the female population pays more attention to their own health compared to males [10].

In the study conducted by Capela et al. (2018) at the University General Hospital of Cuiabá, which evaluated the length of stay of older patients in the ICU, the average length of stay was 13 days. This result was significantly lower compared to the length of stay in the present study. Despite having a similar population profile in terms of age range and hospital unit, there may be differences in the clinical profile and therapeutic approaches of the individuals [11].

When evaluating the timing of the initiation of enteral nutrition (EN), a study conducted at the Regional Hospital of Mato Grosso do Sul found that 52.4% of hospitalized patients received early enteral nutrition within the first 24 hours of admission. This contrasts with the findings of the present study, where it was common for EN to be initiated after 8 days or more. A possible explanation for the delay in starting enteral nutrition could be that patients were receiving another form of nutritional therapy through a different route in the first days or hours of admission. However, this information was not documented in the medical records [12].

Regarding the nutritional status, it was observed that more than half of the individuals were severely malnourished. This contrasts with the findings of van Nieuwkoop, Ramnarain and Pouwels (2022), who evaluated the profile and nutritional status of hospitalised patients using TNE and observed a diagnosis of severe malnutrition in only 24.24% of the sample. One possible explanation for this difference the population studied did not consist solely of older individuals [13].

When investigating the prevalence of drug-nutrient interactions in hospitalised patients undergoing TNE (transnasal endoscopy). Kampa et al. (2020) found that 28.57% of the drugs had potential drug-nutrient interactions, which is a lower result compared to the present study. Although both studies used TNE, Kampa et al. (2020) did not solely focus on older individuals, which reinforces the hypothesis that older individuals have a higher chance of experiencing interactions [3].

Almeida and Genaro (2019), who also investigated drug-nutrient interactions but did not use software, observed that acetylsalicylic acid can reduce the absorption of vitamin K, B1, and folic acid, and that carbohydrates reduce the drug's absorption time. Hydrochlorothiazide, in turn, can have its absorption reduced by food, making it necessary to pause the diet before administering the drug. The difference in the scientific basis used in investigative methods may be the reason for the divergences in the information [14].

In relation to the interactions investigated in other studies that were not mentioned by UpToDate®, a randomised clinical trial conducted in Spain evaluated the influence of food on the pharmacokinetic parameters of omeprazole, rabeprazole, and pantoprazole. It was observed that consuming food before taking omeprazole delayed the average Tmax of the drug by approximately 3 hours, reinforcing the recommendation to take it on an empty stomach [15].

This study has certain limitations. First, limitations were observed in data collection, as it relied on retrospective medical records, thereby using information that was not gathered by the researchers in real-time. Second, the limitations were present in the potential annotations made by the software used. Therefore, these limitations can be overcome in future studies, that is, suggest the scope for future research in that field [16-17].

5. CONCLUSION

The study findings suggest that the occurrence of possible drug interactions deserves attention, as their consequences can negatively impact the

patient outcome. We found that a large portion of the patients were severely malnourished, which increased the risks for negative outcomes. In enteral nutrition, we can rely on concentrated formulas as a strategy to minimise the risks of malnutrition and unwanted interactions with drugs. This is because they allow for the provision of nutrients in a smaller volume, shorter infusion time, and more time between drug and nutritional intake.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

ETHICAL APPROVAL

The study was developed following the technical criteria defined by Resolution No. 466/2012 of the Health Council for the development of research in humans, and it was approved by the Ethics Committee of the Júlio Muller University Hospital (CEP-HUJM) with the approval number CAAE 5,214,651.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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