Identification and analysis of antinutritional factors in possible interactions between medications and food/nutrients in hospitalized patients

Identificação e análise dos fatores antinutricionais nas possíveis interações entre medicamentos e alimento/nutrientes em pacientes hospitalizados

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ABSTRACT

Objective: To identify and analyze the presence of antinutritional factors in possible interactions between medications and foods/nutrients of the diets prescribed for patients of the *Hospital Regional Justino Luz,* in the city of Picos (PI) in order to suggest their likely mechanisms. **Methods:** The sample was made up of 120 medical records of hospitalized patients. The charts were analyzed to verify the presence or absence of interactions between medications and foods/nutrients of the diets prescribed to the patients at the *Hospital Regional Justino Luz*, emphasizing the action of antinutritional factors in these interactions. **Results:** Of the 189 medications prescribed, 128 (67.7%) had a possible interaction with food, totaling up 98 possible interactions between nutrients/foods and medications. Therefore, 20 (20.4%), 12 (12.2%) and 11 (11.2%) possible interactions were identified with captopril, acetylsalicylic acid and spironolactone, respectively, representing, in this order, the greatest frequencies of possible interactions among drugs and foods. A total of nine antinutritional factors were found in seven vegetable foods prescribed to inpatients, in which five (55.6%) were capable of interacting with the medications. Phytates and tannins had the largest quantity of possible interactions with drugs, each with 4 (26.7%) in a total of 15 interactions. The medications aluminum hydroxide, digoxin, and paracetamol attained greater probability of interaction with antinutrients, with 5 (33.3%), 3 (20%) and 3 (20%) interactions, respectively. **Conclusion:** Due to the large quantity of antinutritional factors capable of interacting with drugs prescribed for inpatients, the involvement of a multiprofessional team is indispensable so that these possible interactions between foods, antinutritional factors and drugs might be foreseen, detected, and resolved.

Keywords: Food-drug interactions; Biochemical phenomena; Food; Pharmaceutical preparations

RESUMO

Objetivo: Identificar e analisar a presença dos fatores antinutricionais nas possíveis interações entre os medicamentos e os alimentos/nutrientes das dietas prescritas aos pacientes do Hospital Regional Justino Luz do Município de Picos (PI) para sugerir seus prováveis mecanismos. **Métodos:** A amostra foi constituída por 120 prontuários médicos de pacientes hospitalizados. Os prontuários foram analisados para verificar a presença ou não de interações entre os medicamentos e os alimentos/nutrientes das dietas prescritas aos pacientes internados no Hospital Regional Justino Luz, dando ênfase à ação dos fatores antinutricionais nas interações. **Resultados:** Dos 189 medicamentos prescritos, 128 (67,7%) apresentavam possível interação com a alimentação, totalizando 98 possíveis interações entre nutriente/alimentos e medicamentos. Dessa forma, foram identificadas 20 (20,4%), 12 (12,2%) e 11 (11,2%) possíveis interações com o captopril, com o ácido acetilsalicílico e com a espironolactona, respectivamente, representando, nessa ordem, as maiores frequências de possíveis interações entre os medicamentos/alimentos. Um total de nove fatores antinutricionais foram encontrados nos sete alimentos vegetais prescritos aos pacientes hospitalizados, sendo que cinco (55,6%) eram capazes de interagir com os medicamentos. Os fitatos e taninos apresentaram a maior quantidade de possíveis interações com os fármacos, cada um com 4 (26,7%) em um total de 15 interações. Os medicamentos hidróxido de alumínio, digoxina e paracetamol obtiveram maior

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probabilidade de interação com os antinutrientes, sendo 5 (33,3%), 3 (20%) e 3 (20%) interações, respectivamente. **Conclusão**: Devido à grande quantidade de fatores antinutricionais capazes de interagir com fármacos prescritos para pacientes hospitalizados, a atuação de uma equipe multiprofissional é indispensável para serem previstas, detectadas e resolvidas essas possíveis interações entre alimentos, fatores antinutricionais e medicamentos.

Descritores: Interações alimento-droga; Fenômenos bioquímicos; Alimentos; Preparações farmacêuticas

INTRODUCTION

Food, regardless of the individual's culture and time of life, is an essential and indispensable factor for health maintenance and order. Its importance is associated with its capacity to supply the human body with the nutrients necessary for its maintenance. For the harmonic balance of this task, it is fundamental that food be ingested in adequate quantities and with quality, so that specific effects, such as plastic, regulatory and energy functions, are satisfied, thus maintaining the structural and functional integrity of the organism[1].

Many pathological processes in recovery require of the body an adequate nutritional supply besides the administration of effective and safe medications[2]. However, nutrients are also capable of interacting with drugs, creating a highly relevant issue in clinical practice, due to modifications in the risk/benefit ratio of the medicine use[1]. Interactions between food and drugs can alter the effects of the food and of the drugs, and the therapeutic or side effects of the medications can also cause modifications in patients' nutritional status[3].

Despite few well investigated reports of the pharmacokinetic and pharmacodynamic mechanisms of the possible interactions between drugs and foods, some studies suggested that these interactions may occur due to the presence of antinutritional factors in food items. The term "antinutritional factor" has been used to describe the compounds or classes of compounds present in an extensive variety of vegetable-based foods, which in high concentrations may originate toxic reactions and/or interfere in the bioavailability and digestibility of some nutrients[4,5]. The antinutritional factors that are a part of foods are of a varied nature, and due to divergences in knowledge of their physical and chemical structures and their physiological mechanisms of action, to investigate them in detail is essential from the nutritional and pharmacological point of view[6].

The antinutrients present in vegetable species, such as green and yellow vegetables and cereals, may have their harmful effects minimized depending on the type of processing they undergo[7]. The study of these factors is especially important in reference to feeding inpatients, since many times the adequate diet therapy for each clinical picture is neglected. In fact, there is a concern with the choice, the parts, and the most adequate processes for the diets prescribed for hospitalized patients[4].

Hospitalizations may have varied causes or consequences, such as polypharmacy, genetics, parenteral nutrition, alcohol ingestion, drug abuse, and also due to the antinutritional factors present in foods[3]. Antinutritional factors are substances with the capacity to alter the possibilities of benefiting from the nutrients contained in foods, making them unavailable to the body, and which, at high concentrations, may originate toxic reactions. The antinutritional factors are classified as endogenous and exogenous, where the former are related to toxic substances or naturally occurring antinutritional substances in ingredients, while the exogenous refer to chemical or biological contaminants present in a given product (agrotoxic substances, fungi, among others)[8,9].

OBJECTIVE

Within this contextualization, the present study had the objective of identifying and analyzing the presence of antinutritional factors in the possible interactions among medications and foods/nutrients of the diets prescribed to patients of the *Hospital Regional Justino Luz* (HRJL), in the city of Picos (PI) in order to suggest likely mechanisms of these interactions.

METHODS

Study design

The results were obtained by means of an exploratory-descriptive study with a quantitative approach, with use of the technique of direct observation by means of analysis of 120 medical records and the diets prescribed for the inpatients at the HRJL. The data from the medical records were collected at the care units of the HRJL, in the city of Picos, during the period from August 2009 to July 2010. The study was carried out at the HRJL, a secondary 120-bed reference hospital in Picos, maintained by the Brazilian Unified Healthcare System (SUS), which also provides emergency care.

The following inclusion criteria were adopted for the study: 1) all the records of inpatients at HRJL during the study period, who had used at least one medication orally for clinical treatment; 2) and those who agreed to and signed the Informed Consent Form (ICF) to participate voluntarily.

In order to avoid any methodological bias, the following exclusion criteria were adopted: 1) patients at risk; 2) patients under emergency care; 3) and patients who did not receive oral medications during their hospital stay.

Data collection and independent variables

The interviews followed the methodology proposed by Cipolle et al.[10] and were conducted as described below. Data collection from the patient records was done by Nursing undergraduate students and grantees of the Universidade Federal do Piauí (UFPI) trained under supervision, and performed by means of direct examination of the medical records. During the patient record analysis, a standardized and validated questionnaire was filled in with the purpose of collecting the following pieces of information from the records: age, self-reported skin color, health problems, presumptive diagnoses, medications given, and diets prescribed. Later, the Pharmacy undergraduate students and grantees of the Study Group on Medication Use (GEUM) of the UFPI conducted the analysis of the presence of antinutritional factors in the foods detected during analysis of the possible interactions. The study was approved by the Technical Administrative Board of the HRJL. Also furnished to the group of students were the authorizations by means of signatures on the ICF given by patients for collection of data, enabling the analyses of their prescriptions and diets. There was no nominal identification, nor any moral risk to the patients, since only statistical data was accessed. In this way, analysis was made of information in the patient records in reference to prescription of medications during hospitalization and the diets prescribed for them, in order to identify the presence of antinutritional factors in foods detected during the analysis of possible interactions.

The research protocol followed the ethical principles set forth in the Declaration of Helsinki and the norms of Resolution 196/96 of the National Health Council, having been approved by the Research Ethics Committee of the UFPI (CAAE 0099.0.045.000-09).

RESULTS

One hundred and twenty medical records of inpatients at the HRJL, in the city of Picos, were analyzed. On average, 85% of patients were over 41 years of age and 15% were between 15 and 40 years of age. As to the analysis of the records regarding skin color, 80, 15, and 5% of the charts referred mulatto, white, and black, respectively (Table 1). After investigation of the medical records, it was noted that 35% of the patients were smokers and that the main reason for their hospitalizations was systemic arterial hypertension (40%). Among other reasons that resulted in hospital admissions recorded in the medical charts, the following stand out: wounds in lower extremities, gastric ulcers, gastritis, apnea, hepatic cirrhosis, intestinal infection, stroke, fever, burns, pneumonia, abdominal pain, thrombosis, renal problems and diarrhea.

Table 1. Self-reported socioeconomic profile in records of inpatients surveyed during identification of antinutritional factors in possible interactions between foods/nutrients and prescribed drugs

Socioeconomic profile	Users	
	n	%
Age group		
15 - 40 years	18	15
31 - 40 years	102	85
Self-reported skin color		
White	96	80
Black	18	15
Mulatto	6	5
Marital status		
Single	18	15
Stable relationship	102	85
Schooling level		
Literate	12	10
Incomplete junior school	6	5
Complete junior school	6	5
Incomplete high school	12	10
Complete high school	6	5
Illiterate	78	65
Family income		
0 - 1 wages	72	60
1 - 2 wages	36	30
2 - 3 wages	12	10

From the study of the 120 medical charts, it was noted that most patients were married or were in a stable marital condition (85%). On the other hand, in analyzing type of residence, it was observed that 32 (26.7%) of them lived in homes they owned, and as to schooling level, most were illiterate (65%) (Table 1). Regarding profession, 66 were agricultural workers and had family incomes of about one minimum wage (60%). Also identified was the fact that 45 (37.5%) patients were alcohol users. The average number of medications prescribed to inpatients at the HRJL and followed in the study was 1.58. The number of medications administered was 58 during the morning period (6:00 am to 11:59 am), 67 during the afternoon (noon to 5:59 pm), 48 during the evening period (6:00 pm to 11:59 pm), and 16 during the early morning hours (midnight to 5:59 am).

Of the 189 medications prescribed during all periods, 128 (67.7%) medications were identified as

Table 2. Distribution of possible interactions between foods/nutrients and drugs prescribed in medical charts of inpatients

Possible interactions	Distribution	
	n	%
Cardiovascular	49	50.0
Amiloride	6	6.0
Captopril	20	20.0
Carvedilol	10	10.0
Digoxin	6	6.0
Nifedipine	4	4.0
Propanolol	3	3.0
Anti-inflammatory agents	18	18.4
Acetylsalicylic acid	12	12.2
Diclofenac	5	5.1
Paracetamol	1	1.1
Diuretics	18	18,4
Spironolactone	11	12.2
Furosemide	5	5.1
Hydrochlorothiazide	2	1.1
Anti-ulcer agents	12	12.1
Aluminum hydroxide	7	7.1
Omeprazole	4	4.0
Ranitidine	1	1.1
Laxatives	1	1.1
Mineral oil	1	1.1
Total	98	100.00

having possible interactions with food, totaling 98 possible interactions between nutrients/foods and drugs. Therefore, we identified 20 (20.4%), 12 (12.2%), and 11 (11.2%) possible interactions with captopril (cardiovascular drug), with acetylsalicylate acid (ASA, anti-inflammatory), and spironolactone (diuretic), respectively, representing as well, in this order, the greatest frequencies of possible interactions among the pharmacological classes investigated. Also detected was the fact that of the total number of possible interactions among foods/nutrients and medications, 49 (50%) corresponded to possible interactions with cardiovascular drugs; 18 (18.4%) with anti-inflammatory medicines, 18 (18.4%) with diuretic agents, and 13 (13.2%) with drugs that act on the digestive tract - anti-ulcers (12.1%) and laxatives (1.1%) (Table 2).

On the 11 foods studies, there is literature confirming that the seven (63.6%) vegetables have antinutritional factors that could interact with the drugs prescribed for the inpatients. In the case of soy milk, it is believed that even in small quantities there is the presence of the antinutrients contained in soy. The green vegetables salad was removed from the study, due to lack of specific information.

Chart 1. Identification of antinutritional factors in possible interactions between foods/nutrients and drugs prescribed in medical records of inpatients

Drugs	Mechanisms of the possible interactions between foods/nutrients and drugs/Recommendations
Cardiovascular	
Amiloride	Medication depletes calcium (Ca) absorption. Avoid administration with foods rich in Ca (milk and cheese) and in antinutritional factors (milk (soy): phytates, protease inhibitors and saponins)
Captopril	Foods in general decrease absorption of the drug. Administer 1 hour before or 2 hours after meals
Carvedilol	Foods in general decrease orthostatic hypertension. Administer with foods
Digoxin	Carrots (fibers) decrease absorption of the drug. Avoid administration with foods rich in antinutritional factors (carrot: lecithins, tannins, phytates, nitrates and fibers)
Nifedipine	Foods in general increase bioavailability of the drug. Administer with foods
Propanolol	Milk increases bioavailability of the drug. Administer with high protein content foods
Anti-inflammatory agents	
Acetylsalicylic acid	Foods decrease absorption of vitamins. Do no eat foods rich in vitamins C and K, folic acid, thiamine and amino acids, and rich in antinutritional factors (passion fruit: cyanogenic glycosides, and lettuce: nitrates) close to or during administration of the medication
Diclofenac	Foods in general decrease the risk of lesion in the gastrointestinal tract. Take it with foods to reduce the risk of mucosal lesion
Paracetamol	Carrot and lettuce decrease absorption of the drug. Avoid foods rich in antinutritional factors (carrot: lecithins, tannins, phytates, nitrates and fibers) close to or during administration of the medication
Diuretics	
Spironolactone	Medication retains potassium (K). Avoid administration with foods rich in K and in antinutritional factors (milk (soy): phytates, protease inhibitors and saponins)
Furosemide	Medication depletes sodium (Na). Avoid administration with foods rich in Na and in antinutritional factors (rice: phytic acid)
Hydrochlorothiazide	Fatty foods increase absorption of the drug. Administer with fatty foods (cheese, fried egg and meat). Avoid administration with foods rich in Na and in antinutritional factors (pumpkin: protease inhibitors, lecithins, tannins, saponins, nitrates, cyanogenic glycosides)
Anti ulcer agents	
Aluminum hydroxide	Medication decreases absorption of iron (Fe). Do not eat foods containing Fe close to or during administration of the medication and rich in antinutritional factors (beans: phytates, tannins and oxalic acid)
Omeprazole	Medication decreases absorption of vitamin B_{12}. Do not eat foods rich in vitamin B_{12} and in antinutritional factors (milk (soy): phytates, protease inhibitors and saponins) close to or during administration of the medication
Ranitidine	Medication decreases absorption of vitamin B_{12}. Do not eat foods rich in vitamin B_{12} close to or during administration of the medication
Laxatives	
Mineral oil	Medication decreases absorption of vitamins. Do not eat foods rich in vitamins A, D, E and K and in antinutritional factors (pumpkin: protease inhibitors, lecithins, tannins, saponins, nitrates, cyanogenic glycosides) close to or during administration of the medication

In this study, nine antinutritional factors were found (phytates, protease inhibitors, saponins, lecithins, tannins, nitrates, fibers, cyanogenic glycosides, and oxalic acid) present in vegetable foods consumed by the hospitalized patients. According to a bibliographical search, five (55.6%) of these are capable to interact with medications (Chart 1). Phytates and tannins present the greatest prevalence among the possible foods capable of interacting with drugs, each one with 4 (25%), in a total of 16 interactions. With the medications aluminum hydroxide, digoxin, and paracetamol, five (31.3%), three (18.8%), and three (18.8%) possible interactions with antinutrients were noted, respectively. Of the other drugs (amiloride, omeprazole, mineral oil, and ASA), only one (6.25%) interaction was reported of each medication with the antinutrients present in the vegetable foods. As to the four medications capable of interacting with foods in general, only captopril proved capable of interacting with the antinutritionals. On the other drugs that were not mentioned there was no evidence in the literature as to the antinutritionals investigated (Chart 2).

Chart 2. Identification of the main antinutritional factors in possible drug interactions observed with the medicines prescribed in medical records of inpatients

Drugs	Antinutritional Factors
Cardiovascular	
Amiloride	Phytates
Captopril	Fibers
Digoxin	Phytates, tannins and fibers
Anti-inflammatory agents	
Acetylsalicylate acid	Nitrates
Paracetamol	Tannins and fibers
Anti-ulcer agents	
Aluminum hydroxide	Phytates, tannins and oxalic acid
Omeprazole	Phytates
Laxatives	
Mineral oil	Nitrates

DISCUSSION

In the medical literature, there are various experimental and clinical studies evaluating interactions among drugs, but there are few studies conducted to assess interactions between medications and foods[11]. In the case of individuals admitted to hospital, among the many types of care needed, those related to food and nutrition merit special attention, since nourishment is an indispensable factor for full recovery of health[12].

These interactions are facilitated by the fact that medications and foods are mostly administered orally. The nutrients may modify the effects of the drugs, by interfering in pharmacokinetic processes, hindering therapy. On the other hand, medications can modify the metabolism of nutrients resulting in a modification of the patient's nutritional status. In treating illnesses, the prolonged use of some medications that cause loss of nutrients is common[1].

As it is already known, interactions may have several causes, including alcohol ingestion[3]. Our results demonstrate that a large number of patients were alcohol users, which may have contributed towards a diminished effect of nutrients, as well as of medications administered, making them unavailable to the body.

Prior studies reported that interactions between foods/nutrients and drugs may be caused by the presence of antinutritional factors present in foods[3]. Among these, we draw attention to phytates that represent a complex class of compounds naturally occurring in various foods[13-15]. The phytate content present in foods reduces the bioavailability of minerals and proteins[16,17]. Our results have shown possible interactions between cardiovascular and anti-ulcer drugs with foods, due to the presence of phytates. Thus, it might be recommended that the administration of drugs such as amiloride, digoxin and omeprazol be avoided close to the consumption of foods rich in phytates, due to the decreased absorption of calcium, an additive effect of the very medications that are also capable of chelating calcium.

One the other hand, iron deficiency in the body may be a result of prolonged treatments with antacids (magnesium or aluminum hydroxide)[18]. In light of our results, it is important that the dietitians observe the prescription of medications in patient records before establishing the diet, as well as recommending that foods containing phytic acid, such as beans, for example, be avoided close to the time of drug administration (aluminum hydroxide).

Another antinutritional factor identified in our study is protease inhibitors, proteins broadly distributed in the vegetable kingdom[19]. Studies on the possible interactions between protease inhibitors and some drugs are scarce in literature, but protease inhibitors are used as instruments in the investigation of enzymatic mechanisms and in the development of drugs for various diseases[20]. Still among the antinutritional facts identified, it is important to stress saponins, which are important components for the action of many vegetable-based drugs[21], and lecithins, which may be found in an broad variety of plant and animal species[4,22] and can interfere in the absorption of nutrients[19]. Despite the presence of these antinutritional factors in the foods prescribed in diets for inpatients, it was not possible to identify interactions among the medications identified on the prescriptions and lecithins, protease inhibitors, and saponins found in foods/nutrients recognized during the study.

Contributing to these facts, some studies demonstrated that there is a concern to evaluate the capacity of tannins to form insoluble complexes with iron, and scientific evidence points towards a negative effect of tannin on the absorption of iron which could be effectively prevented by the simultaneous administration of ascorbic acid; therefore, it is believed that the ingestion of beans and other foods rich in iron close to the time of administration of the drug aluminum hydroxide, decreases the absorption of this mineral in the body[17,23]. Tannins are also capable of promoting the induction of enzymes[24]; in this way, it is believed that the administration of drugs, such as digoxin and paracetamol, should be avoided along with sources rich in tannins, due to the likely decrease of the therapeutic effect of the drugs.

In our studies, potential interactions between ASA and lettuce were observed, and because of this, it is believed that the consumption of food rich in nitrates might facilitate the process of nitration (complex of nitrate with ASA), thus hindering the absorption of ASA[4].

Additionally, in the presence of diets rich in fiber, some medications may have their pharmacological effect diminished. In the stomach, fibers retard gastric emptying, increasing satiety, and this is relevant for weight-loss diets[25]. However, studies conducted on the influence of the ingestion of a soluble fiber on the absorption of paracetamol noted a 65% reduction in the maximum concentration of the anti-inflammatory in the blood, a phenomenon explained by the modification in the rate of gastric emptying, which hinders the delivery of the drug to the intestinal portion that absorbs it[26,27]. On the other hand, in the small intestine, fibers retard the uptake of sugars, amino acids and drugs, such as digoxin and paracetamol, due to the fact that they have the capacity of increasing the thickness of the water layer, which acts as a barrier to the diffusion of nutrients and drugs[28]. In the case of the cardiovascular drug captopril, studies demonstrated that its action may be potentiated in association with oil rich in pumpkin seed fibers[13].

Also noted in our study was the presence of cyanogenic glycosides, which have been confirmed in various plants[7,29,30]. The presence of these glycosides was verified in diets prescribed to hospitalized patients; however, despite their known and reported danger to human health, no data was found in literature to support any possible mechanism of interaction between these antinutritional factors and the drugs (ASA, furosemide and mineral oil).

Finally, we underline the presence of oxalic acid, an organic acid found in certain vegetables of the diets prescribed for patients in hospitals. This acid blocks the phytotoxic action of aluminum, with the formation of chelates[31]; in this way, the formation of a possible complex of oxalic acid present in beans and the anti-ulcer drug, aluminum hydroxide might be suggested. It is important to point out that oxalic acid is also capable of forming insoluble chelates or macromolecules with the iron in the diet, which leads to decreased absorption of the iron, an effect that could be exacerbated by the capacity of the aluminum hydroxide to decrease the absorption of iron and consequently, cause anemia or aggravate a preexisting anemia[32].

The considerable quantity of antinutritional factors capable of interacting with drugs prescribed for hospitalized patients reinforces the importance of correctly following the medication dosing schedule and the need for adequate treatment of food. The presence of a multiprofessional team, with physicians, pharmacists, dietitians and nurses can assist in the prevention, detection and resolution of the possible interactions between foods, antinutritional factors and drugs.

CONCLUSION

Based on our results, it is possible to conclude that antinutritional factors (phytates, tannins, nitrates, fibers, cyanogenic glycosides, and oxalic acid) present in food in the diets prescribed for patients hospitalized may be capable of interacting with medications when given concomitantly. Among the possible antinutritional factors, phytates and tannins have the greatest prevalence among the foods capable of interacting with the drugs prescribed. Nevertheless, further studies should be conducted, since most of the medicines identified in the possible interactions have no evidence in the literature as to antinutritional factors (lecithins, protease inhibitors, and saponins) present in the diets prescribed the hospitalized patients.

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